BASIC TOXICOLOGY

1.0 INTRODUCTION

Toxicology is the study of the effects of chemicals on living organisms. The variety of potential effects and the diversity of chemicals present in our environment combine to make toxicology a very broad science. However, it is important to realize that toxicity is an inherent characteristic of all chemicals, and that at the right dose, any substance may cause illness, injury or death. As Paracelsus, the father of toxicology, states: "All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy."

This module presents the general concepts and principles of toxicology. By understanding this information, you can better protect yourself against chemical or biological hazards.

Learning Objectives

At the end of this module, you will be able to:

- Define basic toxicology fundamentals
- Understand how you may be exposed to hazardous chemicals and substances
- Recognize the effect various chemicals may have on your body
- Explain current occupational exposure guidelines (PELs, TLVs, etc).

2.0 DOSE-RESPONSE RELATIONSHIP

The characteristics of exposure and the spectrum of effects come together in a correlative relationship referred to as the dose-response relationship. In general, a given amount of a toxic agent will elicit a given type and intensity of response. This dose-response relationship is the basis for measurement of the relative harmfulness of a chemical.

2.1 Dose

In toxicological studies, the dose given to a test organism is a function of the concentration and the duration of exposure.

The **concentration,** or the amount administered, is usually expressed in units based on the route of exposure, for example:

- Per unit mass or weight (mg/kg)
- Per unit area of skin surface (mg/m^3)
- Per unit volume of air inhaled (ppm or %).

The **duration** of exposure, or period of time over which the dose has been administered, is dependant upon how rapidly the substance is administered and how often the dose is given. In experimental toxicology studies, the duration of exposure to a toxic substance is usually classified as follows:

Acute: Refers to a single exposure over a short period of time (less than 24 hours). In the field, examples include exposure from chemical releases or chemical splashes.

Subacute: Refers to single or multiple doses delivered within 30 days (in animals)

Subchronic: Refers to single or multiple doses delivered within 90 days in animals (7 years in humans)

Chronic: Refers to repeated or continuous exposure over long periods of time (more than 90 days in animals, more than 7 years in humans). Exposure from long-term remedial site work would be a chronic exposure situation.

The type and severity of the toxic effects caused by any specific agent will vary depending on the concentration and duration of exposure - or the dose.

2.2 Response/Effects

Before a dose-response relationship can be evaluated, the type of effect or endpoint that is being measured must be identified and defined. The toxic effects seen following chemical exposure can be categorized as follows:

- Local Effects
  Local effects occur at the site of contact between the toxin and the body. For example if a chemical comes in contact with the skin, it may cause a rash or a burn.
- Systemic Effects
  Systemic effects are those that occur if the toxin has been introduced into the body from its initial contact point, transported to another part of the body, and has caused adverse effects in target organs or organ systems. For example, some chemicals that are ingested may travel through the body and exert their toxic effect on the liver, which would be the target organ.

- Immediate vs. Delayed Effects
  Immediate effects are those effects that develop rapidly after a single administration of a substance. Delayed effects occur after some time has passed since administration, or after repeated exposure to a chemical.

- Reversible vs. Irreversible Effects
  Some toxic effects of chemicals are reversible, such as a rash or nausea. Others, including corrosion of eye tissue and the induction of cancer, cannot be reversed.

Often, the ability of the tissue to regenerate will largely determine whether a toxic effect is reversible or irreversible.

2.3 Measures of the Dose-Response Relationship
The results of dose-response evaluations can be expressed in a number of ways. Some of the more common terms used in toxicology are:

LD_{50}/LC_{50}: The lethal dose or lethal concentration at which 50% of the test population was killed

TD_{50}/TC_{50}: The dose or concentration at which 50% of the test population showed a specific toxic effect during a defined time period

NOEL: No observable effect level; the maximum dose at which there was no response in the test population

LD_{Lo}/LC_{Lo}: The lowest dose or concentration to cause death within a defined time period

TD_{Lo}/TC_{Lo}: The lowest dose or concentration to cause a given toxic effect within a defined time period.

3.0 Routes of Exposure

In order for a chemical to exert its toxic effect, it must get into the body and reach its target. There are four major routes for chemicals to enter the bloodstream, and consequently the organ system(s) that may be affected: inhalation, skin or eye absorption, injection, and ingestion. Industrial exposure to toxic agents most frequently is the result of inhalation and dermal exposure.

The following sections discuss these four major routes in more detail.

