A Primer on Toxics

IN THIS CHAPTER:

"All things are poison and nothing is without poison. Solely the dose determines that a thing is not a poison."
Paracelsus (1493-1541)

Part 1: Toxicology Basics

Toxics are substances capable of causing injury, illness, or death by chemical means. "Toxic" is synonymous with "poison." **Toxicity** is a measure of the relative ability of a chemical to do biological harm. Many naturally-occurring substances are toxic, such as elemental arsenic, mercury and lead, snake venom, and poison ivy.

Toxics are a public health concern for many reasons:

- they can have severe and permanent effects on our health;
- they are so prevalent in our lives;
- the cause-effect relationships between toxics and human health are often poorly understood and difficult to identify;
- little is known about the effects of multiple chemical exposures or the interactions among various chemical metabolites; and

There is no such thing as a harmless chemical. Almost any substance is capable of causing injury, illness or death if it is present in a sufficient amount. For example, even ordinary table salt will kill a human if enough is eaten. Toxicity is relative: some chemicals are *more* toxic than others. The relative danger posed by a chemical is related to:

- **Dose -** How much of a chemical enters the body,
- **Route of exposure** - How the chemical enters the body**,**
- **Duration or frequency of exposure –** Whether an exposure is acute (single

- exposure) or chronic (prolonged or repeated exposure),
- **Response** – How the body handles it once it does enter, and
- **Vulnerability** – Different populations can respond differently to the same chemical (e.g., infants vs. adults).

Adverse effects of a chemical do not occur in a biological system unless that chemical reaches a target site in the body in sufficient concentration and for a long enough period of time to cause damage. In some cases, the body removes the chemical before it has a chance to take effect.

A. Dose

There is a very wide spectrum of doses needed to produce harmful effects. For example, Table 1 shows the various amounts of different chemicals needed to produce the same toxic response in lab animals, in this case to kill 50% of the animals tested. (This is referred to as LD_{50}, or the median dose lethal to 50% of a population).

Table 1-1. Approximate LD_{50} of some representative chemical agents.

Agent	LD_{50} (mg/kg)*
Ethyl alcohol	10,000
Sodium chloride (table salt)	4000
Ferrous sulfate	1500
Morphine sulfate	900
Ethylene glycol (antifreeze)	50
Nicotine	1
d-Tubocurarine	0.5
Hemicholinium – 3	0.2
Dioxin (TDCC)	0.001
Botulinum toxin	0.00001

*** LD_{50} is the dosage (mg/kg body weight) causing death in 50% of exposed animals (SOURCE: Klassen, Curtis, D., *Casarett & Doull's Toxicology: the Basic Science of Poisons*, Fifth Edition, 1996, p.14.**

Toxicologists study the relationship between the dose of a toxic chemical and the resulting effect using dose-response relationships. Some key aspects of dose-response relationships are:

- **potency:** the range of *doses* that produce increasing effects. A more potent chemical produces harmful effects at a lower dose than a less potent chemical;
- **efficacy:** the range of ***effects*** a chemical can produce at a given dose. A more efficacious chemical produces more effects than a less efficacious chemical;
- **threshold:** the lowest dose that will produce an effect;
- **hypersusceptibility:** individuals who respond to *significantly lower* doses than the average population
- **resistance:** individuals who respond to *significantly higher* doses than the average population.

B. Routes of Exposure

Exposure to chemicals may occur by the following routes:

1. inhalation (by breathing)
2. ingestion (swallowing)
3. contact with skin and eyes (absorption)
4. injection (piercing of skin)

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Generally, the fastest route of exposure is inhalation, and the slowest is absorption through the skin. The route of exposure can determine the biological system affected. For instance, ingestion affects the organs of the digestive system. But all blood supply from the digestive tract must first pass through the liver before entering the general circulatory system, thereby affecting that organ as well. However, the liver sometimes metabolizes toxics, decreasing their relative toxicity.

Employees who work with toxic chemicals are the most vulnerable to toxic exposure. However, all populations are at risk of exposure to chemicals. Toxic chemicals are pervasive in our society, and there is virtually no way to avoid at least some exposure to toxics from:

- Household products, such as cleaners, disinfectants, paints and pesticides;
- Food treated with pesticides;
- Natural sources such as radon gas (an invisible, odorless, but highly toxic material that occurs naturally in some environments); and
- Water, air, and soil contaminated by environmental releases from industry and other facilities.

