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REVIEW ARTICLE OPEN AACCESS

An Effective Approach towards Heavy Metals and their Effects on Different Organs of the Body

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Abstract

Most common heavy metals include chromium, cadmium, lead, copper, zinc and nickel and these all are cause of risks for human and environment. Harmful and beneficial effects of Heavy metals depend upon the presence of their concentration. Human health might be severely damaged by these heavy metals including impaired psycho-social behavior, neurological disorders, decrease in immunity and cancer of upper gastrointestinal tract. Substantial metal lethality has demonstrated to be a significant danger and there are a few wellbeing dangers related with it. The lethal impacts of these metals, despite the fact that they don't have any organic job, stay present in a few or the other structure destructive for the human body and its appropriate working. Study sources indicate attention to the discharging of such metals in condition by both anthropogenic and normal methods. Ingestion of such metals lead to frame stable bio lethal mixes by obstructing bio responses of capacities just as ruining their structures. It might prompt different issue and initiate free extreme arrangement. This audit gives insight regarding danger and effect on health. Eco harmfulness test along with chemical concentration monitoring extremely helpful instrument for looking at remediation proficiency of such metals in soil.

Keywords : Heavy Metals, Toxicity, Transferring, Blood Pressure, Ingestion, Lethal

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Introduction

Metals a significant class of comprehensively dispersed contaminations are characteristic components that have been removed from the earth and outfit for human industry and items for centuries. Metals are remarkable for their wide natural scattering, their propensity to be aggregated in chosen tissues of the human body, and their general potential to be lethal even at low degree of introduction. A few metals, for example, copper and iron, are basic to life and assume vital job in it. Different metals are xenobiotics, they have no valuable job in human physiology and, far more atrocious, as on account of cadmium (Cd), lead (Pb), iron (Fe), chromium (Cr), nickel (Ni) and Zinc (Zn), many are harmful even at low degree of introduction. Indeed, even those metals that are fundamental, in any case, can possibly turn destructive at extremely significant levels of introduction. The natural defilements by the dangerous substances are developing that cause significant worry to the neighborhood clients [13].

A wide scope of contaminants are persistently brought into the amphibian condition chiefly because of expanded industrialization, mechanical turn of events, developing human populace and abuse of common assets, horticultural and local squanders run-off. Among these contaminants, overwhelming metals comprise one of the most risky gatherings on account of their persevering nature, lethality, inclination to collect in life forms and experience evolved way of life intensification all the more still, they are non degradable. Overwhelming metals with antagonistic wellbeing impacts in human digestion (counting lead, mercury, cadmium and arsenic) present evident worries because of their diligence in the earth and recorded potential for genuine wellbeing outcomes. Intense overwhelming metal inebriations may harm focal anxious capacity, the cardiovascular and gastrointestinal (GI) frameworks, lungs, kidneys, liver, endocrine organs, and bones. It is beyond the realm of imagination to totally stay away from presentation to lethal metals [22].

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Indeed, even individuals who are not occupationally uncovered convey certain metals in their body because of presentation from different sources, for example, nourishment, drinks, or air. It is, in any case, conceivable to decrease metal poisonous quality hazard through way of life decisions that lessen the likelihood of hurtful substantial metal take-up, for example, dietary estimates that may advance the sheltered digestion or discharge of ingested overwhelming metals [15]. Because of development of innovation, the ascent of enterprises at or along the bank of water bodies is one of the fundamental driver of contamination which may cause the wellbeing perils for the populace devouring the sullied water and other related eatables [22].

Recognition of overwhelming metals and their evil impacts on the individual are consistently of worry of a researcher/toxicologist. The dangerous impacts of overwhelming metals are durable, reason being the non corruption properties of substantial metals. The overwhelming metals can‟t be debased while natural contaminants deteriorate into different synthetic compounds with time [22]. Heavy metals have poisonous impacts even at low fixation, which may demonstrate deadly to any living being. Their focus in biota can be expanded through bioaccumulations [28]. Poisonous metals are normally present in mechanical, city and urban spillover, which can be hurtful to people and biotic life [13].

