

HISTORY OF LEAD POISONING IN THE WORLD

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Introduction

The Center for Disease Control classified the causes of disease and death as follows:

50 % due to unhealthy life styles

25 % due to environment

25% due to innate biology and

25% due to inadequate health care.

Lead poisoning is an environmental disease, but it is also a disease of life style. Lead is one of the best-studied toxic substances, and as a result we know more about the adverse health effects of lead than virtually any other chemical. The health problems caused by lead have been well documented over a wide range of exposures on every continent. The advancements in technology have made it possible to research lead exposure down to very low levels approaching the limits of detection. We clearly know how it gets into the body and the harm it causes once it is ingested, and most importantly, how to prevent it! Using advanced technology, we can trace the evolution of lead into our environment and discover the health damage resulting from its exposure.

Early History

Lead is a normal constituent of the earth's crust, with trace amounts found naturally in soil, plants, and water. If left undisturbed, lead is practically immobile. However, once mined and transformed into man-made products, which are dispersed throughout the environment, lead becomes highly toxic. Solely as a result of man's actions, lead has become the most widely scattered toxic metal in the world. Unfortunately for people, lead has a long environmental persistence and never loses its toxic potential, if ingested. The lead dispersed through gasoline exhausts, smelter emissions, and peeling paint, etc. never fully disappears from our environments nor has man evolved a good biological system to offer any protection from it. In the course of evolutionary time, the global contamination of this highly toxic substance into man's environment has been a very short and recent period.

It is believed that mankind has used lead for over 6000 years. Lead mining probably predated the Bronze or Iron Ages, with the earliest recorded lead mine in Turkey about 6500 BC. The oldest artifact of smelted lead is a necklace found in the ancient city site in Anatolia. The estimated age of this necklace is 6,000 to 8,000 years ago. There were many reasons for lead's use other than its abundance and ease in obtaining it. Some of the properties which make it commercially attractive include: easy workability, low melting point, ability to form carbon metal compounds, hold pigments well, very easily recycled, stands up well to the outside weather elements, a high degree of corrosion resistance, it is inexpensive, etc. There are also several habits and customs of cultures that contributed to human exposure, such as using lead in medicines and cosmetics.

Lead's toxicity was recognized and recorded as early as 2000 BC and the widespread use of lead has been a cause of endemic chronic plumbism in several societies throughout history. The Greek philosopher Nikander of Colophon in 250 BC reported on the colic and anemia resulting from lead poisoning. Hippocrates related gout to the food and wine, though the association

between gout and lead poisoning was not recognized during this period (450-380 BC). Later during the Roman period, gout was prevalent among the upper classes of Roman society and is believed to be a result of the enormous lead intake.

Rome: The First Mass Distributor of Lead:

The Romans conducted lead mining on a massive scale and had several huge lead mine and smelter sites. Lead was in big demand and was a byproduct of refining silver and gold ore. One smelter site located in Spain required tens of thousands of slaves to operate. Another large site was in Greece and the emissions from these two sites would rise high into the atmosphere and get picked up by the world's air currents. Some lead would fall back to earth in the snow and recently, scientists measured lead particles deposited in Greenland's ice to determine the history of lead production. The massive mining and smelting of lead went on for hundreds of years and the production of Roman lead was not surpassed till the period of the Industrial Revolution.

In ancient Rome, lead poisoning was a disease of the wealthy who used lead extensively: leaden cooking utensils and pots, leaden wine urns, lead plumbing (also to line the aqueducts) (Plumbing is derived from plumbum, Latin for " Lead"), vessels used to concentrate grape juice, containers used to store wine, and lead-based makeup. In those days there were no substances (like sulfites) to act as preservatives for the wines. Lead is naturally sweet in taste and was found to enhance both the color and bouquet of wine. The Romans shipped wines all over their empire, as far way as northern Germany. A preservative was needed to prevent bacteria from turning the wines into vinegar. The Greeks added pine tree resin to their wines but the Romans preferred sweet Sapa, a boiled down concentrate of grape juice. The problem with Sapa was that the kettle used in boiling unfermented grape juice into a concentrate was made of lead, which leaches into the liquid because of the high acidic content of the grape juice. The final product, Sapa, is a sweet aromatic syrup containing about one gram of lead per liter. Because of its sweet taste, many Romans used it as a sweetening agent in many dishes. When taken together, all the pathways of lead in Roman society, and the intake of lead in Roman times is estimated to have varied from about 35 mg/day to about 250 mg/day, compared to today's daily intake of 0.3mg in the United states in the 1980's (National Academy of Sciences 1980).

