THE LEGACY OF TETRAETHYL LEAD

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Abstract

Accounts of lead exposure are sprinkled throughout human history. Lead poisoning remained a rare disorder, confined mostly to mine workers, until the early 20th century when lead found its way into the consumer market in the form of lead solder on food cans, paints, pesticides, toothpaste packaging and water stored in lead-lined tanks. However, it was the introduction of tetraethyl lead, a gasoline additive that prevents common engine knocking, that dramatically introduced lead into the Earth's biosphere. Tetraethyl lead increased lead levels in every inhabitant of earth, and years after the protracted battle to ban lead from gasoline, remains a legacy that is with us today and in our bodies.

Introduction

The first significant mining and refining of metallic lead is recorded around 3000 BCE. Hippocrates is credited with the first account of lead poisoning (370 BCE), but the first clinical account comes from the Greek physician Nicander (200 BCE), who describes the characteristic palsy and dull pallor associated with lead poisoning (1). In the ancient world, lead miners were the most likely to be exposed, but lead was also used in cooking utensils and added to food in the form of a sweet-tasting syrup called "sapa," containing a mixture of one gram of lead per liter of grapes (1, 2).

During the Middle Ages, lead was widely used by alchemists in their attempts to convert base metals to gold, and in a more insidious ways, it was sometimes used as a poison. In the New World, lead mining and smelting began almost as soon as the first colonists had settled. The low melting point of lead made it malleable, and it was also resistant to corrosion. During the 19th century lead made its way into the consumer market in the form of food cans sealed with lead solder and water stored in lead-lined tanks. By the time tetraethyl lead was introduced into gasoline, lead was already in many consumer items.

Biological Fate of Lead

Through most of history, lead poisoning was limited to individuals working with lead directly or those drinking wine out of contaminated containers (3). Charles Dickens writes of lead poisoning in his book the *Uncommercial Traveler* (4),

> The lead, Sur. Sure 'tis the lead-mills, where the women gets took on at eighteen-pence a day, Sur, when they makes applicaytion early enough, and is lucky and wanted; and 'tis lead-pisoned she is, Sur, and some of them gits lead-pisoned soon, and some of them gets lead-pisoned later, and some, but not many, niver; and 'tis all according to the constitooshun, Sur, and some constitooshuns is strong, and some is weak; and her constitooshunis lead-pisoned, bad as can be, Sur, and her brain is coming out at her ear,

and it hurts her dreadful; and that's what it is, and niver no more, and niver no less, Sur.

Lead is a known inhibitor of protein function, and proteins that utilize a divalent cation such as Zn^{2+} and Fe^{2+} are particularly sensitive to inhibition from lead (5, 6). Lead enters the human body through ingestion, inhalation or dermally in the case of organic lead. Once in the human body, lead can be found in the blood, mineralizing tissues (bones) and soft tissue. In times of stress, like pregnancy or lactation, the body can mobilize lead and thereby increase blood levels. The human body accumulates lead over a lifetime and releases it slowly (7).

Lead is a neurotoxin, and the nervous system is the most sensitive target of lead exposure (8). It can produce irreparable damage to the nervous system and resulting symptoms are blindness, insomnia, kidney failure, hearing loss, palsies, convulsions and eventually death.

Children suffer neurological effects at much lower exposure levels. There is a large body of evidence that associates decreases in IQ performance and other neuropsychological defects with lead exposure (9, 10). Lead interferes with a hormonal form of vitamin D, which affects multiple processes in the body, including cell maturation and skeletal growth. Lead also interferes with the body's ability to make hemoglobin by interfering with several enzymatic steps in the heme pathway. Maternal blood lead from exogenous and endogenous sources can cross the placenta and put the fetus at risk (10).

Today lead levels in the environment are much higher than in the 19th century, and levels found today in most people are orders of magnitude greater than those of ancient times (11). The circumstance that significantly increased lead levels in the bodies of every animal on the food chain was the addition of tetraethyl lead to gasoline.

