Book Review

Jorge A. Santiago-Blay[1]

In ***Life: The Excitement of Biology*** 4(1):80-85, I reviewed the book *Silent Sparks* but time limitations precluded me from also reviewing *Modern Poisons: A Brief Introduction to Contemporary Toxicology* by Dr. Alan S. Kolok. Below, I do that. As *Silent Sparks*, *Modern Poisons* is an enjoyable read for those with broad interests in science who may not have been trained in biology and/or chemistry. As Kolok says (p. 175), "I want to bring those ideas … not just to scientists and students but to the interested layman as well." The most obvious differences between both tomes is the surprising - at least to me - lack of illustrations in Kolok's book. Thus, herein I supply a few images for the benefit of readers of *Modern Poisons*.

Modern Poisons: A Brief Introduction to Contemporary Toxicology
by Alan S. Kolok. 2016. Island Press. Washington, District of Columbia, USA.
208 pp. ISBN: 978-1-61091-382-9 (softbound, in English)

As a life-long learner, I make every effort to have a well-rounded training in whatever I am pursuing. For instance, while completing my graduate degrees in the USA, I took almost all entomology and botany courses available at the time. Making the funny sign of the crossbones with my arms, I avoided toxicology. Nevertheless, toxicology has chased me as I have had to teach its principles to generations of science majors and non-science majors alike. The onset and expansion of the Industrial and Scientific Revolutions in the so-called "Western world" have transformed toxicology into an applied and interdisciplinary science. As the world becomes more environmentally aware and new chemicals are manufactured, toxicology has become more important. A classification of some of the basic terms related to entities (chemicals or radiation) that can be harmful (or hazardous), including toxins is summarized in Figure 1.

Chapter 1, entitled *The Dose Makes the Poisson*, introduces us to the Father of Toxicology and creator of the dictum that constitutes the title of the chapter, the controversial Swiss-German scholar Philippus Aureolus Theophrastus Bombastus von Hohenheim, self-renamed Paracelsus (1493-1541)[2] or beyond Celsus, the Roman scholar (ca. 25 BCE to 50 CE).

---

[1] 217 Wynwood Road, York, Pennsylvania, USA 17402. E-mail: blayjorge@gmail.com

[2] Paracelsus is also notorious for considering that a miniscule living human, called homunculus, could be formed by alchemical means. Wikipedia Contributors. 2017. Homunculus. *Wikipedia, The Free Encyclopedia*. Accessed on April 11, 2017. https://en.wikipedia.org/wiki/Homunculus . Grafton, A, 1999. *Natural Particulars: Nature and the Disciplines in Renaissance Europe*. MIT Press. 426 pp.

DOI:10.9784/LEB4(4)SantiagoBlay.01
Electronically available on April 23, 2017. Mailed on April 20, 2017

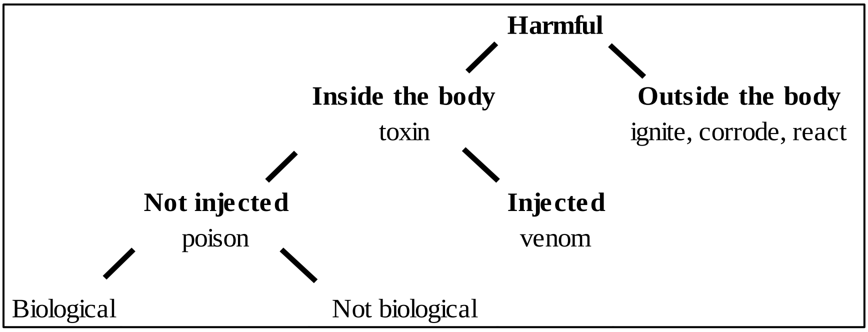


Figure 1. A classification of potentially harmful (or hazardous) chemicals or radiation.

A dramatic example of this aphorism, excess water can kill, as in drowning, or harm, such as in the rare disease, aquagenic urticaria. Besides Paracelsus dictum, the dose-response curve (Figure 2) is another cornerstone of toxicology. The dose (horizontal axis) refers to the concentration of the active ingredient (or radiation) that contacts or gets into the living organism (or part of it, such as cell). The response (vertical axis) refers to what happens to that living entity when it is exposed to the agent. In general, as the concentration of a chemical increases, the response of the living organism, increases although not necessarily at the same rate.

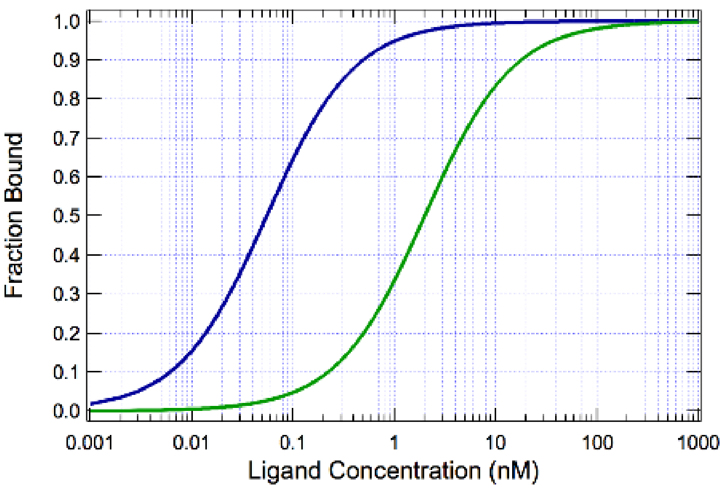


Figure 2. A hypothetical example of a dose-response curve. Image from https://upload.wikimedia.org/wikipedia/commons/4/42/DoseResponse.png . Author, “Pronchik”.

The dose of the active ingredient is not the only important consideration in toxicology. *The Nature of a Chemical* (Chapter 2) is also an essential consideration. How do chemicals enter the cells? Chemicals enter the cell through its membrane (Figure 3). The cell membrane is made from a double layer of phospholipids. Phospholipids have a region with negative electrical charges, represented by spheres in Figure 3. The inside portion of the lipid bilayer is made from the water insoluble portions of the phospholipids, represented by two "tails" of each sphere. The tails of the phospholipid bilayer make it difficult for water-soluble, electrically charged substances, such as ions, to go through the cell membrane. How do electrically charged particles travel through the membrane? The proteins that are interspersed within the phospholipid bilayer assist in those movements. Ions traverse the cell using proteins (pores, gates, or carriers). These proteins are not perfect in recognizing ions compatible with life from those that are not. On the other hand, the oil soluble chemicals, which are often electrically neutral, can go through the cell membrane with relative ease. Taking an organismocentric point of view, most chemicals important to life can generally be classified using a 2 by 2 table: whether the chemical has carbon (organic) or not (inorganic) and whether the substance is water- or oil-soluble (Table 1). Some chemicals are not soluble in either.

Table 1. Mode of entry into the cell through the cell membrane of basic chemical types important to organisms. Most chemicals important for life can be fitted into a 2 by 2 table: inorganic (or without carbon) vs. organic (or carbon-bearing) and water- vs. oil soluble.

	Inorganic Compounds (chemicals without carbon)	Organic Compounds (chemicals with carbon)
Water-soluble chemicals, such as ions	Through proteins (pores, gates, or carriers); "game of mistaken identity" (p. 15)	Through proteins (pores, gates, or carriers); "game of mistaken identity" (p. 15)
Lipid-soluble chemicals	"…can move around within an animal without constraint." (p. 15)	Can move without constraint, however, these compounds are often associated with larger charged proteins making their entrance into cells difficult.

