

## Lead Toxicity

Mention “lead” and many people will remark “isn’t it poisonous?”. In this section, we look at what makes something toxic in general and what we know about lead’s toxicity specifically. As has been our practice throughout this text, we begin by trying to sketch a stock and flow model of the factors that we think are going to be important as we begin our study of lead toxicity. After our initial draft of the model, we’ll learn how it has to be refined to account for some of the special issues associated with human metabolism of toxic materials.

In the case of lead toxicity, we’re clearly interested in how lead gets into people. So what might a stock and flow model look like? Where is lead found in the environment? How does it get from where it is found in the environment into humans? What are the forms it is found in and what are the routes it takes?

Lead is found in the environment in rocks. It is found primarily as PbS, galena. Because of lead’s properties, it has been mined by humans for centuries, and added to a number of products humans use. The first evidence for lead mining comes in 3800 BCE. Lead is easily malleable and has a low melting point, which makes it easy to manipulate and so was used initially for goblets and kitchen utensils. The use of lead in ancient Rome, and the mining of it, led to ill effects that were recognized by some as being due to lead exposure.

More recently, we have used lead as an additive in paint and pottery. In the United States, lead paint was used heavily in the 1940s and 1950s. It was outlawed in the US in 1978, but it is estimated that 74% of all houses built before 1980 still contain lead and in some regions of the country, the percentage of pre-1980 houses with lead is higher. PbO, lead oxide, is a yellow solid. PbCrO<sub>4</sub>, lead chromate, was initially used to make school buses yellow. Pb<sub>3</sub>(CO<sub>3</sub>)<sub>2</sub>(OH)<sub>2</sub> is the primary form of lead that was used in white lead paint. Lead has also been used as a pesticide in the form of Pb<sub>3</sub>(AsO<sub>4</sub>)<sub>2</sub>, lead arsenate. Pb(CH<sub>2</sub>CH<sub>3</sub>)<sub>4</sub>, tetraethyl lead, has been widely used as a gasoline additive because it reduces engine knock. Finally, lead metal is used for solder and for pellets in bullets and other structural uses.

How does it get from those forms inside humans?

Paint wears and creates dust. These dust particles can be inhaled or ingested. When gasoline is burned, the additives in it are released into the atmosphere where they can be inhaled. The particles can also fall out of the atmosphere and be deposited along the side of roads where they can be ingested. Plants grown in lead-contaminated soils can take up the lead. This in fact is a strategy sometimes used for lead remediation (known as *phytoremediation*). However, when vegetables are grown in those soils, consumption of those vegetables can provide another route for human exposure. Lead can, to an extent that depends on its chemical form (see notes on factors that affect the flow of matter) dissolve in water. Drinking water into which lead has dissolved can also provide a route of exposure.

With this information now draw a stock and flow model of lead going into and out of a child.

Unlike most of the models we have worked with, there is no reason to assume that this system is at a steady state. If a child consumes more lead than he releases, the concentration of lead in his body will increase. Conversely, if a child is removed from an environment in which he is exposed to lead, the levels of lead in his system will decline.

As with all scientific issues, we need next to get a feeling for the orders of magnitude that are important.

The most important point in considering the effects of lead exposure is that it affects children and adults differently. The effects on children occur at considerably lower levels than with adults. In children, lead affects neuronal development, leading to irreversible developmental effects.

Lead accumulates in many different compartments within humans. It is measured, however, only in the blood and health standards are set accordingly to these levels. In children, a blood lead level (bll) greater than 10 micrograms per deciliter of blood ( $\mu\text{g}/\text{dL}$ ) is cause for concern and indicates that the child is exposed to lead in her environment. Levels as low as 10  $\mu\text{g}/\text{dL}$  are associated with a decrease in IQ, hearing, and growth. Levels above 100  $\mu\text{g}/\text{dL}$  can cause death in both children and adults.

