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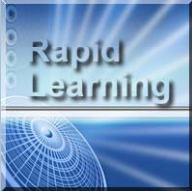
Rapid Learning Center Presents ...

Teach Yourself  
**Toxicology** in 24 Hours




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Disclaimer: All contents in this tutorial are for informational purposes only and not intended to be a substitute for professional medical advice, diagnosis, or treatment. Reliance on any information provided by this tutorial is solely at your own risk. 

 **Introduction to Toxicology**

Toxicology Rapid Learning Series

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**Rapid Learning Center**  
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## Learning Objectives

By completing this tutorial, you will learn about:

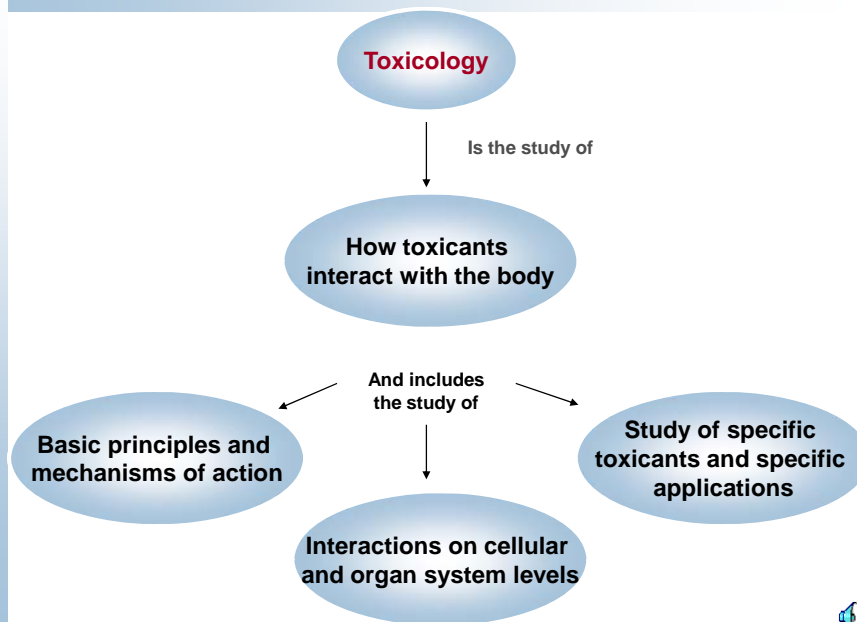


- Introduction to toxicology terminology
- Characteristics of exposure and effect
- Interactions with toxicants
- Dose-response

