



Insinuation of Toxic Metal on Smokers' Lungs

^{1,2*}Aprajita Singh, ¹Atul Thorat, ²Anamika Tripathi, ¹Mohammed Zahid, ¹Mrithulabashini J

¹School of allied health care and sciences, Jain (deemed to be university), Bangalore- 560066, India.

²Pollution ecology research laboratory, Department of Botany, Hindu College, Moradabad-244001, India.

*Corresponding author's E-mail: S.aprajitha@jainuniversity.ac.in

Received: 03-05-2022; Revised: 14-07-2022; Accepted: 21-07-2022; Published on: 15-08-2022.

ABSTRACT

Heavy metals are major cause of environmental pollution and due to their toxicity, they persist long in atmosphere. Toxic metals or heavy metals have ability to accumulate in human body and cause various respiratory disorders. Heavy metals sometimes become highly toxic by reacting with different environmental elements. Tobacco smoking is one of the major concerns for the accumulation of toxic metals in smokers' lungs and people residing with smokers (known as passive smokers) also being affected, especially children. ETS (environmental tobacco smoke) represents inhaling of tobacco and release heavy metals in ambient air involuntary. The development of children pulmonary function severely gets affected due to passive smoking. Every year millions of people die because of tobacco. Heavy metal content is present in the lung tissue of smoker and non-smokers, and which get mixed with the blood at time of gasses exchange in alveoli and circulate in the body. Therefore, tobacco smoking is considered one of the serious global health concern due to its carcinogenic effects on human body. This majorly happens because of the presence of toxic metals like Arsenic (As), Cadmium (Cd), Mercury (Hg), Lead (Pb), Chromium (Cr). The concentration of both Pb and Cd, are potent human carcinogen. This study presents important information regarding effect of heavy metals inhaled content in tobacco and its transference to cigarette smoke and their accumulation in smokers' lung tissue.

Keywords: Heavy Metals, Metal Pollution, Pulmonary disorders, Tobacco, Carcinogens.

QUICK RESPONSE CODE →

DOI:

10.47583/ijpsrr.2022.v75i02.002



DOI link: <http://dx.doi.org/10.47583/ijpsrr.2022.v75i02.002>

INTRODUCTION

Toxic metals are release in environment due to various anthropogenic activities. These activities have increased drastically in recent decade ¹. Electronic waste, industrial smoke, and diesel soot playing prominent role in effecting the health of the people. People residing in developing countries are suffering from various respiratory disorders especially the population involved in smoking². Metals occurs naturally among other environment pollutants and persist for long. Hence, human exposure to metals is inevitable, and some studies have reported gender differences in the toxicity of metals ¹. High-dose heavy metals exposure, particularly arsenic, mercury, cadmium, and lead, may induce severe complications such as breeding trouble, abdominal pain, and kidney dysfunction or Failure². Smoking and chewing tobacco kill millions of people around the world every year. The tobacco was determined to contain 11 toxic metals, the total metal content in cigarettes is present in its ashes⁴. The metals content was also determined in the lung tissue of smokers and non-smokers. The number of heavy metals is said to be increased in the lungs of smokers as heavy

metals are getting accumulated due to inhaling of polluted air and because of smoking³.

Several acute and chronic toxic effects of heavy metals affect different body organs. Gastrointestinal and kidney dysfunction, nervous system disorders, skin lesions, vascular damage, immune system dysfunction, birth defects, and cancer are examples of the complications of heavy metals toxic effects². Humans are exposed to these heavy metals every second by ingestion (drinking or eating) or inhalation polluted air (breathing). Most of the toxic heavy metals like lead, cadmium, antimony, mercury, arsenic, and thallium, are common in industrial operations and are substantial polluters of the environment due to electronic waste burning (PCBs) ⁵. Thallium has a more severe effect than other heavy metals but is less abundant in nature ⁶; it is a cause of alopecia in humans. Followed by mercury and arsenic most abundant metals in biosphere and carcinogenic in nature if inhaled⁷. The main objective of this review is to provide insight into the sources of heavy metals and their harmful effects on the humans with smoking habits.

