ATINER CONFERENCE PRESENTATION SERIES No: HEA2017-0027

ATINER's Conference Paper Proceedings Series
HEA2017-0027
Athens, 14 November 2017

Low Socioeconomic Status (LSES): A Susceptibility Determinant in Chemical Exposure and Toxicity

Gloria O. Anetor

Athens Institute for Education and Research
8 Valaoritou Street, Kolonaki, 10683 Athens, Greece

ATINER's Conference Paper Proceedings Series
HEA2017-0027
Athens, 14 November 2017
ISSN: 2529-167X

Gloria O. Anetor, Department of Public and Environmental Health, Faculty of Health Sciences, National Open University of Nigeria, Abuja, Nigeria

Low Socioeconomic Status (LSES): A Susceptibility Determinant in Chemical Exposure and Toxicity

ABSTRACT

Socioeconomic status has been explored in a number of diseases in the past. Low socioeconomic status or class (LSS; LSC) was considered protective against the major non-communicable diseases such as cardiovascular disease and cancer. It was in contrast highly regarded to be a greater susceptibility factor to infectious diseases that are very prevalent in the resource poor countries. But LSC has largely been ignored in chemical exposure and toxicity which are on the increase in these countries owing to progressive industrialization. In light of the current spate of industrialization with increasing chemical utilization and chemical waste generation it appears desirable to examine the contribution of low socioeconomic class to increased chemical exposure and toxicity. It is noteworthy that the resource poor countries have the poorest regulatory policies and monitoring procedures of chemicals. Low socioeconomic class is often associated with poverty with attendant low nutritional status; including micronutrient deficiency disorders (MDDs) and reduced antioxidant status. This implies greater free radical burden implicated in many pathological processes including chemical toxicity. Optimum nutritional status may modify or mitigate chemical toxicity through the antioxidant hypothesis which can be highly achieved by LSC through health education. Increased susceptibility factors are associated with a raised disease burden or risk. Nutritional status may therefore modify susceptibility to chemical toxicity in LSC associated with nutritional deficiency states that may otherwise enhance vulnerability. Lead poisoning, a well-known toxicant occurs most frequently in disadvantaged populations; lead and iron share a common divalent metal transporter 1 (DMT-1). Iron deficiency, one of the commonest nutritional deficiencies is reported to enhance lead absorption and toxicity. Women and children are particularly vulnerable. Indeed, cognitive disorders caused by the co-existence of both nutritional deficiency and increased chemical exposure (double burden) have been described as a silent pandemic. Sub-optimal nutritional status from LSC may lead to reduced optimal health and development. Low socioeconomic status potentiates even relatively small risk factors, causing more marked contribution to disease when a huge population is involved. Most toxicants

from the environment are cumulative and could lead to high cost of health care and well-being in low socioeconomic class individuals and communities. It therefore seems rational for future investigations to examine low socioeconomic status in chemical exposure and toxicity as a possible useful approach to pragmatically formulate policies to creatively address the growing problem of chemical exposure and toxicity in industrializing developing countries.

Keywords: Socioeconomic status, chemical exposure, Toxicity, Ill-health, susceptibility determinant

Introduction

Economic and social drivers such as income, education and social relationship have a direct bearing on health status.[1] These socioeconomic determinants strongly interact to influence health in general. An improvement in any of the drivers can produce an improvement in both health behaviour and outcomes among individuals and the community. Populations with very low incomes (very common in many developing countries) often lack resources and access to nutritious foods, adequate housing and working conditions which can exert negative impact on health (Public Health Agency of Canada).[2] Although, socioeconomic status is one of the strongest predictors of ill health and early death worldwide, it is often overlooked in health policies. Low socioeconomic status is also linked to significant reduction in life expectancy and should be considered a major risk factor for ill health and early death in national and global health policies. This observation was made very recently after a study that involved 1.7 million participants, largely drawn from the most economically advanced nations of the world; United Kingdom, France, Switzerland, Italy, Australia, United States and Portugal. Remarkably, although rising chemical exposure is becoming an important issue particularly in the rapidly developing countries was not considered (Stringhini et al., 2017)[3]

Health disparities associated with socioeconomic status have been recognized for a number of centuries, Smith et al, 1992; Gallows and Matthews, 2003)[4, 5] and have been described by investigators for decades.