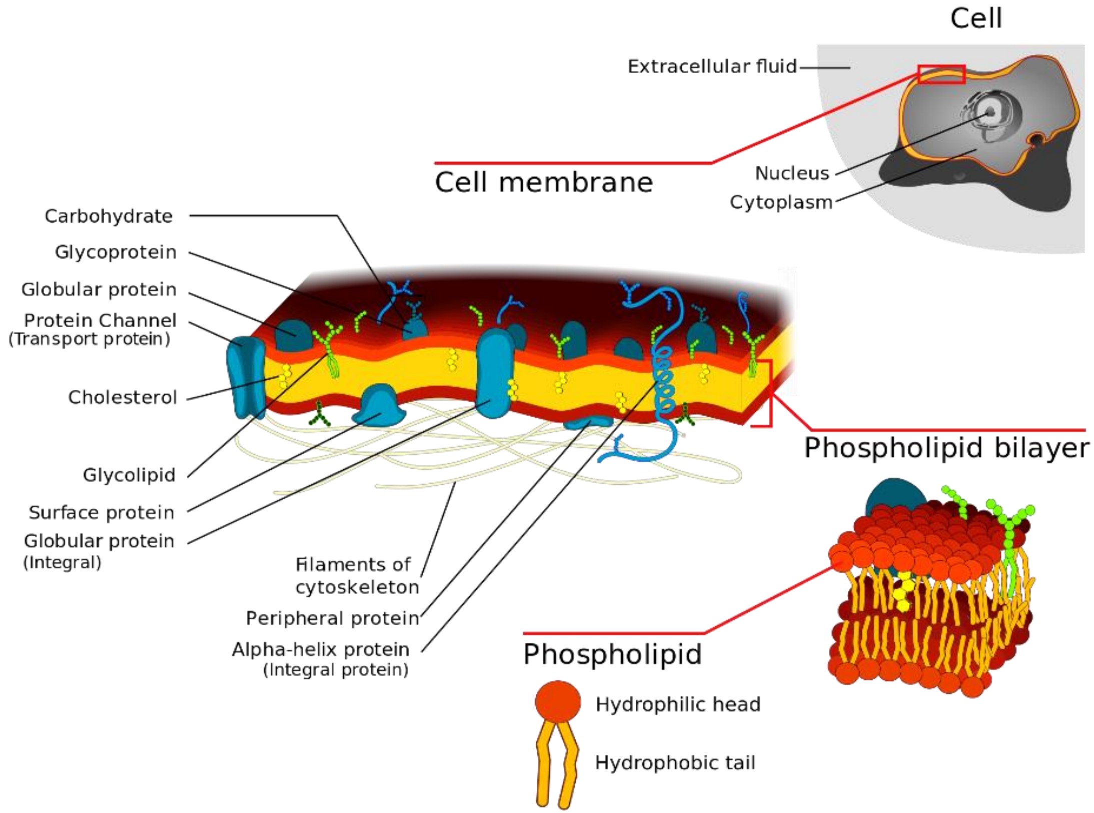


Figure 3. Diagram of the cell membrane of eukaryotic cells, such as plants, fungi, animals, etc. Image from: https://upload.wikimedia.org/wikipedia/commons/thumb/1/11/Cell_membrane_detailed_diagram_3.svg/2000px-Cell_membrane_detailed_diagram_3.svg.png

One important aspect of science is experimentation. *The Human Animal* (Chapter 3) explains that all organisms have a common genetic heritage (Figure 4). For many practical reasons, scientific ideas are not tested on every single species. Yet, as more diverse types of organisms are tested, greater confidence is generated so that the principle is generally applicable to all forms of life.

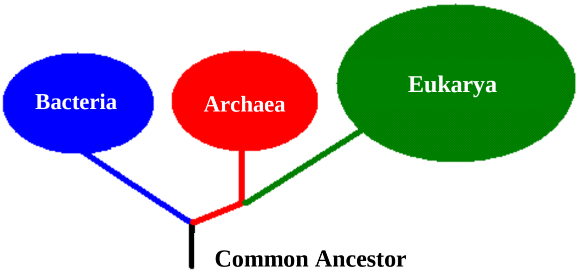


Figure 4. Basic family tree, or phylogeny, of the domains of life. Note the common ancestry of all life, https://upload.wikimedia.org/wikipedia/commons/3/3e/3_domains_of_life.png , ovals in the figure with slight modifications on the labels. These types of genetically-based trees are the basis for scientists' ability to use model organisms and apply the principles learned to other, non-model organisms. Importantly, the Bacteria have been shown to possess the greatest molecular diversity of all domains. Author: C3lin.

Although the model organism approach is often called "Krogh's Principle", like so much in the history of science, this idea is older. In 1865 Claude Bernard (*Introduction à l'étude de la médecine expérimentale*) said (translated from French), "In scientific investigation, each process is of the utmost importance. The happy choice of an animal, an instrument built in [an appropriate] way, the use of a reagent instead of another, are often enough to solve the highest general questions." For years, "the happy choice" of an organism is the basis of the model organism approach to biological sciences. In neurobiology, for example, a genus of squid, *Loligo*, which is endowed with very large axons, has served as a model organism. The forces of evolution, such as genetic drift, mutation, migration, non-random (or assortative) mating, and natural selection, have introduced genetic differences among living things. These genetic differences, in part, explain the differences in susceptibility of different organisms' nervous systems to the same chemical under controlled conditions.

How do chemicals get into the body from a source? *Chemical Journeys: Absorption* (Chapter 4) discusses the different pathways, such as: 1) through the skin, 2) via the respiratory organs (gas exchange), such as lungs, and 3) via the digestive system (ingestion, Figure 5). The dose and the chemical makeup of the substance are as important in toxicology as the physical barriers the body imposes on the passage of all substances through the cell membranes. Once a chemical is absorbed, it is truly "inside" the body. Once the chemical travels through the body, via the blood or whatever other ways it may do, the substance reaches the cells. If the chemical gets inside the cells, what can happen to the molecules? Just as in the case of Napoleon Bonaparte's death, toxic chemicals can be sequestered by the body.

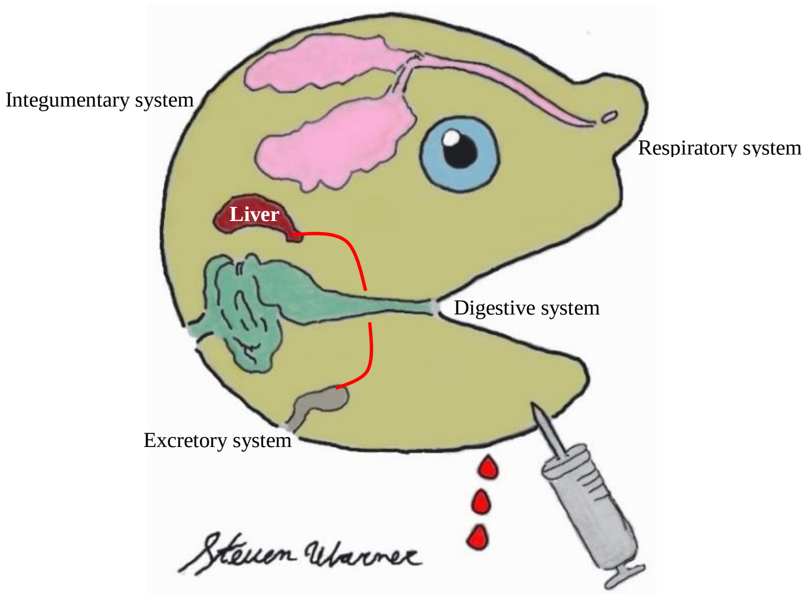


Figure 5. Modes of entry of toxins (skin – integumentary system, facilitated if wounded; nose – respiratory system; and mouth – digestive system). Depending on the organism and toxins, the body may dispose of them in diverse ways (sequestration, chemical transformation, excretion, including the liver) in a generic animal. Concept by author JASB, drawing by Steven Warner (McLean, Virginia, USA).

In addition to sequestration in less vital parts of the body, such as fat cells, if a toxin gets into a body, organisms can defend themselves using several mechanisms (Chapter 5, *Bodily Defense*). For instance, the chemical can be chemically transformed in the body and eventually removed via different avenues of excretion (e.g., urinary system, respiratory system, etc.). If the concentration of toxic molecules is too large, the body may not be able to handle all of them and negative effects may ensue.