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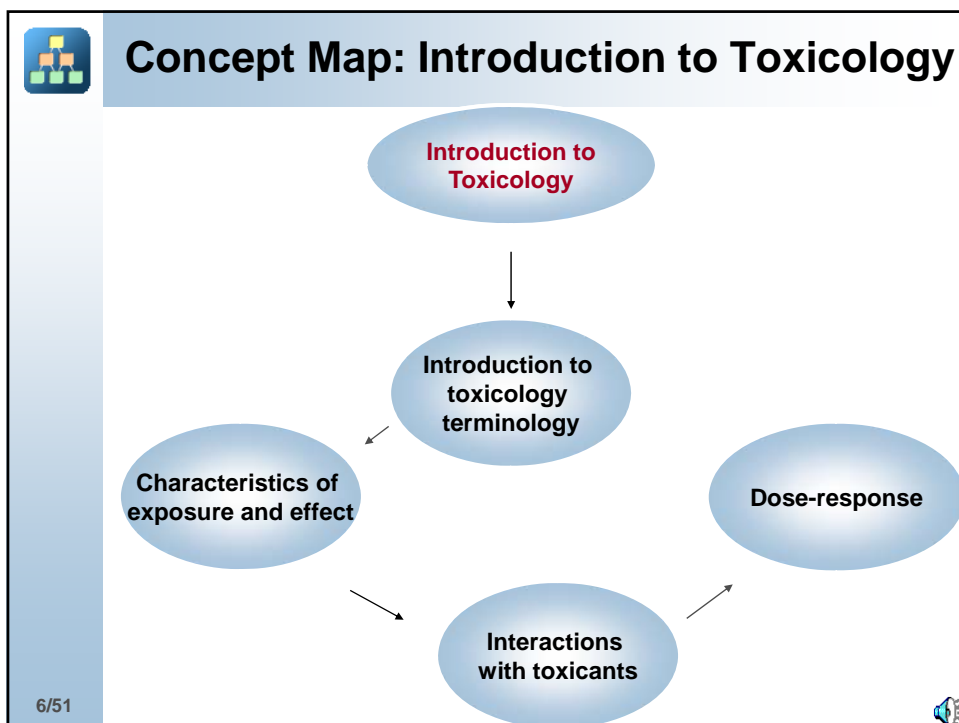
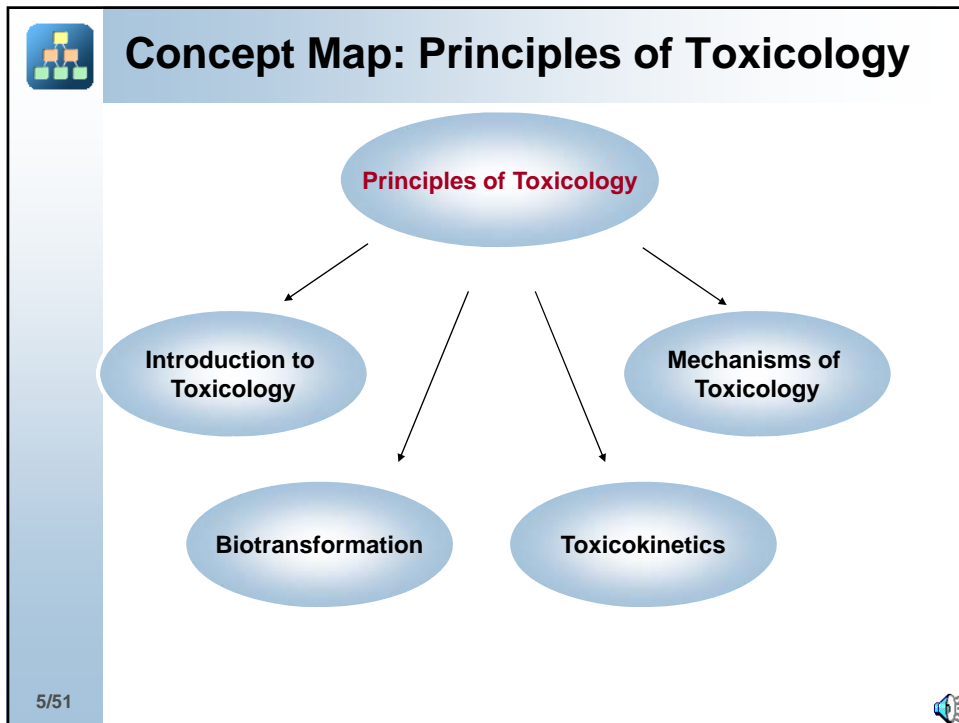


## Concept Map: Toxicology



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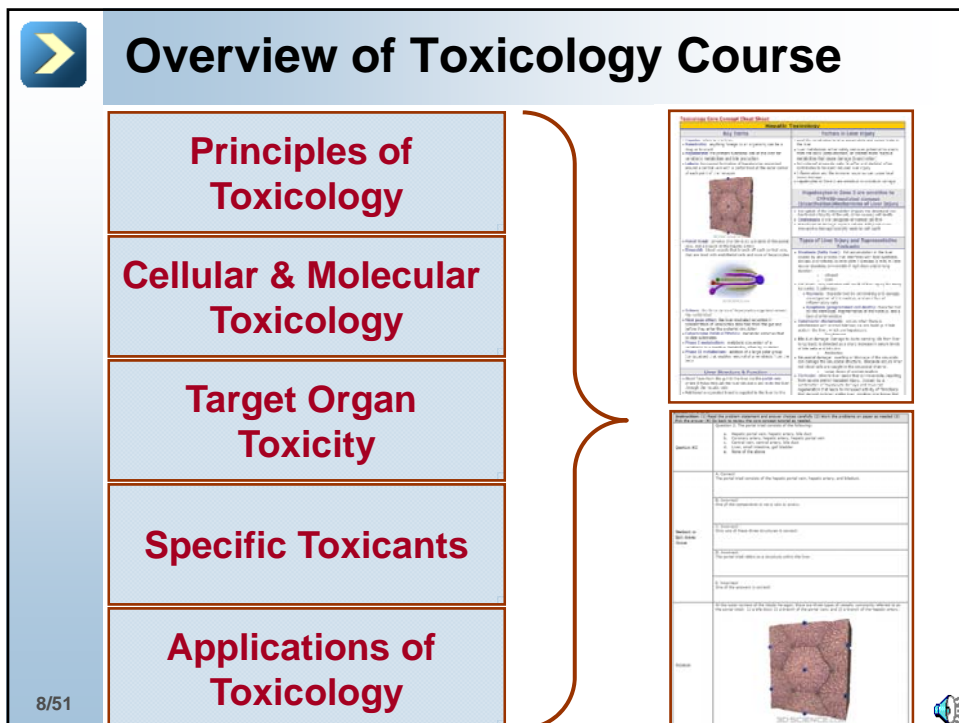