Relatively recent studies in the more industrialized nations demonstrate that socioeconomic status is associated with diverse health outcomes.[1] What appears more disconcerting is that socioeconomic status and inequalities in morbidity and mortality may even be widening.[1] Despite this growing understanding, the concept has not been related to the increasing environmental exposure to chemicals in the developing countries that are rapidly industrializing and consuming a lot of chemicals and generating a lot of chemical wastes with poor regulations and resources for waste management that accentuate chemical exposure and concomitant toxicity.

At least in part, SES disparities in health arise from differences in the distribution of basic resources such as health care (including health education), nutrition and sanitary living environment.

The American Psychological Association defines socioeconomic status as the social standing or class of an individual or group. It is often measured as a combination of education, income and occupation. Examinations of socioeconomic status reveals inequalities in access to resources, including issues related to privilege, power and control. (Stringhini, 2017) Chemical exposure has often been ignored in the examination of socioeconomic status but should be admitted in such discussion owing to the undeniably pivotal position chemicals in the domestic or work environment occur in our modern world. Indeed is thought that modern man lives in a chemical habitat.

Goldman and Tran (2002)[8], some of the few investigators that have examined chemical exposure social disadvantage or poverty, observed that chemical

exposure and toxicity indicate that a person may have had contact with the chemical with potential and real deleterious effects. Toxicants can enter the body in a variety of ways. They can be inhaled, ingested, or absorbed through the skin. Conditions characterizing low socioeconomic status enhance absorption of chemical through these routes. An illustration of a far reaching consequence is that of women and children that are usually more vulnerable. A pregnant woman can transfer toxicants to her fetus through the placental and mothers can transfer toxicants to children through breastfeeding. Goldman and Tran (2002) have warned that all chemical substances can cause injury or disease in humans at sufficient doses.[2]. Though they indicated at sufficient dose, it is recognized that in these countries with the prevalent widespread malnutrition even what is considered innocuous may be toxic. This has recently called for rethinking risk assessment and the need to embrace better ways of accounting for low dose effects (Boobis et al., 2011; Colacci and Kleinstreuer, 2015, Goodson et al, 2015).[9,10,11] A toxicant effect may be visible damage, or a decrease in performance or function measurable only by an investigation. Traditionally, when a small amount can be harmful, the chemical is considered highly toxic. When a very large amount of the chemical is required cause damage, the chemical is considered to be relatively non-toxic. A growing body of evidence suggests that chemicals present in air, water, soil, food, building materials and household products are toxicants that contribute to the many chronic diseases typically seen in human beings; cancer is the most well-known; others are increased susceptibility to infection as a result of suppression of the immune system by chemicals (Bijlsma and Cohen, 2016).[12] It is perhaps rife to recall an observation by a passionate environmentalist, John Last three decades ago.

He drew attention to the situation as follows: The combination of population pressure and malnutrition has sapped the vitality of developing countries for generation. Now new problems are being added, industrial development, often without the restraining laws of affluent industrial nation, is causing serious environmental damage and occupational disease (Last, 1987).[13]

In the developed countries, population exposure to chemicals is monitored, but in many developing countries chemical use may not be regulated or monitored (Grandjean and Landrigan, 2006).[14] The contribution of most chemicals to neurological and developmental disorders and subclinical neurotoxity in children is unknown but considered to be of high magnitude given the enormous amount of chemicals used and released into the environment in these countries. This may also be true of other health outcomes in children and adults.