The piece of the metals fluctuates as indicated by the time and the encompassing fixation. As per the properties of the metals their appropriation is checked identified with the ecological components. The metals are useful just as unsafe; it relies upon the centralization of these substantial metals. On the off chance that their fixation is low it implies they are gainful and keep up the different biochemical and physiological elements of the living body while the most extreme focus makes it destructive for body [16].

Literaure Review

Effect of heavy metals on human body

Iron

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On earth's crust 2nd abundant element is iron and it is a crucial metal for survival and growth of living organisms [26]. The necessary mineral for the body and for many biological systems is iron which is present in the trace amount. As we know that excess of everything is bad so excessive iron causes the toxicity. The toxicity of iron is mostly present in cats, dogs and in the several other animals. Unpremeditated deaths of the children (below 6 years) are occurring due to iron day by day [2].

In normal aging, brain iron accumulates but in any neurological disorder its amount increases. In case of hemochromatosis iron carrying capability of transferrin increases that increased its transportation against blood brain barrier ultimately iron level in brain cells is elevated. Iron on reacting with hydrogen peroxide produce reactive oxygen species and these easily react with proteins, lipids and DNA [20]. Hemochromatosis occurs due to deposition of dietary iron in various organs including brain. HFE gene is involved in hemochromatosis. Cys282Tyr mutations in this gene cause various types of iron storage related disorders that might be a cause of Parkinson's disease and Alzheimer's disease. The presence of this HFE protein on ependymal cells, blood vessels and choroid plexus has been increase iron uptake of brain [6].

The evidence of excessive raise in brain iron level leads to AD. The main causes of AD are amyloids-β (Aβ) plaques formed by impaired clearance and overproduction of (Aβ). Elevated level of iron show interaction with Aβ peptide and reduce molecular oxygen into superoxide and ultimately to hydrogen peroxide by reducing iron. Free iron enhanced oxidative stress that is basically involves in pathogenesis of AD. However, disturbances in iron regulatory protein cause problems in iron de-compartmentalization and homeostasis resulting in oxidative processes [20].

Cellular effect of iron toxicity

A wide range of dangerous free radicals has been produced due to improper iron binding with protein which extremely affects the level of iron in biological fluids and mammalian cells. This unbound iron when circulates in body have certain corrosive effects on biological fluids and gastrointestinal tract. Elevated level of iron saturates in body by crossing the rate limiting absorption steps. Free form of iron easily penetrates in brain, liver and heart and disrupt oxidative phosphorylation eventually convert ferrous form into ferric form of iron which increase

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metabolic acidity on releasing hydrogen ions. Free iron also damage mitochondria, cellular organelles and microsomes by inducing lipid peroxidation [2].

Iron toxicity also leads to tissue damage and oxidation-reduction mechanisms. Excess dietary iron is a potential source of cellular damage. Free radicals produced by iron also induce malignant transformations and mutations which is a cause of several diseases [9].

Lead

All over the world, lead is dangerous metal and it has created many health issues and surrounding contamination because of huge usage of this metal. The color of lead is silver but in dry aerosphere its color is slightly bluish [24]. The origin of lead display consists of food, industrial process, drinking water, smoking and domestic sources. Similarly, other origin of lead were house paint and gasoline which increased to Lead directly affect smooth muscles of heart vessels by restraining Na-K-ATPase activity and the level of intracellular calcium also raised [10]. Blood pressure might be affected by lead. Bagchi & Preuss elaborated that when Sprague-Dawley rats have been exposed with 1% Pb acetate in drinking water for about 40 days the systemic blood pressure has been changed. With the continuation of treatment the level of blood pressure gets high and ultimately returned to normal. But its level again elevated when lead exposure ends for several months. This experiment revealed that elevated level of lead in rats lead to reduction of nitric oxide which basically involves in blood pressure regulation, down regulation of guanylate cyclase enzyme that is a nitric oxide activated vasodilation mediator, changes in adrenergic system [4].

