Toxicology and You
Or
An Introduction to A Small Dose of Toxicology

A book chapter of
A Small Dose of Toxicology - The Health Effects of Common Chemicals

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Supporting web sites
web: www.asmalldoseof.org - "A Small Dose of Toxicology"
web: www.toxipedia.org - Connecting Science and People
Toxicology and You

Toxicology originally developed as the study of poisons and is now more formally described as the study of the adverse effects of chemical or physical agents on living organisms. During our lives, most of us begin to develop an intuitive sense of toxicology that guides many of our personal day-to-day decisions. This process can start first thing in the morning over a cup of coffee or tea or a can of cola. These common beverages contain caffeine, the most widely consumed stimulant in the world. Most consumers of caffeine are well aware of the benefits of this drug as well as the consequences of consuming too much. Through trial and error we have learned how to moderate our consumption of caffeine to avoid any undesirable effects. In regulating our consumption of caffeine we are applying the most basic principle of toxicology: dose / response. We apply this principle as we judge how much and what to eat or drink, or how much suntan lotion we should use before going to the beach. As we shall see in a future chapter, caffeine provides an excellent example of how we apply knowingly or unknowingly the principles of toxicology. Understanding how caffeine interacts with the body can even explain why the coffee and soda companies make so much money from this amazing drug. Looking at the world through the lens of toxicology provides a very interesting perspective on current, historical, and personal events.

The purpose of A Small Dose of Toxicology is to build upon our intuitive understanding of toxicology into knowledgeable and comfortable application of the principles of toxicology. Placing some form and structure around what we already intuitively know about toxicology will allow more critical analysis of not only our immediate environment but many of the current events that shape our local and global society. Toxicological considerations shape directly or indirectly many decisions about our home, play, school, or work environments. As citizens in a democratic society, we must be able to meaningfully engage decision makers in industry, government, and the news media to influence the development of our local environment as well as society. This book is not about the thousands of commercial chemicals that are in use, but rather about the principles that guide decisions about their use and distribution. A little knowledge about toxicology will allow us to better judge the potential effect on our lives, ask insightful questions, and ultimately influence the decision makers.

Historically, toxicology was most often concerned with how much of a substance it took to kill you. Literature has some splendid examples of the awareness of naturally occurring poisons. The ancient Greeks were very knowledgeable about the properties of the plant, Hemlock, part of the parsley family, even though they did not know what specific chemical in it caused death. In 399 BC Socrates was condemned to die by Hemlock after being charged with religious heresy and corrupting the morals of local youth. We now know that the active chemical is the alkaloid coniine, which when
ingested causes paralysis, convulsions, and potentially death. More modern examples of the knowledge of poisons can be seen in the following from a well-known playwright, Shakespeare:

From Romeo and Juliet - act 5
Come bitter pilot, now at once run on
The dashing rocks thy seasick weary bark!
Here’s to my love! O true apothecary!
Thy drugs are quick. Thus with a kiss I die.

Historical events can also be interpreted from the perspective of toxicology. For example, Great Britain acquired Hong Kong during the Opium War of 1839-42, which was really about the toxic and additive properties of this opium. Medical uses of opium included the treatment of diseases such as dysentery and cholera. Users soon found that smoking a mixture of tobacco and opium increased the absorption of opium, resulting in a more rapid onset of its effects. The Chinese government was trying to curb the smoking of opium because of its debilitating effects, which was at odds with the British desire to increase the opium trade. Opium was not made illegal in the United States until 1921(?). The popularity of drug use continues and governments are engaged a variety of efforts to curb their use including “drug wars” with neighboring countries.

Knowledge about the physiological and toxicological properties of drugs (legal or illegal) is important in developing sound public policy. Looking at historical and current events through the filter of toxicology (see below) provides a new perspective on the underlying issues. Life has many examples of toxicology, if one only thinks or sees in terms of a toxicologist.

Every Day Examples of Toxicology
Or
What do these have in common?

