**Learning Scenario – Dosing Model (Vensim)**

**Basic Model:**

**Description**

 This is a system model of the concentration of a drug in the bloodstream as a function of time and the doses. The user determines the dosage and doses per day, as well as the half-life of the drug and the blood volume of the patient. A graph shows the concentration of the drug in the body over the course of 48 hours as well as showing when the concentration exceeds the toxicity level or does not reach the medicinal level.

**Background Information**

 Ideally, medicine would function best if it could maintain a constant concentration throughout the body, but this is not feasible. Instead, it is important for pharmacologists to set the dosages and timing such that the concentration of the drug stays within a certain range. The two quantities of note are the concentration of medicine in the intestines and that in the plasma. As medicine is taken in pill form, it first passes through the digestive system before reaching the bloodstream. From there, it is slowly excreted, requiring additional doses to maintain concentration.

**Science/Math**

The fundamental principle behind this model is HAVE = HAD + CHANGE. The concentration of medication in the blood stream depends on the amount of medication previously in the intestines and on the rate of excretion. The more medicine in the blood stream, the more that will be excreted each time step.

Every time step, the following things happen:

1. Medicine moves into the intestines according to the player-set doses per day and dosage per day.
2. Medicine in the Intestines is absorbed into the blood stream according to the player-set absorption rate constant.
* Absorption = Absorption rate constant \* Medicine in Intestines
1. Medicine in the plasma is excreted according to the excretion rate constant and the player-set medication half-life.
* Excretion = Excretion rate constant \* Plasma level
1. The concentration of medication in the plasma is determined by the player-set blood volume of the patient.
* Plasma Concentration = Plasma Level / Blood Volume

This model exhibits characteristics of a periodic function and an exponential decay function. The following equation for exponential functions is referenced in Learning Objective 1:

The equation for an exponential decay function is the following:



where a is the initial amount of the substance, r is the rate of decay, and t is the time period when the decay is taking place. In this dosing model, this equation changes to the following:



In this model the excretion rate constant is defined as .693.

**Example:** In Objective One students are asked to find out the amount of medicine in a patient’s blood after 6 hours with the following parameters: the initial amount in the blood is 6,000mg and the half-life of the medication is 3 hours. Below is the solution using the above equations:

mg

**Teaching Strategies**

 An effective way of introducing this model is to ask students to brainstorm the process medicine takes in passing through a patient’s body. Ask the following questions:

1. How do people medications? What are the different forms of medication? *Pill, syrup, injection, under the tongue*
2. How do these different forms of medication eventually enter the bloodstream so the patient can feel the effects? What parts of the body/organs do they have to pass through?
3. Once the medication gets into the bloodstream, how long does it stay there? What characteristics of the medication and the person determine how long the effect lasts?
4. How do doctor’s try to make sure a medication is at the right concentration in a patient’s body throughout the day? What factors do they have to consider?

**Implementation:**

**How to use the Model**

This relatively in-depth model has a number of parameters that can be manipulated to produce different results:

1. The “Blood Volume” parameter determines the liters of blood in the patient’s body through which the medication will be distributed.
2. The “doses per day” parameter determines the number of doses of medicine taken by the patient each day.
3. The “dosage per day” parameter determines the total dose of medication taken by the patient throughout the day.
4. The “Absorption rate constant” parameter determines the proportion of the medicine absorbed from the intestines into the blood stream each time step.
5. The “Half-life” determines the half-life of the medication and indirectly determines the rate that the medication is excreted from the blood stream.
6. The “Start Time” and “End Time” parameters determine when the dosing begins and ends. They have very little affect on the model.
7. The “Time Step” parameter determines how long the dose is given.

 All of the aforementioned parameters are manipulated by clicking and dragging their respective sliders. The maximum, minimum, and step values for each parameter are pre-set. Any changes made to the sliders take effect immediately.

 To run the simulation with adjustable variables, click the “Automatically Simulate on Change” button: . The concentration of medicine in the blood over time is displayed immediately in graphical form to the right of the model.

 For a complete tutorial on how to use Vensim, please go to the following link: <http://shodor.org/tutorials/VensimIntroduction/Preliminaries>.

**Learning Objectives:**

1. Understand exponential decay as it relates to the saturation of medicine in the bloodstream
2. Recognize and understand the applications of periodic functions
3. Understand the effect of each parameter on the medicine concentration in the intestines and blood over time

**Objective 1**

To accomplish this objective, have students run the simulation with the default parameters, and observe the graphs. Write on the board the equation determining the amount of medicine excreted from the blood every time step (Excretion = Excretion rate constant \* Plasma level). Ask the following questions:

1. Why does the patient have to keep taking medication at regular intervals? Why does the amount of medicine in the blood stream decrease slowly over time?
2. What is the rate at which the medication is being excreted from the system? What parameter controls that rate?
3. Supposing the patient has 6000 mg of a medication in their blood stream. If the medication has a half-life of 3 hours, how much of the medication will be in their bloodstream after 3 hours? 6 hours? 12 hours? 24 hours? Etc. If the medicinal level of the medication is between 2,000 mg and 6,000 mg, for how many hours will there be enough of the medicine in the patients’ blood for it to have an effect? Make sure to use the exponential decay equation mentioned in the Science/Math section.
4. In what ways is this model showing exponential decay? In what ways is it not? Explain.

**Objective 2**

Have students experiment with the doses per day and the dosage per day and observe the changes in the graph. Explain periodic functions and ask them to explore the model with those ideas in their head. Ask the following:

1. Is this model an example of a periodic function? Why or why not?
2. What would we need to change about the model to make it a periodic function?
3. What parameter determines the “period” of the function? Explain. *Doses per day*
4. What other activities could be modeled using periodic functions?

**Objective 3**

Have students experiment with each of the parameters to see the effect on the graph. Ask the following questions to guide their exploration:

1. What changes do you notice in the graph if you increase the absorption rate? What if you decrease the absorption rate? How important is the absorption rate to the effectiveness of the medicine? Why?
2. Try increasing the blood volume. What affect does that have on the overall medicine concentration in the bloodstream? Why is this the case? Why do larger people have to take more medicine for it to have the same effect?
3. What happens when you increase the doses per day? What about the dosage per day? Describe the changes this makes to the curves on the graph.
4. How does increasing and decreasing the time step affect the graph? How does this relate the patient’s intake of medicine?

**Extensions:**

1. Explore the use of models for predicting outcomes before they happen
2. Think about the qualities this model still lacks when compared with the real world

**Extension 1**

Encourage students to discuss the use of this model in designing medications. Ask the following questions:

1. How could a pharmaceutical company use this model to design medications? Explain.
2. Why would a company want to use a model such as this one before moving on to testing on animals and humans?
3. How could the parameters in this model be changed to represent different types of medications?

**Extension 2**

Have students consider the ways in which this model is *not* an accurate representation of the real world. Ask the following questions:

1. What factors can you think of in the real world that this model leaves out? Explain.
2. What parameters could be added to this model to make it more realistic?
3. What other aspects of medication could be explored using a model similar to this one?
4. What other parameters would need to be added to this model to make it an accurate guess at the correct dosing for a specific person?
5. Would you ever trust a model to determine the information for your medication dosages? Why or why not?

**Related Models**

**Pharmacology Dosing Model**

<http://www.shodor.org/talks-new/excel>

This is the Excel version of the Vensim Dosing Model. Students should discuss the similarities and differences between the two different modeling devices.

**Nutria Population Model**

<http://www.shodor.org/talks-new/vensim>

This Vensim model represents the population of nutria, a type of aquatic rodent, over time. Students should discuss the difference between an exponential growth model and an exponential decay model.