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# Lead Poisoning and Measurement of Body Burdens of Lead : A Perspective

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**ABSTRACT**

The measurement of lead in archaeological bone forms the basis for providing insight into ancient societies, including disease, lifestyle and eating habits. It is sometimes asserted that in the 5th century AD lead toxicity played a key role in the eventual fall of the western Roman Empire. Others view the effect of lead exposure at that time to be less significant. The debate concerns the idea that clinical lead poisoning mainly affected the aristocratic population and caused a strong reduction in fertility and reproduction .Choosing bone over soft tissues or blood for lead measurement is due to the fact that the bone represents a long-term store of a range of elements, including lead, and can survive over many thousands of years. Different elemental analysis techniques both *in-vivo* and *in-vitro* have been developed over the years, including X-ray fluorescence (XRF), the latter being the main technique described within this review. The main advantages of *in-vitro* techniques are that they have excellent detection limits and data processing times but on the down side they are very expensive. On the other hand, while *in-vivo* techniques are non-invasive they suffer from relatively poor detection limits, pointing to the need for validation using *in-vitro* analysis.

**Keywords**: lead poisoning, XRF, Roman Empire, archaeological bone

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## INTRODUCTION

Lead, found in the earth's crust, is an abundant but nevertheless relatively toxic element. When inhaled or ingested, lead accumulates in the bones (Hoon Lee, P. Gardner, & C. Todd, 2001); in the body some 90% of the lead is to be found in the skeleton (Barry, 1975). The lead is also capable of crossing the blood-brain barrier, resulting in potential neurotoxicity (Liu et al., 2014). It has been found that even low doses of lead can carry appreciable risks to health (Yu et al., 2011). When studying lead poisoning effects it is crucial to have access to measuring facilities that are capable of low minimum detectable concentrations (MDC). For example, for lead in the tibia *in vivo* measurement systems with an MDC of about 10-20 ppm lead are in use (mainly being applied in studies of lead exposure of industrial workers) (Hoon Lee et al., 2001).

Bone, which as previously mentioned can survive over many thousands of years, represents a long-term store of lead. The biological half-life of lead has been estimated to be of the order of many years up to several decades. Therefore, bone is an excellent indicator of long-term exposure to lead for both domestic and occupational purposes. Other tissue types have a much more rapid turnover, eg blood, resulting in measurement of only recent exposure. Lead poisoning was observed in the Roman Empire, traced to excessive use of lead utensils and storage vessels, assumed by some to play a key role in the 5th century AD in the eventual fall of the Roman Empire in the west (Woolley, 1984).

Later, during the Industrial Revolution, poor work conditions and low safety legislation were common, and with this occupational lead poisoning was observed. Riva et. al. have reported that in the early 20th century lead poisoning was also seen among painters who worked with leaded paints

(Riva, Lafranconi, D'Orso, & Cesana, 2012). In the 21st century different cases of non-occupational lead poisoning have continued to be reported in children and adults, resulting from for instance use of Chinese medicine as well as other reasons. Some of these cases are described within this review.

## PRE-INDUSTRIALISED ERA

For 6,000 years lead has been mined and used in different applications, from cooking utensils to cosmetics, as in ancient Egypt (Hernberg, 2000). Therefore, the effects of lead have also been widely documented; the earliest material written on lead toxicity have been found in Egyptian papyrus scrolls (Hernberg, 2000). In the 2nd century BC, Nicander, a Greek physician-poet, was the first to describe lead palsy (Retief & Cillier, 2006 ) but he did not relate the palsy to lead exposure (Hernberg, 2000; Riva et al., 2012). The connection between the two was not realised until the 1st century AD, by Dioscorides, a Greek physician (Hernberg, 2000).