Many previous epidemiologic reports have shown that low socioeconomic status is associated with environmental exposures (Kordas etal., 2007).[15] Itaiitaibyo (osteomalacia) a well-known classical poisoning from the environment as a result of excessive exposure to the potent environmental pollutant and toxicant, cadmium from a mine located up stream (Kaji, 2012).[16] The population affected in the community of Fuchu Toyama prefecture was mainly that peasant farmers using contaminated water from the mine laden with cadmium oxide (CdO). It is remarkable that another well known outbreak of a toxic exposure also from Japan involved mercury, the - Minamata bay disease. This arose from waste

from the Chisso plastic factory dumped in the sea or water bodies around the bay. This waste was consumed by fish and other sea creatures and biomagnified in them such that when this poor community solely dependent on the sea and its resources consumed these food items went down with what is now known as Minamata disease, a form of neuropathy (Eto, 2000).[17] As is evident from these two examples most of the affected populations were mainly individuals in the low socioeconomic class. They were often nutritionally disadvantaged, a factor which promotes susceptibility to chemical toxicity owing largely to compromised or ineffective xenobiotic metabolic mechanism, In the field of environmental health, exposure to environmental risk factors are unequally distributed and tend to be influenced by social characteristics which include income, social status, employment and education. (Kordas et al)[15] Minority groups and those with lower socioeconomic status are likely to bear a greater burden of environmental toxicants given their lifestyle, proximity to waste sites, industrial emissions and poorer quality ambient air. Biomonitoring studies have identified toxicants in all individuals, the type and amount of which varies, depending upon lifestyle factors and geographical variation.

Most toxicants from the environment are cumulative and could lead to high cost of health care and well-being in low socioeconomic class individuals and communities. Studies reveal that the relationships among poverty, environment, and disease remain elusive and that residential environment is linked to the etiology of illness. (EH, 2017).[18] A recent article suggests that neurodevelopmental disorders caused by chemical exposures constitute a modern "silent pandemic" (Gradjean and Landrigan, 2006).[19]

Scientific evidence implicates environmental exposures as discernable contributors to adverse health outcomes, such as cancer, neurodegenerative diseases, reproductive health problems, and learning and developmental disabilities. (Tyrell et al., 2013).[20] Importantly, the outcomes depend on the route of exposure (i.e., ingestion, inhalation, and dermal contact). Additionally, for most environmental chemicals, available information on health effects is generally limited to high exposures in studies of humans (e.g., occupational studies of workers) or laboratory animals. Some specific circumstances that may affect chemical exposure and toxicity are discussed below.

The Role of Nutrition in Susceptibility to Chemical Toxicity

Many well conducted studies have demonstrated consistently that nutritional status and nutrients play a beneficial role in modifying (largely mitigating) susceptibility to chemical exposures. (Grandjean and Landrigan, 2006; Kordas et al., 2007)[19,15]. The relationship between environmental chemical exposure and nutritional status is complex, probably more so in the resource poor countries. With a double burden of nutrient deficiencies and greater environmental exposure, a substantial proportion of the world's population may never realize their right optimal health and development.

The interaction among nutritional, nutrients and vulnerable populations in disadvantaged populations in search of economic progress needs better understanding for more creative approaches to managing the consequences of chemical exposure and toxicity. Nutritional deficiency and susceptibility to the increasing chemical exposure in these countries should be recognized as a pivotal determinant in chemical exposure and toxicity. This appears to corroborate an observation made four decades ago that nutritional or therapeutic supplementation of the prime micronutrient, zinc may be beneficial in treating and preventing one of the widest spread chemical toxicity, lead toxicity (Finelli, 1977).[21] In the developing countries, very large numbers of chemicals, many mixtures of chemicals are encountered. The effect of multiple exposure particularly in nutritional deficiency is largely unknown but may have multiplier synergistic adverse effects that could be transgenerational.