On Chapter 6, *Wider Journeys: Pollution*, we learn that the world can be divided into realms or compartments: the atmosphere, the hydrosphere, lithosphere, and the biosphere. In each, different components, air, water, and solids, respectively, predominate. Living things are particularly abundant at the intersection of those three and form the biosphere (Figure 6). Cycles of matter and flows of energy happen in those spheres (Figure 7). Once inside organisms, toxic chemicals may reach the target cells and may become bioactive. If those chemicals are accumulated, their concentrations may increase as organisms become food items of others (Figure 8), as in the case of the Clear Lake (California) Gnat, *Chaoborus astictopus* Dyar and Shannon, 1924, a fly placed in the family Chaoboridae, leading to biological magnification.

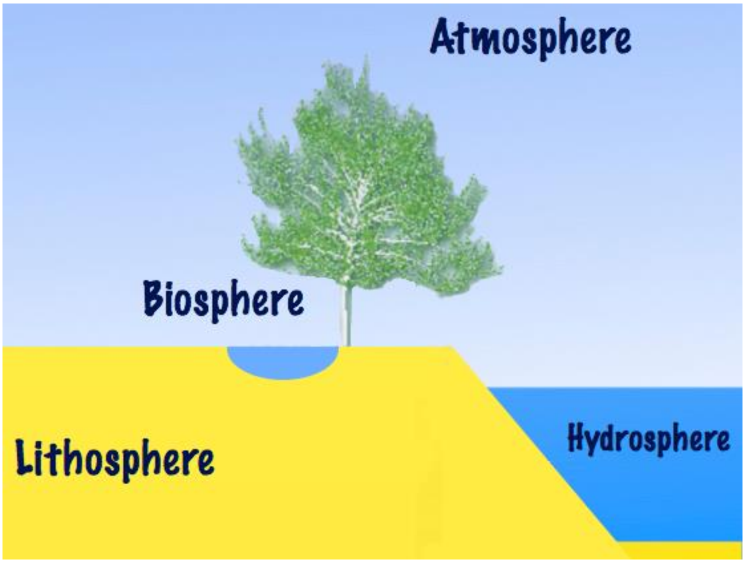


Figure 6. The "spheres", or compartments, of Earth. Author: CK-12 Foundation. Image from https://commons.wikimedia.org/wiki/File:Atmosphere-Biosphere-Hydrosphere-Lithosphere.png

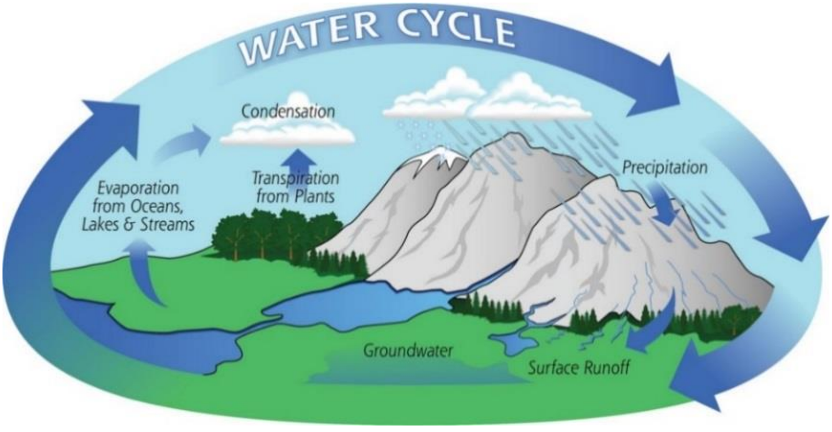


Figure 7. An example of how matter cycles in nature: the hydrologic cycle. Image from NASA. Source: https://c1.staticflickr.com/9/8083/8265046380_4bfb79a5c4_b.jpg

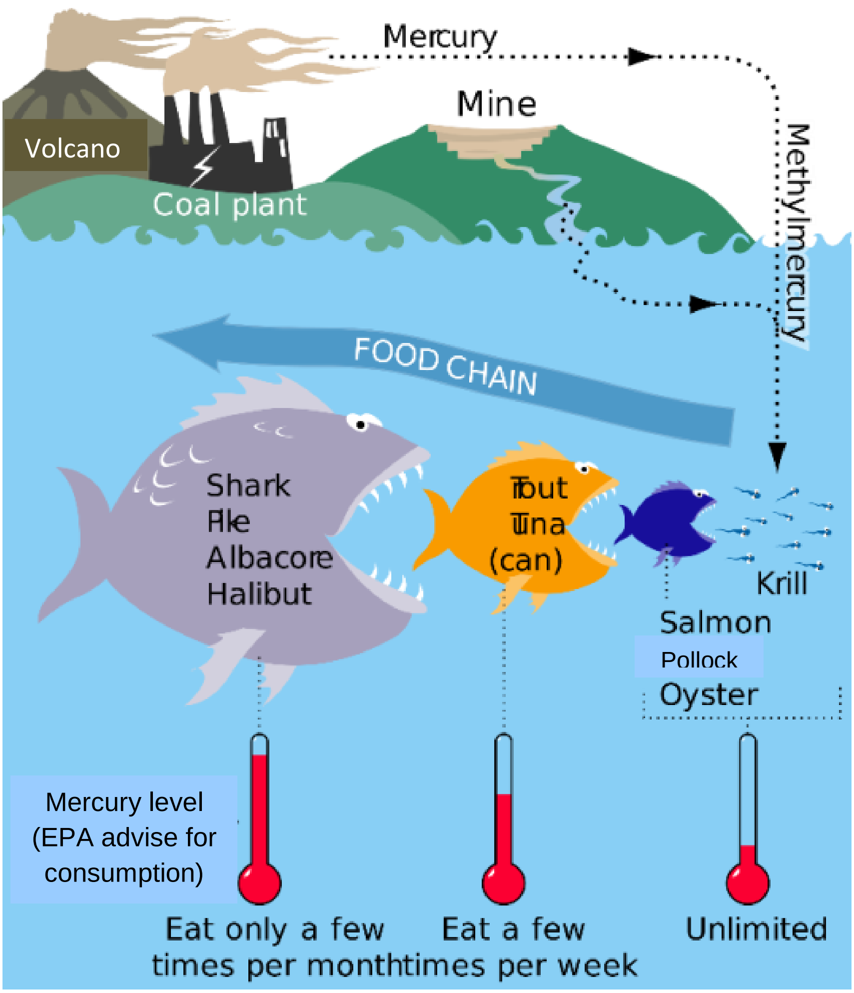


Figure 8. An example of biological magnification. As a chemical gets sequestered in organisms and passed through the food web, its abundance in the sequestering tissues increases. Author: Bretwood Higman, Ground Truth Trekking. Source: http://www.groundtruthtrekking.org/Graphics/MercuryFoodChain.html . Font of some text modified by JASB.

Small Particles (Chapter 7) teaches us that tiny soil particles, colloids, which tend to have a negatively charged surface, can serve as conveyors of toxins between the lithosphere, and/or the atmosphere, and/or the hydrosphere. A basic classification of soil textures is given in Figure 9. Colloids are often found in clay or humic soils. In water, colloidal particles tend to aggregate forming larger particles. The little spaces between the small particles tend to retain toxic compounds, particularly in slow-moving currents. In the air, colloids are generally dry yet they can also carry toxins (Figure 10).

