Lead, Isotopes and Ice

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ABSTRACT

The earliest known use of lead was in the Neolithic period; by Roman times, it was in widespread use, despite recognition that it could have adverse effects on human health. The early smelting processes were inefficient, giving rise to atmospheric pollution; as this reduced with modern improvements in furnace design, so pollution due to the addition of tetraethyl lead to motor fuel emerged. The military use of lead was a further source of environmental contamination, whilst individuals were exposed to lead from water pipes, paint and solder in food cans. Studies of lead in ice cores recovered from Greenland demonstrated a 200-fold increase in lead concentration from 800 BCE to the 1960s, with the greatest increase occurring after 1940. The isotope signatures of lead enabled the sources of environmental contamination to be determined, indicating that industrial lead was responsible throughout most of the last millennium, with lead in fuel making the greatest contribution in recent times. The human impact was demonstrated in studies of archaeological and modern skeletal lead levels. This paper explores the history of the use of lead and the development of an understanding of its toxicity, and examines its impact on human health.

Lead is known today to be a hazardous and persistent pollutant which is harmful both to humans and to the environment, but prior to the recognition of the extent of the risk it presented, its use had been widespread for 4,000 years, reaching a peak in the mid-20th century. This paper explores the history of the use of lead and the development of an understanding of its toxicity, and examines its impact on human health.

Lead (chemical symbol Pb) is a dense, soft, malleable metal of low melting point which is categorised as one of the 'heavy metals'. It has an atomic number of 82 and occurs as four stable isotopes (^{204}Pb, ^{206}Pb, ^{207}Pb and ^{208}Pb) and a number of radioisotopes. The stable isotope ratios vary with geographical region and can be used to indicate the source of allochthonous lead (van Geffen 2013), whilst ^{206}Pb and ^{207}Pb are end products of the uranium decay series and are used in radiometric dating. Lead melts at the relatively low temperature of 327.5 deg C. The fresh surface is bright and silvery but it quickly forms a protective oxide layer in air, becoming a dull grey. Lead is most commonly found in nature as the sulphide, galena (PbS), from which it is extracted commercially. It occurs widely and the largest producers are Australia, China and the United States although many other countries produce lead commercially. Global mining production is of the order of 5 million tonnes annually, whilst a similar amount is recycled (secondary lead) (Guberman 2013).

Decorative beads of galena have been found in Turkey dating from the Neolithic period, around 6,400 BCE (Stech 1999), whilst in southern Scotland a necklace of lead beads was found in an Early Bronze Age burial site (Davis et al 1995). It seems possible that the discovery of metallic lead came about when stones containing galena were used as the base for a hearth; the unexpected globules of bright metal would have been treasured and their early use as jewellery is no surprise. The ease with which the newly-discovered metal could be worked, compared with bronze and the other metals and alloys known to early

civilisations, was no doubt welcomed and new uses were soon developed. By 2000 BCE lead was in use as currency in Assyria, and by 1500 BCE it was also employed in glassmaking in the Middle East, both for the strength it imparted to glass and for its ability to colour glass. Documents comprising rolled lead sheets with incised marks are known from the Hittite period (700-800 BCE) (Bregante 2010).

By Roman times, lead was in widespread use for weights, coins, water pipes, glass and glazes, and in burials. It was also used for cooking pots, and for vessels to store wine, for which it was highly prized owing to the property of such vessels to sweeten sour wine, arising from the sweetness of the lead acetate ('sugar of lead') formed by the action of acetic acid on the storage vessels. The toxicity of lead was only just beginning to be recognised, although it was known to have certain medicinal properties, and lead compounds were used in the treatment of eye and skin diseases (Tapsoba et al. 2010). Lead compounds were also widely used in cosmetics; kohl, a black powder used as an eyeliner, was often based on lead sulphide (and remains in use today), whilst white lead (lead carbonate, $PbCO_3$) was used to lighten the skin. Rouge to redden the cheeks was made from red lead (lead tetraoxide, Pb_3O_4), although the similarly hazardous cinnabar (mercuric sulphide, HgS) was also popular as a rouge. Lead continues to be found in lipsticks although at levels deemed not to be a safety concern, and is permitted as a colour additive in hair dyes (Food and Drug Administration 2014).