LINK
A list of common food and agricultural products treated with pesticides is given in Chapter 3.

C. Duration and Frequency of Exposure
There are two types of toxicity:

- **acute toxicity** – the ability of a chemical to do damage to the body or its functioning as a result of a *one-time* exposure to a relatively large dose of a chemical. Acute toxicity is a concern, for example, when children are exposed to toxic household products left carelessly within their reach.
- **chronic toxicity** – the ability of a chemical to cause health effects as a result of *many repeated exposures* over a

Not all toxic effects are harmful. In fact, therapeutic drugs produce a number of effects, some of which are highly desirable.

prolonged period of time to relatively low levels of a chemical. Chronic toxicity is a concern when considering, for example, low-level occupational exposures to a chemical over a regular period of time. Individual exposures may not necessarily cause adverse health effects, but *cumulative exposures* to that chemical can result in a *threshold* effect at which point illnesses occur.

In most situations, it is the long term, low-level environmental exposures to chemicals in our communities, homes and workplaces – and the chronic effects of those chemicals – that are more common and cause more adverse health effects.

D. Response

In general, there are two broad categories of responses to toxics: acute and chronic responses. Acute responses range from skin irritation to coma or death. Chronic responses include cancer, liver disease, and nervous system damage.

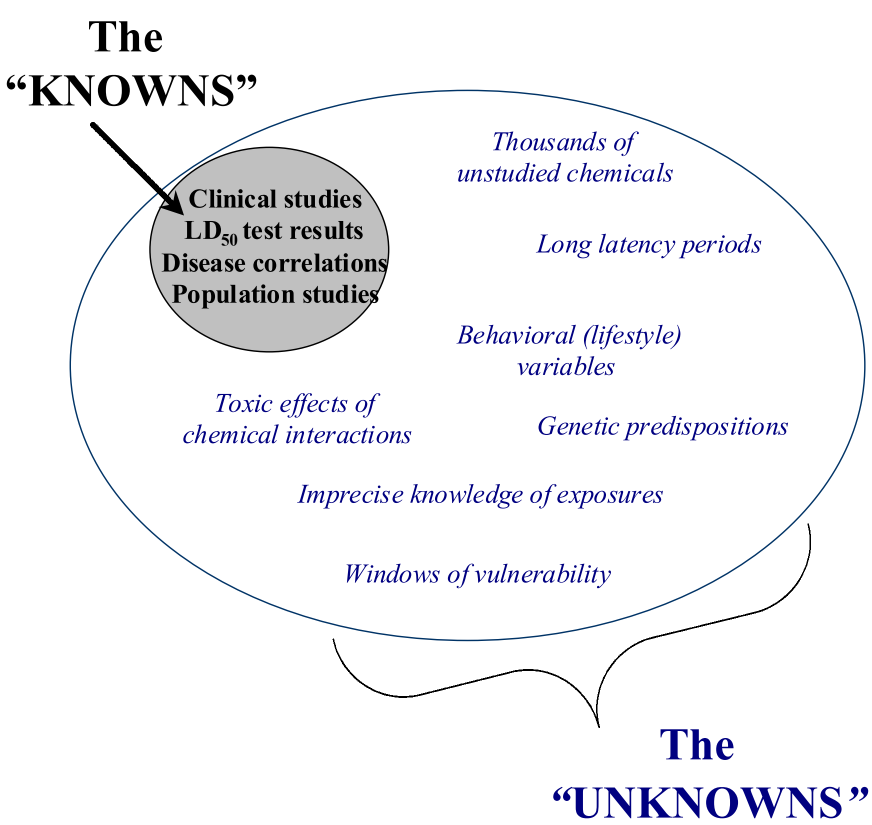
Acute effects are much easier to measure than chronic effects, simply because they manifest themselves so much more readily.