## Overview of Toxicology Course & Study Tips

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## Overview of Toxicology Course

- Principles of Toxicology
- Cellular & Molecular Toxicology
- Target Organ Toxicity
- Specific Toxicants
- Applications of Toxicology

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## Study Tips

- **Actively watch and listen to tutorial**
  - Take notes
  - Pause where necessary
- **Memorize basic information to save time later**
  - Review basic biology where necessary
- **Learn vocabulary quickly for understanding in-depth topics later in series**
  - Make flash cards if necessary



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## Additional Study Tips

- Look for patterns
- **Connect information to topics learned in earlier tutorials**
  - Each tutorial builds off earlier tutorials!
- **Ask for help**
  - Don't be afraid to seek out help early: tutors, teaching assistants, knowledgeable friends can all help



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## Mnemonics

- Great way to memorize lists
- Simple 3-step process:
  - List key words in logical order
  - Write down first letter of each keyword
  - Create an easy-to-remember word, phrase, or sentence from first letters of these keywords
- Example: symptoms of organophosphate poisoning = **DUDE SLOP** (**d**iarrhea, **u**rination, **d**ecreased consciousness, **e**mesis, **s**alivation, **l**acrimation, **o**cular miosis, **p**aralysis)



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## History of Toxicology



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## Toxicology in Ancient Times

- Earliest humans used animal venoms and plant extracts for hunting and warfare
- 1500 BC: hemlock, opium, arrow poisons & metals used to poison enemies and for state executions and assassinations
  - Became widely used
  - Notable victims: Socrates, **Cleopatra**, Claudius



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## Paracelsus (1493-1541)



- Physician-chemist
- Determined that specific chemicals were responsible for toxicity of plant or animal poisons
- First recorded documentation of dose-response relationship, a major concept in toxicology

*All substances are poison; there is none which is not a poison.  
The right dose differentiates a poison from a remedy.*

*- Paracelsus*

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## Orfila, Father of Toxicology (Early 1800s)

- Spanish physician
- First to publish comprehensive works devoted to toxicity of natural agents
- First toxicologist to use autopsy material and chemical analysis as legal proof of poisoning
  - Basis of modern forensic toxicology



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## Modern Toxicology

- **Xenobiotic:** foreign substance taken into the body
  - May be beneficial or toxic, depending on dose



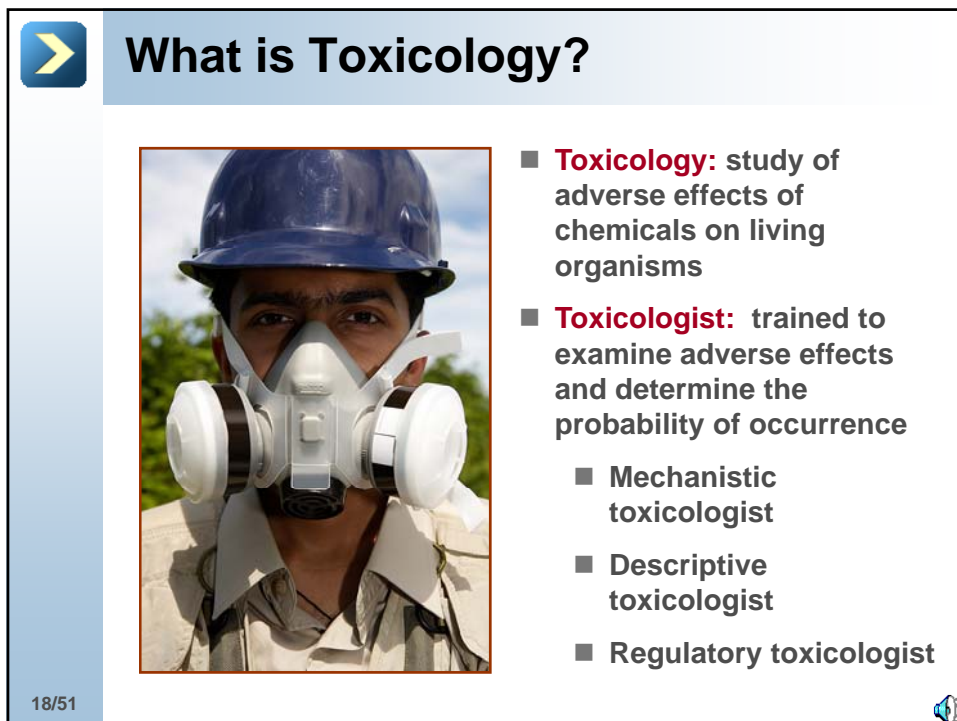
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## Introduction to Toxicology Terminology

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## What is Toxicology?