Today, lead is widespread in the community, either as an intrinsic part of industrial processes such as smelting, welding, soldering, battery manufacture and plumbing (which derives its name from the Latin *plumbum*, lead), or as a by-product. It is used in roofing for buildings, both as flashing to prevent water ingress at joints (where its malleability allows it to be moulded closely) and as a roof covering in buildings of architectural importance. It was formerly commonly used for water pipes, being easily shaped and joined, but it has been

banned in the UK since 1970 because of the risk of contamination of drinking water, especially in soft water areas (Drinking Water Inspectorate 2010). In the past, lead compounds were used as pigments in paints, including for domestic use and for children's toys, but these have now been banned throughout the Western world because of their toxicity. The sweetness of lead compounds made them particularly attractive to children, who were at risk of toxicity as a result of sucking the paint. Nonetheless, much lead-based paint remains in older properties, where its deterioration generates dust which may be inhaled, or ingested by children. About half of all lead produced in the Western world is used by the motor industry where it is an important component of vehicle batteries and, as tetraethyl lead ($(CH_3CH_2)_4Pb$), it was formerly added to petrol (gasoline) as an 'anti-knock' agent. The density of lead makes it particularly important as a component of military projectiles.

MINING AND SMELTING

The history of lead mining and smelting on a large scale is closely allied to the extraction of silver, the process of cupellation to extract silver having been developed in the early Bronze Age period (third millenium BCE) in Asia Minor (Wagner et al. 1979). Originally, the use of lead appears to have been restricted to the manufacture of votive or decorative objects but the establishment and expansion of the Roman Empire saw a rapid increase in demand for lead for a wide range of uses. As new territories were conquered, so lead mines were opened up; lead mining was established in Britain only 6 years after the Roman conquest. In Scotland it is likely that the lead mines of Leadhills and Wanlockhead date from Roman times (Groome 1885). It is believed that Roman lead was smelted in induced-draught shaft furnaces, which are inefficient for recovery of lead and result in substantial losses in fume and slag. Where lead ore with a sufficiently high silver content had been mined, the silver was recovered by cupellation. Lead for pipes and cisterns was cast as sheets in shallow trays and welded at the edges. Inexpensive tableware, for those unable to afford silver, was made from pewter, a 50:50 lead/tin alloy. By the Middle Ages, the enormous demand for silver points to a high production of lead, much of which was exported, and by the 17th century, lead and tin accounted for half of Britain's exports. The lead mining and smelting industries were major employers, not only of men but also of women and children. The basic draught furnace remained in common use, often situated on a hill-top to minimise the impact on the land, as it was recognised that the fumes spoiled the vegetation and poisoned the soil (Tylecote 1992) (Figure 1). A series of paintings depicting lead smelting at Wanlockhead, now in the Scottish National Portrait Gallery, present a sanitised portrayal of a gentle industry; the reality was undoubtedly somewhat more hazardous. In the 17th century there were several attempts to introduce a better design of furnace aimed at reducing fume, but

change came slowly and the process of lead smelting continued to contribute to the burden of atmospheric pollution until the advent of modern health and safety controls in the developed world; it remains problematic in some developing countries.

AUTOMOTIVE USE

Early motor vehicle engines, using poor-quality low octane petrol (gasoline), were prone to pre-ignition or ‘engine knock’, which not only gave rise to unpleasant engine noise but caused damage to the engine, increasing cylinder wear and in the worst cases resulting in rupture of the compression chamber. Tetraethyl lead is reputed to have been developed in 1853 by Carl Jacob Loewig (1803-1890), a German chemist working as Professor of Chemistry at the University of Zurich (Kovarik 2012), who is better known for his discovery of bromine simultaneously with (but independently of) Antoine Jerome Balard. It had no known use until 1921 when Thomas Midgely (1889-1944) tested it as a potential anti-knock agent as a fuel additive at the Dayton Research Laboratories of General Motors. It proved effective but almost immediately, concerns were expressed about potential toxic effects and several members of staff, including Midgely himself, were affected by lead toxicity, with a number of deaths. A laboratory director at the Public Health Service wrote to the US Assistant Surgeon General in October 1922 warning prophetically of a “serious menace to public health”. Midgely himself, still unwell from the effects of lead exposure, issued reassurance that poisoning of the public was "almost impossible, as no one will repeatedly get their hands covered in gasoline containing tetraethyl lead - it stings and burns... The exhaust does not contain enough lead to worry about, but no one knows what legislation might come into existence fostered by competition and fanatical health cranks" (Kovarik 1999). Following further deaths and ill-health within the industry, in 1925 the Surgeon General appointed a committee of experts to examine the safety of tetraethyl lead but they concluded that there were no good grounds to prohibit its use, noting that there may be a requirement to reassess it should the use of leaded gasoline (petrol) in motor vehicles become more

widespread. Tetraethyl lead went on to become the industry-standard additive in motor fuel, finding utility both as an anti-knock agent and to protect against valve seat wear.