In the Roman conquest of Britain, lead was used extensively (Hernberg, 2000; Retief & Cillier, 2006 ; Woolley, 1984); it has been estimated that 80,000 tons of lead annually were used at the peak of the Roman Empire (Woolley, 1984). The uses of lead included lead pipes for domestic water plumbing, lining to cooking pots, in the sweetening of wine through containment in lead vessels, shipbuilding, medicine, and paint (Retief & Cillier, 2006 ). In fact, the word plumbing is derived from the Latin word plumbum (for lead). Furthermore, both in Rome and ancient Egypt, galena (essentially lead sulphide) was applied as an ointment and as a skin whitening agent. Archaeological bones from the Roman era have been shown to contain high concentrations of lead, especially those retrieved from patrician tombs graves (Hernberg, 2000). With extensive use of lead during the Roman era it was not surprising that it resulted in a greater propensity of lead poisoning.

## MODERN ERA/INDUSTRIAL REVOLUTION

Hernberg reported that the first modern clinical description of lead poisoning was in 1839 by Tanquerel des Planches, based on over 1,200 cases (Hernberg, 2000). The large number of cases studied has given great weight to the findings, it seeming unlikely that others would have investigated such numbers of cases, either before or since. These days, lead poisoning is rarely seen in developed countries. Conversely, lead intoxication from different non-occupational sources is still being observed elsewhere (Riva et al., 2012). Chronic lead poisoning was seen in miners and workers during the industrial revolution as a result of poor safety legislation. It was not until the 19th century when the Factories (Prevention of Lead Poisoning) act (1883) was approved in the UK that occupational exposure to lead was minimized (Meiklejohn, 1963).

## LEAD POISONING IN THE HUMAN

Symptoms of lead toxicity throughout the body were established more than a century ago (Hernberg, 2000). These include effects on the nervous system, the kidneys and blood. Lead in high concentrations can have an adverse effects on probably every single biological function and enzymatic action in the body (Hernberg, 2000; Retief & Cillier, 2006 ). The interest these days is in a search for the effects of very low concentrations of lead in an effort to define a limit for safe exposures (Hernberg, 2000).

The alimentary canal and the lungs are the main two pathways for lead absorption. In adults, some 8% of the orally ingested lead is absorbed but the percentage increases to 50% in children. Most of this absorbed lead is excreted by the kidneys and typically more than 90% of the remaining lead ends up accumulating in the skeletal system (Barry, 1975; Retief & Cillier, 2006 ). It should be mentioned that this lead is not harmful to the body unless it is re-released into the blood circulation as a result of extensive decalcification or overly efficient chelation therapy. The presence of lead in other tissues such as kidneys, muscles or nervous system carries risk at various levels (Retief & Cillier, 2006 ).

Lead poisoning may be either acute or chronic. Typically, acute lead poisoning is rare and characterised by symptoms such as immediate abdominal pain, nausea, vomiting, metallic taste, thirst and later diarrhoea. Large exposure to lead can lead to shock, muscle weakness or kidney failure; followed one or two days later by the possibility of death (Retief & Cillier, 2006 ).

As previously noted, chronic lead poisoning can affect various parts of the body, as in for example in the digestive system. The symptoms can start with loss of appetite, a metallic taste in the mouth severe constipation and typical attacks of severe abdominal colic. Manifestations in the neuro-muscular system appear in for example peripheral paralysis or lead encephalopathy (especially in children) and may result in learning difficulties to mental retardation or death (Grandjean, 1978).

Another effect is anaemia in the haemopoeitic system; this can result from either inhibition of haemo-synthesis or haemolysis. It should be mentioned and stressed at this point that lead poisoning is preventable if proper inhibitory actions are applied. If toxicity is related to poisoning then we can say that apart from exposure ($E$), other factors that can affect toxicity ($T$) are dose ($c$) and time ($t$), as indicated in the following equation (Rozman, Doull, & Hayes Jr, 2001).

$$T = f(E(c,t)) \qquad (1)$$

For human physical growth and development there are a number of factors that can influence this process, including nutrition, various physical environmental effects and exposure to pollutants. The effect of pollutant on growth might seem small but with the accumulation of different pollutant types taken together this can be large (Schell & Knutsen, 2002).