3.1 Inhalation

Inhalation is the primary route of exposure for humans, and is the most rapid and efficient route of entry for chemicals found in the form of vapors, gases, mists, or particulates.

Inhaled chemicals can cause different types of adverse effects depending on the depths of the respiratory tract which the substance can reach. Local effects are caused by chemicals that cannot reach the deepest portion, or alveolar region, of the lung and may include:

- Irritation of the nose, throat and upper respiratory tract
- Respiratory tract injury, including damage to the tissues of the throat and bronchi.

Systemic effects occur when the chemical reaches the alveoli where gas exchange can occur. In this portion of the lung, the substance can enter the bloodstream and cause adverse effects in any target organ system.

3.2 Skin/Eye Contact and Absorption

In the workplace, skin and eye exposure can occur from accidental contact with a hazardous chemical, from a chemical spill or splash, and from handling contaminated materials.

Both skin and eye effects can be local or systemic. For example, some substances can cause damage, such as irritation, burns or dermatitis (i.e., local effects) when they contact the skin. Others can be absorbed through the tissue and enter the bloodstream to cause adverse effects elsewhere in the body. For some chemicals, absorption can occur through unbroken skin, however, in most cases, cuts or scrapes on the skin will increase the rate that the chemical is taken into the body.

Examples of chemicals that can be absorbed into the skin include:

- Benzene
- Carbon disulfide
- Carbon tetrachloride
- Toluene.

3.3 Ingestion

In the field, this route of exposure is usually of lesser concern than the routes discussed above. Accidental ingestion of toxic substances usually occurs from ingestion of contaminated food and drink and from poor personal hygiene practices. For example, people who do not wash their hands following work in the fields or an exposure may accidently ingest a substance by putting their hands in or near their mouth.

Again, as with the other routes of exposure, the toxic effects can be either local (nausea, vomiting) or systemic.

3.4 Injection

For injection of a hazardous substance to occur, the skin must be penetrated or punctured by contaminated objects. Situations in the field that can lead to accidental injection include:

- Misuse of contaminated tools

- Misuse or improper disposal of contaminated needles/sharps
- Improper handling or disposal of contaminated glass/metal objects
- Accidentally stepping on nails or other sharp, rusty objects
- Cuts with contaminated tools

4.0 TOXICOKINETICS

Toxicokinetics, or pharmacokinetics, is an approach used to gain an understanding of how the body handles any given substance over time. Mathematical functions are used to quantify where a chemical goes once it enters the bloodstream and how much is absorbed, distributed, excreted, or metabolized.

To understand toxicokinetics, the following definitions should be reviewed:

4.1 Absorption

Absorption is the process in which a toxic agent crosses body membranes and enters the bloodstream.

4.2 Distribution

After entering the blood, a chemical is available for distribution or translocation throughout the body. Although a chemical can be distributed to more than one organ system, the organ that receives the highest dose will show the most adverse effects.

4.3 Metabolism

Metabolism refers to the biotransformation processes that convert lipid (fat) soluble compounds to water soluble compounds so the chemical can be excreted. When a substance is metabolized, the resulting compounds, or metabolites, may be more toxic than the original chemical.

4.4 Excretion

Excretion is the elimination of substances from the body. Excretion can occur by several routes including urine, feces, perspiration, respiration, and human milk.

5.0 TOXIC HAZARDS

Toxic hazards include a wide range of categories, or classes of substances which are based on the type of effects produced from acute and chronic exposure. These hazard classes are described below.

5.1 Irritants

Irritants are materials that cause inflammation of tissue membranes, usually following acute exposure to high concentrations of a substance. Examples of irritants include:

- Primary Irritants
  May cause contact dermatitis within hours of exposure. Most organic solvents and detergents are considered to be primary irritants

- Strong Irritants
  Strong irritants produce observable effects, including ulceration and tissue destruction, within minutes of exposure. Corrosive agents (e.g., acids and bases) are examples of strong irritants

- Respiratory Irritants
  Respiratory irritants cause slight to severe irritation of the nose, mouth, throat and lungs. Examples of respiratory irritants include:

  - Anhydrous Ammonia
  - Bromine
  - Chlorine
  - Phosgene

- Lacrimators
  Some chemicals irritate the mucous membrane, stimulating lacrimation (excessive watering of the eyes). Examples include acrolein, chlorine, and ethyl iodoacetate.

