THE USE OF HAIR AS A BIOPSY TISSUE FOR TRACE ELEMENTS IN THE HUMAN BODY

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Abstract

Scalp hair has been recognized as a tissue which incorporates elements into its structure during the growth process, after which it becomes separated from the continual metabolic activity of the body. It has many advantages for being used as an indicator for screening population groups exposed to environmental pollutants. Such usage is not free from criticisms. Sometimes the so-called "normal ranges" of trace elements in hair quoted in the literature can be wide. Various factors can influence the trace element content of hair. In this report we have attempted to summarize the available literature on the levels of arsenic, cadmium, mercury, lead, selenium and chromium in human scalp hair.

1. INTRODUCTION

During the past three decades, the determination of trace element concentrations in human scalp hair has become increasingly popular for: monitoring environmental exposure, evaluating systematic intoxication, assessing nutritional status, and diagnosing diseases. Blood and urine analysis are the more traditional approach to evaluating trace element levels in the human body, but trace element levels in blood and urine fluctuate rapidly in response to changing physiological and/or environmental conditions. Hair provides a more permanent record of the trace elements associated with normal and abnormal metabolism as well as the trace elements assimilated from the environment.

2. BIOLOGICAL BASIS FOR TRACE ELEMENTS IN HAIR

In 1942, Schoenheimer [1] described the body tissues as being in a state of dynamic equilibrium. Hair is an exception. Unlike the other body tissues, hair is a metabolic end product that is thought to incorporate trace elements into its structure during its growth process. During the growth phase of a hair cycle the matrix cells at the papilla of the follicle show intense metabolic activity, and they produce hair at a rate of approximately 0.4 mm/day. The developing hair is exposed to the metabolic milieu for only a short period of time. As the growing hair approaches the skin surface, it undergoes a hardening process or keratinization, and the trace elements accumulated during its formation are sealed into the protein structure of the hair. It is in this way that the trace element concentrations of the hair are possibly related to the trace element concentrations in the body. Flesch [2] recognized this possibility some thirty-five years ago when he suggested that the hair functioned as a minor excretory organ for arsenic and possibly for other toxic elements. More recently, Hopps [3] and Chittleborough [4] have speculated upon the possibility of interpreting the results of hair analysis for information on trace elements in other parts of the body.

The popularity of using hair as a biopsy tissue for trace elements resides, in part, in the ease with which samples may be collected and in the stability of the samples after collection. In addition, the concentrations of most trace elements are frequently one or two orders of magnitude greater in hair than they are in more conventional biopsy tissues such as blood or urine. Some typical values are compared in Table I.

3. TRACE ELEMENTS AND THEIR NORMAL RANGES IN HAIR

Before hair analysis can be applied to monitoring environmental exposure, evaluating systematic intoxication, assessing nutritional status, or diagnosing disease, it is necessary to establish normal values. Copper, iron, zinc, and the other elements that are essential for normal human metabolism are hemostatically regulated. Consequently, their concentrations in hair as well as in other biological tissues are expected to fluctuate within relatively narrow limits under conditions of normal human metabolism. Unfortunately, the literature abounds with a diverse array of frequently contradictory normal values for the concentrations of the essential trace elements in human hair. Ideally, normal values for cadmium, mercury, lead, and other toxic elements in human tissues should be essentially zero. However, environmental factors rather than normal metabolic activity have contributed to the entry of these toxic elements into the human body. Their concentrations in the hair and other tissues are not hemostatically regulated. These toxic elements may demonstrate dose-tissue concentration relationships, and hair analysis may be a useful index for approximating environmental exposures to and/or body burdens of toxic elements.

Sanders [6] has classified the essential trace elements into three groups. Group I contains those that the human body requires in well defined amounts, *i.e.* iron, iodine and zinc. Group II contains those needed by the human body, but in what exact amount is not yet determined, *i.e.* chromium, cobalt, copper, manganese, molybdenum, and selenium. Group III contains those that are required by various other animals, but have not yet been found to be needed by humans, *i.e.* arsenic, fluorine, nickel, silicon, tin, and vanadium. Falkner [7] has also included these trace elements, with the exception of arsenic, in his list of the micro and macro nutrients essential to normal metabolism, and Owen [8] has identified chromium, cobalt, copper, fluorine, iodine, iron, manganese, molybdenum, nickel, selenium, tin, zinc, and possibly arsenic as the essential trace elements. The essential trace elements and some of their biochemical functions are summarized in Table II.

Several collections and tabulations of the normal values for the concentrations of the essential trace elements in human hair have been published [10-14]. In general, these tabulations for human hair show much wider ranges of normal values than similar tabulations for the normal values of the essential trace elements in a more conventional biopsy tissue like blood [15-17]. In addition, the normal values for some essential trace elements in human hair sometimes differ by as much as an order of magnitude when the experimental results of different investigators are compared. The reported values for the normal hair concentration of chromium are typical of such disagreements.

