PENNSTATE 1855

eTOXIC
Environmental Toxicology Inquiry Curriculum

Module 1: Everyday Toxicology
Lesson 1: What is the Relationship Between Dose and Response?

Lesson Overview

Summary:

"Everyday Toxicology" is meant to be the first module in an environmental toxicology curriculum. It aims to use commonplace substances in order to illustrate basic concepts of toxicology and pharmacology, in order to serve as a basis for further study of selected topics in subsequent modules.

Students will apply the concepts of dose and response and the tool of the dose/response curve in order to design and execute an experiment to investigate the effect of salt on plants in lesson 2.

Objectives:

By the end of the lesson, students will be able to:

1. differentiate between exposure and dose to instructor satisfaction.
2. calculate dose with 100% accuracy.
3. discriminate substances as beneficial or harmful dependent on dose to instructor satisfaction.
3. interpret dose/response curves with 100% accuracy.
4. differentiate between median lethal dose, median effective dose, and the therpeutic index to instructor satisfaction.
5. evaluate toxicity and risk by comparing the dose/response curves to instructor satisfaction.

Grades:

9th through 12th

Prepping the Lesson

Instructions:

Materials/Technical Resources:

It is our recommendation that you walk through the teacher and student materials for this lesson to ensure that students will be able to receive the information through the modes of delivery that we intended prior to using the material in the classroom. If you or your school does not have the resources needed, you may need to make some modifications depending on the resources you have available.

The following materials/technical resources will be needed to complete the lesson. We recommend using Option #1 to provide the materials to your students in the manner in which they were intended to be delivered.

Option #1 (Preferred Technology Requirement)
You will need to have access to a computer, the Internet, and a projection device during the entire lesson. Your students will need to have access to computers and the Internet. You and your students will simultaneously step through the module while using their given computers. You may have to make special arrangements for all of your students to have a computer. Be sure you and your students will not be blocked from Google Documents, YouTube, and your selected online collaborative tool. You may be currently using an online collaborative tool but if not, we recommend Facebook groups, Edmodo, or eChalk.

Option #2 (Minimum Technology Requirement)
If you do not have a way for your students to access the Internet individually, then you will need to facilitate their access to the information. You will need access to a computer, the Internet, and a projection device during the entire lesson. You will step through the module as your students watch and complete the presented activities. There may be modifications to the delivery of the materials that you will need to make, depending upon the resources you have available. Be sure you have access to Google Documents, You Tube, and your selected online collaborative tool. You may be currently using an online collaborative tool but if not, we recommend Facebook groups, Edmodo, or eChalk.

Lesson Time and Supply List:

This document will provide you with information on prep time needed, a list of supplies, and total lesson time for this particular lesson. See appendix for the Lesson Time and Supply List document.

Student Homework:

Prior to starting this module, it is important to determine which online collaborative tool you and your students will be using. Once you have had an opportunity to review all of the lessons, decide how you will facilitate the homework discussions and submissions using your selected online collaborative tool. Be sure to give your students clear directions and objectives on your expectations of the use of this tool and their participation in their homework activities. We highly encourage you to participate with your students in their homework discussions to enhance the quality of the experience.

Essential Vocabulary: biological response, dose, exposure, dose/response curve, logarithmic scale, median effective dose or ED_{50}, median lethal dose or LD_{50}, pharmacology, therapeutic index, toxicologists, toxicology

Student Notebook: Laboratory notebooks are arguably the most useful tool at an experimenter's bench. Remind students of the critical importance of recording all experimental observations, and especially recording all experimental conditions (e.g., the type of chemical treatment, the range of concentrations, number and species of seeds, etc.) when starting an experiment so that they can maintain comprehensive, unambiguous control over those variables when they follow up with subsequent experiments.

Implementing the Lesson

Instructions:

1. Video (3 Minutes)

Getting Started with Everyday Toxicology

Start with your normal opening remarks to your students. Explain that they will be starting a series of lessons about environmental toxicology. Have the students view the **"Getting Started with Everyday Toxicology**" video. This video introduces a "narrative" that will connect the whole module.