5.2 Sensitizers

Sensitizers are materials that trigger an immune response in the body. Unlike the other classes of toxic hazards, these chemicals are not dose dependent, and they usually require an initial or preconditioning exposure. Types of sensitizers include:

- Allergic Sensitizers
  Allergic sensitizers are substances that promote sensitization upon initial exposure. When first exposed to an allergic sensitizer, the immune response system produces antibodies to neutralize the effects of antigens. An antigen is a foreign substance, such as a chemical, that has entered the body. The first reaction to chemical may be mild or even nonexistent. Following subsequent exposures, the concentration of antibodies increases until a threshold is reached. At this point, the antibody level is high enough so that another exposure to the chemical may cause an antigen-antibody reaction, known as an allergic reaction.

  Allergic sensitizers primarily affect the skin and respiratory tract and can show the same symptoms as irritants. Examples range from malathion and isocyanate to poison ivy.

- Photosensitizers

Chemicals that cause an increased reactivity of the skin to UV and/or visible radiation on an immunologic basis. Examples include tetracyclines, xenobiotics, and certain dyes, such as eosin and acridine orange.

5.3 Systemic Poisons

Systemic poisons are chemical agents which exert their toxic effect on specific target organs or organ systems following exposure to any of the four major routes of exposure. These toxic hazards can be grouped in categories based on the organ or organ system targeted or on the effect produced, such as:

- <u>Central Nervous System Depressants</u>
  These cause symptoms such as headaches, nausea, uncoordination, lethargy, and confusion. Examples include toluene, methanol, and benzene.

- <u>Convulsants</u>
  Convulsants cause convulsions and possible coma. Examples include parathion, malathion, and phenol.

- <u>Neurotoxins</u>
  Neurotoxins affect the nervous system. Examples include methanol, mercury, lead, chlordane, and DDT.

- <u>Hepatotoxins</u>
  Hepatotoxins affect the liver. Examples include carbon tetrachloride, kepone, chlordane, and chloroform.

- <u>Hemolytic agents</u>
  These agents affect blood and blood components. Examples include arsine, benzene, and lead.

- <u>Nephrotoxins</u>
  Nephrotoxins affect the kidney. Examples include carbon disulfide, chloroform, mercury, and parathion.

- <u>Reproductive System Toxins</u>
  These affect the male or female reproductive system. Examples include steroids, cadmium chloride, and alkylating agents.

5.4 Carcinogens/Mutagens/Teratogens

- <u>Carcinogens</u>
  Carcinogens are physical or chemical agents which may initiate cancer (abnormal growth of cells; development of malignant neoplasms). Examples include asbestos, DDT, kepone, chlordane, and coal tar pitch volatiles.

- Mutagens
  Mutagens are chemical or physical agents that cause changes in the genetic material that alters the egg or sperm cell. The parent is unaffected, but the offspring suffers consequences. One example is ionizing radiation.

- Teratogens
  Teratogens are agents that cause physical defects in the developing embryo or fetus. Examples include thalidomide, diethylstilbestrol, and ionizing radiation.

5.5 Asphyxiants

Asphyxiants are materials that deprive the body of oxygen. There are two general types of asphyxiants:

- Simple asphyxiants
  These dilute or displace atmospheric oxygen, lowering the concentration of oxygen in air. Normal air contains about 21% oxygen. Simple asphyxiants may create an oxygen deficient atmosphere (<19.5% oxygen) resulting in headaches, unconsciousness and eventually death. Examples include carbon dioxide, nitrogen, helium, and methane.

- Chemical asphyxiants
  These prevent the take-up of oxygen into the blood or prevent normal oxygen transfer from the blood to the body. Examples include hydrogen sulfide, nitrobenzene, and hydrogen cyanide.

6.0 FACTORS INFLUENCING TOXICITY

Many factors affect the reaction of an organism to a toxic chemical. The specific response that is elicited by a given dose varies depending on the species being tested and variations that occur among individuals of the same species.

6.1 Factors Related to the Toxic Agent

Examples of factors related to the toxic agent are as follows:

- Chemical characteristics: The behavior of a chemical in the body can be influenced by many factors related to its chemical composition. For instance, charged or ionized molecules cannot be absorbed through the skin as easily as neutral molecules. Other factors include lipid solubility and water solubility.

- Physical properties: The physical properties of a chemical may affect the degree of the toxic response. For instance, only asbestos particles of a certain size can reach the alveolar region of the lungs and cause fibrosis.