The concept that heavy metal toxicity may be greatly modified and indeed modulated by the nutritional status of population has a firm basis in a great number of reports some of which are long standing (Cerklewski and Forbes 1976; Petering et al, 1977).[22,23] Indeed Petering et al.[23] suggested that nutritional status and dietary intake should be viewed as one of the most important preventive measures available to public health experts to reduce the consequences of environmental or occupational exposure to chemicals.

Low socioeconomic class is often associated with poverty with attendant low nutritional status; including micronutrient deficiency disorders (MDDs) and reduced antioxidant status. This implies greater free radical burden implicated in many pathological processes including chemical toxicity. Optimum nutritional status may modify or mitigate chemical toxicity through the antioxidant hypothesis. Increased susceptibility factors are associated with a raised disease burden or risk. Nutritional status may therefore modify susceptibility to chemical toxicity in LSC associated with nutritional deficiency states that may other- wise enhance vulnerability. Lead poisoning, a well-known toxicant occurs most frequently in disadvantaged populations; lead and iron share a common transporter, divalent metal transporter 1 (DMT-1) . Iron deficiencies, one of the commonest nutritional deficiencies may other- wise enhance vulnerability to lead toxicity.

Many chemical exposed populations are also at risk of nutritional deficiencies. Iron (Fe) deficiency is common in low socioeconomic populations and increases in severity with chemical exposure e.g. Pb with which Fe shares metal transporter such as the DMT-1. This may be seen as a double burden. Of the several nutrients that affect major toxic substances, mercury (mercury toxicity) and selenium (Se) is the most widely examined (Curvin-Aralar and Furness 1991).[24] Selenium affects Hg toxicity at various levels. Mercury decreases the activity of several enzymes in the synthesis of glutathione (GSH) leading to decreased GSH concentration and antioxidant activity and subsequent increase in free radical load. Selenium prevents the depression of the enzymes in the GSH synthetic path way caused by mercury. Investigations have shown that the salt of Se, sodium selenite also decreases the amount of inorganic mercury bound to renal metallothionein. Generally, it is known that

Se delays the onset of inorganic and alkyl mercury toxicity or reduces the severity of the toxic effect. This appears a cheap veritable tool that can be exploited to address the greater susceptibility of low socioeconomic class populations to chemical exposure and toxicity.

Though the cost of mining gold which involves exposure to Hg is great, as every year, huge amounts of mercury pollute the atmosphere and poison hundreds of thousands of people some of the world's poorest countries where mining takes place, selenium appears a promising prophylactic therapeutic agent.

Housing and Residential Location

Housing has been identified as one of the determinants of health and quality of life. The quality of housing and residential location is directly and indirectly associated with social determinants, and mostly socioeconomic parameters (such as income, purchasing power, employment status and education). Populations in LSES tend to live in crowded and unclean residential location and since they are also poorly nourished, they are at greater risk of chemical exposure and chemical toxicity. Furthermore, poor people tend to have their houses located in environmentally polluted places, such as being located near highways, intersections, municipal waste sites or incinerators, and industrial facilities. (Kordas et al., 2007).[15] Many low-income tenants usually live in rental properties. Tenants have little or no decision-making power to fix structural problems (such as chipped lead-based paint or leaking pipes) that increase exposure to environmental hazards. Also, relocating from a home with a hazardous indoor environment to a place with a healthier one is economically difficult for the poor and populations in resource poor countries generally (Environment and health risk; Raul et al., 2008)[25,26] Of all the toxicants commonly discussed, the ones that are recognized to most severely affect people living in poverty the most are lead, mercury, cadmium and pesticides (Goldman, 2002).[8]

Lead

Low socioeconomic status has played a central role in efforts to characterize the magnitude of the risk that lead poses to children, on a transgenerational level, low SES might be a proxy for vulnerability to lead.[9] Studies reveal that appropriate diet and enriched environments might actually prevent and mitigate the biochemical changes induced by lead exposure (e.g., they lower the pro/ antioxidant ratio, which would otherwise be too high in the presence of lead) and actually prevent or revert the pathological damage done by lead. However, the environmental situation in low SES people appear to also have poor environment which lack antioxidants and high lead impact.[10] Prenatal exposure to lead is associated with premature births, reduced growth, learning difficulties and decreased IQ.