Below are a few examples (Table 1.1), there are many more and they occur everyday in the news. Can you add to this list? What toxicology related or biology related issues have been in the news recently?
Table 1.1 Every Day Examples of Toxicology

<table>
<thead>
<tr>
<th>What Aspect of Toxicology?</th>
<th>Comment</th>
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<tr>
<td>Thalidomide</td>
<td>Developed as a sedative in the early 60’s but found to cause a rare birth defect, phocomelia. In 1962 legislation was passed that new drugs must undergo sufficient animal and human testing prior to approval for use by the FDA.</td>
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| Hong Kong                 | a) Many chickens and birds in Hong Kong were killed to stop the spread of a potentially deadly avian virus that could move to humans  
b) Why was Hong Kong a British colony? This was in part due to the opium wars, when England and other countries wanted to promote the use of opium to Chinese population. Consider our own current “war on drugs”. |
| Princess Diana            | At the time of death her driver may have had too much alcohol to drink. |
| Ambassador to Mexico      | A number of years ago a former governor of Massachusetts (Weild) was denied the opportunity to become the ambassador to Mexico because US Senator Jesse Helm thought he was “soft on drugs”. Yet this senator was from a key tobacco growing state and a major supporter of the tobacco industry (and hence nicotine). Who is soft on drugs? |
| $276 Billion              | Money lost or spent due to the consumption of alcohol or drug abuse, car accidents, lost work etc…. |
| $65 Billion               | Money lost or spent due to tobacco related illnesses or disease. |
| Food                      | Our food supply is demands on and is contaminated with pesticides. Artificial sweeteners, flavors, and colors are used. Mercury contaminates some fish. |
| Noise                     | Loud noise can damage hearing and can cause an even greater effect in combination with certain drugs |
| Dust                      | The dust in your home may contain many hazardous contaminants, e.g. lead or pesticides. Many of these can be tracked in the home on shoes or by pets. Removing shoes can reduce contamination in the home. |
| 12,000 Children           | Estimated number of children with Fetal Alcohol Syndrome |
| Coeur d’Alene, Silver Valley, ID | Town contaminated by lead |
| Solar Radiation (ultraviolet light) | Sunburn, cancer |
| Arsenic                   | Found in drinking water, and old smelter and mining sites, cause skin disease and cancer |
Toxicology, while formally considered a new science, has ancient roots and is closely linked to medicine. Toxicology’s counterpart in medicine is pharmacology, the study of the beneficial and side effects of medicinal drugs. The adverse effects of drugs, often termed side effects, are really the toxicological or undesired aspects of the drug that one must endure along with the benefits. The basic principles of pharmacology and toxicology are very similar, with just a different emphasis on the outcome. For example, one can study both the pharmacological or beneficial aspects of caffeine and at the same time be looking at the undesired or toxicological aspects of too much caffeine. Caffeine at the right dose is commonly consumed for its stimulant effects on the nervous system, but too much produces equally recognizable and undesirable effects.

As knowledge of the effects of poisons grew so did the definition of toxicology. A more contemporary definition of toxicology is the study of the adverse (undesired or harmful) effects of chemical and physical agents on living organisms. While this definition may appear relatively simple there are important aspects worth exploring. “Adverse effects” can range from obvious ones like death, cancer, an injury such as an acid burn, or the undesired effects of too much caffeine. We quickly note these unpleasant effects and easily relate them to the consumption of or exposure to the agent. As our understanding of toxicology has increased, there has been a shift in focus by recognizing the unique sensitivity of individuals and to more subtle effects such as a decrease in learning and memory. Subtle damage to the nervous system, which can result in a decrease in intelligence, is more difficult to assess in an individual and to relate to exposure. To assess subtle changes it is often necessary to evaluate exposure and effect in a large group or population of people. Our increased awareness of the adverse effects of lead exposure on young children is an excellent example of the changing perspective on toxicology. It is not nearly as important to know how much lead will kill a child as it is to understand the sensitivity of the child’s developing brain to even low levels of exposure to lead. Harming the learning and memory of child results in a lifetime of undesirable effects and consequences for the individual and society.