Invention of Leaded Gasoline: Tetraethyl Lead as a Gasoline Additive

Thomas Midgley (1889-1944) played a significant role in the introduction of tetraethyl lead into gasoline. Midgley majored in mechanical engineering at Cornell University, and in 1916 he joined Dayton Engineering where he was given the assignment to work on a way to prevent engine knock (12). Engine knock was the metal on metal pinging sound that occurred in an internal combustion engine and one cause of fuel inefficiency.

To eliminate this problem, Midgley first tried an oil-soluble dye with iodine, which proved too expensive. In 1921, he discovered several antiknock agents, but all had a terrible stench. Midgley noticed that almost every successful anti knock agent was made of heavier elements like tellurium or selenium, so lead seemed like a good candidate.

Carl Jacob Löwig was the first to report the preparation of an alkyl lead compound in 1853 (13). The field of organometallic chemistry had begun in earnest in 1849 when Edward Frankland reported preparing the ethyl radical (actually butane) by the action of metallic zinc on ethyl iodide (14). Several years later, George Bowdler Buckton isolated and characterized pure tetraethyl lead (Figure 1) (15).

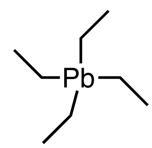

***Figure 1**. Tetraethyl lead*

Midgley and his assistant Carroll Hochwalt turned to the procedure published more than 60 years prior, and in 1921, successfully prepared a tiny amount of tetraethyl lead in their laboratory (12). Midgley learned that 0.05% by volume of lead additive made fuel burn more slowly and prevented engine knock. Leaded gasoline gave greater power and better mileage. It appeared at the time that tetraethyl lead was the most effective and least expensive anti-knock compound.

As Midgley's laboratory developed tetraethyl lead, there were immediate health concerns. Physicians knew about acute lead poisoning among lead workers, and they understood that small amounts of lead accumulate in the body, but little was known about the long-term effects of low-level exposure to lead. At that time, there were no federal laws to require testing of new compounds for toxicity. The Environmental Protection Agency (EPA) and the National Institute of Occupational Safety and Health (NIOSH) were not created until 1970.

Although there were no federal regulations requiring him to do so, Midgley approached the US Bureau of Mines to examine the health hazards of exhaust from fuel burned with tetraethyl lead. He also devised his own experiments to find lead in automobile exhaust. At the time there were no instruments designed to detect small amounts of metals in the air, and he concluded that the exhaust contained no lead. However, after years of working with lead compounds both Midgley and his assistant developed symptoms of lead poisoning. As a precaution, he switched to using rubber gloves in the laboratory (12). Midgley was convinced that since lead was already contained in so many consumer products, the risk to the public was minimal and exposure in the laboratory could be avoided with proper precautions.

Gasoline containing tetraethyl lead went on sale to the public in 1923 and was given the name "Ethyl" (Figure 2). Car owners immediately noticed a difference. The additive stopped knocks, gave more power on hills and a cooler running engine. Ironically, it was already known that ethyl alcohol has a significantly higher heat of evaporation than gasoline providing a cooling effect, which helps reduce engine knock (16).

Midgley then turned his attention to solving the problem of modern refrigeration and developed chlorofluoromethanes for refrigeration and air-conditioning. These compounds were later linked to the destruction of the stratospheric ozone layer that protects earth from UV rays (17).

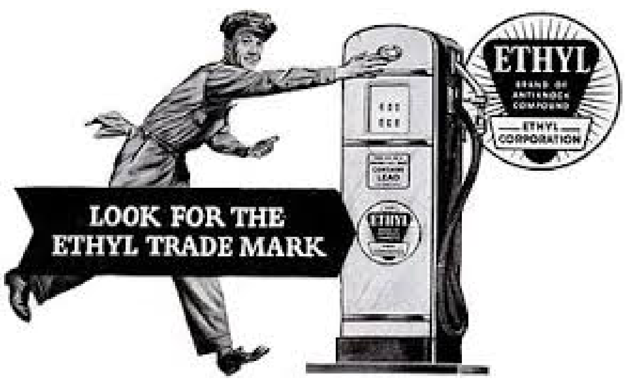

Figure 2*. Early ad for gasoline containing tetraethyl lead (18), which first went on sale in 1923.*

Early Health Concerns about Tetraethyl Lead

During the first two years of leaded gasoline production, at least 15 tetraethyl lead workers died at different plants and dozens of others suffered the characteristic neurological symptoms of lead poisoning (19). The newspaper headlines called the fumes "Looney gas" when workers in a Du Pont factory became psychotic. During this time, the Bureau of Mines announced that the additive posed no peril (20).