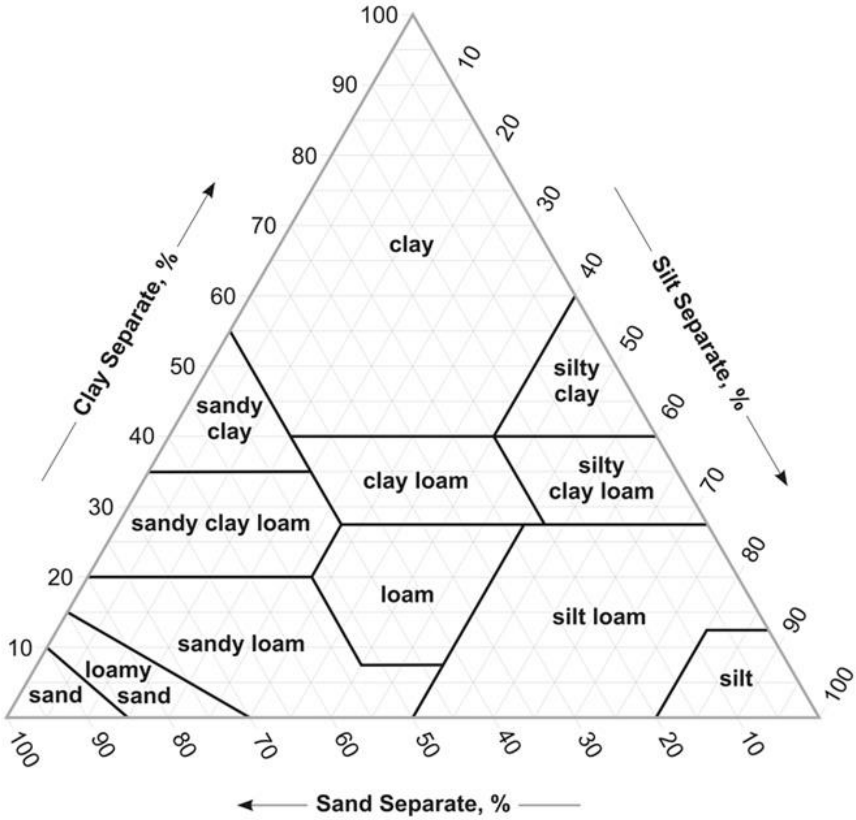


Figure 9. Soil texture triangle. Image from: http://www.nrcs.usda.gov/wps/portal/nrcs/detail/soils/edu/kthru6/?cid=nrcs142p2_054311

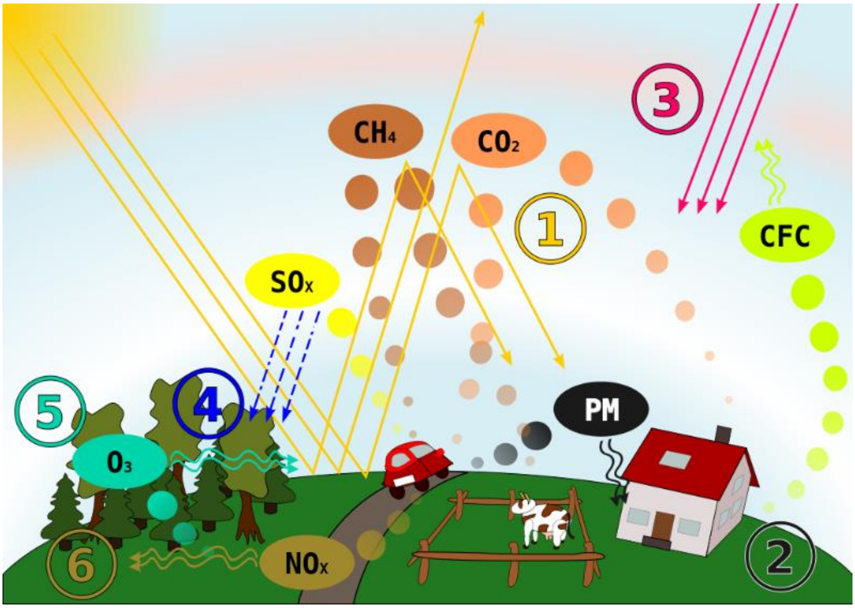


Figure 10. Causes and effects of air pollution: (1) greenhouse effect, (2) particulate contamination, (3) increased UV radiation, (4) acid rain, (5) increased ground level ozone concentration, (6) increased levels of nitrogen oxides. O_3 is ozone, NOx represents oxides of nitrogen, SOx represents oxides of sulphur, PM is particulate matter, CH4 represents methane, CO2 is carbon dioxide, and CFC represents chlorofluorocarbons. Image from: https://en.wikipedia.org/wiki/Air_pollution#/media/File:Air_Pollution-Causes%26Effects.svg

Having worked with (and been stung by) venomous animals, I am often asked to look for information at a poison control center. Chapter 8, *Toxins, Poisons, and Venoms*, discusses these biological compounds (Figure 1). How do venoms, those hazardous substances that are injected, work? They can alter: 1) the neuromuscular junction (Figure 12), 2) the nerve to nerve junction, or 3) the circulatory system.

Metals (Chapter 9), drugs (Chapter 11), and pesticides (Chapter 12) have had a powerful impact on human civilization. Chapter 9, *Metals: Gift and Curse*, sheds light on these important components of human civilization. Metals tend to lose one or two electrons, forming ions and reacting with other substances. Metals generally enter animal bodies through ingestion, as in the case of boiled wine, or *sapa*, or boiled *amurca* from olives. In the case of aquatic animals, metals enter the body through the respiratory organs, such as gills. Metal-carrier proteins, located in the cell membrane, bring the correct (and sometimes the incorrect) metal ion into the cell. The impact of metal ions on living things depends on many factors, such as the relative concentration of colloidal materials in water. This is known as the biotic-ligand model.

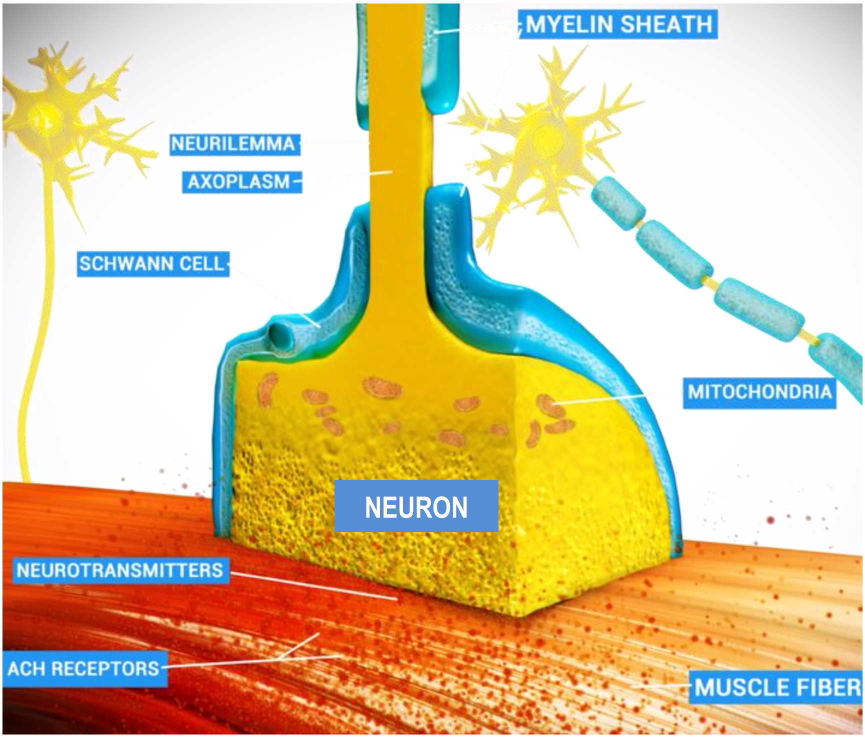


Figure 12. The passage of a nerve impulse, through the nerve cell, or neuron, to a muscle. Image from https://en.wikipedia.org/wiki/Neuromuscular_junction#/media/File:Neuro_Muscular_Junction.png The label, "neuron", was added by author JASB.