## MEASUREMENT OF LEAD POISONING IN ARCHAEOLOGICAL BONE

While atomic absorption spectrophotometric techniques can be used to determine lead and other metal content in bones and teeth, these techniques have three main limitations: (i) the possibility of contamination by lead from the burying environment, minimised in the case of well-preserved bones; (ii) although total lead content is measured, periodic poisoning peaks are not, and; (iii) lead diffuses through the skeleton in a non-uniform way so that for example the skull and ribs have higher levels of lead when compared to pelvic bone or teeth. It should be noticed that due to the destruction of the organic bone matrix, ancient bones can typically be found to have greater concentrations of lead (as well as calcium) than more recent bones (Retief & Cillier, 2006 ). It should be mentioned that hair can also be used to measure lead content but since hair is constantly replaced, it has limited applications in archaeology (Grandjean, 1978).

## ACTIONS TAKEN AGAINST LEAD EXPOSURE IN MODERN SOCIETIES

It has been reported that typical lead levels during the late Roman era were some 41-47% of present-day European levels. The levels reduced post AD 500 to 13% of modern levels, increasing again during the Middle Ages to practically the same levels as those found in ancient Rome (Retief & Cillier, 2006 ). In modern societies actions have been taken against increase in lead levels. Even though the institution of some of these actions has been suggested to be rather late they can nevertheless be considered as successful steps towards avoiding greater hazards. Examples of such action include: lead-free technologies in industry, abandonment of different leaded gasoline, and abandonment of lead plumbing (Hernberg, 2000). In addition, greater attention and research has now focused on the effects of low levels of exposure to lead.

## LEAD POISONING CASES REPORTED IN RECENT YEARS

In recent literature lead poisoning cases are still to be encountered, even in the light of increasing awareness of lead hazards, abandonment of lead in products and other important actions that have been taken. Typically after a brief period subsequent to acute exposure (sometimes of the order of a week), these cases develop into severe symptoms of toxicity especially when, as has sometimes been reported, lead containing medicines have been applied on damaged or affected tissues (Wu, Deng, Lin, & Tsai, 2013). Lead poisoning in children has sometimes been found to be due to ingestion of paint flakes and dust from paintwork maintained in poor conditions (Rollin, Carré, & Garnier, 2008), also in poorly-regulated toys containing lead. Recommendations for reducing risk include: avoiding contact with such paint surfaces, and encouraging diets that provide sufficient supply of calcium and iron to reduce absorption of lead (Rollin et al., 2008; Yabe et al., 2015). It must be noted that while blood lead levels greater than 5 µg/(dL) are considered to be elevated, signs of lead poisoning are not usually manifest until the concentration exceeds 10 µg⁄(dL). Concentrations in excess of 45 µg⁄(dL) need medical intervention (Rollin et al., 2008; Yabe et al., 2015). In one reported case of lead poisoning, due to inappropriate use of Chinese medicine, a 75 year old patient developing signs including anorexia, weight loss, constipation, nausea, after a 3 month use of a herbal medicine for chronic leg ulcer. The patient blood lead level was 226 µg⁄(dL) (Wu et al., 2013). In another case, a 3 year old boy and a 6 month old sister were hospitalised due to the use of the herbal mixture, Hongdan, added to talcum. An average of 817,000 mg/kg of lead were found in samples of this medium, sold as a herbal medicine, the lead being mainly in the form of lead tetraoxide ($Pb_3O_4$) (Lin, Wu, Yan, Li, & Liu, 2012).

