SOME BASIC PRINCIPLES OF TOXICOLOGY

This exercise is designed to help you to understand some of the general principles that are important to toxicologists in their quest to understand the biological effects of chemicals. What follows is a description of several terms that will help you to understand how to think about foreign chemicals in natural systems. There are no reference materials necessary for this exercise except the list of Toxicology terms provided.

TOXICOLOGY

is a science that combines biology and chemistry to study poisons and their effect on biological systems.

Name several poisons.

Toxicologists talk about the **TARGET** of a toxicant. They are referring to the particular macromolecule, cell, organ or biochemical process that the toxicant disrupts. The way the toxicant is able to disrupt that process is called the **MECHANISM OF ACTION** of the toxicant. Not all toxicants are lethal. They may also cause disease, tissue damage, genetic alterations, cancer, etc.

For example, consider carbon monoxide (CO). This poisonous gas is released from the combustion of fossil fuels (car exhaust) and cigarette smoke. The CO molecule competes with O_2 for the same binding sites on hemoglobin. The hemoglobin molecule cannot distinguish between the two molecules, so CO gets transported in the blood instead of O_2 causing oxygen starvation of the tissues (in fact, carbon monoxide binds more tightly than O_2). At lower concentrations, this can cause changes in heart rhythm, headache, weakness, nausea, dizziness and dim vision. At greater concentrations, CO poisoning leads to unconsciousness, coma, convulsions and possibly death. The effects of CO intoxication can be reversible, except when severe oxygen deprivation causes permanent neurologic damage. Thus, the target of carbon monoxide poisoning is hemoglobin and its mechanism of action is competitive binding to hemoglobin causing hypoxia (oxygen deprivation).

Describe, in general terms, the target and/or mechanism of action for one of the poisons you named above.

Again consider the poisons you named. What organism do they effect? Humans? Animals? One of the primary ideas to appreciate in toxicology is that *all* living things are potential victims of poisons. We most often think of toxicant effects on humans and other animals, but all living things can be affected adversely by chemicals that are not part of their own metabolism.

Name a drug or chemical product designed to kill…

Bacteria _____

Fungi _____

Plants _____

Animals _____

SOME BASIC PRINCIPLES OF TOXICOLOGY

All living things are potential targets of poisons. So, too, all chemicals are potential toxicants. Paracelsus, a scientist from the Middle Ages, summed up this concept by stating "all substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy."

Restate this famous quote in your own words.

The simplest and most common substances can be toxic—even water.

How do you suppose water could be toxic?

Name at least 3 substances which you normally consider safe, and explain the circumstances by which they could be harmful.

You should now be able to realize the importance of those "circumstances" you described above. These conditions are critical to the study of toxicology and are described further below.

For an organism to have an adverse effect from a chemical, it must first have been in contact with it. This is called **EXPOSURE.**

Name at least 5 xenobiotics to which you have been exposed in the last 24 hours.

Next you might think about how you came into contact with those xenobiotics. The answer to this question determines the **ROUTE** of exposure. For example, you breathe in air pollutants, thus the first contact points in your body would be your nasal passages, airways, lungs, etc. (This would be the route of carbon monoxide poisoning.)

SOME BASIC PRINCIPLES OF TOXICOLOGY

Below are some other routes of exposure for humans.

For each type of exposure, list the organ(s) that will first have contact with potential toxicants.

Touch _____

Ingestion _____

Injection _____

Toxicologists are also interested in other characteristics of exposure.

Pretend you are a detective at a "toxic" crime scene, and think of as many questions as you can regarding the details of exposure.

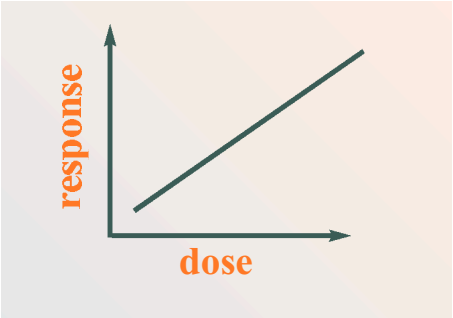
One question you may have imagined is something regarding the length of exposure, or duration. Toxicologists define two types of exposure based on its duration. **ACUTE** exposure is of brief duration. **CHRONIC** exposure is a persistent exposure, over a long period of time.