Lead effects on children brain

Children are more sensitive to lead absorption than adults that's why ingested lead is absorbed in large proportion in gastrointestinal tract of children. Large proportion of circulating lead reaches to brain of children and increases the vulnerability of developing nervous system to lead toxicity. In children the initial symptoms of lead poisoning include irritability, lethargy, anorexia and abdominal cramps. Progressively it leads to ataxia, vomiting, clumsiness and coma. If children

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survive then they will be mentally retarded. Lead poisoning is a syndrome that is associated with lead level in blood 70mg/dl and in some children it develops at 50mg/dl [9].

Effects of dietary lead on kidney

The effect of poisonous agents on kidneys can damage the renal and also can cause the renal failure. Severe prominent dose of lead induced brakeage of proximal tubular function distinct in glycosuria, aminoaciduria and hyperphosphaturia (a Fanconi-like syndrome); these impacts seem to reversible. Nevertheless, repetitive or continuous exposures may cause poisonous stress on kidney, it may grow in chronic and unchangeable lead nephropathy (interstitial nephritis), verifying the sight of deleterious contribution for lead [8]. There are the two ways of renal toxicity (1) reversibly by serious exposure of Pb acetate in children (2) irreversibly during interstitial nephropathy results by long term exposure of [4].

Ghorbe illustrated that the oral administration of the lead acetate resulted in the vital increase of blood urea and serum creatinine. Blood lead concentration increases upto 50 µg/dl due to the large uptake of lead. As a result of this uptake the rate of glomerular filtration slows down and produces glomerular sclerosis. Renal damage causes due to the increased concentration of the calcium, phosphorus, uremia and creatinemia as well as due to the decreased concentration of creatinuria and glycemia

Lead entrance in Body and Blood

Lead enters the human body in many ways. It can be inhaled in dust from lead paints, or waste gases from leaded gasoline. It is found in trace amounts in various foods, notably fish, which are heavily subject to industrial pollution. Some old homes may have lead water pipes, which can then contaminate drinking water. Most of the lead we take in is removed from our bodies in urine; however, there is still risk of buildup, particularly in children. Exposure to lead is cumulative over time. High concentrations of lead in the body can cause death or permanent damage to the central nervous system, the brain, and kidneys (USGAO, 2000). This damage commonly results in behavior and learning problems (such as hyperactivity), memory and concentration problems, high blood pressure, hearing problems, headaches, slowed growth,