- **Toxicology:** study of adverse effects of chemicals on living organisms
- **Toxicologist:** trained to examine adverse effects and determine the probability of occurrence
  - Mechanistic toxicologist
  - Descriptive toxicologist
  - Regulatory toxicologist

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## Types of Toxicology

- **Forensic toxicology:** combines analytic chemistry and toxicology to study specific poisoning events
- **Environmental toxicology:** effects of chemicals in the environment on organisms
- **Developmental toxicology:** effects of chemicals on developing organisms
- **Reproductive toxicology:** studies adverse effects of chemicals on the male or female reproductive system



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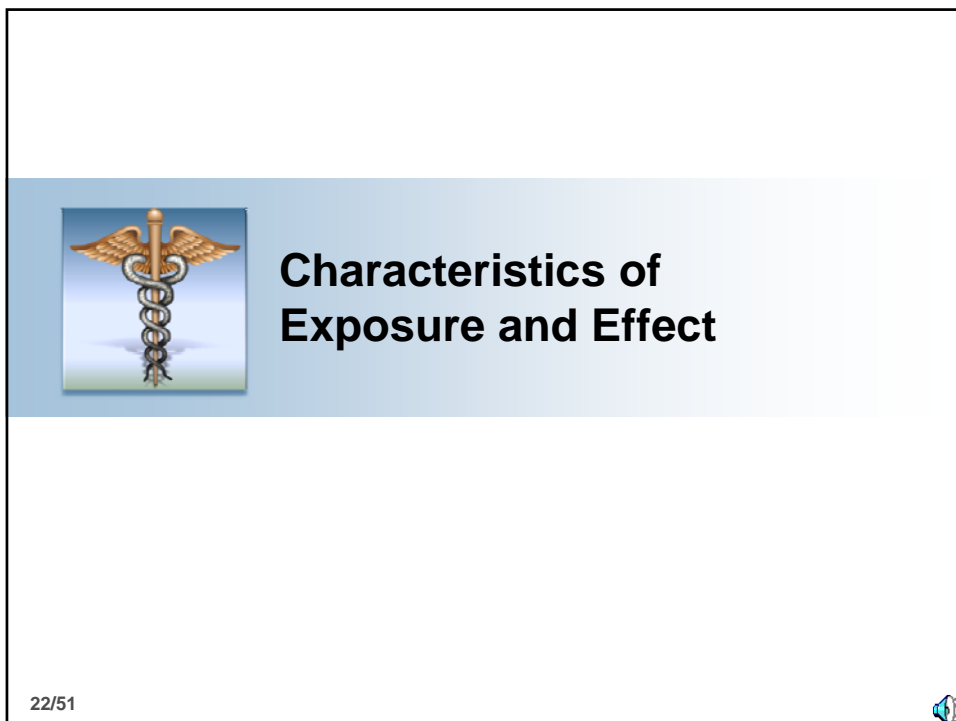
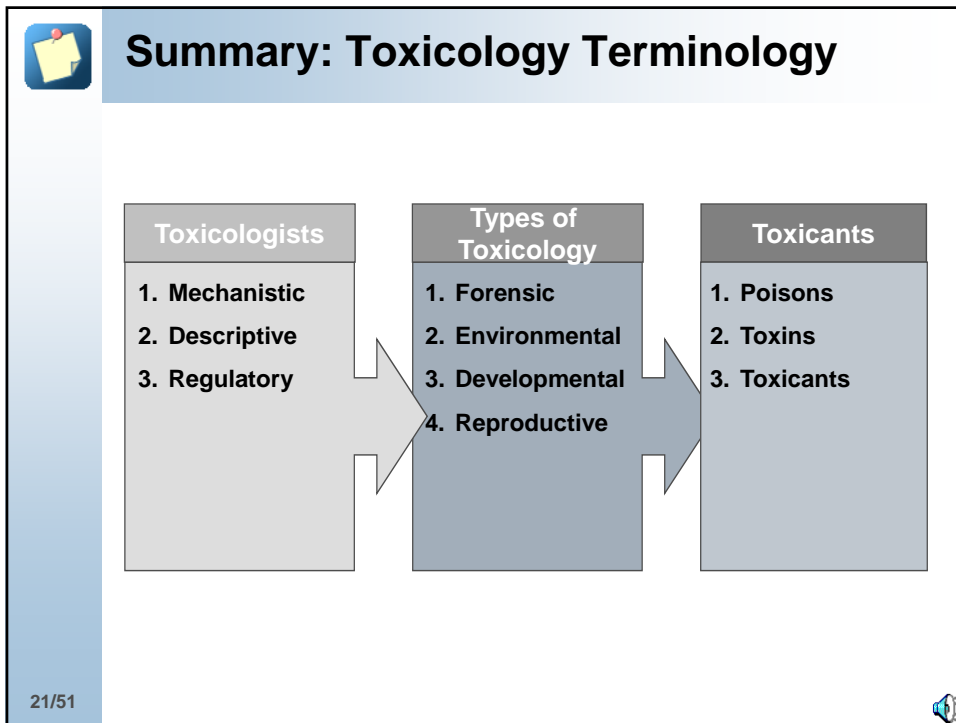
## Poisons, Toxins and Toxicants