Think about oil spills from ocean tankers that transport the hazardous substance. You've probably heard about the Exxon Valdez spill in Alaska because of its magnitude, and the pristine area in which the spill occurred. This is an example of *acute* exposure to oil by marine fish, mammals and birds. Compare this to the *chronic* exposure that animals that live along tanker routes or near oil terminals receive from slow leaks and small spills that may not be nearly as great in magnitude, but occur much more frequently.

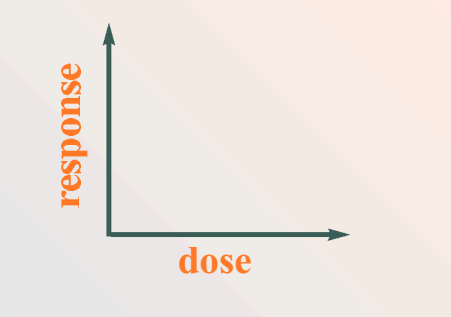
Which do you think is more significant? Why?

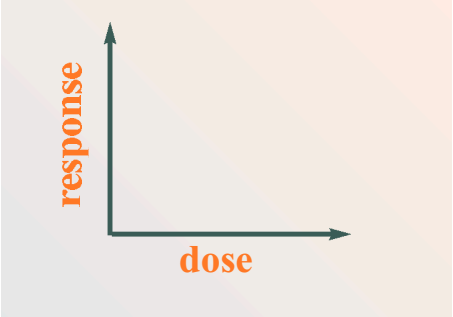
SOME BASIC PRINCIPLES OF TOXICOLOGY

Duration is not the only significant aspect of exposure. One of the most important questions that toxicologists ask about exposure is — "how much?" This is called the **DOSE**. This is important because for each chemical, a certain dose produces certain biological effects in the individual organism. Any biological effect caused by the exposure is called the **RESPONSE**. Most of the time, the greater the dose, the greater the response (as shown to the right), but this is not always true. Dose *vs*. response curves can take many different shapes. The previous graph depicts a linear relationship between dose and response.



Draw a dose *vs*. response curve when a toxicant has no response at low doses, but requires a high dose to observe a response. Draw another for a toxicant which produces responses at low doses, but at some larger dose, the magnitude of the response does not increase.





Earlier in this exercise, you listed at least 5 xenobiotics to which you were exposed in the last 24 hours. Did you experience any adverse effects to any of these chemicals? If so, describe these responses.

SOME BASIC PRINCIPLES OF TOXICOLOGY

Regulatory toxicologists control the toxicity testing that is done on foods and pharmaceutical products. They must think about: What responses are considered "adverse?" To what doses are the consumers most likely to be exposed? Further, they must define the risk associated with each chemical, and the level of risk that the public will accept.

For example, think about an allergic reaction as an adverse effect of a xenobiotic. The "toxicant" in this case might be a food or type of pollen. The adverse reactions vary from individual to individual. They might include skin rashes, asthma attacks, and even severe reactions (anaphylaxis) that, if untreated, can lead to death. One food that causes some allergies in people is peanuts.

Should regulators ban peanuts and peanut-containing food from the public market since it is a huge risk to some? Why or why not?

That was an extreme example, but regulators ask and answer these same types of questions when they set standards for food contaminants and drugs. The analysis of the nature and magnitude of risk is called **RISK ASSESSMENT**.

You have now been introduced to some of the basic principles of toxicology. Perhaps now the next time you sit down to a meal, take medication or breathe in some second-hand smoke, you will think of the toxicologist!

Describe something you have learned or thought about in a new way as a result of this exercise.