It is well known that chromium is involved in glucose metabolism [18]. Hambidge *et al.* [19] have shown that the concentration of chromium in the hair of diabetic children is significantly below that of normal children: the geometric means were 0.65 and 0.85 ppm, respectively. Benjanuvatra and Benion [20] have reported similar findings for adult

victims of this disease in which the mean hair chromium concentration of the adult diabetics was 0.094 ppm and that of the control group was 0.241 ppm. While both studies clearly demonstrate depressed chromium concentrations in the hair of the diabetics relative to the respective control groups, there appears to be little agreement on the normal value for chromium in hair; is it 0.95 ppm, or is it 0.241 ppm? In this respect, the compilation of values for the elemental composition of human tissues by Iyengar, Kollmer and Bowen cited above [10] lists 0.77, 0.85, 0.55, 0.13, 3.30, 3.25, 3.65, 3.10 and 3.20 ppm under the values for the concentration of chromium in human hair.

A review of the literature on the concentrations of trace elements in human hair cited above [11] revealed a range of form 9.1 to 49.8 mg/kg for the average copper contents. When compared to the normal values reported for copper in blood serum [15], where 31 of the 36 arithmetic means fell between 0.85 and 1.23 mg/L, the reported normal values for copper in hair show wide variations.

The wide divergences for the normal values of essential trace elements in hair is not limited to those for chromium and copper. The literature contains similar broad ranges of results for the normal values of the essential trace elements in human hair. Some [21-24] interpret these broad ranges of normal values as serious impediments to the utilization of hair analysis for assessing nutritional status or diagnosing diseases. Katz [25], Chatt [26], Katz and Chatt [27] and others [28,29] have considered variables such as length of hair, colour of hair, anatomical location of hair, age of donor, gender of donor, race of donor, and habitat of donor as well as the procedures used for the collection and preparation of hair samples. The current consensus recommends using a standardized procedure for collecting the hair samples from age-matched, gender-matched cohorts, using a standardized procedure for preparing (cleaning) the hair samples prior to measuring their trace elements contents, and employing a rigorous program of quality assurance to validate the analytical results. More research is needed to fully define the relationships between the levels of essential trace elements in human scalp hair and nutritional status of the hair donor. At present, the research is incomplete, and the assessment of nutritional status on the basis of trace elements in human scalp hair is premature. By the same token, relationships between trace elements levels in human scalp hair and disease must be more firmly established in terms of etiology and application before the diagnostic potential of hair mineral analysis can be fully developed.

Some progress has been made in establishing normal values for some trace and minor elements in human scalp hair. Table III contains a listing of these values for both the essential and the toxic elements. While there is a general reluctance to utilize the former for the assessment of nutritional status or for the diagnosis of disease, the latter have been frequently employed to monitor environmental exposure and to evaluate systematic intoxication.

The determination of trace element concentration in hair has been applied to the evaluation of heavy metal exposures in the domestic and occupational environments. In these applications, hair has been characterized as a biological dosimeter, as a recording filament, and as a mirror of the environment. The heavy metal contents of hair reflect both the exposure dose and the absorbed dose. The former is most often established from ambient air and water quality monitoring programs, and the latter is determined from blood or urine analysis. While hair analysis maybe not able to differentiate between the

endogenous and exogenous depositions of heavy metals in every instance, there is no question that the results reflect exposure to heavy metals.

4. SELECTED TOXIC ELEMENTS IN HAIR

The interests of the toxicologists are directed towards the physiological effects of heavy metals. Cadmium, mercury, and lead were recognized as occupational hazards long ago, and compounds of arsenic and thallium have been used as commercial poisons for many years. These elements have no known biological functions, and their presence in the human body often interferes with the normal metabolic processes. The toxic effects of some of the heavy metals are listed in Table IV. Because of the ease with which the samples can be collected, transported, stored, and analyzed, hair analysis is valuable in screening individuals and populations for exposures to and intoxications with heavy metals. Sheldon *et al.* [32] have reviewed the methodologies and techniques for the routine analysis of human tissues and excreta as direct or indirect evidence of exposure to chemical substances. These approaches to biological monitoring included measurements of concentrations of chemicals in blood, urine, tissue and hair for the assessment of human exposures in the worker and non-worker populations.

4.1. *Arsenic*

The symptoms of acute arsenic poisoning usually begin a half hour after exposure. They include stomach pain and a tightness in the throat. Vomiting and intense diarrhoea quickly follow. The output of urine is characteristically decreased. Death from total cardiovascular collapse usually results within a few days, but deaths that occur up to 14 days after acute arsenic poisoning are usually caused by nephritis. In chronic arsenic poisoning, diarrhoea and vomiting occur, but these are less pronounced than they are in cases of acute arsenic poisoning. Tremors and peripheral neuritis are present in some cases. The afferent motor and sensory nerves in the lower extremities are affected. Ankle jerk disappears, and leg muscles atrophy begins. Arsenic stimulates the horny layer of the skin, which leads to the appearance of dark brown scales. Skin keratoses frequently result from prolonged exposure to arsenic. These may become malignant.