A further case was reported of an infant who suffered acute lead exposure as a result of nursing-associated plumbism (Kokori et al., 1999). Added to this has been the report of seven lead poisoned pregnant women (Shannon, 2003). Another study, in children living in a Zambian villages near a closed mine worked for the period from 1902 to 1994 and published in 2014, was conducted in an effort to measure blood lead levels (blood indicating recent exposure, due to its typical 60 day turnover). Despite the fact that the mine was closed it has continued to be a source of pollution because of the waste stored on-site. One of the interesting findings was that all children under 7 year old included in the study had blood lead levels above 5 µg⁄(dL), the greatest values being among children around the age of 2 years old (Yabe et al., 2015). Finally, observation of lead poisoning in bovine tissues of animals has been reported for cases in a farm in the United States (Buchweitz, McClure-Brinton, Zyskowski, Stensen, & Lehner, 2015). The measurements in this study were carried out using inductivity coupled plasma-mass spectrometry (ICMP-MS).

## LEAD POISONING AS A RESULT OF EXPOSURE TO COSMETIC PRODUCTS

Kohl is a common cosmetic product in the Arabian world and in south Asia, with lead sulphide (PbS) as a main constituent (commonly known as galena); it may also contain different natural substances in a very fine powder form, typically applied around the eyes (Mahmood, Azhar, & Ahmed, 2015).

## TECHNIQUES FOR MEASURING LEAD (*IN VIVO* AND *IN VITRO*)

### In vivo measurements

X-ray fluorescence (XRF) is one of the major non-destructive tools for measuring lead and other elements in different media (Rebôcho, Carvalho, Marques, Ferreira, & Chettle, 2006; Valerio et al., 2014). In making use of this, it is important to note that the selection of tissue site is extremely important. Bone is an excellent indicator of long-term exposure to lead with a biological half-life of the order of many years, compared to the more rapid turnover of body fluids (in the healthy individual the turnover of blood for instance is of the order of 60 days) (Roels et al., 1995). Skeletal remains of the upper echelons of ancient empires can be potentially linked with study of modern exposures, both occupational and domestic. As an example, and relating to occupational lead exposure, the work of Roels et al. (Roels et al., 1994) typifies *in vivo* XRF study, linked to potential nephrotoxicity, renal dysfunction being known to occur at elevated levels of lead exposure (A. C. Todd & Chettle, 1994; Trzeciakowski, Gardiner, & Parrish, 2014).

The detector type, source and measurement geometry all play crucial roles in the accuracy of data obtained. As an example, high purity germanium (HPGe) detectors coupled with use of a gamma-ray source of $^{109}$Cd represents a particularly good choice, the 88.03 keV gamma emission of this nuclide being just above the K absorption edge of Pb (88.012 keV), exciting K-shell fluorescence ($K_\alpha$ and $K_\beta$, resolvable using the excellent energy resolution of the HPGe detector) with high probability, ensuring competitive MDC. A description of an XRF set-up using $^{109}$Cd source and HPGe can be found in this practical description by Todd (A. Todd, 2014). The particular choice of bone site is known to affect the accuracy of the measurement, related to the amount of tissue overlying the bone. As suggested by Chettle et al (Chettle, Scott, & Somervaille, 1991), tibia is the preferred bone for measurement, with only a thin layer of overlying soft tissue, producing minimal attenuation. The arrangement provides for relatively low effective dose of the order of nGy for MDCs of the order of 10 µg Pb per g bone.