In the 1950s, Clair Cameron Patterson (1922-1995), a geochemist at California Institute of Technology, was working on methods of dating geological samples by measuring the ratio of different lead isotopes. He discovered that many of his results were inaccurate due to contamination of his samples with anthropogenic lead (i.e. lead derived from human activity). Further investigation showed a higher concentration of industrial lead in water sampled from the ocean surface than from the deep ocean, and he surmised that this surface pollution was due to washout of atmospheric lead by rain. In order to test this hypothesis, he sampled successive annual layers of old preserved snow and ice in northern Greenland and the Antarctic and found a substantial increase in anthropogenic lead during the Graeco-Roman period (Hong et al. 1994). Overall, there was a 200-fold increase in lead concentration in the northern polar ice-sheets from 800 BCE to the 1960s, with the greatest rate of increase occuring after 1940 (Boutron et al. 1991). Patterson postulated that during the period of gradual rise prior to the mid-20th century, smelting of lead was responsible, especially in the early years of the Industrial Revolution when there was a greatly increased demand for the metal but furnace design was still poor, allowing substantial losses to the atmosphere in the form of dust and vapour. By the mid-20th century, although improved furnace design was reducing industrial losses, output of lead from fuel additives was increasing. Patterson and his colleagues estimated that 4,000 tonnes of lead was burned annually in the northern hemisphere in 1930 as fuel additives, rising rapidly to 36,000 tonnes ten years later and 310,000 tonnes by 1966, of which 40% would be converted to aerosols (Murozumi et al. 1969).

Patterson believed his evidence of the harmful effects of automotive lead on the environment to be so compelling that in 1965 he published an article, 'Contaminated and Natural Lead Environments of Man', to raise public awareness of the problem (Patterson 1965). Further scientific controversy ensued, particularly from industry, and there was much political debate, but by the early 1970s cars fitted with catalytic converters which did not require leaded fuel had been developed and unleaded petrol was available in garages. From then on, the use of lead in fuel decreased rapidly and many countries had banned leaded fuel completely by the end of the 20th century. Geochemical evidence of improvement was rapid. In 1989, a French team took fresh snow core samples from Greenland and showed that lead concentration had decreased by a factor of 7.5 over the preceding 20 years, coinciding with a fall of over 90% in use of lead-based fuel additives in the US (Boutron et al. 1991).

MILITARY USE

Lead has been used as a military projectile for many centuries. Prior to the development of firearms, it was used to make slingshot ammunition; an example in the British Museum dates from the 4th century BCE, and with the development of the firearm in the 15th century, cast lead bullets were manufactured. All military munitions share a similar structure. A cartridge or round (for small arms such as hand-guns or rifles) or a shell (for field guns or artillery) comprises a projectile and a casing containing the propellant and a primer (or detonator), the major difference being size. Detonation of the primer, usually by impact, ignites the propellant which generates a large volume of gas, expelling the projectile along the barrel of the weapon at high velocity. Many projectiles, especially for small arms, continue to be based on lead as its mass both enhances stability in flight and increases transfer of kinetic energy, and hence penetration and/or destructive power, on impact.

In the modern high-velocity rifle bullet, the lead projectile is encased in a copper jacket which prevents the lead melting due to the heat generated during firing. Both the lead and copper may be alloyed with other metals to increase resistance to deformation during firing; World War 1 shrapnel shells were typically filled with half-inch (1.27cm) balls of a lead-antimony alloy. Ammunition intended for low-velocity weapons such as the .22 rifle, often used on indoor firing ranges for practice, is not jacketed. Airborne lead may be generated by direct vaporisation from the surface of the projectile during firing, by disintegration of the projectile on impact, or by explosive vaporisation of the primer, composed of lead azide (introduced in 1944 as a substitute for the highly toxic mercury fulminate), lead styphnate or other lead compounds.