In *Combustion*, Chapter 10, Kolok presents another historical example supporting the statement that cancer-causing chemicals can be present in the environment in which we are immersed, as in the case of British climbing boys of the 1700's who used to clean the products of combustion present in chimneys. Showers and protective clothing could have prevented their maladies. Another example of cancer, or uncontrolled cell division, caused by chemicals is that of the polyaromatic hydrocarbons (PAHs). These carbon-rich compounds may cause mutations, or changes in the DNA, that, at times, may alter the pattern of cell division by transforming genes regulating cell division, like proto-oncogenes, into genes that accelerate cell division (Figure 13). In other cases, genes that protect cells from cancer, called tumor-suppressor genes, can mutate and lose their protective function.

Any chemical that alters "normal" cellular function is considered a "drug". Chapter 11, *Drugs and the Toxicology of Addiction* discusses numerous examples of such chemicals. We may believe that drugs are a modern phenomenon but these chemicals have been around for millennia. For time immemorial, people have chewed coca or areca-betel leaves as pain-killers, or use drugs to socialize and/or to attain what some of us like to call “altered states of consciousness”. Some drugs are addictive, as they lead to seeking more of them as they stimulate the reward centers of the brain. Oher drugs cause dependency by altering the “normal” state of cells.

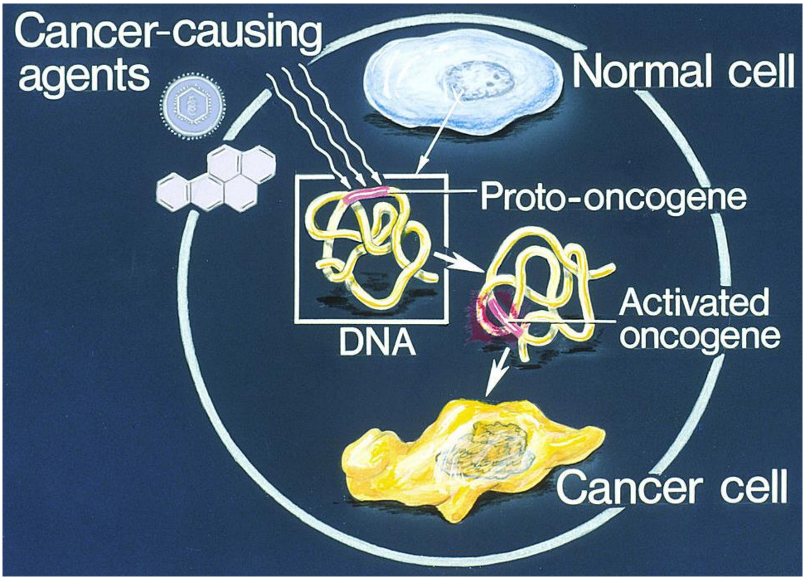


Figure 13. A mechanism of cancer: the formation of activated oncogenes. https://upload.wikimedia.org/wikipedia/commons/thumb/d/de/Oncogenes_illustration.jpg/1200px-Oncogenes_illustration.jpg

Years ago, a paper that could not be published in the pages of *Life: The Excitement of Biology* dealt with bed bug control in dormitories using plant products. This idea is not new as Chapter 12, *70,000 Years of Pesticides*, reveals. Botanicals and mineral compounds were the so-called first generation, or wave, of “pesticides” and they were introduced as ways to get rid of unwanted organisms, or pests. Simultaneously, biological control agents, many of them insects, were tested with some success. The second wave of pesticides began in in the late 1930’s to 1940’s with the meteoric rise in the use of dichlorodiphenyltrichloroethane (DDT, Figure 14). DDT, however, is a lipophilic and it penetrates cells. Recently, a new PBS (USA’s Public Broadcasting Service) television special on Rachel Carson, the author of *Silent Spring*, aired. The treatment of Carson greatly expanded on her personal life and on the political atmosphere at the time and on the impact of her work had after her death[3]. Topics, such as biomagnification (Figure 8), became part of the cultural discourse.

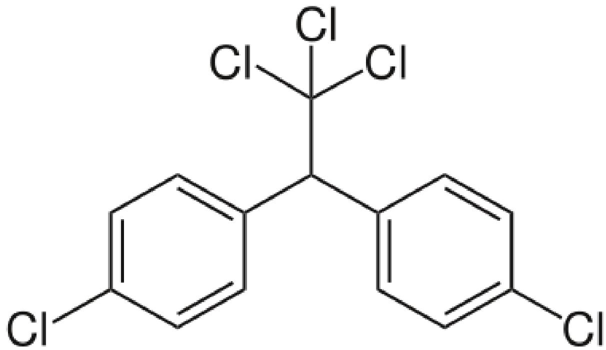


Figure 14. A depiction of a molecule of dichlorodiphenyltrichloroethane (DDT). https://en.wikipedia.org/wiki/Dichlorodiphenyltrichloroethane#/media/File:P,p%27-dichlorodiphenyltrichloroethane.svg

Have you ever wondered why are there so many rules pertaining to what we can ingest? Chapter 13, *The Origins of Regulation*, sets the stage of the USA by the end of the 19th century. As someone who examines relatively older literature regularly, I can attest to the numerous advertisements I have read containing what looked like "bogus claims … regarding the therapeutic capabilities" of products. In the USA, the trend towards regulation of these products in the second half of the 19th century involved several factors, including the urbanization of our country as well as the increased concern for food and drug safety. In the USA, Harvey Wiley (Chief Chemist of the Division of Chemistry, US Department of Agriculture) spearheaded the testing of products, sometimes using methods we would now consider questionable. The efforts of Wiley and his "poison squad", along with the publication of *The Jungle*, contributed to the creation of the US Food and Drug Administration (FDA) in 1906. The importance of the FDA was augmented by the mishaps resulting from the use of chemicals (e.g. Prontosil) that were later found to be toxic to humans as well as the accelerated manufacturing of newer chemicals (e.g., thalidomide) and use of radiation during and after World War II by the so-called "military-industrial complex"[4].

---

[3] For additional information, please consult these references: Kinkela, D. 2011. *DDT and the American Century. Global Health, Environmental Politics, and the Pesticide that Changed the World*. The University of North Carolina Press, Chapel Hill, North Carolina, USA. 256 pp. Lear, L. J. 1992. Bombshell in Beltsville: The USDA and the Challenge of "Silent Spring". Agricultural History 66(2):151-170. Rubin, C. (Foreword by R. Bateman). 2003. *How to Get Your Lawn & Garden off Drugs*. Second Edition. Harbour Publishing. Toronto Ontario, Canada. 126 pp.

[4] The expression, military-industrial complex, comes from the farewell speech of former US President, Dwight D. Eisenhower (Eisenhower, D. D. 1961. *Military-Industrial Complex Speech, Public Papers of the Presidents, Dwight D. Eisenhower, 1960*, pp. 1035-1040,

Days before completing this book review, a person I consider trustworthy communicated to me a case where a friend had been slowly poisoned and killed using tainted meats. Chapter 14, *Low-Dose Chemical Carcinogens*, made me remember the products some of us consume. The change in food processing was parallel to urbanism in the USA and to the technological changes in the drug and pesticide industries. In the context of foods and their additives, what is "safe"? Generally regarded as safe is "the risk to humans of developing cancer within one person's lifetime is less than one in a million". A sweet case in point is that of artificial the sweetener, cyclamate, a possible cancer-causing agent. It took years to get cyclamate banned in the UK and the USA although it is allowed in many other countries. How many food items do we ingest that are not good for us?

In chapter 15, *POPs and Silent Spring*, Kolok introduces us to the historical disconnect between the so-called "closing" of the western frontier and the feeling that the USA was still vast (*Digital History* 2016. http://www.digitalhistory.uh.edu/disp_textbook.cfm?smtID=2&psid=3154). It was realized that some chemicals can act slowly and that diluting waste products was not sustainable. In the USA, *Silent Spring* catalized major laws pertaining to the environment (e.g., Clean Air Act 1963, Clean Water Act 1972, Figure 15). New discoveries mave shed light on how those chemicals persist in the environment (Figures 16-17).