2. Group Activity (20 Minutes)

Teacher Tip: *Be sure to give scenario #1 to one of your groups. This grandfather and granddaughter example will be used throughout the module.*

Who Receives a Higher Dose?

Conduct the group activity "**Who Receives a Higher Dose?**" Ask students to divide into groups of 2-3 or assign students to groups. **The students will be working within in these groups for the rest of the module.** The scenarios are divided into 3 parts. Give each group part 1 of a numbered scenario in which they will read and answer the questions. Remind each group of students that they will be reporting their results during the whole group discussion. You should be available to assist groups as needed. Students will need to answer the questions to each part correctly before moving on to the subsequent parts.

You may want to develop a system to ensure students are answering each part correctly before moving on. **(The scenarios are located in the appendix.)** It is important to note that depending on your class size, you may not use all six scenarios.

3. Post-Activity Discussion (10 Minutes)

Teacher Tip: *Students may confuse this technical definition of dose (dose = exposure / body mass) with our everyday usage of the word "dose" as used, for example, in the directions on over-the-counter drug labels.*

These two uses of the word "dose" are very different. After reviewing the scenarios above, the following example should help draw this distinction:

If a husband weighing 130 kg (286 pounds) and a wife weighing 65 kg (143 pounds) both have a headache and reach for a bottle of Tylenol (acetominophen), they will read that the adult "dose" is two tablets, or 650 mg. However, following the actual definition of dose, the husband, who is twice as big,

Who Receives a Higher Dose?

Monitor each group of students, ensuring they are completing the "**Who Receives a Higher Dose?**" activity. Call on each group of students and ask them to report out on each of the following questions, which they should have already answered within their groups.

- Who were the two subjects?
- What were they exposed to?
- Describe the effect.
- How was the dose calculated? (Each group should discover the answer that Dose = Exposure/Body Weight, with units mg/kg.)
- What were their doses?

As students are reporting back, list information in a table that all students can see. Below is an example of what the completed table might look like. (Note that students are given data in their scenarios that allow them to make calculations with two significant figures.)

Scenario	Subject	Substance	Effect	Dose
1	Grandpa	Caffeine	(none)	3.0 mg/kg
1	Granddaughter	Caffeine	Jittery, shaking hands	10 mg/kg
2	Husband	Tetrodotoxin	Numb, tingly lips	0.00080 mg/kg
2	Wife	Tetrodotoxin	Sweating heavily, headache, weakness, & shortness of breath	0.0015 mg/kg
3	Mom	Tylenol	Still has headache	1.1 mg/kg
3	Baby	Tylenol	Goes to sleep	11 mg/kg
4	Mom	Tylenol	No longer has headache	4.5 mg/kg
4	Baby	Tylenol	Goes to emergency room	45 mg/kg
5	Husband	Vitamin D	Slightly ill, with a low appetite, & nausea	0.0096 mg/kg
5	Wife	Vitamin D	Low appetite, nausea, excessive thirst, urination & kidney problems	0.019 mg/kg
6	Husband	Vitamin D	Pain in limbs, weakness in limbs, diagnosed with osteoporosis & ostemalacia	0.000012 mg/kg
6	Wife	Vitamin D	(none)	0.000023 mg/kg

If students do not call out the following insights spontaneously, prompt them with the suggested questions.

- **"Good" vs. "Bad."** One key insight is the notion that the very same substances in the table can be **both good and bad for human health, depending only on the dose.** (See below, homework for lesson 2, regarding vitamin D and

receives half the dose (650 mg / 130 kg = 5.0 mg/kg) that the wife receives (650 mg / 65 kg = 10 mg/kg).

It may be worthwhile to discuss the implications of this distinction, and to stress that all subsequent discussion of "dose" in this module refers to the toxicological definition, which normalizes for body size.

Teacher Tip: *For more about the differences in response to acetominophen between adults and children, see the discussion of metabolism and elimination in Lesson 5.*

cholesterol). *Suggested question: "Which of these substances is good for you? Which is bad for you?"*

- **Dose = Exposure/Body Mass.** The second key point that this activity aims to steer participants toward is the formal relationship between exposure and dose.

  - In these discussions, we define "exposure" to mean the amount of a substance that is actually absorbed into the body, and not merely in the immediate environment.