In 1974 three US police small-arms instructors developed symptomatic lead poisoning, with blood lead levels >80mcg/dL, after prolonged working at an indoor firing range (Landrigan et

al. 1975). The report into that incident was followed by others, and generated much concern amongst preventive medicine specialists in the British Army. The UK Army Physiological Research Establishment (APRE) conducted a survey of indoor ranges in 1981 which showed that there were significant levels of airborne lead at some locations, and in due course controls and monitoring were introduced. It is likely that many thousands of soldiers were exposed in the years before the problem was recognised, as indoor firing range training was widely used to practice weapon skills at greater convenience, and much lower cost, than using outdoor ranges. Nothing was known about the hazards presented by the firing of artillery shells until Lt Col R Brown, based at the Army Occupational Health Research Unit (AOHRU, the successor organisation to APRE) conducted a study in which he measured lead in air at the point of exposure of the gun crew in 35 Royal Artillery soldiers and also compared their blood lead levels with those found in a group of 292 recruits who had not been exposed to weapon firing. In the exposed cohort, he noted that 60% of the men smoked and were at risk of direct ingestion of lead due to contamination of their cigarettes from lead-contaminated surfaces, and also that they were exposed to environmental lead from exhaust fumes. The time-weighted average for lead in air when high explosive charges were used was found to be 19mg/m^3, which exceeded the Lead in Air Standard of 15mg/m^3 although it was estimated that this level would only be reached on 3 days per month and hence the overall weighted average was within acceptable limits. Blood lead levels for the exposed soldiers ranged from 9.6mcg/dL to 30.1mcg/dL with a mean of 19.25 (SD 4.9). The unexposed recruit controls had a mean blood lead level of 14.5mcg/dL (SD 6.3), similar to the mean of 13.1mcg/dL in adult males found in the US National Health and Nutrition Study (NAHNES) from the same period. The increase in exposed soldiers compared with unexposed recruits was highly statistically significant, $p<0.001$ (Brown 1983). All the exposed soldiers had a minimum of 18 months' service and although this exposure in Royal Artillery personnel was

not typical of the majority of soldiers, it did provide objective evidence of elevated blood lead levels at that time in serving military personnel.

Evidence of the effect of firing on indoor ranges in military personnel was provided by a study conducted on US Special Forces between 2000 and 2005 which found an average blood lead level of 10.2mcg/dL (range 1-48), compared with the mean for the wider population of 2.0mcg/dL at the same period. The mean level in the study population declined over the period of the study from 13.1mcg/dL in 2000 to 6.8mcg/dL in 2005 as control measures were implemented, but remained well above the population mean (Mancuso et al. 2013), and lead levels on some US military indoor ranges remain in excess of permitted levels (Soos 2012).

The manufacture of ammunition was also a source of potential lead exposure to the civilian population, particularly in wartime when large amounts of ammunition were required. Over 200 million shells were expended on the Western Front alone (War Office 1922); they were manufactured at a wide range of locations including the Royal Arsenal at Woolwich and Cardonald on the outskirts of Glasgow. Many of the ammunition factory workers were women. Within the ammunition works, lead was also widely used for flooring, guttering and lining vats (Environment Agency 2001). Remediation of contaminated sites remains problematic. The aftermath of warfighting has also left its impact on battlefield sites. Localised soil contamination has been described at many sites in Europe, not only with lead but also with other heavy metals such as copper, antimony, mercury and cadmium (Meerschman et al. 2010; Souvent and Pirc 2001), where it may affect crops grown on what is now agricultural land.

Military personnel were also, in the past, exposed to lead from vehicle fumes, as noted by Brown in his study of Royal Artillery soldiers (Brown 1983). On military exercises, vehicles often halted in relatively enclosed surroundings such as woods to provide concealment, and

were camouflaged with netting or vegetation which served to further increase the local concentration of exhaust gases as engines were kept running to provide power and heat. Travelling in military vehicles such as Land Rovers and trucks also presented a risk of exposure to exhaust fumes in consequence of the open, canvas-covered passenger compartments, especially when travelling in convoy. From 1985 the British Army began to convert its ageing petrol-engine Land Rover fleet to the new diesel-engine 90/110/Defender model, purchasing around 20,000 of the new vehicles by 1994. The petrol Bedford RL 3-ton truck had already been phased out in favour of the diesel Bedford MK 4-tonne truck by 1977, and thus by the mid-1990s, UK military personnel were no longer at risk from leaded fuels.