Under pressure from scientists, activists and public health experts, the US Surgeon General convened a hearing in May of 1925 to examine possible public health consequences of the manufacture, distribution, or use of leaded gasoline (21). At the time, there was no data that examined how low-level chronic exposure to lead affects the human body (22). In January of 1926, the PHS (Public Health Service) committee released a report that found "no good grounds" for prohibiting Ethyl gasoline but recommended continued tests (23):

> It remains possible that, if the use of leaded gasoline becomes widespread, conditions may arise very different from those studied by us which would render its use more of a hazard than would appear to be the case from this investigation. Longer experience may show that even such slight storage of lead as was observed in these studies may lead eventually in susceptible individuals to recognizable lead poisoning or to chronic degenerative diseases of a less obvious character. In view of such possibilities the committee feels that the investigation begun under their direction must not be allowed to lapse…

By the 1960's tetraethyl lead was in 90% of fuel and was one of the most lucrative chemical enterprises in the United States.

The Age of the Earth and Lead-Contaminated Rock Samples

In 1948, in a seemingly unrelated area of science, a young geologist at the University of Chicago named Clair Patterson (1922-1995) began work on a project to determine the age of the earth. He was using a similar logic to that of Willard Libby who won the Nobel Prize for developing radiocarbon dating (24). Libby had been able to determine the age of organic remains by looking at the relative amounts of carbon-14 in samples using the half-life of 5,600 years. Patterson applied a similar technique, developed by Harrison Brown. The idea was to measure the decay rate of uranium to lead, calculate the age of rocks and ultimately determine the age of the earth. He assumed that the interior of meteorites, which were deposited during the formation of the earth, would have an unchanged interior chemistry, with the exception of radioactive decay (25).

Patterson immediately noticed unusually high lead contamination in his rock samples that were exposed to air. While at University of Chicago and later at California Institute of Technology, he devised a sterile laboratory to prevent contamination from environmental lead. In 1953, he announced at a meeting the age of the earth at 4,550 million years, a monumental breakthrough for which he was never awarded a Nobel Prize (26).

After completing his objective, he turned his attention to measuring lead in the atmosphere. Initially, Patterson collected samples and measured lead isotope ratios in oceans and ocean sediments. He measured lead on land, in layers of ocean water and sea floor sediments. Patterson secured funding through the American Petroleum Institute, which hoped that information about ocean sediments would locate oil.

Patterson and his postdoctoral fellow, Tsaihwa Chow, discovered a modern surge in the amount of lead flowing from rivers into the oceans. They compared lead to barium, which behaves like lead but is not heavily used in industry. Barium in terrestrial rocks and ocean sediment was essentially the control to compare with how lead should appear prior to industrialization. His conclusion: surface layers of the Pacific Ocean contained about 80 times more lead than expected in the natural erosion of igneous rocks on land. He also uncovered elevated lead levels in fresh snowfall, concluding that lead was airborne. The source was tetraethyl lead.

In 1963, Patterson published a paper in *Nature* describing industrial lead in snow and seawater (27). Representatives from the Ethyl Corporation immediately visited him. He carefully explained how their operations were poisoning the environment and people with lead, and one day this information would be used to shut down their operations. After that meeting the US Public Health Service refused to renew his research contract and the American Petroleum Institute discontinued funding. Lead industry officials pressed school trustees at California Institute of Technology to silence him or let him go (28).

To prove that atmospheric lead was caused by automobile exhaust, Patterson turned to ice-core samples. It was known at the time that snowfall in the Arctic accumulates into distinct layers with different colors for summer and winter. He was able to count through the layers and measure the amount of lead in each and essentially establish the concentration of lead in the atmosphere going back hundreds of years. This technique is also used in climate change studies to measure CO_2 levels since the industrial revolution. Patterson found that since 1923, when lead was introduced into gasoline, the level climbed steadily. He states, "…the average resident of the United States is being subjected to severe chronic lead insult" (29).