**In vitro measurements**

For this type of analysis, a bone biopsy must be obtained. Bone biopsy is a medical procedure that aims to obtain a small piece of bone tissue, a procedure that is not without risk. The main advantages of conducting *in vitro* measurements are that results can be obtained in wet, dry or ash weight. Thus said, *in vivo* measurements remain important for living studies, providing non-invasive tools for analysis. In atomic absorption spectrometer (AAS), the sample preparation relies on digesting the bone sample using a concentrated nitric acid ($HNO_3$) solution by either allowing the sample to dissolve within the solution for 48 hours or using a microwave oven to accelerate the process, taking of the order of ten seconds. A study carried out by Zong et al. (Zong, 1996) to compare the two methods, found that the microwave method is favoured since it saves time and lies within the same uncertainty boundaries as the first method. The sample is then converted into a gaseous state in a process called atomisation. The atomisation is usually obtained by placing the sample within a narrow graphite tube that is heated by electrical current. A very specific wavelength of light is produced using a combination of a cathode lamp and a monochromator to match the excitation energy of the element of interest. The presence of this element will result in absorption of some of the light as the atoms of the element are promoted to higher energy level. The amount of light absorbed is proportional to the amount of the element contained within the sample. Further, the results can be compared to calibration values obtained from samples with known quantities of the element (Levinson, 2001). The prime advantage of AAS is that it can provide a quantitative analysis of small samples. In inductivity coupled plasma mass spectroscopy (ICP-MS), the sample is ionised with inductivity coupled plasma. The plasma is energised by inductively heating a gas, usually argon, with an electromagnetic coil. The plasma is sustained at temperatures of order of 10000 K using a quartz torch so it sustains ionisation. The sample is introduced to the plasma and thus is rapidly ionised. Then the ions within the plasma pass through a mass spectrometer and strike a dynode of an electron multiplier that acts as a detector. A pulse of electrons is produced which is proportional to the number of ions entering the electron multiplier. Using this technique for measuring lead content within a sample requires extra care as the lead has many isotopes. Therefore, several mass to charge ratios would select a lead ion. At this same time this can be used as an advantage of this technique since it can provide details on whether the lead within the sample is a result of ingestion or decay from other elements (Inc, 2011). Another method used to introduce the sample to the plasma is laser ablation. The laser will vaporise a portion of the sample resulting in a shallow hole with a diameter of the order of micrometres in the sample. The ablated material is picked up by the gas flow and introduced to the plasma. Further, the use of laser allows for lateral profiling of lead deposition. The ICP-MS is a non-destructive technique, not requiring a sample digestion process (Beauchemin, 2010).

## CONCLUSION

Measuring lead levels in different media has the potential for providing insight into the health status of a community. The major toxic elements including lead can enter to the blood circulation as a result of different industrial activities, presently an issue in developing countries. The mining and use of lead affected the upper echelons of the ancient world, especially during the Egyptian pharonic period and the Roman era; it was even assumed that lead played a key role in the eventual fall of the Roman Empire in the 5th century AD (Woolley, 1984). Lead exposure carries risk at any level, and more so in children since it can affect all the body systems. It is most common in developing countries and poor communities (Meyer, Brown, & Falk, 2008). In different parts of the world attention is usually paid to lead poisoning due to mining and smelting with yet less attention being given to use of leaded paints in historical buildings or the use of leaded gasoline. Therefore, blood lead needs to be screened for individuals (mainly children) who are still living in these conditions. It is also recommended to perform lead soil mapping in big cities and near mining sites.

## REFERENCES

Barry, P. S. I. (1975). COMPARISON OF CONCENTRATIONS OF LEAD IN HUMAN TISSUES. *British Journal of Industrial Medicine, 32*(2), 119-139.

Beauchemin, D. (2010). Inductively Coupled Plasma Mass Spectrometry. *Analytical Chemistry, 82*(12), 4786-4810. doi: 10.1021/ac101187p

Buchweitz, J., McClure-Brinton, K., Zyskowski, J., Stensen, L., & Lehner, A. (2015). Lead isotope profiling in dairy calves. *Regulatory Toxicology and Pharmacology, 71*(2), 174-177. doi: http://dx.doi.org/10.1016/j.yrtph.2014.12.015

Chettle, D. R., Scott, M. C., & Somervaille, L. J. (1991). Lead in bone: sampling and quantitation using K X-rays excited by 109Cd. *Environmental Health Perspectives, 91*, 49-55.

Grandjean, P. (1978). Widening perspectives of lead toxicity: A review of health effects of lead exposure in adults. *Environmental Research, 17*(2), 303-321.