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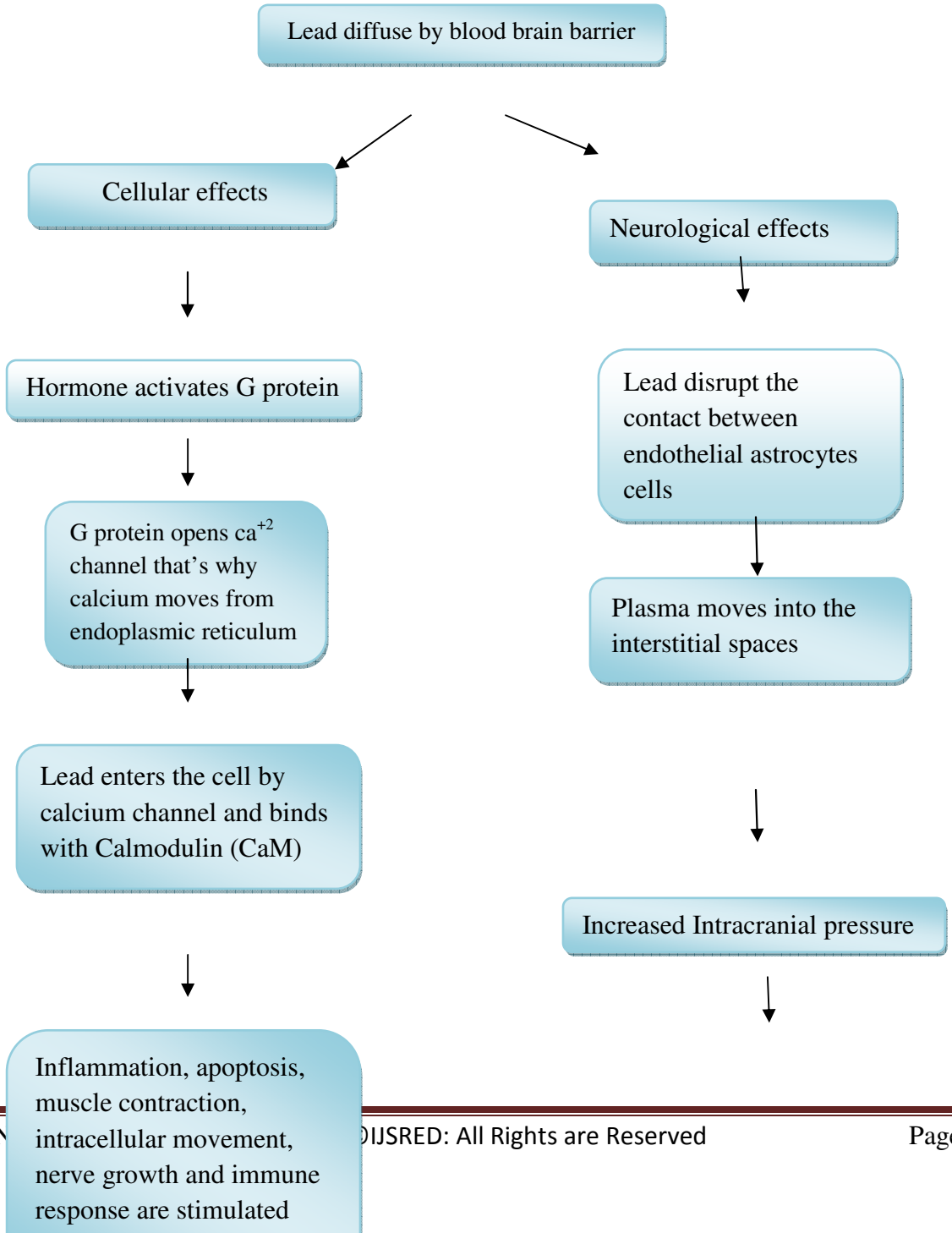
reproductive problems in men and women, digestive problems, muscle and joint pain. Studies on lead are numerous because of its hazardous effects. Lead is considered the number one health threat to children, and the effects of lead poisoning can last a lifetime. The increased level of lead in blood causes the following effects shown by the figure 1 below.



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Edema, encephalopathy and irreversible brain damage.

Figure .1. Effects of increased lead in the blood

Cadmium

According to ATSDR ranking cadmium is characterized as 7th most toxic metal. Oncecadmium is absorbed in humans it is continuously accumulate in the body. Researchers indicate that about 11,000 hectares in China is polluted by this metal and 680 tons of cadmium discharged in environment annually. Cd is predominantly present in vegetables and fruits because it has high rate of transfer from soil to plant [23]. It is highly toxic heavy metal and well recognized due to adverse effect on cells enzymatic processes and induces oxidative stress [11].

Cadmium job in Diabetic nephropathy

A portion reaction relationship has been seen between urinary cadmium and albuminuria among Torres Strait subjects with type 2 diabetes. For people with diabetes, the geometric mean for urinary cadmium with albuminuria was 61% higher than for those without albuminuria. For those without albuminuria, the normal urinary cadmium level was 0.74 µg/g creatinine. The higher urinary cadmium levels among diabetic subjects could be the consequence of broad kidney harm that prompts the arrival of cadmium in the kidney into the pee. One approach to decipher these information is to recommend that the edge urinary cadmium for individuals with diabetes ought to be no more prominent than 0.74 µg/g creatinine to forestall or defer the beginning of renal complexities. Such a translation believes albuminuria to be an indicator of glomerular debilitation, endstage renal disappointment, and unfriendly cardiovascular results. A

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comparable limit was recommended in another investigation that discovered glomerular hindrance related with the urinary cadmium 0.8 µg/g creatinine [14].

Impact on Hypertension.