- **Poison:** any agent capable of causing harm in a biological system
- **Toxin:** toxic substance produced by biological systems
  - Plants, animals, fungi, and bacteria
- **Toxicants:** toxic substances produced by human activity (**anthropogenic**)



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## Characteristics of Exposure

- Toxicity heavily influenced by:
  - Route
  - Concentration
  - Duration of exposure
- Major routes of exposure:
  - Gastrointestinal tract
  - Lungs
  - Skin
- Greatest effects when introduced directly into the blood stream



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## Duration of Exposure

- **Acute:** exposure for less than 24 hrs
- **Chronic:** repeated exposure for more than 3 months
- **Subchronic:** 1 to 3 months
- **Subacute:** 1 month or less



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## Toxicant Effects

- Route and duration of exposure = direct impact on adverse effects
- Categories based on severity of effect, increasing severity



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- Adverse
- Deleterious
- Toxic



## Allergic Reactions

- **Allergic responses:** mediated by immune system
  - Prior sensitization to chemical or structurally similar chemical
- Variety of manifestations:
  - Skin rash
  - Anaphylactic shock – may be fatal



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## Idiosyncratic Reactions

- **Idiosyncratic reaction:** genetically determined, abnormal adverse response to a chemical
  - Extreme version of response seen at high levels of exposure in normal responders
  - Insensitivity to highest dose compared to majority of population



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## Timing of Reactions



- **Immediate:** develop quickly after exposure to toxicant
- **Delayed:** becomes evident days, weeks, or even years after exposure

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## Severity of Reactions

- Reversible vs. irreversible
  - Difference depends on severity of exposure & regenerative capacity of affected tissue
    - Liver & skin can regenerate – reversible damage
    - Nervous system cannot regenerate – irreversible damage



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## Locality of Reactions

- **Local effects:** take place at the site of exposure (where the chemical comes in contact with the organism)
- **Systemic effects:** require absorption into the body and distribution to the site of action



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## Selective Toxicity

- **Selective toxicity:** significant differences in the response to a toxicant that varies between species or between individuals of the same species
- **Species differences:** stem from differing gene expression patterns
  - Important to understand mechanism of action to extrapolate to humans
- Individual differences in response
  - Genetic polymorphisms
  - Underlie idiosyncratic responses



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## Summary: Characteristics of Exposure and Effect

- Route and Site of Exposure
- Duration of Exposure
- Timing of Reaction
- Severity of Reaction
- Locality of Reaction



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## Interactions with Toxicants

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## Combined Effects of Chemicals

- **Additive:** effect of two or more chemicals equals sum of action of each individual chemical alone.  $2 + 2 = 4$
- **Synergistic:** the combined effects of two chemicals are greater than the sum of the effects of each individual chemical.  $2 + 2 = 7$
- **Potentiation:** occurs when a chemical is not toxic itself alone, but contributes to the toxicity of another chemical, making that chemical much more toxic.  $0 + 2 = 7$

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## Antagonism

- **Antagonism:** chemicals work against each other
- Four kinds:
  - **Functional:** two chemicals work against each other by producing opposing effects in the same system
  - **Chemical:** two chemicals interact with each other to produce a less toxic combination
  - **Dispositional:** the biological actions on a chemical reduce its toxicity
  - **Receptor:** one chemical blocks the action of another at its receptor