Hernberg, S. (2000). Lead poisoning in a historical perspective. *American Journal of Industrial Medicine, 38*(3), 244-254. doi: 10.1002/1097-0274(200009)38:3<244::aid-ajim3>3.0.co;2-f

Hoon Lee, S., P. Gardner, R., & C. Todd, A. (2001). Preliminary studies on combining the K and L XRF methods for in vivo bone lead measurement. *Applied Radiation and Isotopes, 54*(6), 893-904. doi: http://dx.doi.org/10.1016/S0969-8043(00)00350-X

Inc, P. E. (2011). The 30-Minute Guide to ICP-MS. 7/3/2015, from http://www.perkinelmer.com/PDFs/Downloads/tch_icpmsthirtyminuteguide.pdf

Kokori, H., Giannakopoulou, C. H., Hatzidaki, E., Athanaselis, S., Tsatsakis, A., & Sbyrakis, S. (1999). An unusual case of lead poisoning in an infant: Nursing-associated plumbism. *Journal of Laboratory and Clinical Medicine, 134*(5), 522-525. doi: http://dx.doi.org/10.1016/S0022-2143(99)90174-9

Levinson, R. (2001). *More Modern Chemical Techniques*. London: Royal Society of Chemistry.

Lin, G.-z., Wu, F., Yan, C.-h., Li, K., & Liu, X.-y. (2012). Childhood lead poisoning associated with traditional Chinese medicine: A case report and the subsequent lead source inquiry. *Clinica Chimica Acta, 413*(13–14), 1156-1159. doi: http://dx.doi.org/10.1016/j.cca.2012.03.010

Liu, J. a., Gao, D., Chen, Y., Jing, J., Hu, Q., & Chen, Y. (2014). Lead exposure at each stage of pregnancy and neurobehavioral development of neonates. *NeuroToxicology, 44*(0), 1-7. doi: http://dx.doi.org/10.1016/j.neuro.2014.03.003

Mahmood, Z. A., Azhar, I., & Ahmed, S. W. (2015). Chapter 7 - Kohl Use in Antiquity: Effects on the Eye. In P. Wexler (Ed.), *History of Toxicology and Environmental Health* (pp. 68-78). Boston: Academic Press.

Meiklejohn, A. (1963). The Successful Prevention of Lead Poisoning in the Glazing of Earthenware in the North Staffordshire Potteries. *British Journal of Industrial Medicine, 20*(3), 169-180.

Meyer, P. A., Brown, M. J., & Falk, H. (2008). Global approach to reducing lead exposure and poisoning. *Mutation Research/Reviews in Mutation Research, 659*(1–2), 166-175. doi: http://dx.doi.org/10.1016/j.mrrev.2008.03.003

Rebôcho, J., Carvalho, M. L., Marques, A. F., Ferreira, F. R., & Chettle, D. R. (2006). Lead post-mortem intake in human bones of ancient populations by 109Cd-based X-ray fluorescence and EDXRF. *Talanta, 70*(5), 957-961. doi: http://dx.doi.org/10.1016/j.talanta.2006.05.062

Retief, F. P., & Cillier, L. ( 2006 ). Lead poisoning in ancient Rome *Acta Theologica 26*, 147-163.

Riva, M. A., Lafranconi, A., D'Orso, M. I., & Cesana, G. (2012). Lead Poisoning: Historical Aspects of a Paradigmatic "Occupational and Environmental Disease". *Safety and Health at Work, 3*(1), 11-16. doi: 10.5491/shaw.2012.3.1.11

Roels, H., Konings, J., Green, S., Bradley, D., Chettle, D., & Lauwerys, R. (1995). Time-Integrated Blood Lead Concentration Is a Valid Surrogate for Estimating the Cumulative Lead Dose Assessed by Tibial Lead Measurement. *Environmental Research, 69*(2), 75-82. doi: http://dx.doi.org/10.1006/enrs.1995.1027

Roels, H., Lauwerys, R., Konings, J., Buchet, J. P., Bernard, A., Green, S., . . . Chettle, D. (1994). RENAL-FUNCTION AND HYPERFILTRATION CAPACITY IN LEAD SMELTER WORKERS WITH HIGH BONE LEAD. *Occupational and Environmental Medicine, 51*(8), 505-512.