The child pictured in Figure 1.1 working in a lead battery recycling factory, illustrates the global implications of toxicology. This child will suffer from the effects of lead poisoning for a live time and well not be able to reach his intellectual potential.
The second part of the definition of toxicology concerns “chemical or physical agents.” Chemical agents can be either naturally occurring or manufactured. Hazardous naturally occurring agents produced by living organisms are called toxins while hazardous manufactured agents are called toxicants. Naturally occurring agents can be as benign and essential as water or as deadly as the venom of a coral snake. Plants, animals, and bacteria produce a range of chemical substances or toxins that usually aid in their survival or defense. Humans and even other animals have learned to use these agents to cure disease as well as poison other plants and animals. Several different plants produce caffeine a bitter compound, mostly likely to protect them from insects. Digitalis, from foxglove, is used in treating heart disease. Bacteria, such as botulism or anthrax, produce toxins that can kill humans, but we take advantage of the yeast that produces alcohol. Our industrial society has learned to manufacture a wide range of chemicals designed for specific purposes. Much of our food supply depends on the use of pesticides. Our households, schools and workplace contain numerous chemicals that are potentially hazardous. The laptop computer essential for writing this book contains thousands of different chemicals. The manufacture of many of the items we depend upon and their
subsequent disposal can create additional hazards. There are numerous examples around the world of contaminated areas that are potentially hazardous to animals, plants and humans.

Physical agents represent a different set of challenges for a toxicologist and are often related to occupational health issues. Temperature and noise are the two most common physical agents that must be considered. In the past decade there has been a growing recognition of the harmful effects of loud noise on hearing and, even more important, a willingness to promote the use of hearing protectors. Changes in stream temperature can affect the ability of fish to live and reproduce. Excessive temperature in the work environment or from wearing protective clothing can decrease performance. Both noise and temperature can increase the stress in the environment and interact with other agents to produce a significant decline in performance. Some drugs can interact with noise to produce greater hearing loss. Sleep deprivation or jet lag can also have serious undesirable effects or just an annoying temporary loss of performance.

Toxicology has progressed along with the biological sciences to place a greater emphasis on understanding the mechanism of action of an agent, greater focus on the subtle responses of the organism, and recognition of the sensitivity of individuals. Thus toxicology has moved away from death as an endpoint to a focus on performance and quality of life. Exposure to hazardous vapor may result in impaired judgment or slowed reaction time, resulting in serious injury to the person responding to an emergency. The child exposed to alcohol during gestation may have permanent learning disabilities because of the sensitivity of the developing brain at that particular point. Recognition that the sensitivity of the individual depends on stage of development, age, or genetic makeup has become one of the most important principles of toxicology. This has modified the thinking and application of the principle of dose/response.

It is possible to take an even broader view of toxicology by defining it as the study of the response of a defined system to some event or exposure to an agent. The principles of toxicology are now applicable to vast systems such as consideration of global warming or the effects of logging on the rain forest. Increased atmospheric carbon dioxide is a toxic event which results in a response of global warming. What dose of logging can a rain forest sustain? The basic principles of toxicology are a framework for considering the small local events to large global events or entire biosystems, which moves us into ecological considerations. Application of the principles of toxicology to even very large events where there is an action or exposure or a reaction and a response results in a simplification that can lead to unique perspective. However, this more ecological perspective on toxicology is not the subject of the book but is worth keeping in mind as one applies the principles of toxicology on a day-to-day basis.

An underlying theme behind this book is to place toxicology in the context of environmental health. How do you define environmental health? What environment are we considering – home, school, workplace, outdoors, indoors, the oceans, the air, or
water? I define environmental health as – “Conditions that ensure that all living things have the best opportunity to reach and maintain their full genetic potential.” While this is a very broad approach to environmental health, its value can be best illustrated by looking at children. How do we ensure that our children can reach their “full genetic potential”? For example, children exposed to even very low levels of lead may have learning disabilities. These detrimental changes may affect the child for a lifetime. How do we as individuals and as a society work to ensure that children are not adversely affected by exposure to lead? This is a complex issue that goes well beyond toxicology, but knowing more about toxicology can help in making small decisions that can influence a child’s future quality of life. The same is true of larger environmental issues. A Small Dose of Toxicology strives to apply the principles of toxicology to the broader goal of increasing the potential for all living things to have an opportunity to reach and maintain their full genetic potential. We will examine the effects of exposure to specific agents on living systems and emphasize changes in performance and function.