In adults, levels above 60  $\mu\text{g}/\text{dL}$  have been connected to elevated blood pressure, digestive problems, kidney damage, nerve disorders and mood changes. The more we have studied the effects of lead exposure, the lower the levels at which ill effects are thought to occur has become. Before the mid 1960's, levels above 60  $\mu\text{g}/\text{dL}$  in children were considered toxic. In 1978, the standard, for children, had changed to 30  $\mu\text{g}/\text{dL}$ . Today, it is 10  $\mu\text{g}/\text{dL}$ .

Since leaded gas was outlawed in the U.S., average blood lead levels in children have steadily declined. Lead is still added to gasoline in some countries. If you are interested, find out which countries still allow lead in gasoline. Students with interest in chemistry may want to investigate in more detail why tetraethyl lead is added to gasoline. As a class, you may want to discuss some of the current controversies in the US surrounded gasoline additives in general.

How does one get poisoned by lead? If 10  $\mu\text{g}/\text{dL}$  in blood is bad for a child and a child has 3-4 L of blood, then 300  $\mu\text{g}$  of lead in a child's body is bad. Does that mean that breathing 300  $\mu\text{g}$  of lead will lead to bll of concern?

With these questions, we enter another realm in the world of stocks and flows. We need to explicitly consider factors that affect the partitioning and transformation of a

substance. 300 micograms may enter the body, but what percentage stays in the body? Where is the percentage that stays in the body located? Ultimately, to make good public policy, we need to know what form of lead actually causes harm to humans and where lead, in that form, needs to be in the body for that harm to occur.

Much limits our ability to gain that sort of knowledge. Do you want to volunteer your child to be dosed with lead and then examined for effects and ultimately dissected to determine where the lead is located? (Even if you do, it is not permissible). There are significant limitations on the sorts of experiments that can be done with people. Most of the information we have about the toxicity of various substances on humans comes from two indirect sources. We use **epidemiological studies** and **studies on animals** to estimate the **dose** of a substance that causes harm to humans.

Epidemiological studies can be done in a number of different ways. (Interested students are encouraged to consult a standard epidemiological textbook for more information on the different types of studies.) Regardless of the study design, an epidemiological study looks for a correlation between exposure and outcome. For example, a group of people can be selected and separated into those who smoke and those who don't smoke and then recontacted in 15-20 years to see who has gotten lung cancer and whether the incidence of lung cancer is higher among the group of people who smoked than those who didn't. Epidemiological studies can be quite sophisticated. They can ask people how much they smoke and see if incidence of lung cancer is highest among those who smoked the most. They can ask people how much they drink and factor out any effect of alcohol on lung cancer from the effect of smoking. However, epidemiological studies certainly have shortcomings. They generally rely on people self-reporting their exposures. They may miss an important confounding variable – for example exposure to air pollution – because it was a factor the study designers did not think about or because it might simply be too hard to gather data about. Small effects are very hard to see and require a large population to resolve. Large epidemiological studies are quite expensive. Epidemiological studies have been the most useful in groups of people with higher than average exposures – e.g. uranium miner workers gave us good data on the effects of radon exposure because radon levels in mines are often quite high. The results from those highly exposed people must then be extrapolated to those of us in the less highly exposed populations and extrapolations raise other issues that will be explored more in the next section. Still, epidemiological studies, because they deal with people, can be useful in determining whether exposure to a chemical causes a health problem and can often be useful in deciding at what level of exposure do certain bad effects occur.

Animal studies have their own sets of strengths and weaknesses. In an animal study, rats or mice (generally, and generally a strain bred to get tumors easily) are divided into groups. Some groups are exposed to relatively high doses of chemicals and at least one group is not exposed but otherwise treated exactly the same way as the exposed animals. After a certain amount of time has elapsed, the animals are killed and autopsied and the number of tumors counted. This makes it easy to correlate exposure level with the number of tumors formed. (A similar procedure can occur to look for other adverse outcomes.) The good points are clear – one has a nice, controlled experiment. A few

mice are not sneaking out of the cage to smoke a cigarette and if one mouse is stressed, they all are. The doses are carefully measured and administered. There is a clear control. If tumors occur at significantly higher numbers in the treated animals and if there is a clear relationship between dose and number of tumors, the evidence that the chemical being used caused the tumors is strong. On the other hand, laboratory animals are not humans. They metabolize chemicals differently. The strains used in these experiments are specially bred to be susceptible to tumors and the doses that they are given are quite high. These later two factors help circumvent the problem that you need a lot of data points to resolve a statistically small effect – by making the effect larger you need fewer data points, which means fewer animals, which means less expense and is ethically preferable. Extrapolations to lower doses and to a different species are required