Chronic arsenic poisoning has been caused by drinking water contaminated with arsenic. Hindmarsh *et al.* [33] reported one such instance in Waverly, Nova Scotia. They examined 92 residents of Waverly after two cases of arsenic poisoning led to the discovery of 29 contaminated wells in the town. Of these, 27 of the residents had clinical features that could be attributed to chronic arsenic poisoning. A positive relationship was established between the frequency of these symptoms and the concentrations of arsenic in the hair and in the drinking water of the victims. Valentine *et al.* [34] were able to show that the arsenic concentrations of blood, urine and hair were correlated with the arsenic concentrations of the drinking water in two California and in four Nevada communities. Olguin *et al.* [35] correlated the arsenic concentrations of drinking water from the Comarca Lagunera region of Mexico with the arsenic concentrations in the blood, urine, hair and nails for residents with the cutaneous signs of arsenic poisoning and for those with known arsenic exposures. In both, the Valentine *et al.* study and in the Olguin *et al.* study, the hair arsenic concentrations appeared to show dose responses. Relationships between the clinical symptoms of arsenic poisoning and the concentrations of arsenic in the hair and/or drinking water have also been made in Chile [36] and in the Republic of Hungary [37,38].

Similar relationships have been established for chronic poisoning from airborne arsenic associated with the combustion of coal in Czechoslovakia [39], the smelting of copper in the United States [40], and the general urban atmosphere in the People's Republic of China [41].

Yamamura and Yamauchi [42] have investigated the possibility of arsenic poisoning in the occupational environment. While they found that the arsenic levels in the urine, blood, and hair of workers exposed to arsenic (III) oxide dusts were significantly higher than those of the control group, no relationship with clinical symptoms was possible. Both groups were asymptomatic. Feldman *et al.* [43] were, however, able to relate peripheral neuropathy to the arsenic concentrations found in hair and urine from workers in a copper smelter who were occupationally exposed to arsenic (III) oxide. Gabor *et al.* [44] also found elevated levels of arsenic in the hair and urine of smelter workers. These elevated levels were correlated with high rates of dyspepsia, astereovegetative, and polyarthralgic symptoms.

Jervis and Tiefenbach [45] reported that children living in the vicinity of a gold refinery had a mean hair arsenic concentration of 6.7 ppm compared to 0.33 ppm arsenic for the controls. Drinking water contaminated with arsenic from the refinery was suggested as the source of exposure. Mitoma *et al.* [46] have reported arsenic levels as high as 3.4 ppm in the hair of those living in the vicinity of a refinery. Ghelberg and Bodor [47] found increased arsenic in the hair and urine of children and adults residing near a copper refinery, and they subsequently recommended the use of hair analysis for screening exposures to arsenic and other heavy metals [48].

Hair analysis has been applied to monitoring non-workers for exposure to arsenic from industries other than mining and refining. Residents of an apartment complex were exposed to airborne arsenic when 75 kg of As_2O_3/Na_3AsO_3 dust was accidentally released from a Dutch chemical factory [49]. In this case, the analysis was able to differentiate between bulk and surface arsenic in or on the hair, and the contamination of the apartment residents was found to be a result of fallout with little or no real intake of arsenic. In what was formerly the Deutsche Demokratische Republik, the hair and urine of children residing in a region with high airborne arsenic showed, respectively, mean values of 5.5 and 0.5 ppm arsenic while the hair and urine of children from a control region contained, on the average, 0.011 and 0.004 ppm arsenic, respectively [50]. Obrusnik *et al.* [51-52] established relationships between the arsenic content of hair from the non-occupationally exposed population and the emissions of coal-fired power stations, and they encouraged the use of hair analysis as an indicator of such exposures.

4.2. Cadmium

Cadmium was recognized as an occupational hazard on the basis of its acute toxicity over a century ago. The chronic toxicity of cadmium became known in 1955 as the painful consequences of bone decalcification in the postmenopausal victims of itai itai byo. In the 15 years that followed, 200 cases of this disease, half of which resulted in death, were recorded in the Jintsu River Valley. The disease was caused by the ingestion of food and water contaminated with cadmium, and it was characterized by rheumatic symptoms with intense pain in the joints, resulting from the loss of bone materials, and by the bones themselves becoming as flexible as soft tissue [53].

Cadmium ingestion also resulted in damage to the kidneys, or renal tubular dysfunction. Some epidemiological evidence appears to relate the accumulation of cadmium with hypertension. The mechanisms of cadmium toxicity are ill defined at present. They may involve inactivation of enzymes containing sulphydryl groups, competition with zinc, and inhibition of copper absorption.