Ensuring environmental health is a complex interaction of the individual as well as society and ranges from the local to the global. Gold miners in the Amazon use mercury to extract the gold. As the mercury evaporates to reveal the gold, it harms the miners as they breathe it in, but mercury is also going into the atmosphere. The wind may take the mercury in the atmosphere far away but eventually it comes back to the ground, where it is modified by bacteria and taken up by fish. Government agencies must then regulate the amount of mercury acceptable in certain species of fish such as tuna and swordfish. Broken thermometers, fluorescent light bulbs, and a variety of consumer products release mercury into the environment. As a society, how much do we spend to curb the release or even the sale of mercury?

Pesticides are chemicals designed to kill unwanted plants, insects, and animals. While necessary in some situations, their widespread use has had unintended consequences. DDT widely used to kill mosquitoes is but one example. It was subsequently found to weaken bird shell eggs, causing serious declines in predatory birds. An interesting property of DDT and a number of related pesticides is that they can be stored in fat. As the DDT moves up the food chain from smaller to larger animals more and more accumulates in the fat. During breast feeding fat is mobilized and along with it the DDT, which appears in the breast milk, consumed by the infant. These are two of the many examples that we must confront as we begin to appreciate the global implication of toxicology and environmental health and impacts on individuals.

State and national government agencies spend our tax dollars on environmental and toxicology issues. Both the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) were formed in an effort to protect the health and well being of people and the environment. For both agencies, 1962 was a year to remember. A turning point in the regulation governing the FDA occurred in 1962 when it was determined that a new sleeping pill, thalidomide, was shown to cause birth defects. Infants in Europe and Australia were born with birth defects when their pregnant women used thalidomide.
Fortunately, Dr. Frances O. Kelsey, an FDA scientist, kept this drug off the American market despite the best efforts of industry to have the drug approved. Following this incident, regulation was passed that significantly strengthened the FDA’s control over approval of new drugs. Also in 1962, Rachel Carson published her landmark book “Silent Spring,” which dramatically documented the impact of chemicals on the environment and raised concerns about the effect of pesticides on human health. In a delayed political response, the EPA was created in 1970 to administer a variety of laws to protect human health and the environment. The EPA is responsible for regulating the use of pesticides, industrial chemicals, hazardous waste, drinking water, air pollutants and other environmental hazards. These two agencies, as well as other federal and state agencies, spend a lot of money based on principles of toxicology.

The title of this book, “A Small Dose of Toxicology”, identifies a primary aim, which is to provide a small but useful introduction to toxicology. Many of the examples were selected to emphasize how toxicology fits into everyday events and life choices. Do we take one or two cups of coffee? What are the consequences of drinking alcohol or the consumption of other recreational drugs? Why are some individuals more sensitive than others? Was food cooked long enough to insure that all bacteria are killed? My focus is on the practical application of toxicology in our day-to-day lives, but I want to keep a perspective on applying the principles of toxicology to bigger issues. I omitted some of the details on the chemistry and mechanism of action knowing that this information is available from other sources. A list of references includes a number of excellent books that contain more specific information on the chemistry and mechanisms of action of both common and obscure toxic agents. It is said that toxicology can be learned in two easy lessons of only ten years each (I think it may be three lessons now). This book is an introduction to the first ten years.

Understanding the principles of toxicology can provide the power to discover new insights into decision-making. The principles of toxicology can then be applied to an ever changing circumstances as we search for some understanding of the issues. The power is in having the knowledge to evaluate a new situation.

“It is not the truth that makes you free. It is your possession of the power to discover the truth. Our dilemma is that we do not know how to provide that power.”

Each of us can benefit from discovering how and why our bodies interact with an agent as well as from understanding how various compounds impact the environment. Appreciating the impact of dose/response and individual susceptibility provides a basis upon which to take action to improve our own health and well being and that of the environment. Knowing that an infant is more susceptible than an adult to an agent such as
lead, because of their low weight and sensitivity of their developing nervous systems, can result in small but important actions that reduce the infant’s exposure and thus improve their quality of life. This knowledge may also translate into changes in the workplace or by government agencies. Knowledge can provide the power to shape and influence environmental health.