In brief		
'Precautionary principle'	Fundamental part of risk management	Concept not endorsed as a basis for policy making
Societal, economic, ethical or environmental concerns	Taken into account in risk management decision in line with the consumer right to information and choice	'other factors' considered as barriers to trade
Approach to ensuring food safety	Integrated "farm-to-fork" approach	Safety mostly verified at the end of the process
Food risk evaluation	Full scientific assessment by EFSA for regulated products such as GMOs and additives.	Largely relies on companies' own private assessment

Figure 15. Some environmental principles in modern environmental laws. Image from http://capreform.eu/wp-content/uploads/2014/06/US-EU-comparative-food-regulatory-approaches.jpg

---

http://coursesa.matrix.msu.edu/~hst306/documents/indust.html). It has been suggested that other expressions, such as "military–industrial–congressional complex" or "military–industrial–academic complex" were present in earlier versions of Eisenhower's speech (Wikipedia Contributors. 2017. *Military–industrial complex*. Accessed on April 11, 2017).

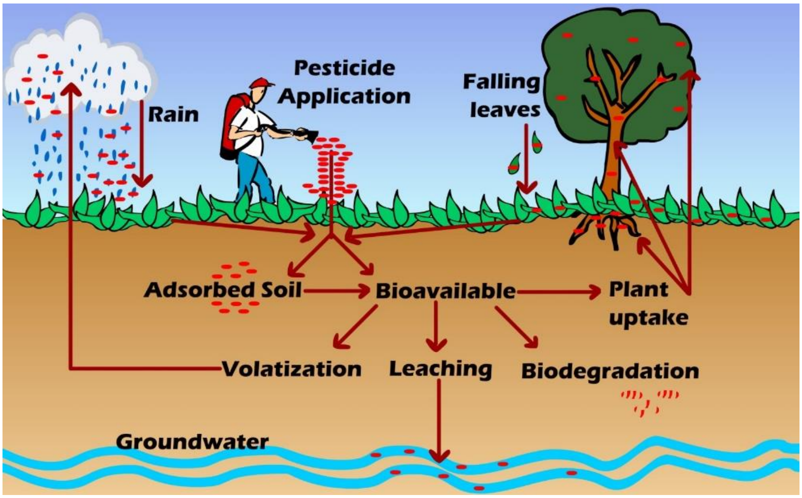


Figure 16. Some possible fates of pesticides in the environment. Image from https://www.intechopen.com/source/html/45279/media/image5.jpeg

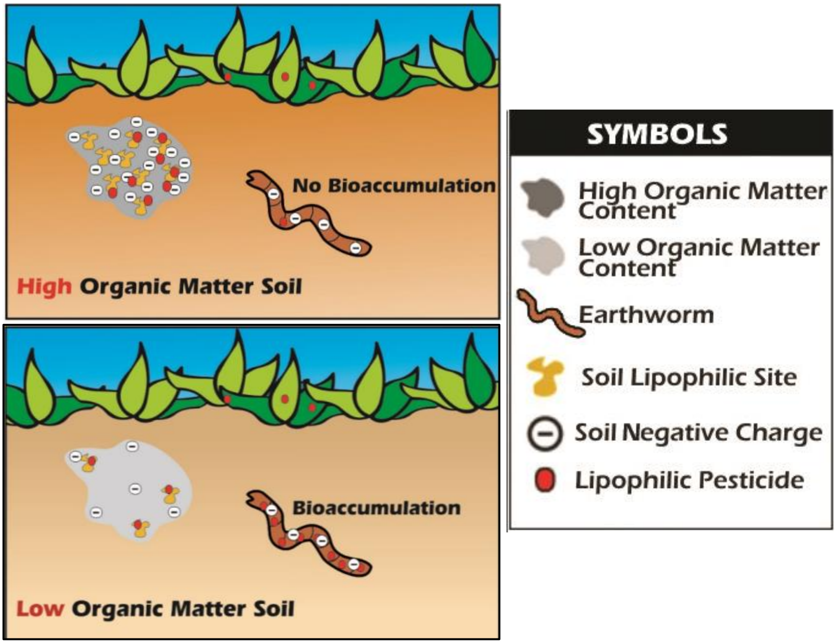


Figure 17. After adsorbed in the soil, some pesticides become part of organisms and where they increase in concentration, or biomagnify, as we move through the food web. Images from https://www.intechopen.com/source/html/45279/media/image2.jpeg .

Chapter 16, *Toxic Toiletries*, discusses the work of Kolpin and collaborators at the United States Geological Survey during 1999-2000. They detected tiny amounts of all sorts of drugs and cosmetics in numerous streams. Dramatic examples include some hair straighteners with bioactive hormones as they contain extracts from animals' placentas. While some of those products "have been shown to increase hair follicle growth", some can have negative health effects, "including "premature development of secondary sexual characteristics (breast development and pubic hair growth)". There are many studies that demonstrate the negative effects of some of those products in non-human organisms (see also Figure 18).

Figure 18. Image taken from https://s-media-cache-ak0.pinimg.com/564x/ee/8a/a9/ee8aa90de3f486bc00e2c95008b01b2c.jpg

During my long professional career, I have had the privilege of teaching many non-science major students. Few topics captivate them – as well as the science or biology majors – more than matters pertaining to reproductive functions. In my classes, I teach that the way humans do things varies immensely. However, the human way is only a small set among the colossal variability of how other organisms work. Chapter 17, *Determining Sex: Chemicals and Reproduction*, exemplifies this and it constitutes a great introduction to the amazing diversity of sex determination mechanisms (genetic and environmental, including temperature Figure 19). How organisms develop their biological sex is not trivial. In humans, numerous steps must work perfectly for a human with a karyoformula of 22 pairs + Xy in his cells to become a boy. One of those steps is the correct functioning of the Sex-determining Region Y (SRY) located in the y chromosome of human males (Figure 20). The development of sex organs is only one aspect of sexual development. What happens if twins (one a male and the other a female) are developing in the same uterus? In cattle, for instance, the female calf will be sterile, called "freemartin", owing to the effect of the neighboring developing male. For eons, humans have attempted to control their reproduction. One of those means has been birth control pills. Although there are various kinds of birth control pills, they have human-made hormones that fool women's bodies into not releasing an ovule every (approximately) 28 days, thus preventing ovulation. Where do we think those synthetic hormones go? Eventually, into the water.

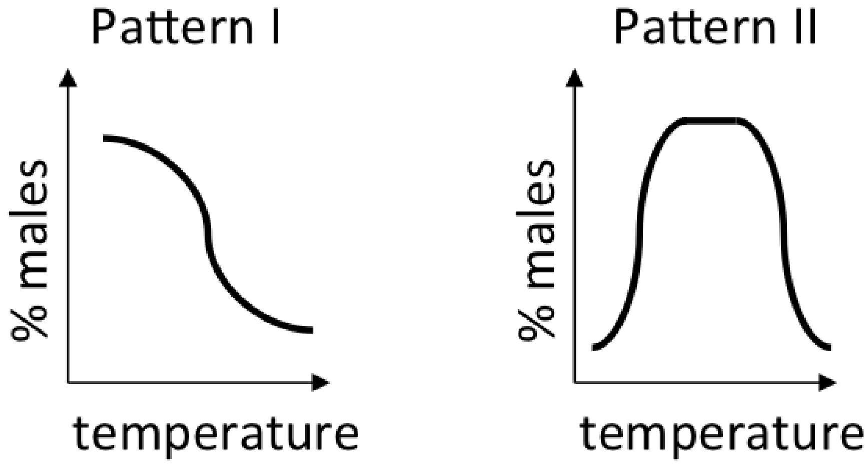


Figure 19. Sex determination can involve environmental factors, such as temperature, as in some reptiles. Image by Peteruetz - PPT, CC BY 3.0, https://commons.wikimedia.org/w/index.php?curid=35348457