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## Tolerance

- **Tolerance:** decreased responsiveness to a chemical
  - Prior exposure to that chemical or to a structurally related compound
- Causes:
  - Reduction in amount of toxicant reaching the site of action
  - Reduced responsiveness of tissue to the chemical



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## Summary: Interactions with Toxicants

Type of Interaction	Characteristics
<b>Additive</b>	Effect of two or more chemicals equals sum of individual chemical effects
<b>Synergistic</b>	Combined effects of two or more chemicals are greater than sum of individual chemical effects
<b>Potentiation</b>	Chemical is not itself toxic, but contributes to toxicity of another chemical
<b>Antagonism</b>	Chemicals work against each other in physiological system
<b>Tolerance</b>	Decreased responsiveness to a chemical

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## Dose-Response

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## What is Dose-Response?

- **Dose-response:** relationship between exposure to a chemical and the magnitude of the response
- Dose typically determines the response
  - Consistent
  - Predictable
  - Can be measured

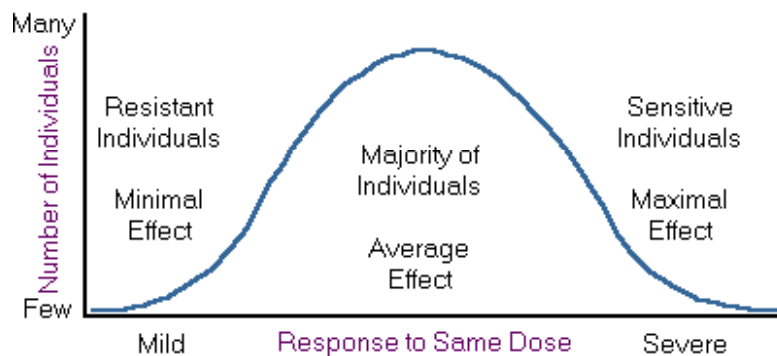


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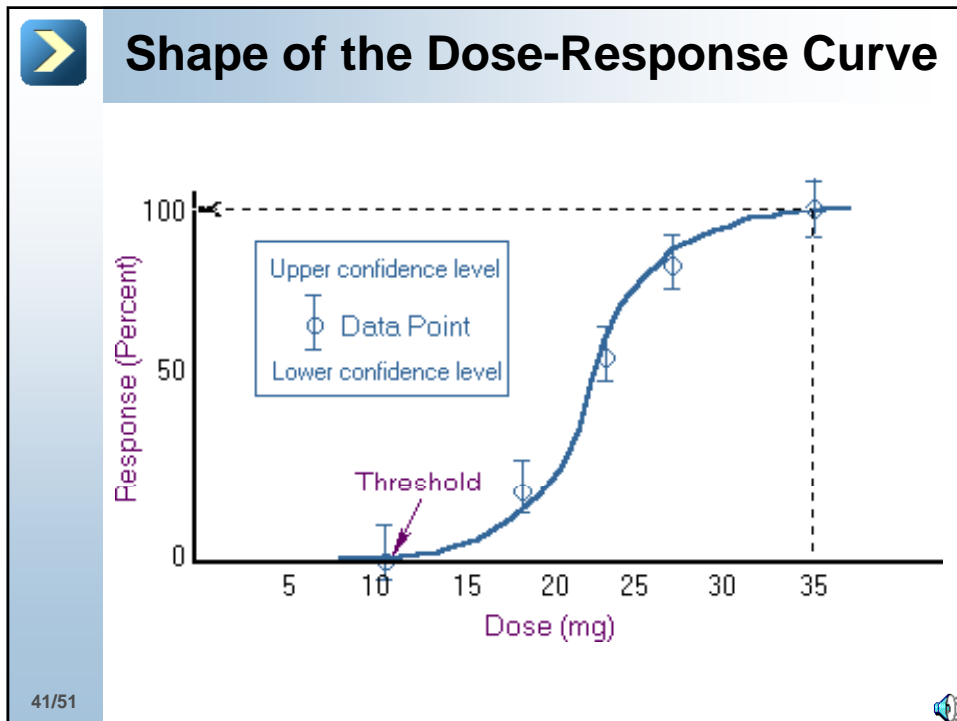
## Types of Dose-Response Relationships

- **Individual:** describes the response of an individual organism to a specific chemical
- **Quantal:** describes the distribution of responses to different doses in a population of exposed organisms