Ellis *et al.* [54,55] were able to determine kidney and liver cadmium concentrations by in-vivo neutron capture γ-ray spectroscopy. They compared these results to the hair cadmium concentrations on a subject-by-subject basis and concluded that the hair cadmium concentrations were not good indices to the cadmium body burden in the occupationally exposed individual. Anke *et al.* [56] found that the hair from occupationally exposed individuals contained 150 times more cadmium than from controls, and that blood and urine cadmium concentrations of the occupationally exposed individuals were, 5 and 15 fold higher, respectively, than those of the controls. Brückner [57] reported a 140 fold increase in the hair cadmium concentrations of exposed workers, and he recommended using the cadmium contents of hair as an indicator of airborne cadmium exposure. The general consensus appears to favour using hair cadmium measurements as indices to cadmium exposure [58-62], but this possibility is not universally endorsed [63-65]. More study and critical evaluation are needed to determine whether or not such measurements might be suitable for assessing systemic cadmium intoxication.

4.3. Mercury

The toxicology of mercury parallels that of cadmium. The acute toxicity of mercury was identified in the workplace before its chronic toxicity to the general public was suspected. Beginning in 1953, increasing number of adults and children residing near Minamata Bay showed loss of coordination, numbness of the limbs, partial blindness, and loss of hearing. Convulsions, coma, and death followed in 46 of 125 cases. By 1956, a congenital Minamata disease was observed in the offspring of symptom-free parents. The disease was subsequently diagnosed as acute methyl mercury poisoning and traced to the consumption of fish that had concentrated, or "biomagnified", mercury from industrial wastes discharged into Minamata Bay [66].

The toxicity of mercury involves both tissue destruction and enzyme inactivation. Gastroenteritis, nephritis, and hepatitis are frequency consequences of mercury poisoning. Mercury poisoning also causes irreversible neurological damage. Collapse of central nervous system (CNS) is often the cause of death from mercury poisoning [67].

Acute poisoning cause by mercury vapour and many mercury compounds is characterized by inflammation of the exposed mucous membranes. Typical symptoms are: stomatogingivitis, pneumonitis with respiratory distress, cough, fever, abdominal pain, vomiting, and diarrhoea. Permanent renal damage may be a result. Constriction of the visual fields, ataxia, and difficulty with speech are some typical signs. Death may result from haemorrhage and either circulatory collapse or renal tubular necrosis [68].

Limited exposure to organomercurials often results in fatigue, memory loss, and poor concentration ability. Chronic exposure to inorganic mercury can lead to weakness, weight loss, anorexia, tremor, and uncontrolled mood swings ranging from depression, shyness, nervousness, and irritability to irrational temper outbursts.

The laboratory diagnosis and assessment of chronic mercury poisoning is frequently aided by urine analysis. Urinary excretion, preferably over a 24 hour period, is a good index to mercury exposure. Normal output is less than 0.05 μmol (= 10 μg) of mercury per litre [69].

Chronic mercury poisoning has resulted from the continued use of consumer products containing this toxic element as well as from the ingestion, inhalation and/or absorption of food, air, and water in the domestic and occupational environments. Elevated mercury levels in hair and in other tissues frequently accompany chronic mercury poisoning.

The suspected chronic systemic intoxication with mercury of six women from the long term use of skin bleach creams containing ammoniate mercury has been reported by Marzulli and Brown [69]. Mercury etiology was confirmed in only one of these cases where the skin bleach was used for over four years. Urine, blood, and hair mercury concentrations were: 250 μg/24 hours, 100 ng/mL, and 125 mg/kg, respectively. Sherlock *et al.* [70] maintain that the major non-occupational source of mercury exposure is the consumption of contaminated fish. They found a linear relationship between mercury in hair and mercury in blood from studies on fish consumption by over 900 persons residing in two coastal regions of the United Kingdom:

$$\text{HAIR MERCURY} = 0.367 \times \text{BLOOD MERCURY} + 0.694$$

where the hair mercury concentration is expressed in mg/kg, and the blood mercury is expressed in μg/L.

Hansen *et al.* [71] investigated possible chronic systematic mercury intoxication in a population of Greenlanders who consumed seal contaminated with mercury. They found a correlation ($r = 0.9222$) between the concentration of mercury in hair and the concentration of mercury in blood:

$$\text{HAIR MERCURY} = 289 \times \text{BLOOD MERCURY} + 63.4$$

where the hair mercury concentration is expressed in μg/kg, and the blood mercury concentration is expressed in μg/L.

The consumption of fish contaminated with mercury is, perhaps, the chief source of non-occupational mercury exposure. Matthews [72] has reported elevated hair and blood mercury concentrations, 27 $\pm$ 15 mg Hg/kg hair, were correlated with the mercury concentrations in fish caught and consumed in the Republic of Seychelles. Riolfatti [73] has investigated the mercury exposure of two Italian populations and found that the hair and blood mercury concentrations, 3.06 mg/kg and 0.07 mg/L, respectively, were correlated with the amount of fish consumed. Similar correlations for hair mercury concentrations have been reported for populations in Senegal (7.33 ppm) [74], the People's Republic of China [75], Malaysia (8 ppm) [76], Thailand [77] and New Guinea (2.6 ppm) [78,79]. Duplicate diet studies in the United Kingdom [80] have shown elevated hair and blood mercury level in the populations consuming mercury-contaminated fish. The scalp hair to blood mercury ratios in a group of 20 English volunteers who consumed known quantities of mercury contaminated halibut for a 100 day period ranged from 200:1 to 340:1 with a maximum mean hair mercury concentration of 25 ppm [81]. Airey [82]