- Presence of impurities: Traces of other chemicals present along with a toxic agent can alter the toxic effect produced by exposure (see also Section 6.5 below).

- Carrier substance or vehicle: The vehicle in which the chemical is present when it enters the body can affect the toxic effects produced. For example, certain vehicles can increase a chemical's lipid solubility, thus increasing the rate at which it is absorbed into the skin.

6.6.2 Factors Related to the Exposure Situation

Examples of factors related to the exposure situation are as follows:

- Dose: The dose, or the concentration of chemical and duration of exposure, can directly affect the type and severity of the toxic response (i.e., the dose response relationship). Often, the higher the dose, the more irreversible damage is seen.

- Rate of administration: In some cases, the severity of the response may be related to the rate at which the chemical is administered. For example, hydrogen sulfide is lethal at high concentrations; however, when it is administered slowly, there is little effect since the chemical is rapidly oxidized in the plasma to a nontoxic substance.

- Route of entry: A specific chemical may exhibit various levels of toxicity based on the route of exposure. For instance, lead is toxic by inhalation and ingestion, but it is more readily absorbed and produces a greater response in the respiratory tract than in the gastrointestinal tract.

6.3 Factors Related to the Individual

Examples of factors related to the individuals are as follows:

- Heredity: Genetic defects in metabolism can render an individual more susceptible to a given toxic agent. For example, individuals lacking the enzyme G6Pd may suffer damage to red blood cells when given aspirin.

- Previous exposure: Previous exposure to a toxic agent can result in tolerance, increased sensitivity or no change in the degree of response. In some cases, previous exposure to a toxic agent may provide protection against subsequent exposure.

- Nutrition: Since diet can change factors related to body composition and physiological and biochemical functioning, a person's nutritional status can affect the body's response to toxic agents.

- Hormones: The level of hormones present in the body may affect the body's response to a toxic agent. For instance, pregnant women are often more susceptible to a chemical's toxic effects.

- Age: Infants, children, adults and senior citizens have differences in their organ systems that contribute to differences in the distribution and toxicity of a substance.

For example, newborns are less susceptible to central nervous system (CNS) stimulants than adults, but are more susceptible to CNS suppressants.

- Sex: A chemical may exert its toxicity on an organ system that is specific for a certain sex. For instance, a chemical that targets sperm production will have a different or no affect in women.

- Presence of disease: Pre-existing diseases may increase a person's sensitivity to a toxic agent. For example, a person with chronic asthma would be more susceptible to the toxic effects of a respiratory irritant.

6.4 Factors Related to the Environment

Examples of factors related to the environment are as follows:

- Carrier: An agent may act to deliver another agent. Formaldehyde adhering to wood dust particles is an example of this phenomenon.
- Additional chemicals present: Other chemicals can interact with a substance to alter its toxicity. (See section 6.5 below)
- Temperature: Many body processes are temperature dependent. In warm weather or during heavy activity, the body's cooling mechanisms of vasodilation and sweating are activated. Both mechanisms can act to increase the amount of a toxin passing through the skin and into the blood system. Therefore, an increase or decrease in environmental temperature can affect the degree of toxicity of a chemical.
- Air pressure: Different altitudes and barometric pressures can affect the toxicity of some chemicals, such as ethanol or digitalis.
- Light/radiation: In the presence of a radiation source, such as sunlight, some chemicals may produce a different or more severe toxic response.

6.5 Chemical Interactions

Some combinations of chemicals produce different effects from those attributed to each chemical individually. Interactions of chemicals include:

- <u>Additive</u>
  When two chemicals are combined they produce an effect equal to the sum of the two chemicals.

- <u>Synergism</u>
  When two chemicals are combined, they produce an effect that is greater than the sum of the effect of each agent given alone.

- <u>Potentiation</u>
  A type of synergism where one chemical (the potentiator) is not usually toxic if present alone, but has the ability to increase the toxicity of other chemicals.

- Antagonism
  When two chemicals are combined, they interfere with each other's actions or one interferes with the action of the other chemical. There are four types of antagonists:
  - Functional
  - Chemical
  - Dispositional
  - Receptor.