There are many distinguished historians who now believe that this high exposure to lead was a contributing force in the decline of the Roman Empire. With the more recent scientific research proving that lead is a highly neurotoxicant and analyzing the strange behavior of most Roman leaders and the upper classes, a good case can be made for lead's role in a declining Roman society. What is ironic is the fact the during Roman times lead poisoning was primarily a disease of the affluent while today it is an affliction of primarily the poorer communities.

The First Law Banning Lead Was for Economic Reasons!

In the German city of Ulm, during the late 1690's, there was a severe outbreak of colic, an illness characterized by a variety of symptoms, including excruciating abdominal pain. Ulm's official physician noted that at a local monastery the monks who did not drink wine were healthy while those that did developed colic. Since the monks lived together, ate the same food, and drank the same wine, they provided the astute doctor with an ideal setting for investigating the cause of the disease. Every time he visited the monks he was offered a glass of wine until he too developed colic. Upon a detailed investigation he found the culprit to be the agent used to sweeten the wine, litharge, a white oxide of lead. When this concentrated sweetener was added to sour wine it brought it back to life and made it drinkable. The entire region depended upon the wine export as a major source of revenue. If the word spread that the wine from Ulm caused colic then the city's economy was threatened. In 1696, Duke Ludwig issued a decree forbidding the use of lead-based additives in any wine product. For anyone who violated this decree, the punishment was death!

There were recordings of Roman wine being banned by German tribes because of the sickness which resulted. Surprisingly, many doctors of that period prescribed preparations of mercury or litharge itself to cure colic! On and off over the next centuries liquor would continue to be a source of lead exposure. In 1763, a physician at the court of King George III, discovering that lead fittings used to press cider caused an outbreak of colic. The great gout epidemics of the eighteenth century in England were traced to the popular port wines from Portugal which were heavily leaded (in 1825, 21 million liters of port was consumed in England). Poorly glazed pottery used to store beers and wines resulted in chronic colic outbreaks in Germany when the lead leached out into the brew. Even today, some wine seals are made of lead and some leaded crystal decanters can leach lead into the liquor. One of America's first public health laws was to ban the use of leaded coils due to the health problems it caused to people who drank the spirits. In colonial America, the Massachusetts Bay Colony banned lead from being added to wine and cider.

But it is not just liquor products where lead can turn up. In Hungary, in 1994, a major health problem occurred when red oxide lead was mixed into paprika to brighten the color of the spice. Research has shown that stone mills, which have lead pieces, can result in putting lead particles into the flour. Lead has shown up in milk where cows have grazed on grasses growing in soil with large lead accumulations from either industrial waste or heavy auto traffic. Weather lead is puffed onto a 18th century noble's wig in the form of white lead litharge, innocently drunk with wine made from grapes grown near a busy highway, or added as a filler to ice cream being sold in India, man seems to create unusual pathways for lead to enter the human system.

Occupational Hazards

In the eighteenth, nineteenth, and twentieth centuries the worst outbreaks of lead poisoning of adults were occupational in origin. It became common knowledge that to work in an industry where you handled lead was certain to make you sick or worse. These workers absorbed lead from inhalation of fine lead dust or fumes, contamination of food eaten at the workplace, or by absorption through the skin. Charles Dickens describes in his essay "Star of the East" the horrible effects of lead poisoning on women who work in London's infamous white lead mills, "her brain is coming out her ear and it hurts her dreadful...". Benjamin Franklin in 1763 wrote about the "dry gripes" (colic) and "dangles" (wrist drop) which affected tinkers, painters, and typesetters.

Lead's hazards to the reproductive process have been known for at least a century. British factory inspectors at the turn of the twentieth century noted that women who were exposed to lead through working in the cottage ceramic industry tended to be barren and that children who were born to those women were often short-lived. In most western countries during the 1930's through the 1970's, awareness among health workers was associated with more lead poisoning cases being reported, and laws protecting workers were being enacted.

Today, occupational exposure to lead remains a big problem in developing countries. Occupational lead exposure is likely unregulated in these countries with little monitoring of poisoning being done. What has become a growing concern among health officials is the prevalence of home-based cottage industries in these countries. These cottage industries are located in the where large numbers of people live, especially children. They are of particular concern since these non-regulated businesses deliver the lead right into the homes or yards where children live or play. Children can also be exposed when the working parent brings the lead dust home from work (on cloths, in hair, or on shoes, etc.). With the enactment of worker safety regulations and more accurate monitoring and reporting, the focus of lead research began shifting towards children's health.