Chronic responses are extremely difficult to link to a particular chemical because there are so many variables to consider:

- Toxic effects are the result of complex interactions between many factors, such as genetics, previous exposure, duration of exposure and lifestyle.
- The toxic effects of some chemicals on an organism may be magnified by interactions with other chemicals.
- Many health effects of toxic chemicals are chronic (take many years to develop) which makes short-term analysis difficult.
- Risk factors, such as elevated mercury levels, are often determined by epidemiological studies

(studies on populations) rather than studies on individuals. These studies are costly and complicated. As a result, not all chemicals in commercial use today have been studied to determine the possible risks they pose to humans and the environment.

- Many toxic effects have been determined by lab animal tests, which do not necessarily predict actual effects of a toxic chemical on humans. Some evidence shows that animal studies may in fact *underestimate* human vulnerability to toxics.[1]



The various types of human responses to toxics may be described by the types of reactions summarized in the table above:

Table 1-2 Types of Reactions to Toxics

Reaction Type	Description
Allergic	An adverse reaction to a toxic chemical resulting from previous sensitization to that chemical. Once sensitization has occurred, reactions usually occur at low doses.
Idiosyncratic	Genetic predisposition to an abnormal chemical response. For example, people who are unusually sensitive to nitrates, all have common biological traits that affect oxygen transport in their blood.
Local	Response at the site of contact with toxics.
Systematic	Response following absorption and distribution of agent.
Immediate	Response develops rapidly after a single exposure.
Delayed	Response develops slowly over time, for example, cancer.
Reversible	Tissue can repair damage from toxic exposure.
Irreversible	Tissue is injured beyond repair.
Additive	Two or more toxic chemicals exert a combined effect which is equal to the sum of effects of the chemicals.
Synergistic	Two or more toxic chemicals exert a combined effect which is *much greater* than the sum of effects of the chemicals.
Antagonistic	Two or more toxic chemicals exert a combined effect which is *less* than the sum of effects of the chemicals.
Tolerance	State of diminished effectiveness of toxics due to prior exposure.

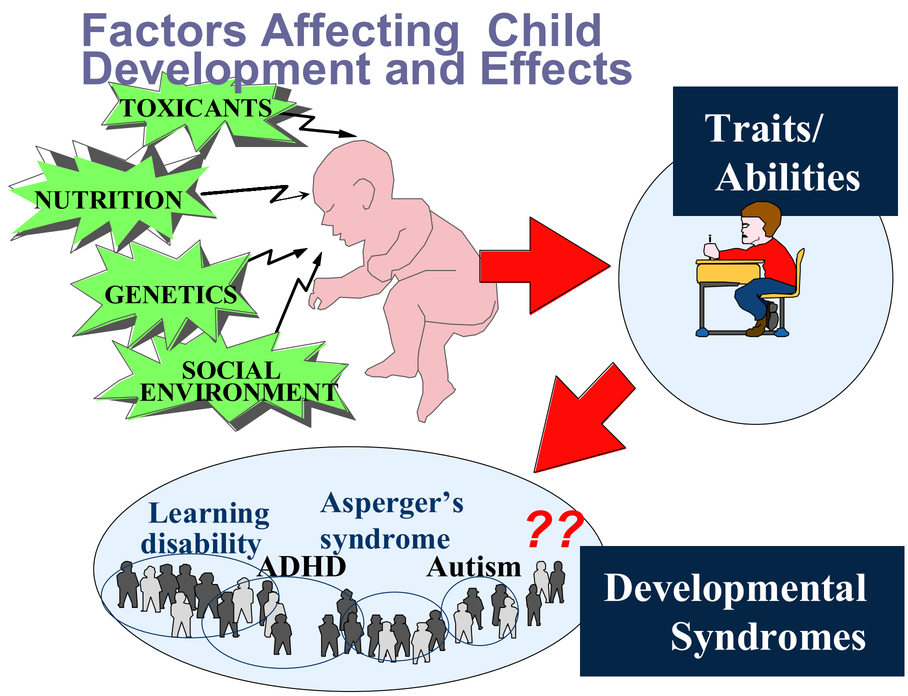
SOURCE: Hall, Stephen, *Chemical Exposure and Toxic Responses*, 1997, p.6.