  - "Dose" is a measure of exposure that accounts for body size. (This meaning is distinct from the connotation of a medically prescribed dose; see the accompanying sidebar.)

- **Connection to the Narrative**. Trace salt concentrations are necessary for all life, but high concentrations of salt can be toxic to crop plants (and all other organisms). *Suggested question: "What does this have to do with plants and salt?"*

4. Video (5 Minutes)

The Poison is the Dose

After the discussion of the **"Who Receives a Higher Dose?"** activity, students will view the **"The Poison is the Dose"** video. This video summarizes the idea of dose/response curves while utilizing the grandfather and granddaughter scenario example. This segment reinforces the concept of dose and that both beneficial and harmful effects depend on dose, and then **quantifies these ideas by introducing the concept of the dose/response curve.** (Alternatively, you may choose to present content from this video directly, in a traditional lecture and discussion format.)

5. Guided Discussion (5 Minutes)

Conclusion

The following two questions can generate a quick discussion that may help **clarify, synthesize, and extend the concepts** of dose and response.

Ask students to reflect on these questions, discuss them in their groups, and share their conclusions with the class.

- Is there a substance that is toxic at any dose?

- Is there a substance that is safe at any dose?

Answer: *In principle, even the most deadly toxin could be rendered harmless by diluting it to a sufficiently low*

dose; in principle, even the most benign substance would be deadly at a high enough dose. (Human deaths due to excessive consumption of water are not unheard of; recall the 2007 case of Jennifer Strange, who died in a radio station's contest.)

However, in practice, if that harmless dose is not detectable by current medical techniques, regulatory agencies will determine that there is "no safe dose." For example, there is no safe dose of lead for small children—any detectable blood level of lead in children has been clinically correlated with harmful effects on brain development.

Conversely, there are substances that must be delivered in such high doses in order to observe a harmful effect that for all practical purposes they are never lethal. For instance, rats had to be force-fed truly huge amounts of vitamin C before a lethal dose (LD_{50} ~12 g/kg!) could be recorded—so much that death could very well have been from the force-feeding itself. (See lesson 3, regarding the rapid elimination of vitamin C.)

Finally, address any questions students may have before prompting them to complete their homework.

Homework

6. Video (5 Minutes)

Comparing Dose/Response Curves

Remind students to complete their homework, **"Comparing Dose/ Response Curves."**

7. Reflective Questions (15 Minutes)

Comparing Dose/Response Curves

Answer the following questions and post your responses within your class's online collaborative tool for all of your classmates to review. Then, review your classmates' responses and comment on at least three of them.

What dose/response curve would you measure in order to evaluate the effects of salt on crops? In particular,

1. Which variable(s) would you manipulate experimentally? In other words: **what specific quantity** would you measure and plot on the X-axis of the dose/response curve?

2. Which biological response(s) would you measure? In other words: **what specific quantity** would you measure and plot on the Y-axis of the dose/response curve?

Answers: *1. Experimentally manipulate salt concentration. Measure responses over a range of concentrations. 2. There are a wide range of possible indicators of toxicity: height of growth, number of leaves, color of leaves, yield of fruit in grams, rate of growth, etc.*

Take your thoughts about your experimental system a step further by posting **your critique of the experiments posted by your classmates.** Respond with comments to three of your classmates' posts on the online collaborative tool, addressing the following issues:

1. Compared with others, are these methods more or less **practical**? (Think: cost, time, resources?)

2. Compared with others, are these methods more or less **sensitive**?

Some representative answers:
Practicality
Experiments that require seeds or small sprouts will obviously be cheaper and easier than those that require full-size plants or trees in the field. For instance, an analysis of fruit or nut yield (while providing potentially critical data) would require a long-term commitment of fairly large resources of test plots, labor, and so forth.

Sensitivity
There is a great deal of variation in salt tolerance among different plant species, or even among different cultivars and varieties of a particular crop species. Plants with low salt tolerance will, in general, serve as more sensitive indicators. Many plants will have different sensitivities at different developmental stages; in general, very young seedlings will be more sensitive than established plants.