The “Principles of Toxicology” chapter provides an overview of the principles of toxicology while subsequent chapters explore specific topics in great depth. The reader is encouraged to pick and choose specific areas of interest; toxicology is fun when explored out of curiosity. One unique feature of the book is that each chapter has a corresponding PowerPoint presentation. This presentation material was designed to aid the student or the teacher by providing a concise overview of the material in the chapter and, in some cases, provide information from a slightly different perspective. A teacher can use this material for classroom presentation or the student can use the presentation material as class notes or for review of the chapter material. As a teacher myself, I have always wondered how many times the same material has been reproduced to accommodate a lecture.

This edition of “A Small Dose of Toxicology” is designed to take advantage of the extensive information in Toxipedia (www.toxipedia.org), a wiki enabled web site that is designed to grow as our understanding of toxicology expands. Toxipedia’s mission is to place scientific information in the context of history, society, and culture and thereby allow us individually and collectively to make better decisions about human and environmental health.

Toxicological Resources

There is a large and ever-growing body of information on toxicology, particularly on the World Wide Web. Many national government, international organization and non-government agencies have excellent web sites with detailed information on the issues discussed in this book. I urge you to consult these sites for more in-depth information. Your local bookstore, particularly a large university bookstore or an ecologically oriented store may have additional information. Unfortunately much of the in-depth medically or highly scientific information is not very accessible. There are also many non-governmental organizations that can provide additional information and a different perspective. Computer networks and local public and university libraries also contain a wealth of information. Teaching aids, including, material directly related to this book are also available on-line or from a variety of organizations.

Below is a list and brief description of a very few of the more detailed web sites and references. Each chapter of has additional specific recourses and reference while the below are more general in nature.

Teaching resources
• A Small Dose of Toxicology presentation material is online: www.toxipedia.org or www.asmalldoseof.org. Web site contains presentation material related to this book for each chapter.

• Center for Ecogenetics and Environmental Health, Department of Occupational and Environmental Health Sciences, University of Washington. Online: http://depts.washington.edu/ceeh/ (accessed: 27 December 2011). K-12 teacher resources and student aids that address toxicology.


• Society of Toxicology (SOT) – K-12 Resources. Online: http://www.toxicology.org/teachers/teachers.asp (accessed: 27 December 2011). U.S. national toxicology organization site has a variety of useful information and links to educational resources on toxicology and related biological sciences.

**European, Asian, and International Agencies**

• Organization For Economic Co-Operation And Development (OECD) – Chemical Safety. Online: www.oecd.org/ehs/ (accessed: 27 December 2011). This OECD Site contains general information on environmental and chemical health and safety.


• England – The National Institute for Clinical Excellence (NICE). Online: http://www.nice.org.uk/ (accessed: 27 December 2011). NICE was set up as a Special Health Authority for England and Wales and its role is to provide patients, health professionals and the public with authoritative, robust and reliable guidance on current “best practice”.
The aim of DOH is to improve the health and well being of people in England.

This international sire has information on large number of agents.

“ITER is a compilation of human health risk values from a number of international health organizations and independent groups.”

IPCS INCHEM is a means of rapid access to internationally peer reviewed information on chemicals commonly used throughout the world, which may also occur as contaminants in the environment and food. It consolidates information from a number of intergovernmental organizations whose goal it is to assist in the sound management of chemicals.

Site has a large list of pesticide data sheets.

IARC's mission is to coordinate and conduct research on the causes of human cancer, the mechanisms of carcinogenesis, and to develop scientific strategies for cancer control.

The World Health Organization, the United Nations specialized agency for health, was established on 7 April 1948. WHO's objective, as set out in its Constitution, is the attainment by all peoples of the highest possible level of health. Information is in English, Spanish, and French.

IPCS is a joint programme of three Cooperating Organizations - ILO, UNEP and WHO, implementing activities related to chemical safety.
Published by the International Labour Organization’s Constitution to promote "the protection of the worker from sickness, disease and injury arising out of employment".