LEAD AND HEALTH

Contrary to popular belief, the Romans were aware of the toxicity of lead, although the contribution of chronic lead poisoning to the fall of the Roman Empire continues to cause controversy among historians (Scarborough 1984) and, in a contrasting view, Patterson proposed that it was the economic consequences of exhaustion of the Roman lead mines which contributed to the decline of the Roman Empire (Patterson 1987). The Roman architect Vitruvius (Marcus Vitruvius Pollio), who took a keen interest in health in relation to construction, wrote;

> "Water conducted through earthen pipes is more wholesome than that through lead; indeed that conveyed in lead must be injurious, because from it white lead [lead carbonate] is obtained, and this is said to be injurious to the human system. Hence, if what is generated from it is pernicious, there can be no doubt that itself cannot be a wholesome body. This may be verified by observing the workers in lead, who are of a pallid colour; for in casting lead, the fumes from it fixing on the different members, and daily burning them, destroy the vigour of the blood; water should therefore on no account be conducted in leaden pipes if we are desirous that it should be wholesome. That the flavour of that conveyed in earthen pipes is better, is shewn at our daily meals, for all those whose tables are furnished with silver vessels, nevertheless use those made of earth, from the purity of the flavour being preserved in them." (Pollio tr. Gwilt 1826)

Lead enters the body predominantly by inhalation and by ingestion, although tetraethyl lead is also absorbed percutaneously. It is taken up by both blood, where it has a half-life of 28-35 days, and bone where it has a much longer half-life of 5-19 years. There is a dynamic turnover between the two compartments, bone acting as a reservoir and holding 90-95% of

the lead in adults (Rabinowitz 1991). It is probably harmful at all levels, and even at levels well below those at which symptoms of acute poisoning are seen, it has been associated with evidence of harm in a wide range of health outcomes. Children are especially sensitive to the effects of lead, where serious consequences include behavioural and neurological problems and developmental delay. Exposure to very high levels of lead causes acute intoxication, a medical emergency. Symptoms include colicky abdominal pain, fatigue, muscle pain and, in severe cases, encephalopathy followed by coma and death. Typically, blood lead levels in excess of 50 mcg/dL are seen in acute intoxication. Chronic low-level exposure is more common and may occur occupationally or as a result of environmental exposure. A blood lead level in excess of 25mcg/dL is considered to be elevated in the US for adults although a lower cutoff, 5mcg/dL, is taken as the public health action level for children aged 17 years and under (Centers for Disease Control 2012) in recognition of their greater sensitivity to the adverse effects of lead, and in this age-group 10mcg/dL is considered to be elevated. Physical symptoms are rare at these levels but a body of evidence is emerging to show that even low levels of lead are associated with adverse long-term health outcomes.

The scale of the impact of the 20th century use of lead on humans may be judged from archaeological studies on bone lead levels in buried skeletons of Pre-Columbian South-West American Indians. After accounting for contamination of the skeletons by modern technological lead in soil moisture, concentrations in bone and tooth enamel indicating a total lead burden approximately 1000 times lower than in modern Americans were found. The researchers surmised that exposure to industrial lead was responsible for the increase, although they cautioned that chemical alteration of bone during burial (diagenesis) or contamination of reagents with modern lead could have introduced inaccuracies (Ericson 1979; Patterson 1987; Patterson et al. 1991). Other studies examining remains from other

civilisations have confirmed the increase in bone lead concentration but at a lower level, of the order of 7-10 times (Grandjean 1979).