Heavy Metal Toxicity

Arsenic is odourless and tasteless. Inorganic arsenic is a known carcinogen and can cause cancer of the skin, lungs, liver, and bladder ⁸. Arsenic is one of the most important heavy metals causing disquiet from both ecological and individual health ⁹. Arsenic is a protoplasmic poison since it affects primarily the sulfhydryl group of cells causing malfunctioning of cell respiration, cell enzymes and



mitosis^{9, 10}. According to the WHO, the major concern for public health is heavy metal that is Cadmium^{5, 6}, and Cadmium is the only metal which can get accumulated in tobacco plant naturally (*Nicotiana tabacum*)⁷. This leads to “hyper-accumulation” to very high cadmium concentrations especially in the leaf part of the tobacco plant⁹. The balance of the oxidant–antioxidant system and induce inflammatory responses can be disturbed in various organs due to poisoning. Exposure to Pb can produce alteration in physiological functions of the body and is associated with many diseases^{9, 13, 15}. It has been reported that Pb gets easily absorbed in the lungs of the children because of passive smoking¹². Each year, between 25,000–30,000 tons of Cd is released into the environment because of many activities, both natural and man-made. However, the main sources through which Cd makes its way into the human body are agricultural produce (food), and smoke produced by the combustion of tobacco¹⁴. It was observed in a study that one cigarette generally contains approximately 1–2 mg of Cd, and half of this amount enters the lungs by way of smoking and becomes part of the systemic circulation¹⁸. Cadmium has many applications, e.g., in batteries, pigments, plastics and metal coatings and is widely used in electroplating¹⁹ Cr (VI) and Cr (III) are the most stable forms and only their relation to human exposure is of high interest²⁰. Occupational sources of chromium include protective metal coatings, metal alloys, magnetic tapes, paint pigments, rubber, cement, paper, wood preservatives, leather tanning and metal plating¹⁷

Schroeder et al.¹⁶ (1970) reported that cigarettes contained 390 g/kg of Cr, but there has been no significant report published on the amount of chromium inhaled through smoking.

Table 1: Showing effects of increased Pb levels in human blood¹¹

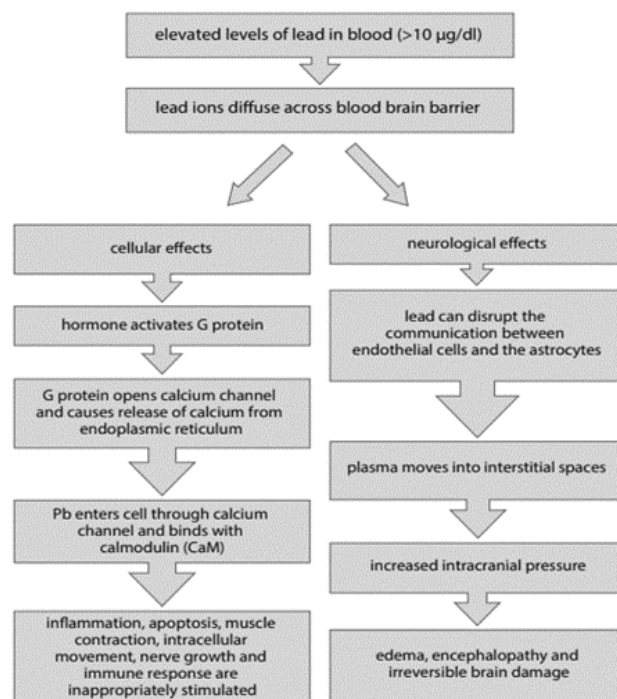


Table 2: Types of Mercury Toxicity SADER²¹

	Elemental mercury	Methyl mercury	Inorganic mercury
Sources	Fossil fuels, dental amalgams, old latex paint, incinerators, thermometers	Pesticides, fish, poultry	Biological oxidation of mercury, demethylation of methyl mercury by intestinal microflora
Absorption	75–85% of vapor absorbed	95–100% absorbed in intestinal tract	7–15% of ingested dose absorbed and 2–3% dermal dose absorbed in animals
Distribution	Distributed throughout the body, lipophilic, crosses blood-brain barrier and placental barrier, accumulates in brain and kidney	Distributed throughout the body, lipophilic, readily crosses blood-brain barrier as well as placental barrier, accumulates in kidney and brain	Does not cross blood-brain or placental barrier, present in brain neonates, accumulates in kidney
Excretion	Sweat, urine, feces, and saliva	90% excreted in bile, feces, 10% in urine	Sweat, saliva, urine and feces
Reason for toxicity	Oxidation to inorganic mercury	Demethylation to inorganic mercury, generation of free radical, binding to thiols in enzymes and structural proteins	Binding to thiols in enzymes and structural proteins