evaluated over 500 hair samples from 32 locations in 13 different countries, and she found hair mercury concentrations of 11.6, 2.5, 1.9, and 1.4 ppm for those who ate fish every day, every week, twice a month, and once a month, respectively. From an extensive review of the literature, she [83] subsequently established a positive linear correlation between hair mercury concentration and fish consumption using data from some 7500 individuals in 35 countries:

$$\text{HAIR MERCURY CONCENTRATION} = 0.13 \times \text{FISH CONSUMPTION} + 1.67$$

where hair mercury concentration is expressed as mg/kg, and fish consumption is expressed as kg/person/year. Some of her [82] data as well as some of the more recent data from Fergusson's tabulations [84] are presented in Table V. Fergusson's tabulations [84] also include a mean hair mercury concentration of 183 ppm for victims of Minamata disease.

The highest concentrations of total mercury found in hair samples from three Iraqi victims of the massive poisoning during the winter of 1971-72 due to the consumption of home made bread contaminated with methylmercury fungicide were, respectively, 649, 564, and 535 ppm. The "inorganic" mercury concentrations were 73, 57, and 70 ppm, respectively [85]. Subsequent evaluations of additional samples of hair as well as blood from other victims were made by other laboratories using different measurement techniques. The results for hair ranged from 250 to 450 ppm total mercury, ten percent of which, approximately, was "inorganic" mercury [86]. Blood mercury concentrations ranged from 10 to 90 μg/L less than ten percent of which was usually present in the "inorganic" form. Clarkson [87] has reviewed the relationship between these methylmercury concentrations in hair and blood, and he has applied these findings to the development of dose-response relations both for adult exposure and for prenatal exposure. Dermelj *et al.* [88] have measured total mercury and methylmercury concentrations in scalp hair samples collected from populations where fish was frequently eaten and from populations with negligible fish consumptions. For the former, approximately 80 percent of the total was found to be present as methylmercury. For the latter, less than five percent of the total mercury was found to be present as methylmercury. Using maternal hair methylmercury concentration data from Iraq, Cox *et al.* [89] used dose-response analysis for developing predictive models of prenatal exposure and subsequent motor retardation CNS abnormality. Using an animal model, Zorn and Smith [90] have demonstrated that the hair and other tissues such as blood, kidney, liver, lung, muscle, and spleen contain methylmercury formed from the in vivo methylation of "inorganic" mercury.

More than 15 years ago, Lenihan *et al.* [91] reported that the mercury concentrations in scalp and public hair from British dentists and their clinical assistants were from two to three times higher than the values obtained with corresponding samples from the office staffs at the dental clinics. Hefferren [92] subsequently recommended that the mercury levels in the hair of dental clinic personnel be considered as an indicative and not as a definite measure of mercury absorption, and the Health Foundation Research Institute of the American Dental Association has recommended safety and monitoring procedures for mercury in the clinical practice of dentistry [93]. Many sources of mercury waste have been identified in the dental practice [94]. Lin *et al.* [95] found geometric means for scalp hair mercury concentrations of 10.77 $\pm$ 4.04 and 3.76 $\pm$ 1.33 ppm for 32 Taiwanese dental professionals and 30 normal controls, respectively. The arithmetic means for scalp hair mercury concentrations in Korean dentists and their clinical assistants

were 8.57 and 5.79 ppm, respectively, while that for the residents of Seoul was 2.57 ppm [96]. In Jakarta, the average scalp hair mercury concentration of dentists was more than five times higher than that of the control population, *i.e.* 15.51 versus 2.80 ppm, respectively [97]. It appears that occupational mercury exposure results in elevated hair mercury concentrations, and that the regular analysis of mercury in hair or urine is recommended for monitoring mercury exposure of dental professional in Japan [89], Great Britain [98,99], and Poland [100].

In addition to workers in dental clinics, workers in laboratories, chlorine producing factories, and granaries experience occupational exposures to mercury or mercury compounds. Cagnett *et al.* [101] have reported that such exposures resulted in elevated mercury concentrations in hair, blood, and urine. Wiadrowska and Syrowatka [102] found the range of hair mercury concentrations for occupationally exposed workers was 170 to 231 ppm; that for the general population of Warsaw was 0.25 to 7.59 ppm. The mercury concentrations in the blood, urine, and hair of workers in a Spanish chlorine production factory with a workplace atmosphere containing from 0.05 to 0.1 μg of mercury per cubic meter were 6.7 μg/100 mL, 0.15 μg/L, and 44 mg/kg, respectively [103]. The urine and hair mercury levels of Czech workers who had treated grain with a mercury containing fungicide were 25 and 300 times higher, respectively, than the values for their controls [104]. The good techniques of Soviet laboratory workers were reflected in normal, *i.e.* 1.42 ppm, hair mercury levels relative to their controls, 1.05 ppm [105].