Childhood Lead Poisoning

Modern understanding of lead poisoning in children has evolved through four stages.

First: when childhood lead poisoning was first described in 1892 in Brisbane, Australia, its very existence was disputed by elitist physicians in Sydney. A.J. Turner, a house officer at the Brisbane Children's Hospital, diagnosed several children with lead intoxication who had been given a previous diagnosis of meningitis. Also at Brisbane, J. Lockart Gibson, an ophthalmologist, recognized lead poisoning in children with retinitis and ophthalmoplegia. They investigated and found the source of lead exposure to be paint on rails in the children's homes. Through their efforts, lead was eventually banned from house paint in Australia in 1914. That same year, childhood lead poisoning was first reported in America.

Second: After its existence was accepted, the prevailing belief among pediatricians was that children who did not die during the acute stage of the disease suffered no lasting ill effects. In 1943, Byers demonstrated the persistence of severe residue in children who had recovered from acute lead poisoning. Dr. Randolph Byers, one of America's first pediatric neurologists, discovered that several children with learning or behavior disorders had earlier been treated for lead poisoning. Along with Elizabeth Lord, a psychologist at Boston Children's Hospital, Byer conducted detailed psychometric evaluations of 20 children who had reported previous lead poisoning. They found that 19 of the 20 children were behavior disordered or intellectually impaired. Dr. Byer's studies in the early 1940's were the first to prove that children who survived acute intoxication were often left with devastating deficits in intellectual function.

Third: The reality of sequelae was then accepted, but sequelae were thought to afflict only those patients who had had the most severe symptoms. In the late 1970s, 1980s, and early 90's, the publication of papers from around the world showing IQ and behavioral deficits at silent doses of lead, the neuropsychological costs of asymptomatic lead exposure were established to the satisfaction of the scientific community. This controversial issue has now been effectively settled. With the release of extensive research from numerous studies, each confirming the other, almost all workers in the field agree that lead at silent doses produces deficits in psychological function; these include intelligence, perception, attention, language function, and perhaps social adjustment.

Fourth: Regulations began to be shaped to accommodate the realization that lead at silent doses damaged the brains of children. Mass public screening programs were enacted to monitor the lead exposure of young children. For the first time the focus of lead exposure was centered on primary prevention, with many laws being enacted to eliminate lead sources in the environment. Mandatory testing programs were being established in many states to detect early identification of lead problems. In 1991 CDC devised a strategic plan to prevent childhood lead toxicity. This was a historic moment in lead poisoning prevention.

There were two important sources of lead for children in America: paint and leaded gasoline. Lead in household paint was recognized as a danger early in the 20th century; it was banned in Australia in 1914 and by international convention in 1925. The United States was not a signatory to that agreement. It was not until 1970 that a statute banning lead in household paint was passed in the United States. Although in the early 1930s the city of Baltimore recognized the widespread hazards of lead paint to children and took steps to control its use, lead paint was not banned by statute in this country until 1970.

Special Note on the Evolution of the Most Widespread Toxin Ever Made!

Letting the " Monster" loose: Propaganda, politics, and the "old boys club" at work

No toxic substance has been more widely distributed throughout man's environment than the lead additive Tet in gasoline. For over seven decades, millions of autos of all descriptions have successfully dispersed this toxic substance to all corners of the world. How did such a toxic substance ever gain approval to expose hundreds of millions of people?

In 1921, competition in the expanding American automobile market was fierce. Ford's Model T outsold all other manufacturers, and General Motor's flagship product, the Cadillac, had a motor knock. The Model T was economical, dependable, and easy to fix. Its performance, however, was unremarkable and it had as much style as an orthopedic shoe. Charles F. Kettering, director of research at General Motors, chafed in second place. He had a plan: he would displace Ford with a high-performance engine in a fashionable GM auto body. The best way to achieve high engine performance is to increase compression in the cylinder. Squeeze the air-fuel mixture in the cylinder into a smaller volume and it will detonate with much more force. But when the gas volume is severely compressed, it acts like diesel fuel and ignites prematurely. This is engine knock, and it causes loss of power and eventual damage to the engine. Kettering set Thomas Midgely, his close associate and principal chemist in GM's Dayton, Ohio, research laboratory, to find an antiknock agent.