E. Vulnerable Populations
But epidemiologists have determined that there are generally five groups of people that are particularly vulnerable to toxic chemicals:[2]

- industrial workers;
- occupants of "tight buildings," including office workers and school children;
- residents whose air or water is contaminated by chemicals;
- individuals who have had personal and unique exposure to various chemicals in domestic indoor air, pesticides, drugs, and consumer products; and
- developing infants and children.[3]

Infants and children are especially susceptible to toxic chemicals.

Fetal and infant brains are uniquely vulnerable to toxic disruption. Brain development begins early in fetal life as the brain takes shape, and continues through adolescence.



SOURCE: Greater Boston Physicians for Social Responsibility, *Training Program for Health Professionals*, April 2001.

Part 2: Types of Chronic Health Effects[4]

Carcinogenic: Cancer-causing substances. Chemically induced cancer generally develops many years after exposure to a toxic agent. Cancer results from a series of genetic alterations that leads to the progressive disruption of the normal mechanisms controlling cellular growth.
Examples of carcinogenic toxicants:

- cadmium, nickel, chromium (lung cancer)
- vinyl chloride (liver).
- arsenic (skin and lung cancer)
- benzene (leukemia)

Cardiovascular or Blood Toxicity: Adverse effects on the cardiovascular or hematopoietic (blood cells) systems. Exposure to cardiovascular toxicants can contribute to elevated blood pressure, hardening of the arteries, abnormal heartbeat, and decreased blood flow to the heart. Exposure to hematopoietic toxicants can reduce the oxygen carrying capacity of red blood cells, disrupt important immunological processes carried out by white blood cells, and induce cancer.

Examples:

- benzene
- arsenic
- lead, cadmium
- ozone

Reproductive and Developmental Toxicity: (Also called teratogens). Adverse effects on the male and female reproductive systems such as decreased fertility, as well as adverse effects on a developing child, such as birth defects and low birth weight.

Examples:

- lead, mercury
- toluene
- vinyl chloride & polychlorinated biphenyls
- (PCBs)
- secondhand tobacco smoke

Endocrine Toxicity: Adverse effects on the endocrine system (organs and glands that secrete hormones, such as pituitary, hypothalamus, thyroid, adrenals, pancreas, thymus, ovaries, and testes). Compounds that are toxic to the endocrine system may cause diseases such as hypothyroidism, diabetes mellitus, hypoglycemia, reproductive disorders, and cancer.

Examples:

- polychlorinated biphenyls (PCBs)
- DDT
- organochlorine pesticides & dioxins

Gastrointestinal or Liver Toxicity: Adverse effects on the structure and/or functioning of the gastrointestinal tract, liver, or gall bladder. The liver functions as a center for metabolism, processing chemicals we are exposed to so they can be utilized, detoxified, or excreted.

Examples:

- beryllium, phosphorus, and urethane
- carbon tetrachloride, chloroform
- arsenic, copper, and vinyl chloride
- chlorobenzene hexachlorobenzene

Immunotoxicity: Adverse effects on the functioning of the immune system. Altered immune function may lead to the increased incidence or severity of infectious diseases or cancer, since the immune system's ability to respond adequately to invading agents is suppressed.

Examples:

- asbestos, benzene
- polybrominated biphenyls (PBBs), polychlorinated biphenyls (PCBs)
- dioxins (TCDD)
- dieldrin (pesticide)

Kidney Toxicity: Adverse effects on the kidney, ureter, or bladder. The kidney not only is the major excretory organ in the body, but also performs nonexcretory functions, such as regulating blood pressure and blood volume. Since the kidneys receive approximately 25 percent of cardiac output, any chemical in systemic circulation is delivered to them in relatively high amounts, making kidneys unusually susceptible to the toxic effects of chemicals.

Examples:

- halogenated hydrocarbons: tetrachloride and trichloroethylene,
- cadmium, lead.

Musculoskeletal Toxicity: Adverse effects on the structure and/or functioning of the muscles, bones, and joints. Although injuries arising from repetitive motion or cumulative trauma are among the most common causes of musculoskeletal disorders, chemical hazards can also play a role in musculoskeletal disease.