In an innovative study on the source of lead in blood, all petrol distributed in the Piedmont area of Italy between 1975 and 1979 was deliberately labelled with lead having a characteristic stable isotope profile. This study, which was to become known as the Isotopic Lead Experiment project, demonstrated that lead derived from petrol contributed around 24% of the blood lead of urban-dwelling adults (Facchetti 1989). More recent UK studies have suggested a much higher contribution from petrol-derived lead, possibly as high as 60-70% (Gompertz 1998). Smokers are also exposed to lead though tobacco, as tobacco leaves may become contaminated with lead both by direct deposition on the leaf and by uptake from the soil. The propensity of leafy plants to take up atmospheric lead was demonstrated by a study of vegetable crops at the former lead-mining village of Wanlockhead in Scotland, where much higher levels were found in cabbages than in turnips (Chandler et al. 2012). Whilst atmospheric lead levels are highly responsive to changes in input, lead in soil is much more persistent, in part due to 'recycling' as lead-bearing plant material rots back into the soil. Lead may also unintentionally enter tobacco plants as a contaminant in mineral-based fertilisers; the phosphate fertilisers commonly used on tobacco crops may contain radium and its decay products including ^{210}Pb lead and ^{210}Po polonium, both of which are found in tobacco. When the tobacco is smoked, these radioisotopes are deposited in the lungs leading to high localised doses of radiation in the bronchioles (Environmental Protection Agency 2012) in addition to absorption of the lead itself from the lungs into the bloodstream. The lead content of tobacco is gradually reducing as controls on lead become effective. A Canadian study demonstrated a fall in the lead content of tobacco from 3.86mcg/g (SEM 0.063) in 1968-1971 to 1.92mcg/g (SEM 0.060), whilst the lead content of mainstream

cigarette smoke fell from 216ng/cigarette to 83ng/cigarette, a decrease of 62%, between 1968 and 1988. (Rickert and Kaiserman 1994).

By 1980, the human benefits of reducing use of lead in fuel were already becoming apparent in the US. Annest and co-workers analysed data from the second National Health and Nutrition Examination Survey (NHANES II) and reported a 37% (5.4mcg/dL) fall in average blood lead levels between 1976 and 1980, with a highly significant correlation with lead levels in motor fuel ($p<0.001$), although the authors cautioned that correlation did not prove causation (Annest et al. 1983). Phase 1 of the third NHANES study provided even more compelling evidence (Pirkle et al. 1994). The geometric mean for adult males (aged 20-74) had fallen from 13.1mcg/dL (95% CI 12.7-13.7) in 1976-1980 to 3.7mcg/dL (95% CI 3.5-3.9) in 1988-1991, with a similar fall in all demographic groups examined although there were differences in absolute values between the groups. Overall there had been a decrease of 80% in average blood lead levels between 1976 and 1991. By 1991, many of the sources of lead had been controlled; lead had been removed from 99.8% of motor fuel, and its use in soldered cans had also greatly reduced, the latter having been phased out in the UK from the 1980s and banned in the US in 1995 (although it could still be found in some imported cans). However, lead-based paint remained in use in some older properties, and it is likely that residual environmental lead from vehicle emissions in earlier years was still entering the food chain.

A subsequent NHANES analysis (NHANES 1999-2002) examined blood lead levels in the sample population to 2002 and also looked at the correlation with chronic diseases known by then to be associated with lead exposure. Only 113 of the 9,961 study participants (1.13%) had a blood lead level >10mcg/dL, compared with 6.6% of the 1988-1991 study population. The age-standardised geometric mean fell from 2.76mcg/dL in 1988-1994 to 1.64mcg/dL in

1999-2002, a decline of 41%. The association was significant ($p<0.001$) for all age, gender and racial groups, and remained significant after adjusting for smoking, alcohol consumption and education. There was a non-significantly higher blood level in the older age groups. The prevalence of chronic kidney disease, peripheral arterial disease and hypertension was progressively higher at each higher quartile of blood lead level after adjusting for confounders (p value for trend <0.001) in nearly all groups, and the authors noted the controversial nature of the association between hypertension and low-level lead exposure, as reported in other studies (Muntner et al. 2005).

Further light on the controversy was shed by the Veterans Administration Normative Aging Study which demonstrated that it is bone lead and not blood lead which is a predictor of the development of hypertension (Cheng et al. 2001). Later studies including animal studies and meta-analyses concluded that there is clear evidence of a positive association between lead and blood pressure, the effect becoming manifest many years after initial exposure, by which time individual blood lead levels may have fallen. A systematic review by Navas-Acien found that there was sufficient evidence to infer a causal relationship for hypertension. For clinical cardiovascular end-points (coronary heart disease and stroke) there were positive but non-statistically significant associations, with a clear dose-response gradient, sufficient to conclude that the evidence was suggestive but insufficient to infer a causal relationship (Navas-Acien et al. 2007). Vaziri explored the mechanisms by which lead affects the cardiovascular system and found multiple pathways operating at the cellular and molecular level. He noted that long-tem exposure to lead resulted in a marked elevation of arterial pressure and an increase in aortic atherosclerotic plaques (Vaziri 2008).