Site has information on improving Europe’s environment.

GINC is a worldwide information network for safe use of chemicals.

EcoNet is part of IGC and was the world's first computer network dedicated to environmental preservation and sustainability.

HERA, on ingredients of household cleaning projects is a voluntary industry program to carry out Human and Environmental Risk Assessments on ingredients of household cleaning products. HERA is a unique European partnership established in 1999 between the makers of household cleaning products (AISE) and the chemical industry (CEFIC) that supplies the raw materials.

This is Australia's national agency for health and welfare statistics and information.

Japan’s MHLW is regulates drug, food and labor safety..

Japan’s NIHS regulates drugs and chemicals.

North American Agencies
Health Canada provides extensive health related information in English or French.

CCOHS promotes a safe and healthy working environment by providing information and advice about occupational health and safety.

The CHEMINDEX database contains information on over 200,000 chemicals; record contains identification information on a unique chemical substance, including chemical names and synonyms, the CAS registry number, and a list of the CCINFO databases containing information on that substance.

Material Safety Data Sheets on over 120,000 compounds from 600 North American manufacturers and suppliers.

This site provides access to probably the greatest sources of reference material in the world. The Health Information section has specific areas related to Toxicology as well as many searchable databases.

Contains a wealth of information on many common environmental pollutants such as lead, mercury and pesticides as well as regulatory information. The site also has a great kids section.

“IRIS is a database of human health effects that may result from exposure to various substances found in the environment.” An excellent souse of information about many compounds – a great starting place.

“The Toxics Release Inventory (TRI) is a publicly available EPA database that contains information on toxic chemical releases and other waste management
activities reported annually by certain covered industry groups as well as federal facilities.”

  All you would ever want to know about the drug approval process as well as basic information on diseases and current event topics.

  Site contains an interesting historical perspective on the U.S. FDA.

  OSHA is responsible for regulating the work place environment. The site has information on current standards and business requirements.

  NIOSH is responsible for conducting research and making recommendations for the prevention of work-related disease and injury.

  CDC is recognized as the lead federal agency for protecting the health and safety of people of the United States.

  CPSC works to save lives and keep families safe by reducing the risk of injuries and deaths associated with consumer products.

  NTP was established in 1978 by the Department of Health and Human Services (DHHS) to coordinate toxicological testing programs within the Department, strengthen the science base in toxicology; develop and validate improved testing methods; and provide information about potentially toxic chemicals to health regulatory and research agencies, the scientific and medical communities, and the public.

Wide range of information linking the environment, toxicology and health.

  “The CalEPA mission is to restore, protect and enhance the environment, to ensure public health, environmental quality and economic vitality.”

  “The OEHHA mission is to protect and enhance public health and the environment by objective scientific evaluation of risks posed by hazardous substances.”

**Non-government Organizations**

  “Environmental Defense is dedicated to protecting the environmental rights of all people, including future generations. Among these rights are clean air and water, healthy and nourishing food, and a flourishing ecosystem.”

  Site has information on health effects and state exposure issues.

  “TERA is a nonprofit (501(c)(3)) corporation dedicated to the best use of toxicity data for the development of risk values.”

  NAAEE is a network of professionals, students, and volunteers working in the field of environmental education throughout North America and in over 55 countries around the world. Since 1971, the Association has promoted environmental education and supported the work of environmental educators.

  ALA fights lung disease in all its forms, with special emphasis on asthma, tobacco control and environmental health.

U.S. based international professional organization for toxicologists.


**Library References**


**Introductions to Toxicology and Risk**


- Risk Analysis and Management, By Morgan, M. Granger Scientific American, July 1993 p 32-41. (This is a good short overview of many of the issues in risk analysis.)


**Reference Books (lots of good information, but costly)**


Goodman and Gilman’s The Pharmacological Basis of Therapeutics (12th Edition), ed. Joel G. Hardman, Lee E. Limbird, Perry B. Molinoff, and Raymond W. Ruddon, 2010, McGraw Hill, New York, p 1808. (A detailed book on the pharmacological (i.e. beneficial) and toxicological (i.e. adverse) effects of drugs. Also considerable basic physiological information.)