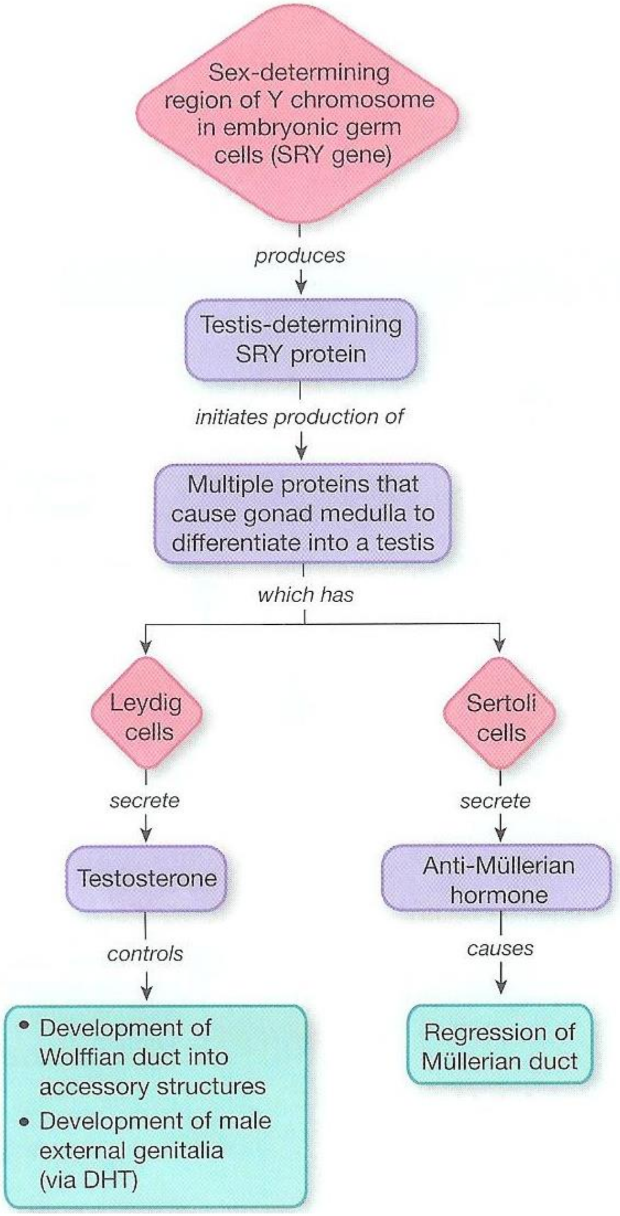


Figure 20. Sex-determining Region Y (SRY) action pathways in humans. This gene, among others, is involved in the development of testicles and in preventing the formation of female reproductive structures. Image taken from https://upload.wikimedia.org/wikipedia/commons/c/c7/SRY_Gene_Pathway.jpg

Numerous studies have shown that those water-borne synthetic hormones can target and alter the expression of male fish reproductive organs making them also develop female reproductive structures, a condition known as intersexuality. Birds that eat those fish experience the effects of those added hormones as decreased interest in reproducing (See Figure 8). Thus, the interactions of genes and hormones can control the development of sex organs. Yet, in other organisms, temperature determines whether an organism will develop as a male or a female. If you have found this interaction between genes and the environment complicated, think now about the psychological expression of our sexuality, gender, as in the rich variety of human expressions, such as male, female, gay, lesbian, bisexual, transsexual, queer, intersex, and asexual.

As an example of environmental effects, I tell my students that if we eat a lot we will gain weight. The molecular mechanisms pertaining to the understaning of environmental effects may include changes in the DNA (or mutations), changes in packing of the DNA, changes in the RNA messages that turn on/off the production of proteins, etc. Importantly, chapter 18, *The Earliest Exposure: Transgenerational Toxic*ology, also discusses the not obvious and cutting edge effects: can our actions affect developing children and the reproductive cells of those developing children (Figure 21)? Evidence supporting the existence of transgenerational effects has come to light with studies of famines, stress, etc. This brings an old biology theme back: is heredity just DNA? Although DNA "won", since, at least, the 1850's, there has been an undercurrent of answers that have included the key role of the environment in heredity. For more information on epigenetics, the interested reader should watch any one or more of the slightly different videos entitled *Ghost in Your Genes*.

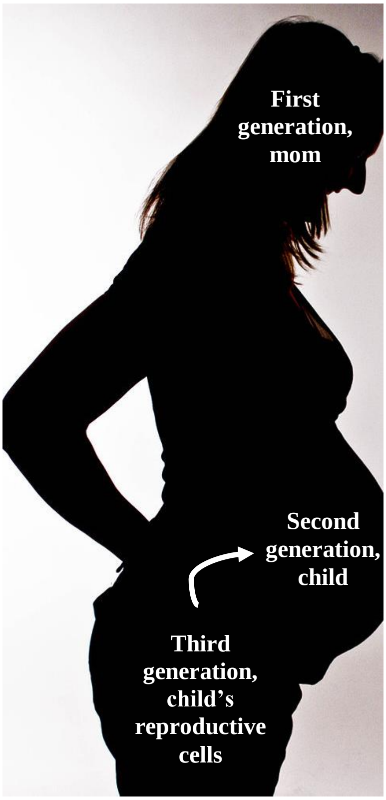
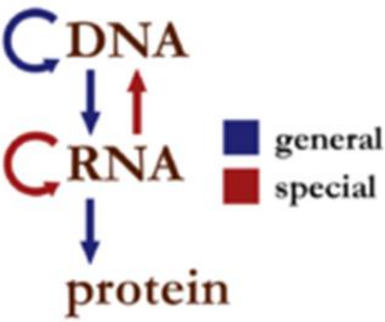


Figure 21. Epigenetic effects: the mother is the first generation, the developing human is the second generation, and the reproductive cells developing in the developing human, the third generation. Image from https://upload.wikimedia.org/wikipedia/commons/thumb/8/86/Silhouette_or_a_pregnant_woman_and_her_partner-14Aug2011.jpg/840px-Silhouette_or_a_pregnant_woman_and_her_partner-14Aug2011.jpg

Chapter 19, *Natural Toxins Revisited*, explores the interface between natural toxins and infectious agents. Infectious agents, reproduce using the nucleic acid machinery, following the so-called "central dogma of genetics" (Figure 22). In contrast, natural toxins are chemicals produced by organisms that have a harmful effect in another organism. Interestingly, that harmful effect does not depend on the organism being alive, as in the case of urushiol, the lipid-soluble chemical produced by many plants, including those in the mango and cashew family, the Anacardiaceae. A relatively mild example of the potent dermatitic effects of urishiol are illustrated in Figure 23. But, what are we to make of proteins, such as prions? Prions are modified proteins that can induce other normally and functional proteins of its kind to misfold. This incorrect folding is not just a matter of curiosity. There are practical medical consequences to some of these misfolded proteins, such as mad cow disease, Creutzfeldt-Jakob disease, and other conditions believed to be caused by these agents, prions, which as far as it has been searched, lack nucleic acids. In other words, prions are proteins that make more of themselves without DNA or RNA.