Lustberg and Silbergeld followed up participants in the 1976-1980 NHANES study to 1992 to evaluate the association between lead exposure and mortality (Lustberg and Silbergeld

2002). Based on an extrapolation of the NHANES findings, they estimated that 29 million Americans, or 15% of the adult (>20 years of age) population had blood lead levels exceeding 20mcg/dL in 1976-1980, although this had reduced to 1.7 million or 0.6% of US adults by 2000. Mortality was compared for three groups: blood lead <10mcg/dL, 10-19mcg/dL and 20-29mcg/dL at baseline. There was a 24% increase in age- and sex-adjusted all-cause mortality in the 10-19mcg/dL group (relative risk (RR) 1.24, 95% CI 0.97-157) and a 74% increase in the highest exposure group (RR 1.74, 95% CI 1.40-2.16). For circulatory disease, the increase was non-significant for the middle exposure group but the relative risk was 1.48 (95% CI 1.10-2.01) for the highest exposure group. The increased risk persisted after multivariate adjustment for age, sex, race, education, income, smoking, BMI, exercise and urban/rural location. There was also an increase in cancer mortality with increasing lead exposure, with a 120% increase in lung cancer mortality (RR 2.20, 95% CI 0.80-6.06) and a 50% increase in mortality due to cancers of other sites (RR 1.50, 95% CI 0.80-2.81) in those with the highest exposures compared with those with levels at baseline <10mcg/dL. There was an interaction with heavy smoking, with those in the higher exposure group who smoked more than one pack of cigarettes per day experiencing an adjusted 5-fold increase in cancer mortality (RR 4.67, 95% CI 2.13-10.25) compared with lighter or non-smokers, although no such interaction was found for circulatory disease. The authors concluded that blood lead level was an important predictor of all-cause mortality and also for cancer and circulatory disease mortality. The population-based nature of this study overcame the problems inherent in earlier studies on occupationally-exposed subjects, such as the healthy worker effect and the confounding effect of other industrial co-exposures.

There may also be behavioural impacts, as lead is known to be associated with sociopathic behaviour such as aggression and impulsivity. A report for the US National Bureau of

Economic Research identified robust evidence linking the rise and fall in violent crime in the 20th century to levels of childhood exposure to lead, concluding that the phasing out of lead in gasoline was responsible for a 56% reduction in violence between 1992 and 2002 (Reyes 2007, Reyes 2015), although association does not necessarily establish causation.

CONCLUSION

The isotope signatures of lead have provided a remarkable insight into the anthropogenic origins of this widespread environmental contaminant. Studies of ice cores have added the dimension of time, providing a clear picture of the evolution of the problem and, more recently, evidence that global control measures are making a difference. The failure to recognise the health and environmental impact of the toxicity and persistence of such a widely-used resource over several thousand years unwittingly resulted in the systematic low-grade poisoning of many generations of humankind. The issue was global, but it particularly impacted on the industrialised nations, reaching a peak with the advent of the motor vehicle and the ubiquity of leaded fuel. The realisation in the 1970s of the need for control resulted in global action which is already demonstrating substantial benefits to human health, although the problem is far from resolved, especially in developing nations where environmental controls and monitoring are poorly implemented. Falling blood lead levels in the developed nations over the last 35 years mask the extent to which older members of the modern population were exposed to environmental lead in their childhood and early adult life and which may still present a risk to their health. With 95% of inhaled or ingested lead sequestered in bone, the very long half-life of lead in bone and the even longer persistence of lead in soil, the legacy of lead smelting, lead-based fuel additives, lead paint, lead water pipes and lead solder on food cans will continue to have an impact on the health of the population, albeit a reducing impact, for decades to come.

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Abbreviations

BCE – Before the Common Era (equivalent to BC)

CI – Confidence intervals

NHANES – National Health and Nutrition Examination Survey

RR - relative risk

SEM – Standard error of the mean

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Figure caption

Figure 1. Barren landscape due to extensive heavy metal contamination at the site of the former lead smelter, Wanlockhead, Scotland. The wooden stakes are all that remains of the wooden flue which carried fumes from the smelter.