Eum watched a portion reaction connection between urinary cadmium and hypertension. Of the Korean subjects in their investigation, 26.2% were hypertensive. For this populace, the mean blood cadmium was 1.67µg/L, and the hazard gauge for hypertension was 1.51 when blood cadmium levels in the most reduced tertile were contrasted and those in the most elevated. An affiliation was likewise found between blood cadmium and circulatory strain levels in a U.S. test populace, where the mean blood cadmium was 3.98-overlay lower than the mean level found in the Korean investigation [18].The quality of the cadmium pulse affiliation was most prominent among nonsmokers, middle among previous smokers, and little or missing among current smokers. These discoveries support "pressor" impacts, which have been demonstrated to be normal for incessant presentation to low-portion cadmium [23].

Impact on Lung

[Lampe inspected the potential impacts of presentation to cadmium on lung work utilizing an example gathering of 96 men who experienced one to three lung work tests somewhere in the range of 1994 and 2002. They found a decrease in constrained expiratory volume in 1 sec (an impression of lung work) related with expanded urinary cadmium among the individuals who smoked. These information recommend that lung illness among smokers might be intervened to a limited extent by cadmium, in light of the fact that urinary cadmium is likewise a marker of aggregate smoking, a set up chance factor in lung infection.

Impact on Periodontal tissues

A 3-crease increment in urinary cadmium (0.18 versus 0.63 µg/g creatinine) has been accounted for to be related with a 54% higher commonness chances proportion (OR) for periodontal malady. For instance, Arora found that among an example of grown-ups, 15.4% had periodontal illness. The age-balanced mean urinary cadmium for subjects with periodontal sickness was 0.50 µg/g creatinine and 0.30 µg/g creatinine for unaffected people [3].

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Impact on Ocular tissues

Higher urinary cadmium was seen as related with AMD among smokers. The middle urinary cadmium level of present and previous smokers with AMD was 1.18 µg/g creatinine. This level was 1.97-, 2.03-, and 2.07-overlay higher than that of smokers without AMD, nonsmokers with AMD, and nonsmokers without infection, individually. Expanded retinal cadmium content has additionally been found in male subjects with AMD [29].

Impact on Mammary organ

Gundacker (by and large, a cadmium substance of 0.086 µg/L and that bosom milk cadmium content was lower among nonsmokers who took nutrients and mineral enhancements ($p < 0.05$) [9]. In an investigation by Kippler said that the middle cadmium level in bosom milk from Bangladeshi subjects was 1.6-crease higher than was the level from Austrian subjects [14]. The specialists watched a relationship among's cadmium and the essential organization of milk, including manganese, iron, and calcium levels. Their discoveries recommend a potential impact of cadmium on mammary organ metal vehicle and emission.

Nickel

In environment, nickel is present in a very low concentration. It has various applications. Mostly it is used as an ingredient of steal and other products of metals. It is found in jewelry as well as in some food goods e.g. chocolate and fats with greater quantity. The chances of nickel uptake increases by eating vegetables grown in polluted soil. An uptake of nickel from plants is very important than from vegetables. At the end nickel is present in detergent as well as in smokers and they have the higher uptake by their lungs [18].

Common disorders cause by dietary nickel

There are several ways of the exposure of nickel in humans like by breathing air, water intake, eating food or smoking cigarettes. Too much large uptake of nickel from soil or by water causes the several types of cancers such as lung cancer, nose cancer, larynx cancer and prostate cancer,

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sickness, dizziness, respiratory failure, lung embolism, birth defects, asthma and chronic bronchitis, allergic reactions such as skin rashes, mostly from jewelry and heart disorders [18].

Nickel metabolism

Most of the nickel is distributed to bone, kidney and lungs after absorption [21]. In gastrointestinal tract nickel is poorly absorbed approximately 10%. Orally administrated nickel is primarily found in kidneys than other organs. Ni^{2+} taken through oral route is accumulated in spinal cord than in frontal cortex or cerebellum. It can cause several allergic reactions and the ratio of allergens is about 10% to 20%.

Nickel toxicity syndrome

Nickel carbonyl exposure leads to nickel toxicity. Initial symptoms involve respiratory tract infections and other non-specific symptoms. Severe poisoning leads to gastrointestinal and pulmonary toxicity. However, cerebral edema and interstitial pneumonitis are the major causes of death. Nickel compounds and nickel itself are the carcinogenic in nature. Nickel toxicity syndrome is characterized by heart failure, decreased estrogen, asthma, vomiting, stomach irritation, elevated RBCs, headache, nausea, angina, hypoglycemia, lowered pulse, skin rashes and increased urine protein [17].