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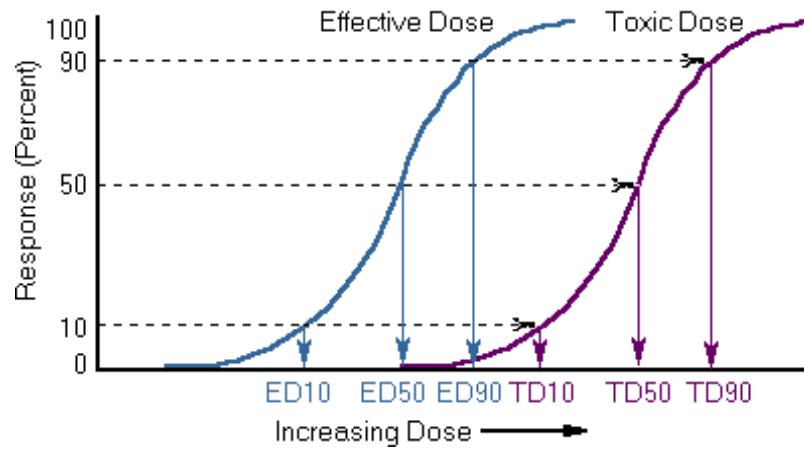
### Assumptions of the Dose-Response Curve

- Assumptions:
  - Direct cause-and-effect relationship
  - Magnitude of the response is directly related to the dose
  - The response can be measured in a quantifiable manner that is accurate and repeatable

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## Comparing Dose-Response Curves



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## Therapeutic Index

**Therapeutic Index (TI) =**

$$\frac{\text{dose required to produce toxic effect}}{\text{dose required to produce therapeutic effect}}$$



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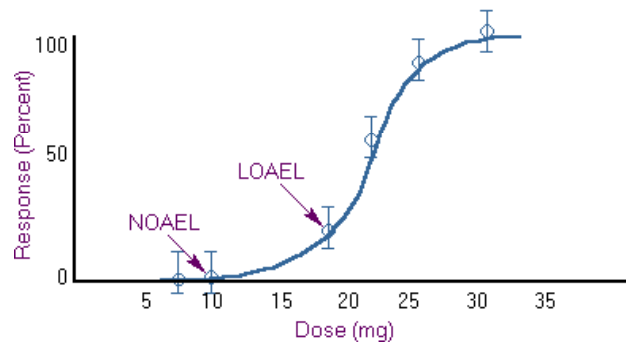




## Margin of Safety

- Margin of safety:** the distance between the estimated dose to which a population is exposed, and the NOAEL, as determined in experimental animals

$$\frac{LD_1}{ED_{99}}$$



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## Potency vs. Efficacy

- Potency:** range of doses over which a chemical produces increasing responses
- Efficacy:** capacity of drug or toxicant to cause a specific functional response





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 **Summary: Dose-Response**


Term	Definition
<b>Dose-Response</b>	Relationship between exposure to a chemical and the magnitude of the response
<b>Therapeutic Index</b>	Dose required to produce toxic effect / dose required to produce therapeutic effect
<b>Margin of Safety</b>	MOS = LD1/ED99
<b>Potency</b>	Range of doses over which a chemical produces increasing responses
<b>Efficacy</b>	Capacity of a drug or toxicant to cause a specific functional response


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 **Question: Review**


A \_\_\_\_\_ is a toxic substance produced by a biological system.  toxin

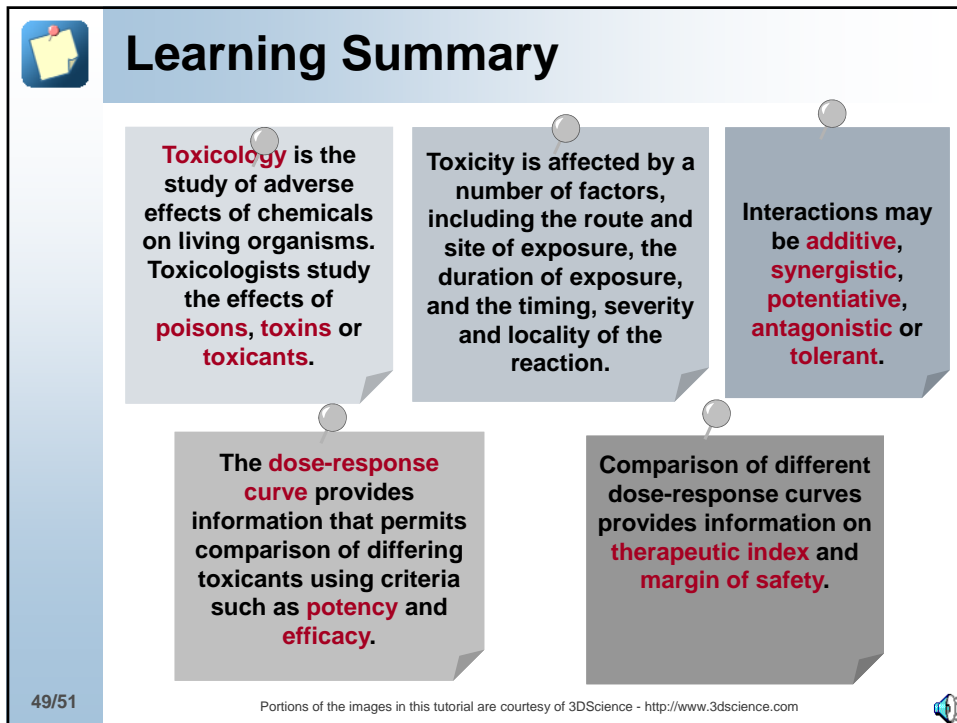
\_\_\_\_\_ is when two chemicals interact with each other to produce a less toxic combination.  Chemical antagonism