In December of that year, after trying and discarding many compounds, Midgely tested an old German patent, tetraethyl lead (TEL), in the laboratory engine, which was knocking on ordinary gasoline. It immediately began to run smoothly and silently. A new product was born, and a new firm, General Motors Chemical Company, Kettering named the new fuel Ethyl Gas. Nowhere was the word lead mentioned on the product label. That Memorial Day the new fuel was used by some of the drivers in the Indianapolis 500. This shrewd marketing step was a spectacular success: the first, second, and third-place winners all ran on ethyl gasoline.

Shortly after production began, workers in all three plants began to go crazy and die, often in straightjackets. Somewhere between 13 and 15 known deaths occurred, and over 300 men became psychotic. Workers called the product "looney gas" and the place where it was fabricated "The House of Butterflies." This last sobriquet was earned by the sight of psychotic workers trying to brush phantom insects off of their arms.

A moratorium on the use of TEL was called and the Surgeon General convened a meeting of industrialists, public health specialists, and academic physicians to determine if this new product was a serious enough threat to be banned or whether it could be sold to the general public.

At the Surgeon General's meeting, a young assistant professor of pathology at the University of Cincinnati, Robert Kehoe, emerged as the principal industrial expert and spokesman. When workers died in the Dayton plant in 1923, General Motors asked Kehoe to consult and make preventive recommendations. He made some measurements of lead levels in the plant and in workers directly exposed to TEL. His control group was workers in the plant who had no direct contact with the compound.

This assignment marked the beginning of a major career shift for Kehoe. C. F. Kettering would, with support from the Ethyl Corp., DuPont, and others, open the Kettering Laboratory on the University of Cincinnati Medical campus and name Kehoe as its director. Kehoe would also become Medical Director of the Ethyl Corp. and a corporate officer at GM. In the Surgeon General's meeting and others that followed his words were put forward as the final opinion on lead by the industry representatives, and he was treated with considerable deference. Kehoe was not burdened with a hypertrophied sense of modesty. He spoke with great confidence that his data was the best, if not the only, guide to the truth. Kehoe's sway in lead toxicology held until the late 1960s. The durability of the extraordinary scientific solecism that lead in the body was natural is a testament to the shielding power of reputation. It pays to advertise.

There were no scientific challengers to Kehoe until Clair Patterson. His methods and conclusions could not have been more different. Patterson aimed his attack at Kehoe's assertion that lead was a normal component of the human body, insisting that what he called "normal" was in fact "typical." This was more than a semantic quarrel. Patterson fundamentally altered the vocabulary with which the debate over the health effects of lead was conducted. Most people, following Kehoe's arguments, referred to "normal levels" of lead in blood, soil, and air, meaning values

near the average. They assumed that because these levels were common, they were harmless. "Normal" also carries some of the meaning "natural." Patterson argued that "normal" should be replaced by "typical." Simply because a certain level of lead was commonplace did not mean it was without harm. "Natural," he insisted, was limited to concentrations of lead that existed in the body or environment before contamination by man.

Kehoe and other workers in lead completely missed this distinction because their reagents, instruments, and the very air in their laboratories were freighted with lead. As a result the baseline measurements of all their samples were raised and their results blurred. In addition, the control subjects in Kehoe's studies, the workers in the Dayton plant who did not directly handle TEL, were nevertheless exposed to it. His second "unexposed" group, the Mexican farmers, ate food that had been cooked in and served from lead-containing ceramic pots and plates.

Patterson was able to demonstrate and correct this fundamental error because of the extraordinary measures he took to avoid contamination of his specimens. Because his lab was cleaner than others, his measurements of isotopic ratios were free of the contamination that confounded the findings of Kehoe and others. Where Kehoe measured lead in "unexposed" workers in a TEL plant and Mexican farmers, Patterson studied pre-iron age mummies and tuna raised from pelagic waters.

Patterson stumbled on the problem of global lead contamination while measuring the concentration of mineral isotopes in his study of the age of the earth. He noticed that the lead levels in his reagents and in soil and ice were much higher than predicted by theory. It would have been understandable if he treated the contamination of his reagents as a severe annoyance to be overcome and then forgotten, but that was not his style. To him it was not a nuisance but a clear signal of the contamination by lead of the biosphere. This was an unrecognized danger, he believed, to everyone. In this regard, he provided facts to flesh out the warnings 40 years earlier of Yandell Henderson, David Edsall, and Alice Hamilton. Alice Hamilton of Harvard Medical School, a pioneer in the study of occupational diseases and a recognized expert in lead poisoning, spoke briefly at the hearings to review TEL:

" I would like to emphasize one or two points that have been brought out. One is the fact that lead is a slow and cumulative poison and that it does not usually produce striking symptoms that are easily recognized. The other is that if this (as does seem to have been shown) is a probable danger, shall we not say that it is going to be an extremely widespread one"? She said that while it might be possible to educate a workforce on avoiding lead poisoning, it would be impossible to control the behavior of a whole country, and that TEL should be replaced with a less poisonous antiknock agent.