The Ethyl corporation believed that lead was hazardous only at high exposure levels and affected only careless factory workers or children who ingested lead paint chips. Patterson believed there was no clear line between what was obviously toxic and what was completely harmless. He was deeply troubled by the lack of objectivity in the health studies on lead (22).

In 1966, hearings on leaded gasoline began in the United States Senate and included testimony from scientists working for industry and Clair Patterson. Patterson told the committee (22)

> It is not just a mistake for public health agencies to cooperate and collaborate with industries in investigating and deciding whether public health is endangered—it is a direct abrogation and violation of the duties and responsibilities of those public health organizations.

The hearings, chaired by Sen. Edmund Muskie, led to an extended debate about the need for new regulatory agencies and new approaches to regulations. Most specifically lead could no longer be considered a one-time exposure hazard limited to factory workers, but rather an insidious airborne danger that accumulates over time and with exposure (22, 30).

During the 1960s the Centers for Disease control (CDC) considered 60 μg/dL of blood acceptable. By 1991 the number was lowered to 10 μg/dL and in 2012 dropped to 5 μg/dL. In children under 5 years, levels above 5 μg/dL require case management and levels above 45 μg/dL require chelation therapy (31).

In 1970 Congress passed the Clean Air Act of 1970. It did not ban leaded gasoline, but gave the EPA (Environmental Protection Agency) authority to ban harmful fuel additives (19, 32). In 1970 the General Motors Corporation began to equip its cars with catalytic converters, which oxidize certain pollutants using palladium, rhodium and platinum catalysts. Tetraethyl lead tends to clog up catalytic converters making the two incompatible. In 1972, the EPA announced that all gasoline stations were required to carry un-leaded gasoline to protect catalytic converters. The EPA delayed the standards until 1973 and was also sued by the Ethyl Corporation. The United States banned lead from indoor paint in 1978, years after many other countries (33).

Between 1975 and 1980, the sales of leaded gasoline dropped by from 160×10^3 tons/year to 60×10^3 tons/year. The ambient air lead concentration dropped correspondingly from 1.23 μg/m^3 to 0.45 μg/m^3. Children and adult blood levels also dropped. The average American child's blood lead level in 1976 was 13.7 μg/dL and by 1991 was 3.2 μg/dL (28). Lead settling on the polar ice cap also decreased and by 1989 was near pre-automobile levels.

Through the 1970s, Patterson examined lead levels in food chains. He and his assistant, Dorothy Settle, turned their attention to tuna, an animal at the top of the food chain. They found that fresh tuna contained 0.3 ng of lead per gram of fresh meat, but that canned tuna contained nearly 5000 times more lead because the containers were sealed with lead solder (34). This called into question lead levels in other canned products, many of which were marketed for children. Patterson was dismayed with the government agencies charged to protect the public and later offered to train government scientists in his clean (lead-free) laboratory techniques that he developed as a young scientist.

Looking Back

Clair Patterson's original research to determine the age of the earth led him to uncover massive lead contamination in the environment. Patterson then set out to educate and remove lead from gasoline and became a constant critic of the lead industry. Armed with the power of strong scientific inquiry, he played a crucial role in removing the lead additives from gasoline and lead solder from food containers. He uncovered a dramatic difference between preindustrial and post-industrial lead levels in the environment. He stimulated medical research on the effect of low-level lead pollution. He was a catalyst for lead remediation in homes and regular lead testing for young children as part of routine medical exams. Lead levels in our bodies have dramatically decreased as a result of his endeavors.

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Anderson Named President and CEO of CHF

The board of directors of the Chemical Heritage Foundation has voted unanimously to appoint Robert Anderson as the new president and CEO of the organization, effective January 9, 2017. Anderson is the former director of the British Museum, London, an internationally recognized historian of science, and a longtime CHF board member. He has been interim president since July 2016. After a very extensive search for a president, the board realized that the best choice was already in place.