7.0 EVALUATING HEALTH HAZARDS

In addition to understanding how chemicals enter the body and cause adverse effects, it is also important to try to obtain specific information on the chemical health hazards you may be exposed to in the field activities so you can decide what protective measures will be necessary. One source of general toxicological information is the material safety data sheet (MSDS). Knowledge of specific hazards of chemicals can help you to:

- Determine whether a hazard exists and the degree of the hazard
- Determine whether air monitoring is needed and whether techniques exist for monitoring exposures present before or during field activities
- Determine whether possible exposures should be documented by medical monitoring
- Determine needs for specific protective equipment and clothing and establish the basis for selecting and using such equipment and clothing.

The following sections outline some information that will assist in evaluating the toxicity of a chemical.

7.1 Exposure Limits/Airborne Concentrations

One of the first considerations in controlling exposures to hazardous chemicals is knowing whether acceptable exposure concentrations have been established for the chemicals in question. There are three major sources of exposure limits:

- The American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs).
- The Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs).
- National Institute of Occupational Safety and Health (NIOSH) Recommended Exposure Limits (RELs).

TLVs are recommended exposure limits which are updated annually, while PELs are legally enforceable standards and are only updated by OSHA when warranted.

The categories of exposure limits are based on time of exposure and concentration, and include:

TWA: Time-weighted average (TWA) concentration for an 8-hour work day

STEL: Short-term exposure limit (STEL): the 15-minute TWA exposure which shall not be exceeded at any time during a work day even if the 8-hour TWA is within established limits. Exposures above the TWA up to the STEL should not be longer than 15 minutes, should not occur more than 4 times per day, and there should be at least 60 minutes between successive exposures in this range.

C: Ceiling (C): the concentration that should not be exceeded during any part of the working day.

In addition to the above limits, the National Institute for Occupational Safety and Health (NIOSH) and OSHA have developed Immediately Dangerous to Life and Health (IDLH) concentrations for use in the decision making process for respiratory selection. IDLH represents a maximum concentration from which one could escape within 30 minutes without any impairing symptoms or irreversible health effects.

7.2 Toxicological Data

Information on the toxic properties of chemical compounds and the dose response relationship can be obtained from animal studies, epidemiological investigations of exposed human populations, and clinical studies or case reports of exposed humans.

- Epidemiological Studies - are based upon the results observed/measured in a given population exposed to a chemical when compared to an appropriate, non-exposed group.

- Clinical Studies - involve individual reports of chemical exposure.

- Animal Data - includes all descriptive animal toxicity testing. Effects produced by the compound in laboratory animals are often applicable to humans.

The extrapolation of human data from animal studies is complex, and these values should only be considered as an approximation for the potency of the compound and used in conjunction with additional data. For example, when comparing chemicals, if an LD_{50} is greater in one, that chemical is said to be less potent than the other, since it would take more of the other chemical to produce the same effect. Those chemicals which will produce death in microgram doses are considered extremely toxic.

Information about the toxicological effects of a chemical can be obtained from the labels and the MSDS. These sources contain data on acute and chronic health effects, including skin and eye irritancy, systemic toxicity, and carcinogenicity.

[Note: Refer to "Hazard Communication" for more information on labels and MSDSs.]

7.3 Signs and Symptoms of Overexposure

During field activities, you must always be aware of the potential for unexpected exposure to toxic chemicals and be able to identify any signs and symptoms of overexposure. Some signs and symptoms may include the following:

- Sneezing and coughing
- Changes in breathing rate
- Headache, dizziness
- Nausea
- Irritation of the eyes and throat
- Redness and swelling of the skin
- Itchiness of the skin
- Changes in behavior.

Anyone who develops signs and symptoms of chemical exposure should seek medical attention immediately.

8.0 SUMMARY

This module has presented the basic toxicology fundamentals. Information was presented on the routes of exposure to hazardous chemicals and the effects these chemicals may have on the body. In addition, the current occupational exposure guidelines were presented.

Key concepts presented in this module are:

- An understanding of the concepts and principles behind toxicology results in increased protection against chemical and biological hazards.
- Toxicity depends upon chemical characteristics, route of exposure, and dose.
- Dose is a function of the concentration and duration of exposure.
- Acute refers to a single exposure over a short time period, while chronic refers to continuous exposure over a long time period.
- Routes of exposure include inhalation (most significant), ingestion, skin contact/absorption, and injection.
- Toxins can act as irritants, sensitizers, systmetic poisons, carcinogens/mutagens/teratogens, or as asphyxiants.
- Toxicity is influenced by the characteristics of the agent, the exposure situation, the subject, the environment, and the effect of chemical interactions.
- Understand the nature of specific chemical hazards prior to engaging in field activities in order to take appropriate protective measures.
- Always consult ACGIH TLVs, OSHA PELs and NIOSH RELs for the most current and applicable exposure limits.
- Toxicological data is drawn from epidemiological studies, clinical studies, and animal data.
- Overexposure to hazardous chemicals may result in acute effects. Understanding the warning signs will help limit exposure.

