INTERDISCIPLINARY LIVELY APPLICATIONS PROJECT

Saving a Drug Poisoning Victim

AUTHORS:
Jodye I. Selco (Chemistry)
jodye_selco@redlands.edu

Janet L. Beery (Mathematics)
janet_beery@redlands.edu

University of Redlands
Redlands, CA

EDITOR:
David C. Arney

CONTENTS:

MATHEMATICS CLASSIFICATIONS:
Calculus, Differential Equations, Mathematical Modeling

DISCIPLINARY CLASSIFICATIONS:
Chemistry, Biology, and Medicine

PREREQUISITE SKILLS:
Exponential growth and decay, Euler's method or other numerical method for solving systems of differential equations

PHYSICAL CONCEPTS EXAMINED:
Kinetics of drug uptake and elimination

MATERIALS INCLUDED:
TrueBASIC programs

COMPUTING REQUIREMENTS:
Numerical differential equations solver, spreadsheet, computer algebra system, or any computer programming language

ILAP Modules: Tools for Teaching 2000, 31-46.

Contents

1. Setting the Scene

You are a physician in a hospital emergency room. A child has just been brought to the emergency room by a frantic parent. The parent takes the asthma medication theophylline in tablet form. Two hours before arriving at the hospital, the child ingested eleven 100-mg theophylline tablets. Like most oral drugs, theophylline is absorbed into the bloodstream at a rate proportional to the amount present in the gastrointestinal tract (stomach and intestines) and is eliminated from the bloodstream at a rate proportional to the amount present in the bloodstream.

Your quick check of the *Physician's Desk Reference (PDR)* [1999] reveals that the brand of theophylline that the child took has an absorption half-life of 5 hours and an elimination half-life of 6 hours. The *PDR* also warns that a blood-level concentration of 100 mg/L or more of the drug is seriously toxic and that a concentration of 200 mg/L or more is fatal.[1]

You estimate that the child has 2 L of blood. You also determine that because of the 2-hour delay, the pills already have passed from the child's stomach to his intestines, so that it is too late to eliminate the drug by inducing vomiting. Your task is to determine if the child is in danger, and, if so, to save his life.[2]

2. Building a Model

You are interested in the amount of theophylline in the child's bloodstream over time. (Actually, you are concerned about the *concentration* of theophylline in the child's bloodstream over time; but since the amount is slightly easier to

[1] These values are the concentrations at which 50% of the patients exhibit these symptoms. In the fatal case, the concentration of of 200 mg/L—the lethal concentration for 50% of the population—is called the LC_{50} value.

[2] In reality, a physician in this situation would contact the local poison center, which would provide information about which symptoms to watch for as well as the appropriate medical treatment.

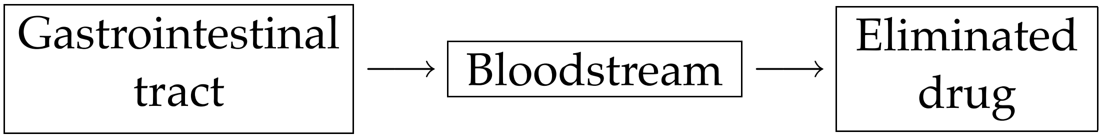

Figure 1. Compartment model for theophylline.

calculate than the concentration and since you can convert easily from one to the other, you decide to calculate the amount.)

To determine the amount over time, you also need to determine the amount of theophylline still in the child's gastrointestinal tract over time. You could calculate also the amount of theophylline eliminated from the bloodstream; however, since theophylline in this form is not dangerous, you decide not to keep track of the eliminated drug. The compartment model in **Figure 1** illustrates the progress of the drug through the child's body.

Requirement 1: First, predict the general shape of the graph of $G(t)$, the amount of theophylline in the child's gastrointestinal tract (in mg) after t (in hours), and of the graph of $B(t)$, the amount of theophylline in the child's bloodstream (in mg) after t hours. Using time $t = 0$ as the time at which the child first ingested the theophylline, make separate rough sketches of the graphs of $G(t)$ and $B(t)$. On each graph, label the point at $t = 0$. (If $t = 0$ is the time when the child first ingested the theophylline, what are the corresponding values for G and B?) Remembering that the half-life for absorption of theophylline from the gastrointestinal tract into the bloodstream is 5 hours, label the points at $t = 5$ and $t = 10$ on your graph of $G(t)$. You need not label any other points on the graphs or mark any other values along their axes—yet.

Requirement 2: Since you have more information about the rates of change of G and B than about G and B themselves, you decide to model the quantities G and B by writing equations for their rates of change (differential equations). Begin with the differential equation for G. Theophylline is absorbed into the bloodstream at a rate proportional to the amount present in the gastrointestinal tract. This means that theophylline is *leaving* the gastrointestinal tract at a rate proportional to the amount of the drug present there. Hence, taking k to be the positive constant of proportionality, you have

$$\frac{dG}{dt} = -kG \text{ mg/h}, \qquad G(0) = 1100 \text{ mg}.$$

Use what you know about initial value problems of this form, along with the fact that the absorption half-life of theophylline is 5 hours, to write a formula for $G(t)$, the amount of theophylline (in mg) in the gastrointestinal tract at time t. (That is, solve the initial value problem for $G(t)$, then solve for k. Record k to four decimal places.) You now should have both a formula for $G(t)$ and a differential equation for G in which k has a numerical value.

Requirement 3: Now write a differential equation for B. Since theophylline is entering the bloodstream at one rate and leaving it at another rate, the differential equation for B is of the form

$$\frac{dB}{dt} = \text{absorption rate} - \text{elimination rate},$$

with units of mg/h.

Consider the first term, the absorption rate. Recall that theophylline is absorbed into the bloodstream at a rate proportional to the amount present in the gastrointestinal tract with an absorption half-life of 5 hours. This should sound familiar; use your work from **Requirement 2** above to write an expression for the absorption rate.

Now consider the second term, the elimination rate. Remember that theophylline is eliminated from the bloodstream at a rate proportional to the amount present in the bloodstream with a half-life of 6 hours. In order to find the constant of proportionality, assume that at some (future) time t_1 there is 20 mg of theophylline in the bloodstream and that no additional theophylline is entering the bloodstream—that is, assume for the moment that

$$\frac{dB}{dt} = -\,\text{elimination rate}, \qquad B_1(t) = 20 \text{ mg}.$$

Under these assumptions, the amount of theophylline in the bloodstream is decaying exponentially. Use what you know about exponential decay to write an expression for the elimination rate. (Record the constant of proportionality to four places after the decimal point.)

You now should have a differential equation for B involving the variables G and B.

3. Using the Model

Now that you have differential equations for G and for B, you are ready to use them to determine if the child is in danger and, if so, how to treat him.

Unlike for the differential equation for G, there is not a simple closed-form solution for the differential equation for B. That is, you may not be able to write an explicit formula for $B(t)$ but instead may have to approximate values of $B(t)$ using Euler's method or another numerical method for solving differential equations. Your instructor will specify the degree of accuracy (number of significant figures) for your calculations.

Requirement 4: Determine the amount of theophylline in the child's bloodstream at the time of his admission to the hospital, $t = 2$ hours. Recalling that the child has 2 L of blood and that a blood-level concentration of 200 mg/L or more of the drug is fatal, what amount of theophylline in his bloodstream,