Appendix

Lesson Time and Supply List

Amount of Prep Time:

We recommend 30-45 minutes depending on your expertise level with the content. Each module will vary depending on your previous experience with the content and technology.

Materials:

Each student will need
- a scenario handout.
- access to a computer to view videos (unless you decide to show the video through the class projector unit.)
- to be added to your online collaborative tool.

You will need
- to print and cut scenario handouts.
- to download or develop a partially completed “Who Receives a Higher Dose?” table to be completed with your students.
- to set up your online collaborative tool.

Total Lesson Time:

Lesson Activity	**Amount of Time in Class**
Video: Getting Started with Everyday Toxicology	3 Minutes
Group Activity: Who Receives a Higher Dose?	20 Minutes
Post-Activity Discussion: Who Receives a Higher Dose?	10 Minutes
Video: The Poison Is the Dose	5 Minutes
Guided Discussion: Conclusion	5 Minutes
Total Time	**43 Minutes**
Lesson Activity	**Amount of Time out of Class**
Video: Comparing Dose/Response Curves	5 Minutes
Reflective Questions: Comparing Dose/ Response Curves	15 Minutes
Total Time	**20 Minutes**

Scenario #1: Grandfather, Granddaughter, and Caffeine

Part 1

Scenario: A thirteen-year-old girl and her grandfather walk into a café together. They each drink a large coffee. Thirty minutes later, the girl feels jittery and her hands are shaking. Her grandfather feels fine. They both consumed the same amount, or had the same exposure, of caffeine, but their responses were quite different. Apparently, one received a larger dose of caffeine than the other.

Question: How might you explain two very different effects in two people who have consumed the same amount of caffeine?

---------- Cut Here ----------

Part 2

Question: Consider these facts. The girl weighs 36 kg (79 pounds) and her grandfather weighs 120 kg (264 pounds). A large coffee contains 360 mg of caffeine. Would you change your answer to the previous question based on these data?

Problem: Using these data, find a method to calculate the dose of caffeine that each person received. What dose of caffeine did each receive?

---------- Cut Here ----------

Part 3

In other words, they both had equal exposures to caffeine, but the girl had a much higher dose—more than three times higher.

Prepare to summarize your findings to the whole class by answering these questions:

1. Who were the two individuals?
2. What chemical were they exposed to?
3. What was the effect on each individual—harmful, beneficial, or neither?
4. How did you calculate their respective doses?
5. What were their respective doses?

---------- Cut Here ----------

Answer Key—Scenario #1: Grandfather, Granddaughter, and Caffeine

Part 1

Possible answers: one is bigger/smaller than the other, one is younger/older than the other, one is more/less sensitive, one is sick, one is male/female, one has built up a tolerance, etc.

Part 2

Answer: The girl's dose was 10 mg/kg; her grandfather's dose was 3.0 mg/kg.

Scenario #2: Husband, Wife, and Improperly Prepared Pufferfish

Part 1

Scenario: Fugu is a pufferfish used in Japanese cuisine that contains a potent neurotoxin called tetrodotoxin. This dish is harmless when prepared correctly by an expert chef, but when prepared improperly, it can cause death by paralysis.

A husband and wife go into a sushi restaurant and decide to be adventurous. They each have an order of fugu. Twenty minutes later, the wife is sweating heavily, complaining of headache, weakness, and shortness of breath. Her husband has numb, tingly lips. They both consumed the same amount, or had the same exposure, of tetrodotoxin, but their responses were quite different. Apparently, one received a larger dose of tetrodotoxin than the other.

Question: How might you explain two very different effects in two people who have consumed the same amount of tetrodotoxin?

---------- Cut Here ----------

Part 2

Question: Consider these facts. The husband weighs 130 kg (286 pounds) and the wife weighs 65 kg (143 pounds). Their servings of pufferfish each contained 0.10 mg of tetrodotoxin. Would you change your answer to the previous question based on these data?

Problem: Using these data, find a method to calculate the dose of tetrodotoxin that each person received. What dose of tetrodotoxin did each receive?

---------- Cut Here ----------

Part 3

In other words, they both had equal exposures to tetrodotoxin, but the wife had a much higher dose—twice as high.