These health scientists predicted at the Surgeon General's 1925 meeting that tetraethyl lead would lead to widespread increases in human lead burden. Patterson began to divert a considerable proportion of his extraordinary mind and energy away from pure geochemistry to the study of lead contamination. By conducting his experiments in his ultra-clean chamber in which the air was filtered, the experimenters gowned and masked, and the reagents and water supply purified of any trace of lead, he was able to avoid contamination and establish the true concentrations of lead in his samples. He showed that technological activity had raised modern human body lead burdens 100 times that of our pretechnologic ancients. In addition to tuna caught in the deep strata of the Pacific Ocean and brought to the surface with great care to avoid contamination on the way up and pre-iron age mummies buried in sandy soil, he sampled cores of the Greenland ice pack. By slicing the ice cores he was able to precisely date the specimen and show the time course of lead in the atmosphere.

The removal of lead from gasoline in 1990, regarded by many as one of the major public health triumphs of the 20th century, had an immediate impact. Between 1976 and 1994, the mean blood lead concentration in children dropped from 13.7 mcg/dL to 3.2 mcg/dL, in direct proportion to the

amount of tetraethyl lead produced. One could want no clearer testimony to the efficacy of a well-conceived and consistently applied public health policy.

In 1993, the National Academy of Sciences verified that lead at extremely low doses caused neurobehavioural deficits.

Role of Lead and Behavioral Toxicology

Behavioral toxicology, the study of chemical toxicants and their influence on brain function, is a young field. The notion that a chemical can affect the brain and that the earliest expression of toxicity could be found in altered behavior, thinking, or mood is not new; it was voiced at least 2000 years ago by the Greek Dioscorides when he wrote, "Lead makes the mind give way." Despite this early warning, the scientific community has until recently paid little systematic attention to the impact of neurotoxicants on behavior. The first textbook on this subject was published in 1975.

Behavioral teratology, the study of the effect on behavior of chemical exposure of the fetus in utero, is an even newer discipline. Until recently, the uterus had been visualized as a time capsule with a 9-month lease, sheltering the developing fetus from most adverse influences such as drugs, toxicants, or nutritional deprivation. The thalidomide and Minamata disasters quickly disabused scientists and laymen alike of this false comfort. It is now clear that many chemicals cross the placenta and impinge on the developing brain. Behavioral deficits have been shown for some agents at doses well below those that cause anatomical alterations.

Three important classes of neurotoxicants are metals, solvents, and pesticides. The clearest data on the deleterious effects of prenatal exposure to toxicants come from the study of two metals, lead and mercury, and from epidemiologic investigations of the effects of alcohol taken during pregnancy. Less complete data are available for two other groups of agents, solvents and pesticides. What we do know about their effects on the fetal brain is convincing enough to demand caution in their distribution.

In the late 1970s, attention began to shift to the question of intrauterine exposure to lead. Scanlon measured umbilical-cord blood lead concentrations in newborns and showed that infants born to inner city mothers tended to have higher blood lead levels than those born to suburban mothers. The observation that lead crossed the placenta sparked studies of prenatal exposure on infant development. The first study examined a large cohort of births at the Boston Hospital for Women. Umbilical-cord bloods were obtained from almost 12,000 births over a 2-year period. Lead was found to be related to minor birth defects in a subsample of 5000 of these infants. A subsample of these subjects that was evenly divided among low exposure (< 3 ug/dl), medium exposure (6-7 ug/dl), and high exposure (> 10 ug/dl) was followed. Subjects were seen at 6, 12, 24, 57, and 120 months of age. Significant deficits in infant IQ scores were found in children in the high cord blood lead group as late as 24 months of age. At 57 and 120 months of age, the effect of umbilical-cord blood was no longer significant, but the effect of the 24-month blood lead level was statistically significant. Similar data have subsequently been reported from studies in Cincinnati and Australia. It is clear that lead exposure during pregnancy is a behavioral teratogen.

Conclusion

Winston Churchill said: "Make no small plans". By this he meant that most enterprises are not completely successful. To diminish one's goals at the beginning is to guarantee that success will be limited. Those who wish to end childhood lead toxicity should aim high: make a large plan. They should also be patient, and expect to spend a considerable amount of time in the struggle to succeed.

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