Tobacco Toxicity

Tobacco is processed from the leaves of plants in the genus *Nicotiana*¹². Smoking negatively impacts on health across the life-course and dramatically reduces both quality of life and life expectancy¹⁹. The negative impacts of tobacco smoking include, among others, increased rates of cardiovascular-related death (e.g., ischemic heart disease and stroke)¹⁴. Nowadays, about 12% of all deaths among adults aged 30 years and over are attributed to tobacco¹⁹. It is estimated that globally tobacco kills around 6 million people each year: five million from direct tobacco smoking while 600,000 deaths are attributable to second-hand smoke effects²¹. On current smoking trends, the annual death toll from tobacco is expected to rise to around 10

million people by 2030³². Direct tobacco smoking and involuntary smoking (exposure to second-hand smoke) have been classified by the International Agency for Research on Cancer (IARC) as agents considered carcinogenic to humans (classified as group 1 exposure circumstances)¹⁶. tobacco smoke can be an important source of know toxic compounds such as nitrosamines, polycyclic aromatic hydrocarbons (PAHs), pesticides, heterocyclic and aromatic amines, and metals.¹⁷

Toxic metals play important role in accumulation in human body due to tobacco smoking as it contains toxic compounds^{8, 9}. Effectively, various toxic compounds are presents in tobacco smoking which while smoking transfer into blood at time of exchange of gases.^{8,20,21}. The extent of



which a metal transfer from tobacco to cigarette smoke varies greatly depending on several factors such as the metal properties, metal content in the tobacco, design of cigarette, length of rod and type of filter used ^{7, 8, 17}.

Anaemia may develop with Pb poisoning via the inhibition of ferro chelatase and aminolaevulinic acid dehydratase (ALAD), the two of many enzymes involved in heme biosynthesis ¹⁹. Exposure to Pb can produce alteration in physiological functions of the body and is associated with many diseases ^{25, 26}. Pb accumulation in human body is highly toxic which causes adverse effects on the neurological dysfunctions, biological disruptions, and cognitive disabilities functions in the bodies. The international level-of-concern for Pb poisoning is 10 µg/dl in the blood ^{27, 19}. In recent years, adulteration of opium with heavy metal (Pb) has been considered a threat to a human life (18). The increasing order of metal content depending on their toxicity is Tl > As > Hg > Cd > Pb > Cr > Al > Mn > Ba > Zn > Ni. Various cigarette brands were analysed for metals contents.

Table 3: Cut-offs for blood metal levels ⁹

Antimony	2 µg/L
Arsenic	3.12 µg/L
Barium	77.6 µg/L
Cadmium	0.15 µg/L
Cesium	10 µg/L
Chromium	1.86 µg/L
Cobalt	0.63 µg/L
Copper	1495 µg/L
Lead	2 µg/dL 5 µg/dL 10 µg/dL
Manganese	18.3 µg/L
Nickel	2.62 µg/L
Selenium	201 µg/L
Zinc	5234 µg/L

Overview of Effect of Tobacco on Lungs of Smoker & Passive Smokers

Lung diseases caused by smoking include COPD, which includes emphysema and chronic bronchitis ^{31, 32}. Cigarette smoking causes most cases of lung cancer ^{13, 2}. If you have asthma, tobacco smoke can trigger an attack or make an attack worse ^{31, 32}. Smokers are 12 to 13 times more likely to die from COPD than non-smokers ^{31, 32}. Smoking can cause lung disease by damaging your airways and the small air sacs (alveoli) found in your lungs³².