Exposure to lead may be also associated with neuropsychiatric disorders such as attention deficit, hyperactivity disorder (ADHD) and antisocial behavior. Needleman et al., (1996)[27] and other investigators for example, have reported intellectual impairments at levels below 10 μg/dL of blood lead. There is also evidence that lead damages brain tissue. Studies have consistently demonstrated that there is no safe level of exposure to lead in humans and this is worse in children. (Ideal blood lead level is zero; no level is safe). Early exposure to lead has been reported to lead to juvenile delinquency.[6] it is important to note that both the dosage and the duration of exposure have significant effects in determining potential health outcome.

Most reports of excessive lead exposure occur most frequently among disadvantaged populations and are associated with cognitive deficits at levels known to produce harm such as the inner cities of the United States or the suburban areas of Australia or the mining communities in Nigeria as the Zamfara lead poisoning episode.

Mercury

Mercury, particularly its organic form, Methylmercury (MeHg, Hg-CH_3), is a global contaminant and toxicant of major concern for humans and wildlife. Mercury is the third (after arsenic and lead) on the 2011 Agency for Toxic Substances and Disease Registry (ATSDR) priority hazardous substances. Emerging evidence indicates it may have adverse effects on the neuro-logic and other body systems at common low levels of exposure, Minamata- Fish are the most important agents of MeHg exposure for humans, and consumption of contaminated fish is a serious public health concern. Kordas et al (2007)[4] have alluded to the potential harm from prenatal methyl mercury exposure which has caused concern among pregnant women. These investigators further observed that the current recommendations in the United States call for reduced consumption of seafood during pregnancy but that in low-income countries such advisories may not exist, and if they do, fish-consuming communities may be economically constrained from changing their diets. This to a large extent or at least in part explains why low socioeconomic class makes populations in that class susceptible to toxicants. It should be noted that low-level exposure, as well as intoxication, has substantial impacts on children's health.

These major toxic metals (lead and mercury) were examined in a previous study by Lim et al (2015)[28] who reported the following findings in the study they carried out in Korea to examine the associations between blood lead and mercury levels and individual as well as community level socioeconomic positions (SEPs) in school-aged children. The risk of high blood lead level was significantly higher for the lower SEP individuals (odds ratio (OR) 2.18, 95% confidence interval (CI) 1.36–3.50 in the lowest educational attainment of the father), with a significant dose-response relationship observed after adjusting for the community SEP. The association between high blood lead levels and lower SEP individual was much stronger in the more deprived communities

(OR 2.88, 95% CI 1.27–6.53) than in the less deprived communities (OR 1.40, 95% CI 0.76–2.59), and showed a significant decreasing trend during follow-up only in the less deprived communities. The risk of high blood mercury levels was higher in SEP individual (OR 0.64, 95% CI 0.40–1.03 in lowest educational attainment of the father), with a significant dose-response relationship noted.[29] Significantly decreasing trends were evident during the follow-up both in the less and more deprived communities. The investigator concluded that from a public health point-of-view, community level intervention with different approaches for different metals is warranted to protect children from environmental exposure. This study largely corroborates the greater susceptibility of low socioeconomic class populations and the need for deliberate attempts to address the problem.