Prepare to summarize your findings to the whole class by answering these questions:

1. Who were the two individuals?
2. What chemical were they exposed to?
3. What was the effect on each individual—harmful, beneficial, or neither?
4. How did you calculate their respective doses?
5. What were their respective doses?

---------- Cut Here ----------

Answer Key—Scenario #2: Husband, Wife, and Improperly Prepared Pufferfish

Part 1

Possible answers: one is bigger/smaller than the other, one is younger/older than the other, one is more/less sensitive, one is sick, one is male/female, one has built up a tolerance, etc.

Part 2

Answer: The husband's dose was 0.00080 mg/kg; the wife's dose was 0.0015 mg/kg.

Scenario #3: Mom and Baby Take Baby Tylenol

Part 1

Scenario: A young mother and her one-year-old baby both have a fever. The mother gives her baby 0.8 ml of acetominophen drops ("Infant's Tylenol"). She doesn't have any adult acetominophen pills, so she gives herself 0.8 ml of the baby drug, too. Thirty minutes later, the baby has stopped crying and settles down to sleep. His mother is relieved that the baby seems better, but her fever doesn't feel any better. They both took the same amount, or had the same exposure, of acetominophen, but their responses were quite different. Apparently, one received a larger dose of acetominophen than the other.

Question: How might you explain two very different effects in two people who have consumed the same amount of acetominophen?

---------- Cut Here ----------

Part 2

Question: Consider these facts. The baby weighs 7.2 kg (16 pounds) and his mother weighs 72 kg (158 pounds). A dropper of 0.8 ml contains 80 mg of acetominophen. Would you change your answer to the previous question based on these data?

Problem: Using these data, find a method to calculate the dose of acetominophen that each person received. What dose of acetominophen did each receive?

---------- Cut Here ----------

Part 3

In other words, they both had equal exposures to acetominophen, but the mother had a much lower dose—ten times lower.

Prepare to summarize your findings to the whole class by answering these questions:

1. Who were the two individuals?
2. What chemical were they exposed to?
3. What was the effect on each individual—harmful, beneficial, or neither?
4. How did you calculate their respective doses?
5. What were their respective doses?

---------- Cut Here ----------

Answer Key—Scenario #3: Mom and Baby Take Baby Tylenol

Part 1

Possible answers: one is bigger/smaller than the other, one is younger/older than the other, one is more/less sensitive, one is sicker, one is male/female, one has built up a tolerance, etc.

Part 2

Answer: The baby's dose was 11 mg/kg; his mother's dose was 1.1 mg/kg.

Scenario #4: Mom and Baby Take Adult Tylenol

Part 1

Scenario: A young mother and her one-year-old baby both have a fever. The mother takes an adult acetominophen tablet ("Tylenol"). She doesn't have any infant acetominophen drops, so she unwisely gives the baby an adult tablet, too. Thirty minutes later, her fever feels better, but the baby's distress is even worse than before, and he is vomiting. A trip to the emergency room is necessary to save his life!

Mother and baby both took the same amount, or had the same exposure, of acetominophen, but their responses were quite different. Apparently, one received a larger dose of acetominophen than the other.

Question: How might you explain two very different effects in two people who have consumed the same amount of acetominophen?

---------- Cut Here ----------

Part 2

Question: Consider these facts. The baby weighs 7.2 kg (16 pounds) and his mother weighs 72 kg (158 pounds). An adult pill contains 325 mg of acetominophen. Would you change your answer to the previous question based on these data?

Problem: Using these data, find a method to calculate the dose of acetominophen that each person received. What dose of acetominophen did each receive?

---------- Cut Here ----------

Part 3

In other words, they both had equal exposures to acetominophen, but the baby had a much higher dose—ten times higher!

Prepare to summarize your findings to the whole class by answering these questions:

1. Who were the two individuals?
2. What chemical were they exposed to?
3. What was the effect on each individual—harmful, beneficial, or neither?
4. How did you calculate their respective doses?
5. What were their respective doses?

---------- Cut Here ----------

Answer Key—Scenario #4: Mom and Baby Take Adult Tylenol

Part 1

Possible answers: one is bigger/smaller than the other, one is younger/older than the other, one is more/less sensitive, one is sicker, one is male/female, one has built up a tolerance, etc.