Cigarette smoking is an important worldwide health problem, and it has been reported that 1.7 million Thai

youths currently smoke ³⁰. In previous studies, cigarette smoking was found to influence the lung function of the adolescent boys and girls ^{13, 14}. The number of cigarettes was the best measure of exposure to husbands’ smoking, while exposure at workplace was more strongly related to the duration of exposure.⁸

Table 4: Hypothetical Mechanisms of Metal Toxicity ³⁴

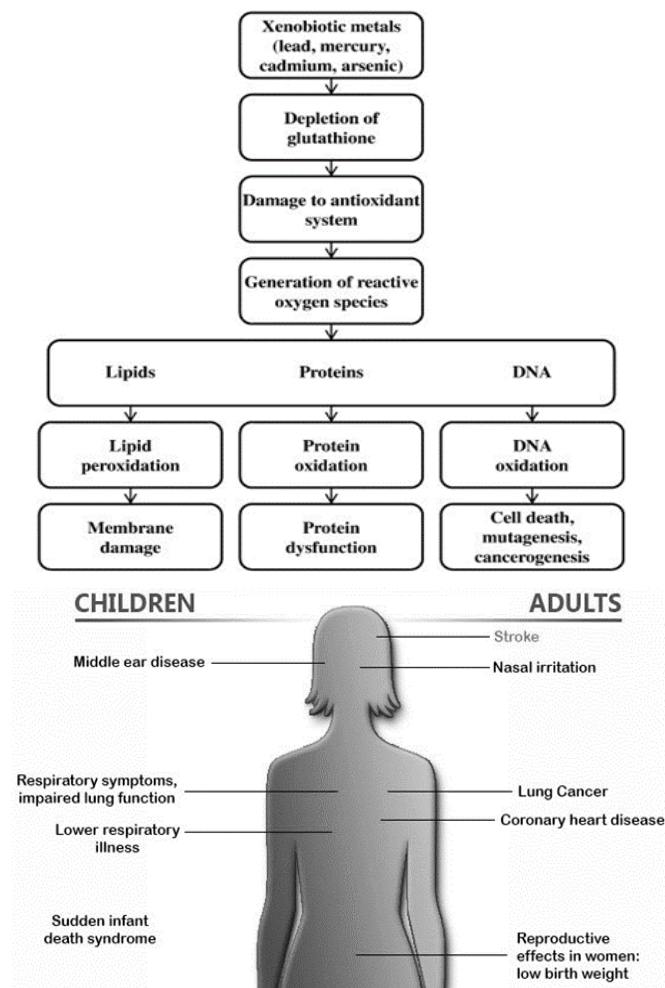


Figure 1: Health Consequences Causally Linked to Exposure to Passive Smoking Smoke ²⁷

It was shown due to smoker misclassification is very unlikely to be responsible for the increased health risks which is being recently observed in the epidemiological studies on humans on ETS²¹. Few studies have shown, longitudinal and cross-sectional in environment tobacco smoke is playing pivotal role in various lung disorders and compared with significant relation with drug response and dose ^{10, 11}. Acute exposure to environment tobacco smoking results in decrease of lung volumes and blood flows which also affected gaseous exchange, effecting whole system¹². Non-smoking individuals with long-term ETS-exposure have an increased risk of lung cancer. Hackshaw et al. reviewed 37 epidemiological studies on the risk of lung cancer in non-smoking persons (4626 cases) ³⁵. It was found that lifetime risk of lung cancer in non-smoking persons who lived with a smoker was 24% (95% CI 13% to 20%). Carcinogens related to tobacco smoking also detected in the blood of the ETS

exposed to passive smoker \ providing clear evidence of the ETS association ³⁸. A dose-response relationship between the non-smoker's risk of lung cancer and cumulative exposure to ETS was also demonstrated in this review.³⁹