Rollin, L., Carré, N., & Garnier, R. (2008). Follow-up of children suffering from lead poisoning or at risk of lead poisoning in Greater Paris, 1992–2002. *Revue d'Épidémiologie et de Santé Publique, 56*(6), 391-397. doi: http://dx.doi.org/10.1016/j.respe.2008.08.002

Rozman, K. K., Doull, J., & Hayes Jr, W. J. (2001). Chapter 1 - Dose, Time, and Other Factors Influencing Toxicity. In R. I. K. C. Krieger (Ed.), *Handbook of Pesticide Toxicology (Second Edition)* (pp. 1-93). San Diego: Academic Press.

Schell, L. M., & Knutsen, K. L. (2002). 8 - Environmental Effects on Growth. In N. Cameron (Ed.), *Human Growth and Development* (pp. 165-195). San Diego: Academic Press.

Shannon, M. (2003). Severe Lead Poisoning in Pregnancy. *Ambulatory Pediatrics, 3*(1), 37-39. doi: http://dx.doi.org/10.1367/1539-4409(2003)003<0037:SLPIP>2.0.CO;2

Todd, A. (2014). Measuring Lead in Bone; A Practical Description. 7/3/2015

Todd, A. C., & Chettle, D. R. (1994). IN-VIVO X-RAY-FLUORESCENCE OF LEAD IN BONE - REVIEW AND CURRENT ISSUES. *Environmental Health Perspectives, 102*(2), 172-177. doi: 10.2307/3431606

Trzeciakowski, J. P., Gardiner, L., & Parrish, A. R. (2014). Effects of environmental levels of cadmium, lead and mercury on human renal function evaluated by structural equation modeling. *Toxicology Letters, 228*(1), 34-41. doi: http://dx.doi.org/10.1016/j.toxlet.2014.04.006

Valerio, P., Soares, A. M. M., Araujo, M. F., Silva, R. J. C., Porfirio, E., & Serra, M. (2014). Arsenical copper and bronze in Middle Bronze Age burial sites of southern Portugal: the first bronzes in Southwestern Iberia. *Journal of Archaeological Science, 42*, 68-80. doi: 10.1016/j.jas.2013.10.039

Woolley, D. E. (1984). A PERSPECTIVE OF LEAD-POISONING IN ANTIQUITY AND THE PRESENT. *NeuroToxicology, 5(3):* , 353-361.

Wu, M.-L., Deng, J.-F., Lin, K.-P., & Tsai, W.-J. (2013). Lead, Mercury, and Arsenic Poisoning Due to Topical Use of Traditional Chinese Medicines. *The American Journal of Medicine*, *126*(5), 451-454. doi: http://dx.doi.org/10.1016/j.amjmed.2013.01.001

Yabe, J., Nakayama, S. M. M., Ikenaka, Y., Yohannes, Y. B., Bortey-Sam, N., Oroszlany, B., Ishizuka, M. (2015). Lead poisoning in children from townships in the vicinity of a lead–zinc mine in Kabwe, Zambia. *Chemosphere, 119*(0), 941-947. doi: http://dx.doi.org/10.1016/j.chemosphere.2014.09.028

Yu, X.-D., Yan, C.-H., Shen, X.-M., Tian, Y., Cao, L.-L., Yu, X.-G., Liu, J.-X. (2011). Prenatal exposure to multiple toxic heavy metals and neonatal neurobehavioral development in Shanghai, China. *Neurotoxicology and Teratology*, *33*(4), 437-443. doi: http://dx.doi.org/10.1016/j.ntt.2011.05.010

Zong, Y. Y, Parsons, P. J. and Slavin, W, (1996). Accurate and precise measurements of lead in bone using electrothermal atomic absorption spectrometry with Zeeman-effect background correction *Journal of Analytical Atomic Spectrometry, 11*, 25-30

 