Pesticides

According to National Institute of Environmental Health Sciences (NIEHS)[30] pesticides are commonly employed to kill, repel, or control certain forms of plant or animal life that are considered to be pests. Pesticides include herbicides for destroying weeds and other unwanted vegetation, insecticides for controlling a wide variety of insects, fungicides used to prevent the growth of molds and mildew, disinfectants for preventing the spread of bacteria, and compounds used to control mice and rats. Accumulating evidence indicates that pesticide exposure is associated with an increased risk for developing Parkinson's disease.[31] It is common knowledge that various reports of outbreak of pesticides poisoning are largely in the developing countries where the bulk of those in the low socioeconomic class are found. The report of increased poisoning in Sri Lanka is well known.[32]

Cadmium

Cadmium (Cd) like lead and mercury just discussed above is a non-essential toxic metal belonging to group IIB of the periodic table of elements (IARC, 1993)[33] which is a wide spread environmental pollutant that has recently gained greater public prominence due to its increased use in industrial processes particularly due to world-wide increase in discard of electronic – waste such as cell phones and computers containing this toxic metal (Rydh and Svärd; 2003; Järup, 2003; Wong et al., 2007).[34,35,36] Unlike essential trace elements such as copper, iron, selenium, zinc and others, Cd largely has no known biological function. Cadmium exhibits considerable toxicity with destructive effects on most organ systems. Human exposure to Cd occurs chiefly through inhalation or ingestion (Bernhoft, 2013).[37] Bernhoft reported that cigarette smoking is considered to be the most significant source of human cadmium exposure, and that inhalation due to industrial exposure can be significant in occupational settings; for example, welding or soldering, and can

produce severe chemical pneumonitis.[37] This again points to the greater risk of those in the low socioeconomic class regarding exposure to cadmium; most of those in the indicated occupations are commonly in the low socioeconomic group and recent evidence suggest that cigarette smoking is becoming a commoner habit in the developing countries (Anetor, 2008).[38] Cadmium exposure may also occur from ingestion of contaminated food (e.g., crustaceans, organ meats, leafy vegetables, rice from certain areas of Japan (itaiitai) and China) or water (either from old Zn/Cd sealed water pipes or industrial pollution) and can produce long-term health effects. Contamination of drugs and dietary supplements may also be a source of contamination[34]. Most of these later effects are also of greater frequency in the low socioeconomic class thus constituting a susceptibility determinant.

Recommendation

There is a need for concerted action at all levels, including actions by individual patients, health educators, clinicians, medical educators, regulators, government and non-government organizations, corporations and the wider civil society, to understand the toxic exposure risk and minimize the extent of toxic exposures on current and future generations. Community groups and government can play a key role in helping to reduce home-related environmental exposures among the poor or low socioeconomic class individuals. One strategy is to raise awareness about the dangers of environmental chemical hazards among disadvantaged populations through health and nutrition education using television, radio, social and print media.

Conclusion

Chronic exposure to environmental chemicals is an increasing problem globally, probably more so in the rapidly industrializing developing countries, adversely affecting the quality of life of a disproportionate part of the population. It therefore seems rational for future investigators to examine low socioeconomic status in chemical exposure and toxicity as a susceptibility determinant to more pragmatically address the growing problem of chemical exposure and toxicity in industrializing developing countries. Although the adverse impacts of toxic chemicals on resource poor populations may seem all too apparent the full consequences and pragmatic implications are insufficiently understood and recognized. Therefore, it appears essential to take a critical look at the problem in order to better understand how to mitigate the effects and improve the conditions in which these disadvantaged and at risk populations live especially through the use of health education.

Better understanding of the interactions between low socioeconomic status and environmental exposure appears needed to guide action from governments and individuals. Future studies on chemical exposure and toxicity need to

consider nutrition and health education interventions as the means to ameliorate and prevent toxicity exposures to environmental pollutants in study populations with low socioeconomic status as a key target susceptibility determinant. Nutritional status may modify susceptibility to chemical exposure and appears a key weapon to hold on to as a useful approach to pragmatically formulate policies to creatively address the growing problem of chemical exposure and toxicity in industrializing developing countries.