4.4. Lead

Lead poisoning from a variety of domestic and industrial sources is a subject of concern because it affects the nervous system of children given to pica and because its effects are so severely and permanently damaging to the fetuses and newborns of mothers ingesting lead.

The symptoms of acute lead poisoning are a sweet, metallic taste, salivation, vomiting, intestinal colic, and lowered body temperature. In addition, there may be cerebral oedema, convulsions, and coma. Kidney damage is frequent, and peripheral neuropathy often causes wrist drop. When death occurs, it is usually due to cardiovascular collapse.

Chronic lead poisoning has CNS manifestations. These are most pronounced in children, and they include irritability, headache, insomnia, restlessness and ataxia. Later, confusion, delirium, convulsions, and coma may develop. Muscle paralysis involving the extensor muscle of the wrist and foot may also develop. The gastrointestinal symptoms of chronic lead poisoning often include stomach distension after meals, constipation, nausea, vomiting, and colic. Appetite loss, weight loss, and fatigue usually follow. A black or purple line sometimes forms at the margin of the gums when lead in the saliva is precipitated with sulphide produced by gingival bacteria. Some other heavy metals, such as arsenic, bismuth, tin, and mercury, produce similar precipitates at the gingival border. Haematologic characteristics of chronic lead poisoning are basophilic stippling and elevated lead content. The urinary lead concentration is also elevated as are the concentrations of the urinary coproporphyrins [106].

Campbell and Baird [107] reported on the symptoms and treatment of lead poisoning in a group of demolition workers who suffered occupational exposure. Many of

these workers were found to have blood lead levels in excess of 3.8 μmol/L (= 775 μg/L) which is the upper limit for the industrially exposed population in the U.K. Urinary coproporphyrin excretion exceeded the normal 500 nmol/day. Weakness of tiredness, anaemia, abdominal pain, blue line at the gingival margin, nausea and vomiting, pleuritic pain, constipation, and elevated blood urea were observed in most cases. Other clinical features were anorexia, headache, hyperuricaemia, metallic taste, joint pain, peripheral neuropathy, irritability, and insomnia.

Chronic lead poisoning has resulted from the continued use of consumer products containing lead, the long term ingestion and/or inhalation of lead and lead compounds in the domestic environment and the exposure to lead and its compounds in the workplace. In many instances, the characteristics of chronic lead poisoning include elevated levels of lead in the hair as well as in the other tissues.

Kopito and his colleagues [108,109] have firmly identified relationships between the concentration of lead in the hair of children and the major clinical and laboratory findings associated with the chronic plumbism in children. The mean lead levels of these children as compared to controls were 282 versus 24 ppm. The source of lead in most cases was attributed to pica. Marzulli *et al.* [110] established a correlation between blood-lead and hair-lead levels in children identified in a lead poisoning surveillance project. From linear regression, they found:

$$\text{WHOLE BLOOD LEAD} = 0.02757 \times \text{HAIR LEAD} + 39.79$$

where the whole blood lead concentration is expressed as μg/100 mL, and the hair lead concentration is expressed as mg/kg For the 11 data points they reported, the correlation coefficient was r = 0.854 at p less than 0.001.

Niculescu *et al.* [111] investigated the relationship between blood-lead and hair-lead levels in two groups of adults with different exposures to airborne lead. A significant correlation between hair-lead and blood-lead, r = 0.72 at p less than 0.001, was found only with the 31 individuals exposed to high airborne lead. For 26 of these 31 individuals, blood lead was in excess of 40 μg/100 mL. For those in the high exposure group, the regression equation was:

$$\text{HAIR LEAD} = 1.505\, e^{(0.018 \times \text{BLOOD LEAD})}$$

where the hair lead concentrations were expressed in ng/cm and the blood lead concentrations were expressed in μg/100 mL.

Clayton and Wooler [112] measured the blood lead and hair lead levels of 38 male workers at a lead-acid battery factory in Sydney. The correlation between blood lead and hair lead concentrations was significant: r = 0.76 at p less than 0.005. The data followed an exponential curve:

$$\text{HAIR LEAD} = 15.2\, e^{(0.067 \times \text{BLOOD LEVEL})}$$

where the blood lead concentration is expressed as μg/100 mL and the hair lead concentration is expressed as μg/g. Fergusson *et al.* [113] reported an average hair lead concentration of 363 mg/kg for New Zealand battery workers. Bencko *et al.* [114] found

elevated concentrations of lead in the blood and hair of workers at a Prague battery factory. They reported concentrations as high as 53 μg/100 mL and 80 mg/kg, respectively, and they proposed the use of hair analysis for monitoring lead exposure. Burguera *et al.* [115] found that the mean lead hair content of petrol garage workers in Merida City, Venezuela, was significantly greater than that of an equal number of age-matched, gender-matched controls. The respective means and standard deviations were 48.7 ± 17.5 and 17.2 ± 8.1 ppm. They also reported than the lead hair contents of these Mexican petrol garage workers appears to increase with increasing duration of employment. Weber *et al.* [116] reported that the concentration of lead in the hair of Mexican pottery workers ranged from 3 to 600 ppm while that of controls ranged from 1 to 40 ppm.