Mechanism of Epigenetics Due to Heavy Metals

Epigenetic alterations can be promoted in heavy metals with help of methylation and modification of DNA and Histones respectively. Some heavy metals are capable of DNA methylations and histones modifications such as As, Hg, Cr, and Pb. On the other hand, only Cd and As are reported to mediate expression of noncoding RNAs, another molecular mechanism of epigenetic regulation ²⁷. The exact mechanism of epigenetic changes due to heavy metals exposure is not fully determined ²². It seems that increased expression of protooncogenes and silencing of tumour suppresser genes via intracellular ROS production are the underlying causes ²⁹. Expressions of some tumour suppressors gene are inhibited by the process of Methylation in DNA which leads to convert protooncogene to oncogene. As a result, changes in gene expression result in the alteration of the cellular division process and facilitation of malignant transformation of cells ²⁵. Epigenetic dysregulations in human bronchial epithelial cells were reported following Cr6+ exposure. Some studies found increased levels of histone H3 methylation marks (H3K9me2 and H3K27me3) and histone methyltransferases (HMTases) ³⁴. Reports suggested Cr-induced methylation of the p16 gene, a tumour suppressor gene, in the same cell line ³⁸. Similarly, various genetic and epigenetic changes may attribute to the Hg, Pb, Cd and As toxic and they show high carcinogenic effects. DNA methylation as well as specific histone modification marks are associated with exposure to Cd and As.^{22, 27, 34}

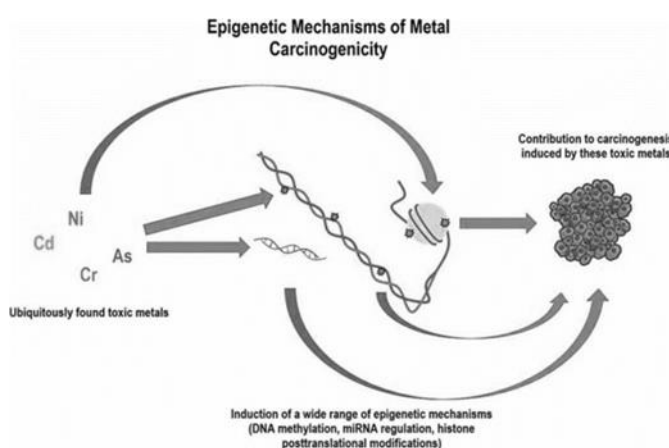


Figure 2: Toxic metals can induce epigenetic mechanisms contributing to carcinogenesis ⁴⁶

CONCLUSION

In this review we reviewed the effects of some heavy metals, i.e., arsenic, lead, mercury, cadmium, chromium, on humans in form of tobacco smoking. We concluded that because of tobacco smoking in any form like cigarettes, hukkah, sheesha, inhaling of tobacco is responsible for accumulation of heavy metals in body. Controlling the

activity of smoking plays crucial role because there are maximum chances that complication will be severe in future and there will adverse and more harmful effects can be imposed to human body by toxic and hazardous metals. Smoking especially in front of children if one of the major reasons for their improper growth and development. Observing the interventions and the exposure probably for decreasing more extra vulnerability to toxic metals in ecosystems and prevent humans to get affected in devastating ways and it can become significant step towards controlling pollution of heavy metals. Extensive steps have been taken by various national and international co-operatives to reduce toxicity of heavy metals in environment. Smoking has a multidimensional impact on lung such as respiratory disorders, breathing problems, pulmonary disorders. It remains the most prominent causative reason for developing the disease and carries a definitive prognostic and predictive value. Adenocarcinoma is more common in never smokers and females even children are getting exposed because of passive smoking. There are various for molecular profiling of never smokers where carcinogenesis stays presumptive but still if someone near then is smoker can be a reason for getting affected. Thus, Heavy metals can disrupt various cellular events including growth, proliferation, differentiation, damage-repairing processes, and apoptosis by disturbing the cell signalling pathways or kinase cascades. Some toxic or heavy metals including Hg, Pb, Cd, and As causes genomic instability. Collectively, these types of studies may substantially improve the understanding of the significance of heavy metal effect in smoking-related lung diseases and the corresponding potential diagnosis, monitoring, or treatment.