Chronic bronchitis

Nickel has many harmful health effects; one of them is the chronic bronchitis as well as cancer of lungs and nasal sinus etc. Chronic bronchitis is the type of chronic obstructive pulmonary disease. In the bronchial tubes inflammation occurs with a lot of mucus. That's why difficulty in breathing as well as cough occurs. The main causes of chronic bronchitis are shown in figure 2.5. It occurs due to presence of nickel in air for a long period of time which spreads air pollution and cigarette smoking is also responsible for it. The level of nickel is higher in those people who work in nickel refineries or in nickel processing plants.

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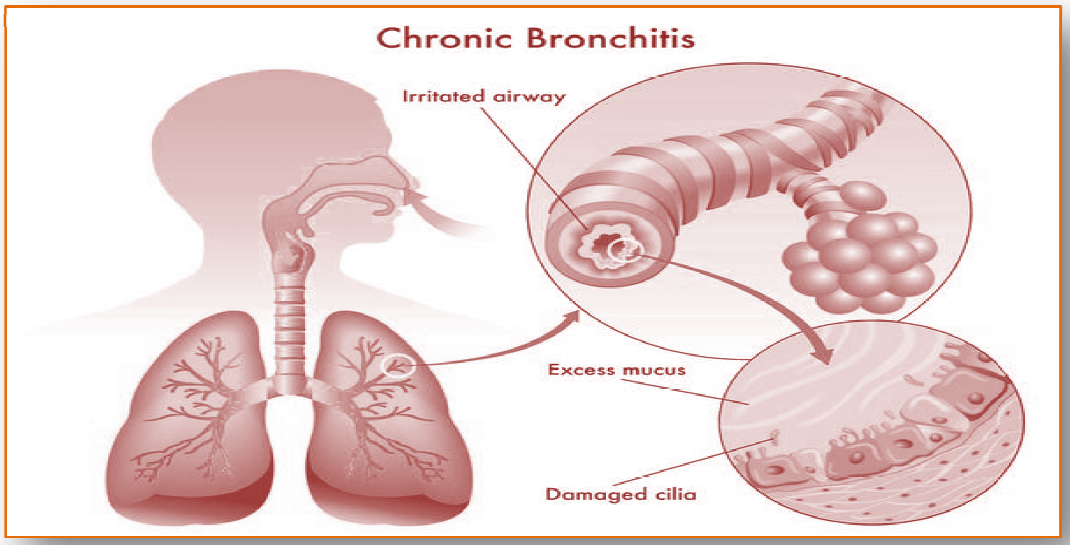

Figure 2. Chronic bronchitis

Chromium

On earth seventh most abundant element is chromium which is present in various oxidation states form Cr^{2+} - Cr^{6+} (Rodriguez *et al*., 2009). Cr^{+3} and Cr^{+6} are most common and toxic to humans, animals and plants [17].

Cr (III) is harmless while Cr (VI) can easily penetrate through iso-structural anions in the cell. Reactive oxygen species like hydrogen peroxide, superoxide ions and hydroxyl radicals are produced by interaction between biological reductants and chromium (VI) and eventually cause oxidative stress within the cell and cause damage to proteins and DNA. Literature survey's shows that Cr (VI) is dangerous than trivalent chromium and it enters easily in cells and quickly reduced to Cr (III). According to International Agency for the Research on Cancer Cr (VI) is included in group 1 human carcinogenic compounds [12].

An essential mineral for the optimum health is chromium which is a trivalent element [7]. For the therapy of type 2 diabetes mellitus intolerance a nutritional supplement is used called chromium picolinate [Cr (pic) 3] which is a comparatively better absorbed form of trivalent

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chromium. Simultaneously including other several effects, it also enhances the sensitivity of the insulin so that glucose homeostasis could be maintained in both animals and humans [1].