\_\_\_\_\_ is decreased responsiveness to a chemical.  Tolerance

\_\_\_\_\_ is the range of responses over which a chemical produces increasing responses.  Potency

The relationship between exposure to a chemical and magnitude of response is the  dose-response curve

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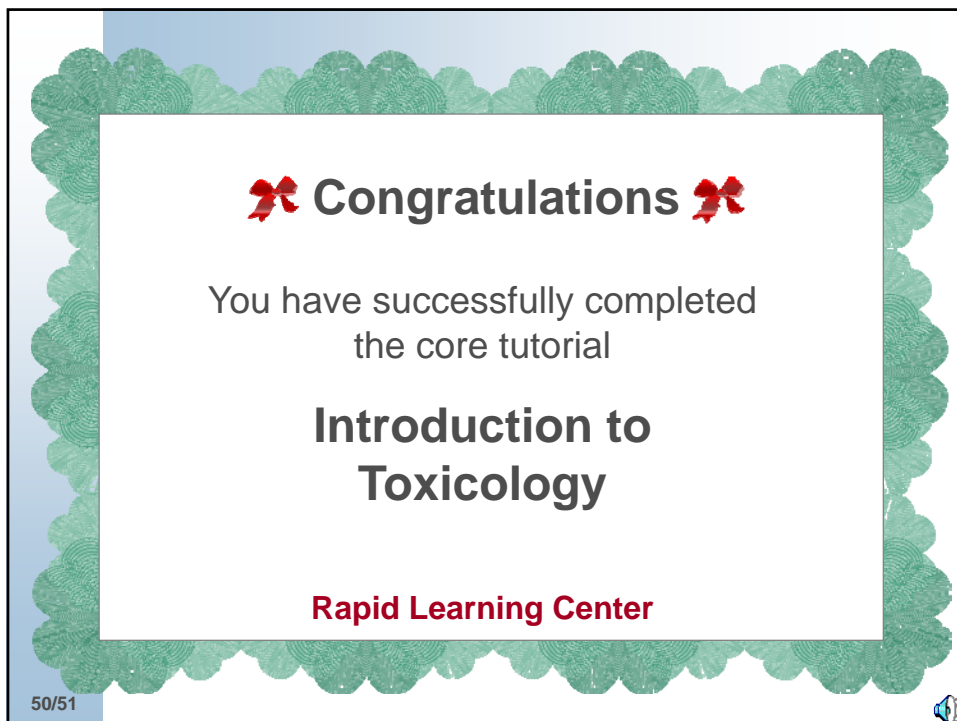


## Learning Summary

- Toxicology** is the study of adverse effects of chemicals on living organisms. Toxicologists study the effects of **poisons, toxins** or **toxicants**.
- Toxicity is affected by a number of factors, including the route and site of exposure, the duration of exposure, and the timing, severity and locality of the reaction.
- Interactions may be **additive, synergistic, potentiative, antagonistic** or **tolerant**.
- The **dose-response curve** provides information that permits comparison of differing toxicants using criteria such as **potency** and **efficacy**.
- Comparison of different dose-response curves provides information on **therapeutic index** and **margin of safety**.

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**🎀 Congratulations 🎀**

You have successfully completed the core tutorial

## Introduction to Toxicology


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**What's Next ...**

Step 1: Concepts – Core Tutorial (Just Completed)

→ Step 2: Practice – Interactive Problem Drill

Step 3: Recap – Super Review Cheat Sheet

**Go for it!**



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