REFERENCES

- 1 Friberg L, Injuries following continued administration of cadmium, preliminary report of a clinical and experimental study, Arch Indust Hyg Occup Med 1950; 1: 458–6.
- 2 Agency for Toxic Substances & Disease Registry (ATSDR). Toxicological Profile for Cadmium. Atlanta, GA, U.S. Department of Health and Human Services: Public Health Service; 2015 March.
- 3 World Health Organization (WHO). Exposure to Cadmium: a Major Public Health Concern. Geneva, WHO; 2010.
- 4 Satarug S, Moore MR. Adverse health effects of chronic exposure to low-level cadmium in foodstuffs and cigarette smoke. Environ Health Perspect 2004; 112: 1099-4.
- 5 Nair AR, Degheselle O, Smeets K. Cadmium-induced pathologies: where is the oxidative balance lost (or not). Int J Mol Sci 2013; 14: 6116–27
- 6 Joseph, C. L. M., Havstad, S., Ownby, D. R., Peterson, E. L., Maliarik, M., McCabe, M. J. Blood lead level and risk of asthma. Environ. Health Perspect 2005; 113 (7):900–4. Doi:10.1289/ehp.7453.
- 7 Jacobs, D. E., Wilson, J., Dixon, S. L., Smith, J., and Evens, A. The relationship of housing and population health: a 30-year retrospective analysis. Environ. Health Perspect 2009;117(4):597–7. Doi:10.1289/ehp.0800086.
- 8 Kianoush, S., Balali-Mood, M., Mousavi, S. R., Moradi, V., Sadeghi, M., Dadpour, B., et al. Comparison of therapeutic effects of garlic and d-penicillamine in patients with chronic occupational lead poisoning.