Jervis, Chatt, and their coworkers have made several studies on pollution from smelters in and around Toronto. Lead levels as high as 20 times normal values were reported in the hair of children residing close to secondary lead refineries [117]. The hair lead concentrations of those living within 500 meters of lead refineries were found to be ten times higher than those of the control population [118]. Median values for the concentrations of lead in hair from residents in rural, urban, and near a smelter areas residents were 9.1, 15.3, and 48.5 ppm, respectively, and a correlation between blood-lead and hair-lead concentrations was obtained for these subjects [119]:

$$\log \text{HAIR LEAD} = 0.8 \times \text{BLOOD LEAD} + 0.025,$$

where the hair lead concentration is expressed in μg/g and the blood lead is expressed in μg/100 mL. Wibowo *et al.* [120] have also reported a correlation between the hair lead and the blood lead concentrations of children residing within 1 km of a lead smelter, but they prefer the measurement of blood lead concentrations and of zinc protoporphyrin concentrations in blood to the measurement of hair lead concentrations for the assessment of total exposure and health risk.

4.5. *Selenium*

Selenium is a "Doctor Jekyll - Mister Hyde" element. It is both, necessary and harmful for life. In animals, selenium deficiency is related to "white muscle disease" while a dietary excess causes the "blind staggars" [121]. In humans, Keshan disease, a well defined, chronic cardiomyopathy endemic in the Keshan region of China, is one consequence of selenium deficiency. Human selenium intoxication frequently produces hair loss, skin lesions, and CNS disorders [122]. Selenium is a beneficial element. It is recognized as a dietary requirement in amounts ranging from 0.04 to 0.10 mg/kg of food, but it is toxic when ingested in amounts greater than 1 mg/kg of food. "Garlic breath", pallor, nervousness, depression, and gastrointestinal disturbances are common symptoms of selenium intoxication.

Thimaya and Ganapathy [123] observed a weak correlation between selenium concentrations in the hair and those in the blood serum of humans. Increased hair selenium concentrations have been reported in experimental animals that were maintained on diets containing selenium supplements [124], and in experimental animals that were brought to mild states of systemic intoxication by chronic, low-dose exposure to selenium [125]. In humans, the frequent use of anti-dandruff shampoos containing selenium has been identified as an exogenous source of this element that could lead to confusion in

interpreting the results of hair selenium measurements applied to monitoring environmental exposure or evaluating systemic intoxication [126-128]. Clearly, further study of the significance of hair selenium measurements is needed.

4.6. Chromium and nickel

Chromium is an essential micronutrient and a chemical carcinogen. Its essentiality or carcinogenicity is determined by its chemical form and dosage [129]. A health assessment document [130] and a toxicological profile [131] have been prepared by federal agencies in the USA.

Saner *et al.* [132] found increased chromium in the hair and urine of 18 Turkish tannery workers, and Randell and Gibson [133] have reported on parallel observations in the hair and urine from 71 Canadian tannery workers. The mean hair chromium concentration obtained from the Turkish tannery workers was thirty times greater than the normal value: in the Canadian study, the respective median values differed by a factor of five. Unfortunately, the data presented do not allow a more quantitative comparison. However, it does appear that hair chromium concentrations, as predicted by Matsubara's and Machida's animal model [134], may reflect environmental exposure and systemic intoxication. More experimental evidence is needed to support the validity of this application.

The essentiality/carcinogenicity of nickel, like that of chromium, may depend on the chemical form and dosage. The possibility of monitoring environmental exposure to and evaluating systemic intoxication with nickel by hair analysis has been demonstrated in two cases of nickel carbonyl poisoning [135]. Further studies are needed to confirm or reject this possibility.

5. CONCLUSIONS

The analysis of hair for toxic elements shows promise as an indicator of exposure or intoxication in the domestic and occupational environments. It has been proven that scalp hair is a "biological monitor" for mercury. In the case of other persistent and accumulative toxic elements such as cadmium, lead, and arsenic, and in circumstances where intakes may be in either single massive or irregular doses, the blood levels may not reliably reflect the total body burden; scalp hair can serve as a better indicator. More work is needed to determine whether or not hair analysis for other elements may have similar applications. Moreover, the hair metal levels can reflect the history of exposure. Hair has many advantages which can be exploited to screen large population groups suspected of adverse exposure. In some cases hair levels along with the biochemical parameters can be used to identify individuals suffering from heavy metal poisoning. Strong correlations between the trace element levels in hair and the abnormal physiologies of various diseases have not yet been established. Also it has not been clearly demonstrated that a dietary deficiency of a particular essential element results in a value lower than the normal concentration in hair. Continued interest, research and activity in the use of hair as a biopsy tissue will establish the place of this approach as a probe for the evaluation of trace elements in the body.