Figures 22-23. 22. The so-called central dogma of genetics. In its most basic inception, it says that the hereditary information is encoded in DNA and transmitted to RNA molecules (transcription) that, eventually, encode for proteins (translation), https://upload.wikimedia.org/wikipedia/commons/thumb/0/06/Centraldogma_nodetails.png/160px-Centraldogma_nodetails.png The curved arrow next to DNA represents DNA semiconservative replication. The curved arrow next to RNA represents the ability of RNA to make more RNA. The arrow going from RNA to DNA represents reverse transcription. 23. A case of inflammation of the human skin or dermatitis caused by contact with urushiol from a poison https://upload.wikimedia.org/wikipedia/commons/thumb/f/f6/Poisonivyrash.jpg/233px-Poisonivyrash.jpg

Have you considered how is it that some bacteria appear to be harder to eliminate these days? Chapter 20, *Chemical Resistance*, discusses the development of resistance in organisms. Besides the intriguing ideas of epigenetics, namely the effects of an environmental factor in subsequent generations that have not been exposed to that factor, there are five major forces responsible for the generation or the spread of resistance. These forces of evolution are: genetic drift, mutation - the ultimate generator of totally new variants in a population, migration, non-random mating, and natural selection. Genetic drift (Figure 24), the beetles randomly killed happen to be green) refers to random changes in gene frequencies which are especially pervasive when the size of a population is small. Mutations are changes in the genetic material. Mutations are classified in two categories: small (affecting a small number of building blocks, or nucleotides, of the DNA) or large (affecting many nucleotides, Figures 25-26). Both genetic drift and mutation are considered "random" forces with respect to the direction of evolution, such as pesticide or drug resistance. Namely, resistance does not evolve "because" a pesticide or a drug directed the organism to develop resistance. Instead, as new variants of a gene enter in a population, every so often one variant may happen to serendipitously confer the organism with the ability to resist a pesticide or a drug. Resistance can spread by migration of individuals carrying the variant from one site to another, as they move by themselves or on a host, such as humans. Natural selection is the differential survival of different organisms in a population of the same species. In contrast to the previous two agents, genetic drift and mutation, natural selection tends not to be random, instead, it favors individuals with specific characteristics, or fitter (not fittest) to a specific environment. Pesticide and drug resistance are excellent examples as organisms that cannot handle the chemical will be precluded from surviving (and reproducing). Those that make it through the chemical challenge, will be available for passing the reistance to future generations. In bacteria, small circular pieces of DNA, known as plasmids, greatly facilitate the process of drug resistance during sexual reproduction by sharing plasmids with other bacteria. If the bacteria receiving the plasmids were sensitive to the drug, they will now be resistant.

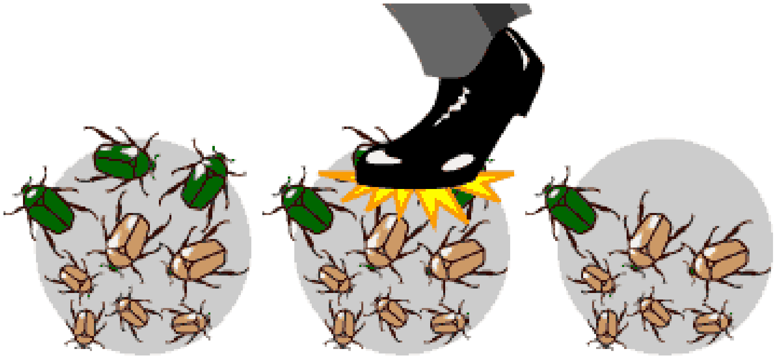


Figure 24. Someone may inadvertently remove a disproportionately number of insects carrying the genes for a specific color (or in this context, pesticide resistance). Everything else equal, the frequencies of the color variants in the genes would have been altered for the next generation. Image from http://hodnett-ap.wikispaces.com/file/view/geneticdrift.gif/228215374/geneticdrift.gif

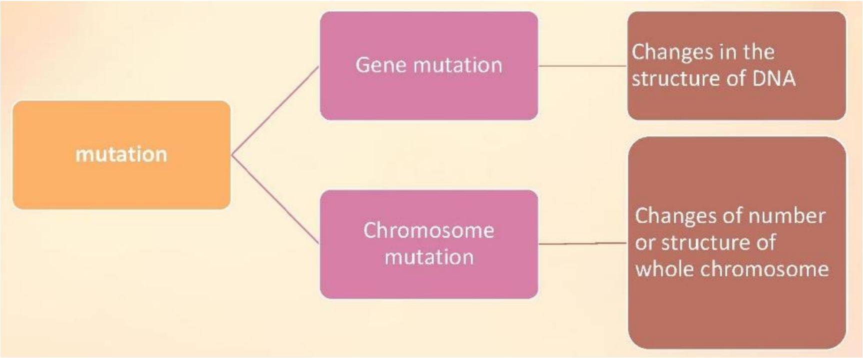


Figure 25. A classification of mutations: small (or "gene mutations") and large (or "chromosomal mutations"). Image from http://www.ask4biology.com/wp-content/uploads/2013/02/Mutation.jpg

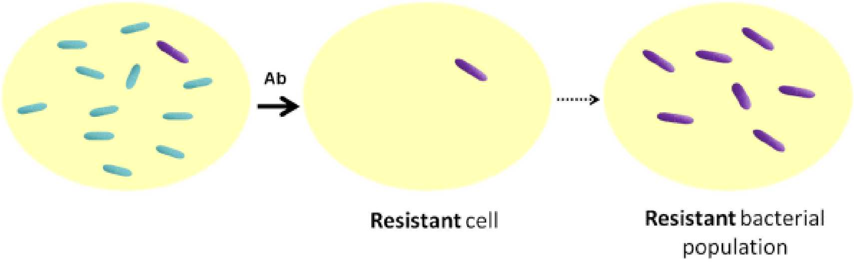


Figure 26 Simplified version of evolution of antibiotic resistance in bacteria. Image from http://4.bp.blogspot.com/-gBazqhef_1Y/U79ZsfmGDuI/AAAAAAAAAzI/mr59y2s-KNs/s1600/Suarezfig1final.gif

The twenty relatively short chapters are followed by an *Afterword*, which reminds readers of the importance of lipid solubility and the ability of living things to chemically transform toxins. Also, emphasis is placed on the future of toxicology through three areas: the effect of small particles, the variety of chemical interactions (Figure 27), and the possible effects of global climate change (Figure 28).

A generous section of additional resources, *References*, for those who want to learn more, as well as an *Index* complete the book. Indeed, a motto of a promotion for this book, "Clear and jargon-free writing on toxicology" will be appreciated by any reader with learning at his/her heart.

Wholeheartedly, I recommend *Modern Poisons: A Brief Introduction to Contemporary Toxicology* by Dr. Alan S. Kolok to non-science major undergraduates and to anyone who may want to learn more about toxicology.

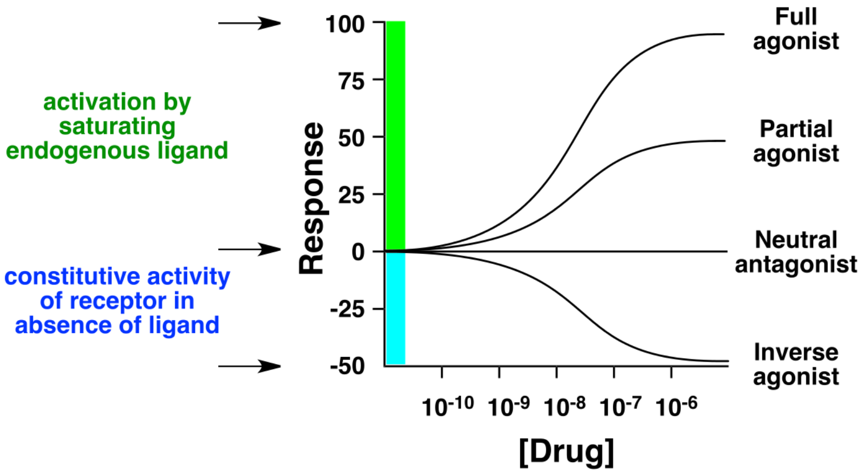


Figure 27. Basic interactions between two different chemicals. Some chemicals cause an increase in the action of another; they are known as agonists. Others cause no change in action ("neutral antagonists") or a decrease in the action of another; they are known as antagonists (or inverse agonists). Many of these effects are non-linear. https://upload.wikimedia.org/wikipedia/commons/thumb/6/6c/Inverse_agonist_3.svg/1200px-Inverse_agonist_3.svg.png

Figure 28. Exaggerated example of unexpected potential interactions between pesticide resistance by biting insects and global climate change. Image by Paula Williams, taken from http://time4wellbeing.wikispaces.com/file/view/CARTOONpwilliams.jpg/74952997/430x358/CARTOONpwilliams.jpg