- Basic Clin. Pharmacol. Toxicol 2012;110(5):476–5. Doi:10.1111/j.1742-7843.2011.00841.x.
- 9 Kianoush, S., Balali-Mood, M., Mousavi, S. R., Shakeri, M. T., Dadpour, B., Moradi, V., et al. Clinical, toxicological, biochemical, and hematologic parameters in lead exposed workers of a car battery industry. *Iran J. Med. Sci* 2013;38 (1):30-38.
 - 10 Kianoush, S., Sadeghi, M., and Balali-Mood, M. Recent advances in the clinical management of lead poisoning: *Acta Med. Iran* 2013; 53: 327–5.
 - 11 Gordon JJ, Quastel GH. Effect of organic arsenicals on enzyme system. *Biochem J* 1948; 42: 337-11.
 - 12 Hughes JP, Polissar L, Van Belle G. Evaluation and synthesis of health effects studies of communities surrounding arsenic producing industries. *Int J Epidemiol* 1988; 17: 407–5.
 - 13 Martin S, Griswold W. Human health effects of heavy metals. *Environmental Science and Technology Briefs for Citizens* 2009;15:11-16.
 - 14 Zhitkovich A. Importance of chromium-DNA adducts in mutagenicity and toxicity of chromium (VI). *Chem Res Toxicol* 2005; 18(1): 3–7.
 - 15 Martin S, Griswold W. Human health effects of heavy metals. *Environmental Science and Technology Briefs for Citizens* 2009;15:1–6.
 - 16 Schroeder HA, Nason AP, Tipton IH. Chromium deficiency as a factor in atherosclerosis. *J Chron Dis* 1970; 23(2): 123–12.
 - 17 Hagstad, S., Bjerg, A., Ekerljung, L., Backman, H., Lindberg, A., Rönmark, E., Lundbäck, B. Passive smoking exposure is associated with increased risk of COPD in never smokers. *Chest* 2014; 145(6):1298–5.
 - 18 Dip, A., Iritas, S.B., Mergen, G., Dinc, A.H., Soylemezoglu, T.J. Effects of age, gender, BMI, settlement and smoking on lead and cadmium accumulation in heart tissue. *Medicine* 2017; 6(3):531–4.
 - 19 P. Jha, Avoidable deaths from smoking: a global perspective, *Public Health Rev* 2012;33:569–31.
 - 20 HHS, U.S. Department of Health and Human Services, How Tobacco Smoke Causes Disease: The Biology and Behavioural Basis for Smoking-Attributable Disease: A Report of the Surgeon General, GA, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, Atlanta 2010.
 - 21 IARC, Tobacco smoke and involuntary smoking, *IARC Monogr. Eval. Carcinog. Risks Hum* 2004;83:1–1452.
 - 22 D. Bernhard, A. Rossmann, G. Wick, Metals in cigarette smoke. *Iubmb Life* 2005; 57: 805–4.
 - 23 R.V. Caruso, R.J. O'Connor, W.E. Stephens, K.M. Cummings, G.T. Fong, Toxic metal concentrations in cigarettes obtained from U.S. smokers: results from the international tobacco control (ITC) United States survey cohort. *Int. J. Environ. Res. Public Health* 2014;11:202-15.
 - 24 E. Pinto, I.M.P.L.V.O. Ferreira, Cation transporters/channels in plants: tools for nutrient biofortification, *J. Plant Physiol* 2015;179:64–69.
 - 25 U. Kramer, Metal hyperaccumulation in plants, *Annu. Rev. Plant Biology* 2010;61:517–11.
 - 26 M.R. Fresquez, R.S. Pappas, C.H. Watson, Establishment of toxic metal reference range in tobacco from US cigarettes, *J. Anal. Toxicology* 2013;37:298–5.
 - 27 R.S. Pappas, M.R. Fresquez, N. Martone, C.H. Watson, Toxic metal concentrations in mainstream smoke from cigarettes available in the USA. *J. Anal. Toxicology* 2014;38:204–211.
 - 28 M. Chiba, R. Masironi, Toxic and trace elements in tobacco and tobacco smoke, *Bull. World Health Organisation* 1992; 70: 269–8.
 - 29 Cancer Research UK. Tobacco and cancer risk statistics. From: <http://www.cancerresearchuk.org/cancerinfo/cancerstats/causes/lifestyle/tobacco/tobacco-and-cancer-risk#Smoking> Accessed: Feb 2013
 - 30 M. Williams, A. Villarreal, K. Bozhilov, S. Lin, P. Talbot. Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. *PLoS One* 2013;8:345-7.
 - 31 N.M. Hepp, W.R. Mindak, J. Cheng. Determination of total lead in lipstick: development and validation of a microwave-assisted digestion inductively coupled plasma-mass spectrometric method. *J. Cosmet. Sci.* 2009;60:405–9.
 - 32 T.G. Kazi, N. Jalbani, M.B. Arain, M.K. Jamali, H.I. Afridi, R.A. Sarfraz, A.Q. Shah. Toxic metals distribution in different components of Pakistani and imported cigarettes by electrothermal atomic absorption spectrometer. *J. Hazard. Material* 2009;163:302-5.
 - 33 M.A.L. Anton, D.A. Spears, M.D. Somoano, M.R.M. Tarazona. Thallium in coal: analysis and environmental implications. *Fuel* 2013;105:13–5.
 - 34 Burki, T. K. Nigeria's lead poisoning crisis could leave a long legacy. *Lancet* 2012;379(9818):60332-8. Doi:10.1016/s0140-6736
 - 35 Jacobs, D. E., Wilson, J., Dixon, S. L., Smith, J., and Evens, A. The relationship of housing and population health: a 30-year retrospective analysis. *Environ. Health Perspect* 2009; 117(4):597–7. Doi:10.1289/ehp.0800086.
 - 36 Joseph, C. L. M., Havstad, S., Ownby, D. R., Peterson, E. L., Maliarik, M., McCabe, M. J., et al. Blood lead level and risk of asthma. *Environ. Health Perspect* 2005;113(7):900–4. Doi:10.1289/ehp.7453.
 - 37 Kianoush, S., Balali-Mood, M., Mousavi, S. R., Moradi, V., Sadeghi, M., Dadpour, B., et al. Comparison of therapeutic effects of garlic and d-penicillamine in patients with chronic occupational lead poisoning. *Basic Clin. Pharmacol. Toxicol* 2012;110(5):476–5. Doi:10.1111/j.1742-7843.2011.00841.
 - 38 Kianoush, S., Balali-Mood, M., Mousavi, S. R., Shakeri, M. T., Dadpour, B., Moradi, V., et al. Clinical, toxicological, biochemical, and hematologic parameters in lead exposed workers of a car battery industry. *Iran J. Med. Sci.* 2013;38(1):30-6.
 - 39 Kianoush, S., Sadeghi, M., and Balali-Mood, M. Recent advances in the clinical management of lead poisoning. *Acta Med. Iran* 2015;53:327–9.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

For any question relates to this article, please reach us at: globalresearchonline@rediffmail.com
 New manuscripts for publication can be submitted at: submit@globalresearchonline.net and submit_ijpsrr@rediffmail.com