References

1. Gallo LC, Matthews KA. Understanding the Association Between Socioeconomic Status and Physical Health: Do Negative Emotions Play a Role? Pschol. Bullet. 2003; 129: 10-51.
2. Socioeconomic status. From http://www.apa.org/topics/socioeconomic-status/ Accessed April 26, 2017.
3. Goldman L, Tran N. Toxics and Poverty: The Impact of Toxic Substances on the Poor in Developing Countries in August 2002. From http://siteresources.worldbank.org/INTPOPS/Publications/20486400/TOXICStext917w.pdf Accessed March 1, 2017.
4. Bijlsma N, Cohen MM. Environmental Chemical Assessment in Clinical Practice: Unveiling the Elephant in the Room. *Int. J. Environ. Res. Public Health*. 2016; *13*(2): 181. doi:10.3390/ijerph13020181
5. Kodas K, Lönnerdal B, Stoltzfus RJ. Interactions between Nutrition and Environmental Exposures: Effects on Health Outcomes in Women and Children. *J. Nutr.* 2007; 137 (12): 2794-2797.
6. *Grandjean P, Landrigan PJ. Developmental neurotoxicity of industrial chemicals. Lancet*. 2006*;* 368:2167*–78.*
7. Environment and health risks: a review of the influence and effects of social inequalities. From http://www.euro.who.int/__data/assets/pdf_file/0003/78069/E93670.pdf Accessed April 26, 2017.
8. Tyrrell J, Melzer D, Henley W, Galloway TS, Osborne NJ. Associations between socioeconomic status and environmental toxicant concentrations in adults in the USA: NHANES 2001–2010. *Environ. Int.*2013; 59:328–335. doi: 10.1016/j.Envint.2013.06.017.
9. Rauh VA, Landrigan PJ, Claudio L. Housing and Health Intersection of Poverty and Environmental Exposures. *Annals of the New York Academy of Sciences*. 2008; 1136: 276-288.doi: 10.1196/annals.1425.032.
10. Learning and Developmental Disabilities and Toxic Chemical Exposures. From http://www.minddisrupted.org/findings.disabilities.php Accessed April 25, 2017.
11. Lanphear BP, horning R, Ho M. Screening housing to prevent lead toxicity in children. *Public Health Rep.* 2005; 120:305–310.
12. Bellinger DC. Lead Neurotoxicity and Socioeconomic Status: Conceptual and Analytical Issues. *Neurotoxicology*. 2008; 29(5): 828–832. doi: 10.1016/j.neuro.2008.04.005.
13. Ferrie JP, Rolf K, Troesken W. Lead Exposure and the Perpetuation of Low Socioeconomic Status. From http://www.pitt.edu/~troesken/vita/LeadAndThePerpetuationofLowSocioeconomicstatus7.pdf Accessed May 2, 2017.