This digression is intended to point out to you that it is difficult to know how much lead at what point in the body causes what specific kind of harm. We'll think about some of this material again as we think more generally about how to assess risk. For now, we want to recognize that our stock and flow model has uncertainty in it – something that we have seen before and pointed out to you is a hallmark of environmental science.

The EPA has worked to come up with numbers that we can use to fill in our stock and flow model. These numbers will help us translate between the amount of lead in the environment and the amount of lead likely to end up in a child's blood. We can then use that number – the estimated amount of lead in a child's blood – to estimate health effects. This later estimate comes courtesy of some pretty good epidemiological studies.

**BEFORE WE PROCEED, TAKE A BREAK AND DO A QUICK BACK OF THE ENVELOP CALCULATION. HOW MANY LEAD ATOMS ARE THERE IN A VERY SMALL DROP OF LEADED PAINT THAT IS 1% LEAD BY WEIGHT?**

There are a couple of different approaches we can take to estimating the amount of lead inside a child. EPA has developed a model that you are invited to use in the lab for this section. In a bit more of the back of the envelop spirit, we can use the EPA estimates for media intake given below. That information, coupled with knowledge about the concentration of lead in various media, which you would need to determine by measuring, will give you an estimate of the amount of lead consumed by a child. Below this chart, there is another chart that converts between amount of soluble and insoluble lead consumed by a child per day and the blood lead levels such ingestion would sustain. See the section in this chapter on factors that influence the solubility of compounds for more information on what makes a source of lead soluble or insoluble.

EPA estimates for Media Intake Rates (Pb intake rate = media Pb concentration \* Media Intake Rates)

Soil/Dust	0-1 yr 0.085 g/d 1-2 yrs 0.135 g/d 2-3 yrs 0.135 g/d 3-4 yrs 0.135 g/d	This number reports a total value for soil intake. It is a ratio of soil ingestion (45%) to dust ingestion (55%)
-----------	---	--

	4-5 yrs 0.100 g/d 5-6 yrs 0.09 g/d 6-7 yrs 0.085 g/d	
Air	0 -1 yr 2 m <sup>3</sup> /d 1-2 yrs 3 m <sup>3</sup> /d 2-5 yrs 5 m <sup>3</sup> /d 5-7 yrs 7 m <sup>3</sup> /d	
Drinking Water	0-1 yr 0.2 L/d 1-2 yrs 0.5 L/d 2-3 yrs 0.52 L/d 3-4 yrs 0.53 L/d 4-5 yrs 0.55 L/d 5-6 yrs 0.58 L/d 6-7 yrs 0.59 L/d	
Diet	0-1 yr 5.53 µg Pb/d 1-2 yrs 5.78 µg Pb/d 2-3 yrs 6.49 µg Pb/d 3-4 yrs 6.24 µg Pb/d 4-5 yrs 6.01 µg Pb/d 5-6 yrs 6.34 µg Pb/d 6-7 yrs 7.00 µg Pb/d	Site specific data may be used to augment the default intake rates
Alternative sources	Site specific data may be used to account of intakes of Pb in sources such as Pb paint	EPA has written an exposure model to account for lead exposure from other sources (IEUBK)

#### Lead accessibility

Blood lead concentration (µg Pb/dL)	Dose of soluble lead to achieve this concentration (mg/kg/day)	Dose of soil lead to achieve this concentration (mg/kg/day)
1	0.03	0.04
2	0.07	0.1
3	0.11	0.17
4	0.15	0.27
5	0.20	0.40
6	0.25	0.60
7	0.30	0.93
8	0.36	1.60

Given this information, go through a couple of different exposure scenarios to see how a child in those environments would fare.