Examples:

- coal dust
- cadmium
- silica
- fluoride (occupational levels)

Neurotoxicity: Adverse effects on the structure or functioning of the central and/or peripheral nervous system. It is well established that exposure to certain agricultural and industrial chemicals can damage the nervous system, resulting in neurological and behavioral dysfunction. Symptoms of neurotoxicity include muscle weakness, loss of sensation and motor control, tremors, alterations in cognition, and impaired functioning of the autonomic nervous system

Examples:

- Methyl mercury, lead are known
- carbon disulfide, n- hexane, trichloroethylene

Respiratory Toxicity: Adverse effects on the structure or functioning of the respiratory system. The respiratory tract consists of the nasal passages, pharynx, trachea, bronchi, and lungs. Respiratory toxicants can produce a variety of acute and chronic pulmonary conditions, including local irritation, bronchitis, pulmonary edema, emphysema, and cancer.

Examples:

- coal dust, aluminum, beryllium, and carbides of tungsten
- cadmium oxide, ozone, nitrogen oxides
- cigarette smoke, asbestos, arsenic, and nickel.

Skin or Sense Organ Toxicity: Adverse effects on the skin or sense organs (smell, vision, hearing, and taste). Sense organs may be injured by a variety of physical, chemical, and biological agents.

Examples:

- cadmium, nickel (smell)
- ammonia, chlorine, hydrogen sulfide, sulfur dioxide (smell)
- formaldehyde, many organic solvents (vision)
- lead (hearing loss)

Part 3: Toxics of Greatest Concern and their Effects

Broadly, the most dangerous toxics can be grouped into four main categories**:**

- **Metals**
- **Pesticides**
- **Solvents**
- **Persistent, bioaccumulative, and toxic (PBT) and Dioxins**
-

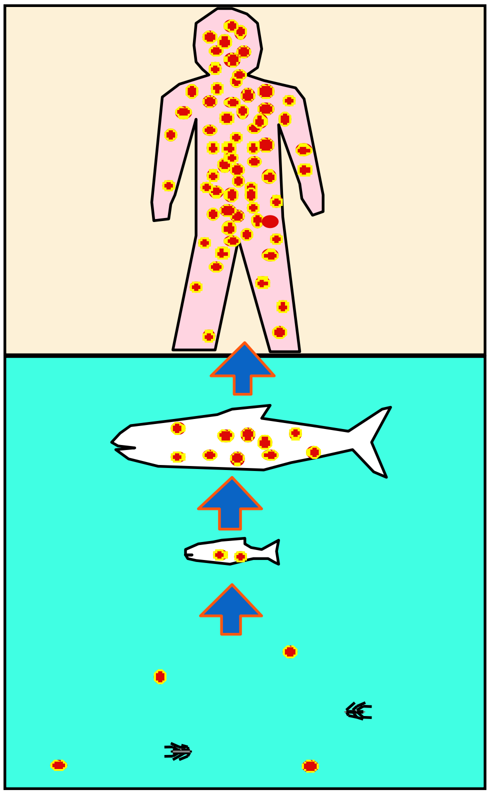
PBT = Persistent, Bioaccumulative Toxic

Many metals and pesticides are considered PBTs.

Metals – Of the approximately 80 elements classified as metals, more than half are of industrial and economic significance. About 12 metals are essential for life, such as calcium, copper, sodium, and zinc. But as with all chemicals, they can be toxic in high concentrations.

Table 3. Metal exposure and Toxic Responses

Metal	Essential element?	Organs Affected	Source
Aluminum	no	Brain - has been linked to Alzheimer's disease	some deodorants, aluminum cookware
Barium	no	digestive system, muscles, circulatory system	paints and inks
Cadmium	no	kidneys, lungs, teeth	batteries, ink, paint
Chromium	depends	skin, lungs	paints, inks, leather tanning, bleaches, adhesives
Copper	yes	liver, brain, kidneys, eyes	plumbing pipes, automotive brake pads, root killer, wood preservatives
Iron	yes	kidneys, liver	metal foundries
Lead	no	brain, central nervous system	paints, fuel additives, water (where lead pipes and solder are used)
Mercury	no	central nervous system	thermometers, thermostats, fluorescent tubes, batteries
Nickel	no	skin, lungs, kidney, stomach, throat	metal plating, coins, jewlery



Bioaccumulative toxics progressively accumulate in the tissues of organisms going up the food chain.