14. Kordas K, LÖnnerdal, B, Stoltfus, R. J. Interactions between nutrition and environmental exposure: effects on health outcomes in women and children. *J. Nutr*. 2007; 137: 2794- 2797.
15. Grandjean, P; Landrigan, P.J. Developmental neurotoxicity of industrial chemicals. *Lancet.* 2006; 368: 2167-78.
16. Kaji M. Role of experts and public participation in pollution control: the case of Itai-itai disease in Japan. *Ethics in Science and Environmental Politics.* 2012; *12*, 99–111.
17. Eto K. Minamata disease. Neuropathology. 2000; 20 Suppl: S14-9.
18. Last, J. M. The state of the world in the 1990s. In: Public Health and Human Ecology. *Appleton Lange*. 1987; pp.340.
19. Karagas MR, Choi AL, Oken E, Horvat M, Schoeny R, Kamai E, Cowell W, Grandjean P, Korrick S. Evidence on the Human Health Effects of Low-Level Methylmercury Exposure. *Environ Health Perspect.* 2012J; 120(6): 799–806. doi: 10.1289/ehp.1104494.
20. Chen C. Methylmercury Effects and Exposures: Who Is at Risk? *Environ Health Perspect*. 2012; 120(6): a224–a225. doi: 10.1289/ehp.1205357.
21. Hornberg C., Pauli A. Child poverty and environmental justice. *Int. J. Hyg. Environ. Health*. 2007; 210:571–580.doi: 10.1016/j.ijheh.2007.07.006.
22. Lim S, Ha M, Hwang SS, Son M, Kwon HJ. Disparities in Children's Blood Lead and Mercury Levels According to Community and Individual Socioeconomic Positions. *Int. J. Environ. Res. Public Health.* 2015; 12 (6), 6232-6248.doi: 10.3390/ijerph120606232.
23. Bernhoft RA. Cadmium Toxicity and Treatment. *The Scientific World Journal.* Volume 2013 (2013), Article ID 394652, 7 pages. http://dx.doi.org/10.1155/2013/394652.
24. Anetor JI, Ajose F, Anetor GO Iyanda AA, Babalola OO, Adeniyi FAA. High Cadmium/Zinc Ratio in Cigarette Smokers: Potential Implications as a Biomarker of Risk of Prostate Cancer. *Nigerian Journal of Physiological Sciences.* 2008; *23*(1-2): 41-49.
25. Sughis M, Penders J, Haufroid V, Nemery B, Nawrot TS. Bone resorption and environmental exposure to cadmium in children: a cross - sectional study. *Environ Health.* 2011; 10: 104. doi: 10.1186/1476-069X-10-104
26. National Institute of Environmental Health Sciences (NIEHS). From https://www.niehs.nih.gov/health/materials/niehs_overview_508.pdf. Accessed May 17, 1017.
27. Pesticides. From https://www.niehs.nih.gov/health/topics/agents/pesticides/ Accessed May 18, 2017.
28. Rajapakse T, Griffiths KM, Christensen H. Characteristics of non-fatal self-poisoning in Sri Lanka: a systematic review. *BMC Public Health.* 2013; 13:331. https://doi.org/10.1186/1471-2458-13-331
29. Burm et al. Representative levels of blood lead, mercury, and urinary cadmium in youth: Korean Environmental Health Survey in Children and Adolescents (KorEHS-C), 2012–2014. *International Journal of Hygiene and Environmental Health*. 2016; 219: 412–418. https://doi.org/10.1016/j.ijheh.2016.04.004**.**
30. Stringhini et al. Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1·7 million men and women. *The Lancet*. 2017; doi: 10.1016/S0140-6736(16)32380-7.
31. Järup L. Hazards of heavy metal contaminations. *Br Med Bull.* 2003; 68: 167-182.
32. Rydh CJ, Svärd B. Impact on global metal flows arising from the use of portable rechargeable batteries. *Sci Total Environ.* 2003; 302: 167-184.

33. Satarug, S. Moore MR. Adverse health effects of chronic exposure to low-level cadmium in food stuffs and cigarette smoke. *Environ Health Perspect.* 2004; 112: 1099-1103.
34. Wong CSC, Duzgorin-Aydin NS, Aydin A, Wong MH. Evidence of excessive releases of metals from primitive e-waste processing in Guiyu, China. *Environ Pollut.* 2007; 148: 62-72.
35. Cerklewski FL, Forbes RM. Influence of dietary zinc on lead toxicity in the rat. *J. Nutr.* 1976; 106: 689.
36. Petering HG, Murthy L, Cerklewski FL. Role of nutrition in heavy metal toxicity In: Lee, S. D. (ed.) *Biochemical Effects of Environmental Pollutants*. Ann Arbor Science, Ann Arbor, Michigan. 1977; pp365-376
37. Needleman HL, Riess JA, Tobin M, Biesecker G, Greenhouse JB. Bone Lead Levels and Delinquent Behavior. *JAMA.* 1996; 275 (5): 363-369.