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TABLE I. FREQUENT "NORMAL" VALUES FOR SOME ESSENTIAL AND SOME TOXIC TRACE ELEMENTS IN BLOOD, URINE AND HAIR [5]

	Blood Serum (mg/L)	Urine (mg/L)	Hair (mg/kg)
Copper	0.8 - 1.8	0.03 - 0.06	7 - 40
Iron	0.7 - 1.5	0.10 - 0.15	15 - 175
Zinc	0.8 - 1.1	0.40 - 0.60	150 - 250
Cadmium	0.001 - 0.007*	0.001 - 0.005	0.4 - 2.4
Mercury	0.002 - 0.006	0.001 - 0.02	0.5 - 10
Lead	0.002 - 0.2*	0.006 - 0.012	5 - 50

*whole blood

TABLE II. SOME BIOCHEMICAL FUNCTIONS OF THE ESSENTIAL TRACE ELEMENTS IN HUMAN AND ANIMAL METABOLISM [9]

Element	Function
Chromium	required for glucose metabolism
Cobalt	component of vitamin B12
Copper	component of oxidative enzymes, required for hemoglobin synthesis
Fluorine	essential for normal growth in rats
Iodine	component of thyroid hormones
Iron	component of hemoglobin, component of oxidative enzymes
Manganese	component of enzymes
Molybdenum	component of oxidative enzymes
Nickel	essential for normal growth in rats
Selenium	component of oxidative enzymes
Silicon	needed for normal growth in rats
Tin	may function in oxidation - reduction catalysis
Vanadium	may function in oxidation - reduction catalysis
Zinc	component of enzymes

TABLE III. NORMAL RANGES FOR TRACE AND MINOR ELEMENTS IN HAIR, (mg/kg)

Element	Doctor's Data [30]	MineraLab [31]
Calcium	204 - 712	200 - 600
Magnesium	29 - 137	25 - 75
Phosphorus	108 - 203	100 - 170
Sodium	346 - 1080	150 - 350
Potassium	42 - 430	75 - 180
Iron	21 - 50	20 - 50
Copper	17 - 67	12 - 35
Molybdenum	0.59 - 2.55	0.10 - 1
Manganese	0.62 - 1.97	1.0 - 10
Zinc	104 - 283	160 - 240
Chromium	1.03 - 3.23	0.50- 1.50
Selenium	0.08 - 0.64	3.0 - 6.0
Lithium	not established	0.10 - 0.80
Nickel	1.80*	1.0 - 2.0
Cobalt	not established	0.20 - 1.0
Vanadium	---	0.50 - 1.0
Lead	15.0*	20 - 30
Mercury	3.0*	2.5 - 5.0
Cadmium	1.6*	1.0 - 2.0
Aluminum	2.9 - 82.5	20 - 40
Arsenic	0.4*	2.0 - 3.0

*Normally tolerated limit

TABLE IV. SOME EFFECTS OF HEAVY METAL INTOXICATION

Element	Toxic effects
Antimony	Acute poisoning may result in vertigo, abdominal cramps, nausea, vomiting, rhinitis, bronchitis, and pneumonitis. Liver and kidney damage may appear at later signs
Arsenic	Intoxication often results in necrosis of the liver, hepatitis, encephalitis, myelitis, and nephritis as well as nerve and kidney degradation
Beryllium	Chronic inhalation often produces weight loss, bone and joint pain, chills, fever, disturbed liver and spleen function, skin lesions, and general physical deterioration
Cadmium	Intoxication produces weight loss, bleeding, rhinopharygitis, perivascular and peribronchial fibrosis, pulmonary emphysema, and damage to the liver and kidneys
Lead	Intoxication causes damage to the Central Nervous System (CNS), the brain, the reproductive system, and the kidneys
Mercury	Damage to the liver, kidneys, brain, and CNS result from intoxication
Selenium	Intoxication may result in liver and kidney damage as well as damage to the CNS and brain
Thallium	Intoxication causes gastrointestinal haemorrhaging, peripheral neuropathy, necrosis of the liver, delirium, and coma. Death is usually due to CNS or circulatory collapse

TABLE V. HAIR MERCURY CONCENTRATIONS FROM FISH-EATING POPULATIONS

Population	Mercury concentration, mg/kg	
	mean	range
Australia[a]	2.5	0.8 - 5.3
Canada[a]	1.2	0.3 - 2.7
China[a]	0.9	0.2 - 2.7
Germany (FRG)[a]	0.5	0.2 - 1.2
Hong Kong[a]	3.0	0.9 - 6.6
Italy[a]	1.5	0.5 - 5.4
Japan[a]	3.9	1.0 - 9.2
Monaco[a]	1.7	0.3 - 4.7
New Guinea[a]	1.8	
New Zealand	1.3	0.4 - 2.8
South Africa[a]	1.9	0.1 - 6.3
UK[a]	1.6	0.1 - 16.5
USA[a]	2.4	0.4 - 7.6
Korea[b]	1.9	0.4 - 9.4
Pakistan[b]	1.7	0.2 - 8.8
Sweden[b]	1.3	0.2 - 4.3

[a]See Ref. [82]

[b]See Ref. [84]