SOURCE:: *In Harm's Way,* Training Program for Health Professionals, Greater Boston Physicians for Social Responsibility, April 2001.

Pesticides – Pesticides are defined as any physical, chemical or biological agent intended to kill an undesirable plant or animal pest. The major classes of pesticides are insecticides, fungicides and herbicides. Of approximately 900 licensed pesticidal active ingredients, about 140 are considered by EPA to be neurotoxic, or toxic to the central nervous system.[5]

Data on long-term effects of pesticide exposures are limited, however, evidence suggests links to developmental disorders and cancer.[6] Some pesticides are considered persistent, bioaccumulative, and toxic (PBT) according to EPA. These are: aldrin, chlordane, heptachlor, isodrin, toxaphene, pentimethalin, and trifluralin. PBT's are discussed in more detail below.

Solvents – Solvents are widely used in industry and, to a lesser extent, in households for cleaning, degreasing, and paint stripping applications. Exposure to solvents is primarily through inhalation. Acute effects range from skin irritation to death. Chronic effects include cancer and permanent damage to liver, kidney, blood, and skin.

There are many different classes of solvents, including: aliphatic hydrocarbons, aromatic hydrocarbons, chlorinated hydrocarbons, alcohols, glycols, ketones, phenols, and ethers, among others.

PBTs - Persistent, bioaccumulative and toxic (PBT) chemicals are especially dangerous because they do not break down in the environment (hence the name "persistent"), they build up in the food chain (bioaccumulative), and they can be extremely toxic even in minute quantities,. The figure below illustrates how PBT concentration builds going up the food chain.

PBTs have been linked to health problems in wildlife and humans, including birth defects, inability to reproduce, and developmental problems. It is estimated that PBTs are present in every human on earth. The Environmental Protection Agency (EPA) has targeted several PBTs as particularly dangerous; these PBTs are summarized in the table at the end of this chapter.

Endocrine disrupters

In recent years, increasing scientific and public attention has been focused on the potential effects of synthetic chemicals on the endocrine system, the glands and hormones that help guide the development, growth, reproduction, and behavior of animals including human beings.

Chemicals that interfere with the normal functioning of this complex system are known as "endocrine disruptors." Disruption of the endocrine system can occur in various ways. For example, some chemicals may mimic a natural hormone, fooling the body into over-responding to the hormone. Other chemicals may block the effects of a hormone in parts of the body normally sensitive to it. Still others may directly stimulate or inhibit the endocrine system, leading, to overproduction or underproduction of hormones. Certain drugs are used to intentionally cause some of these effects, such as birth control pills.

Known or suspected endocrine disruptors include:

- some pesticides – chlordane, DDT, endrin, toxaphene, lindane, atrazine, simazine, kepone, aldrin/dieldrin
- PCBs, dioxin, polyaromatic hydrocarbons (PACs)
- mercury, lead

The EPA has already banned the use in the United States of some of these chemicals, including PCBs, DDT, chlordane, aldrin/dieldrin, endrin, kepone, toxaphene, and it is working with the international community to limit production and use of these chemicals worldwide. The Agency is also revising its testing guidelines for revaluating the effects of pesticides and toxic substances on reproduction and the developing fetus, which will enable EPA scientists to more readily identify chemicals with hormone-disrupting effects.

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- **some pesticides – chlordane, DDT, endrin, toxaphene, lindane, atrazine, simazine, kepone, aldrin/dieldrin**
- **PCBs, dioxin, polyaromatic**
- **mercury, lead hydrocarbons (PACs)**

References

[1] Schettler, Ted, M.D., et al., *In Harm's Way*, a Report by Greater Boston Physicians for Social Responsibility, p. 7. Full text report on-line: http://www.igc.org/psr/
[2] Ashford, Nicholas, Chemical Exposures: Low Levels and High Stakes, 1998, p.3
[3] Schettler, Ted, et. al., *In Harm's Way*, Greater Boston Physicians for Social Responsibility, May, 2000
[4] This information taken from Environmental Defense's Scorecard website, www.scorecard.com.
[5] Federal Register. 64(151):2945-42947, 1999.
[6] Greater Boston Physicians for Social Responsibility, Training Program, April, 2001.