Chromium pathogenicity

Fruits, vegetables and meat are the primary sources for chromium as they contain <10-1300µg/kg of Cr [25]. The ultimate products or intermediates produced during the reduction of chromium VI can enter into Fenton-type reactions in which they produce hydroxyl radicles in association with hydrogen peroxide. Alternatively, by Haber-Weiss like reactions Cr (V) and Cr (VI) produces hydroxyl radicals in the presence to Cr(III), which mediates chromium toxicity during reduction by inducing oxidative stress but chromium intermediates interact with DNA and protein [25].

Hexavalent chromium exposure cause acute tubular necrosis which is marked by reduction in urinary flow rate. ATN is generally characterized by renal failure. Research studies by placing 5ICr intratracheally in animals provide strong evident of 6-20 fold high chromium accumulation in renal cortex than in liver and RBCs. Trivalent chromium has low nephrotoxicity than its hexavalent form and both species of chromium are involved on causing acute renal failure and tubular necrosis [27].

Cr (VI) facilitates entry in cell and circulation and cellular injury is associated with trivalent form of chromium. Chronic renal injury is generated by long term exposure of minute level of chromium which ultimately leads to chronic interstitial nephritis. The biological half-life of chromium is about 1month and it gets accumulate in renal tissues over many months. Chromium as a cause of renal failure can only be evident when some conditions are superimposed on other causes of injury such as hypertension, lead nephropathy and reduction in renal reserve [27].

Effect on heart

The studies of chromium picolinate about the effect on cardiovascular system are limited however it is investigated that it has some relation with the carbohydrate metabolism. Through the standard correlation between the diabetes (type 2) intolerance and several cardiovascular diseases (irregular vascular functions, elevated blood pressure and ischemic heart disease),

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cardiovascular effects due to supplements become more related. In the hypertensive rats the treatment of chromium picolinate attenuates the sucrose-induced intensification of the blood - pressure and also improves the acetylcholine-and nitroprusside-induced vasodilator response [5].

In humans the level of protein, lipids and carbohydrates is maintained by chromium. By binding the insulin with receptors chromium enhances the function of insulin in the cell wall. Many studies include the different forms of growth such as carcass characteristics, immune functions, reproduction and tissue deposition [1].

Zinc

Zinc is a trace element and it is a part of >300 enzymes and a large number of other proteins. Sufficient zinc availability is necessary for optimal protein metabolism and nucleic acid metabolism. Normally 2-3g Zn is present in human body and 90% of which is present in bones and muscles. Dietary zinc is absorbed in small intestine and distributed via serum where it predominately presents in bounded form with various proteins like transferrin, albumin and α-microglobulin [19].

Zinc induced copper deficiency

High concentration of zinc is associated with deficiency of copper. Competitive absorption with enterocytes is mediated by MT. generally, MT binds through high affinity with copper than zinc, however, high amount of zinc depress copper absorption [19].

Impact of zinc on apoptosis

Increased intracellular zinc levels may also induce cell death by inhibition of the energy metabolism. High level of intracellular zinc in different cells and tissues leads to apoptosis as shown in figure 3 Reports show that intracellular accumulation of zinc either by releasing from intracellular sources or due to exogenous administration activates certain pro-apoptotic molecules such as p38 and potassium channels lead to cellular death. Increased level of intracellular zinc can induce death of cell by inhibiting energy metabolism [19].