Part 2

Answer: The baby's dose was 45 mg/kg; his mother's dose was 4.5 mg/kg.

Scenario #5: Husband and Wife Vitamin Overdose

Part 1

Scenario: Many people living in high latitudes don't make enough vitamin D within their bodies. Concerned that they don't have healthy vitamin D levels, a husband and wife decide that they will both take daily vitamin D supplements. They each take ten pills a day. After a few weeks, the husband is slightly ill, with a low appetite and nausea. The wife also experiences a loss of appetite and nausea, as well as excessive thirst and urination. Her doctor diagnoses kidney problems due to very high blood levels of calcium.

Both the husband and the wife have been taking the same daily amount, or have had the same daily exposure, of vitamin D, but their responses were quite different. Apparently, one received a larger daily dose of vitamin D than the other.

Question: How might you explain two very different effects in two people who have consumed the same amount of vitamin D?

---------- Cut Here ----------

Part 2

Question: Consider these facts. The husband weighs 130 kg (286 pounds) and the wife weighs 65 kg (143 pounds). Each pill contains 0.125 mg of vitamin D, so by taking ten pills, both consume 1.25 mg per day. Would you change your answer to the previous question based on these data?

Problem: Using these data, find a method to calculate the dose of vitamin D that each person received. What dose of vitamin D did each receive?

---------- Cut Here ----------

Part 3

In other words, they both had equal exposures to vitamin D, but the wife had a much higher dose—twice as high.

Prepare to summarize your findings to the whole class by answering these questions:

1. Who were the two individuals?
2. What chemical were they exposed to?
3. What was the effect on each individual—harmful, beneficial, or neither?
4. How did you calculate their respective doses?
5. What were their respective doses?

---------- Cut Here ----------

Answer Key—Scenario #5: Husband and Wife Vitamin Overdose

Part 1

Possible answers: one is bigger/smaller than the other, one is younger/older than the other, one is more/less sensitive, one is sick, one is male/female, one has built up a tolerance, etc.

Part 2

Answer: The husband's daily dose was 0.0096 mg/kg each day; the wife's daily dose was 0.019 mg/kg each day.

Scenario #6: Husband and Wife Vitamin Deficiency

Part 1

Scenario: Many people who live at high latitudes, spend most of their time inside, and protect themselves from sunlight do not produce enough vitamin D within their bodies. A husband and wife eat a diet that they think is healthy, but it contains low levels of vitamin D. Eventually, the husband begins to complain of pain and weakness in limbs, and his doctor diagnoses osteoporosis and osteomalacia (weak bones). His wife doesn't have any symptoms.

Both the husband and the wife have been consuming the same daily amount, or have had the same daily exposure, of vitamin D, but their responses were quite different. Apparently, one received a larger daily dose of vitamin D than the other.

Question: How might you explain two very different effects in two people who have consumed the same amount of vitamin D?

---------- Cut Here ----------

Part 2

Question: Consider these facts. The husband weighs 130 kg (286 pounds) and the wife weighs 65 kg (143 pounds). Their meals on a typical day contain a total of 0.0015 mg of vitamin D. Would you change your answer to the previous question based on these data?

Problem: Using these data, find a method to calculate the dose of vitamin D that each person received. What dose of vitamin D did each receive?

---------- Cut Here ----------

Part 3

In other words, they both had equal exposures to vitamin D, but the husband had a much lower dose—half as much.

Prepare to summarize your findings to the whole class by answering these questions:

1. Who were the two individuals?
2. What chemical were they exposed to?
3. What was the effect on each individual—harmful, beneficial, or neither?
4. How did you calculate their respective doses?
5. What were their respective doses?

---------- Cut Here ----------

Answer Key—Scenario #6: Husband and Wife Vitamin Deficiency

Part 1

Possible answers: one is bigger/smaller than the other, one is younger/older than the other, one is more/less sensitive, one is sick, one is male/female, one has built up a tolerance, etc.

Part 2

Answer: The husband's daily dose was 0.000012 mg/kg each day; the wife's daily dose was 0.000023 mg/kg each day.