- Seek medical attention if you develop signs or symptoms of chemical exposure.

Measures you can take to minimize the risks associated with chemical exposure include:

- Understand the basic principles of toxicology and how they relate to exposures you may encounter during field activities.
- Practice applying this knowledge:
  - For example, pick a common hazardous material you are exposed to in the field (for which you know the approximate concentration), look up the TLV or PEL, estimate your daily exposure duration, and try to calculate your dose. Compare your calculated dose to the established values.
- Know the primary routes of exposure for chemicals you commonly encounter in the field.
- Be aware of the different effects toxins can have on your body (e.g., chronic, acute, local, systemic, immediate, delayed, reversible).
- Recognize that toxins present a wide range of hazards (e.g., irritants, sensitizers, poisons, carcinogens, mutagens, teratogens, asphyxiants).
- Identify any relevant factors that may influence your reaction to toxins (e.g., heredity, previous exposure, nutrition, hormones, age, sex, presence of disease).
- Obtain specific information about the chemical health hazards you may be exposed to during field activities so you can decide what protective measures may be needed.
- During field activities, be aware of the potential for unexpected exposures. Signs and symptoms may include:
  - Sneezing and coughing
  - Changes in breathing rate
  - Headache, dizziness
  - Nausea
  - Irritation of the eyes and throat
  - Redness and swelling of the skin
  - Itchiness of the skin
  - Changes in behavior.
- Seek medical attention immediately upon development of signs/symptoms of chemical exposure.

EXERCISE

1. The dose-response relationship evaluates the relationship of which of the following parameters:

   a. Concentration of chemical
   b. Duration of exposure
   c. Effect produced
   d. A and C
   e. All of the above

2. Acute effects are usually seen following repeated and prolonged exposure to a chemical: (Circle One)
   True False

3. A chemical will only cause adverse effects at the point of contact: (Circle One)
   True False

4. The lethal dose or lethal concentration at which 50% of the test population is killed:

   a. LD_{50}
   b. NOEL
   c. TD_{50}
   d. LD_{Lo}

5. Order the following chemicals from least toxic to most toxic based on their LD_{50} values for oral dosage to rates (in mg/kg):

Benzene	3800
Calcium chloride	1000
Caffeine	192
1 ,2-dichloroethane	680
Nicotine	53
Sodium chloride	3000

6. Which two of the following routes of exposure are most significant and common for field personnel:

   a. Ingestion
   b. Skin contact/absorption
   c. Inhalation
   d. Injection

7. Materials that cause inflammation of tissue membranes usually following acute exposure to high concentrations are:
   a. Asphyxiants
   b. Sensitizers
   c. Irritants
   d. Neurotoxins
   e. Carcinogens

8. Materials that cause changes in the genetic material that alters the egg or sperm cell are:

   a. Mutagens

b. Reproductive toxins
c. Carcinogens
e. Allergic Sensitizers

9. Substances that prevent the take-up of oxygen into the blood or prevent normal oxygen transfer from the blood to the body are:

   a. Simple asphyxiants
   b. Irritants
   c. Chemical asphyxiants
   d. a and c
   e. All of the above

10. Factors that can influence the toxicity of a compound include:
    a. Concentration of toxic agent
    b. Age of person
    c. Physical characteristics of chemical
    d. Temperature of environment
    e. All of the above

11. When two chemicals are combined, they produce an effect that is greater than the sum of the effect of each agent given alone. This is called:

    a. Antagonism
    b. Synergism
    c. Carcinogenicity
    d. Summation

12. Signs and symptoms of chemical exposure may include:

    a. Sneezing and coughing
    b. Changes in breathing rate
    c. Irritation of the eyes and throat
    d. Changes in behavior
    e. a, b, and c only
    f. All of the above

EXERCISE KEY

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   True ***False***

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Benzene	3800	***(1)***
Calcium chloride	1000	***(3)***
Caffeine	192	***(5)***
1 ,2-dichloroethane	680	***(4)***
Nicotine	53	***(6)***
Sodium chloride	3000	***(2)***

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    e. a, b, and c only
    f. All of the above