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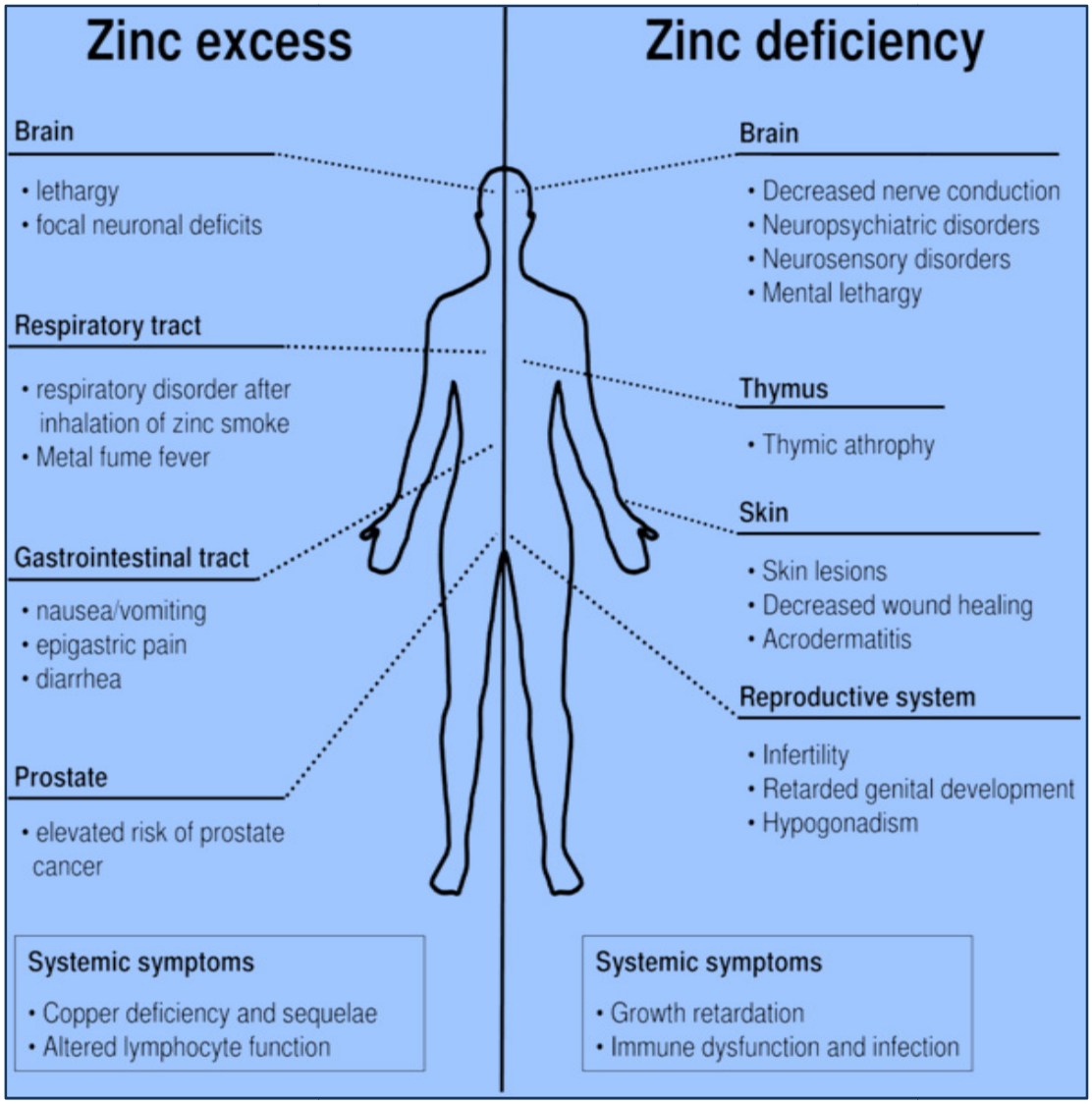

Figure .3. Impact of zinc on human biological structures

Effects on immune system

Dietary intake of zinc from 200-400mg/day can disrupt immune functioning. Pancreatic cells have large amount of zinc then other tissues of body so studies reveal that there is an association between zinc and diabetes [30].

Conclusion

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Taking everything into account, the act of follow component recognition ought to be kept on maintaining a strategic distance from conceivable utilization of polluted eatables. Individuals ought to be careful about the perilous impacts of utilization of heavy metals. As recommended by World Health Organization. The bioaccumulation of Heavy metals may present extraordinary danger to health of people and animals. Studies have shown that some heavy metals (Ni, Cr and Cd) are mind boggling cancer-causing agents, and the instruments fundamental these metals carcinogenesis are multifactorial. Disappointment of controlling heavy metals and their introduction to condition may force antagonistic impacts and lead to extreme intricacies. National just as worldwide collaboration is required to forestall heavy metal lethality.

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