I.11 Specific Dosing Calculations, Thermometry, and Pharmacogenomics

GOAL *To provide practice with several formulas using patient-specific data to determine medication doses.*

OBJECTIVES

This chapter equips students to:

- Define dose, single dose, daily dose, total dose, dosage regimen, and usual adult dose
- Calculate in kilograms the actual, ideal, and adjusted body weight for a patient
- Calculate medication doses based on a patient's weight
- Calculate medication doses based on a patient's body surface area
- Define the Cockcroft-Gault equation, and use this formula to determine a patient's kidney function and medication doses based on it
- Interconvert between degrees Celsius and degrees Fahrenheit
- Define the key points for personalizing warfarin therapy using pharmacogenetic testing

KEYWORDS

Body surface area (BSA)
Cockcroft-Gault equation
Creatinine clearance (CrCl)
Ideal body weight (IBW)
Thermometry

Importance for Medical Math and Clinical Practice

Chapter 11 introduces calculating a drug dose based on a patient's physical characteristics such as body weight, body surface area, body temperature, organ system function, and genetic makeup. Use of these in calculations generally implies the need for a more precise estimate of the amount of drug to get a specific therapeutic outcome. This may be necessary since the difference between a therapeutic dose and a toxic dose for some drugs may be quite small. Or, it may be known that a particular drug's therapeutic effect depends upon accumulation of the drug in a specific body tissue or upon the rate by which a drug is changed chemically (metabolized) in the body or removed from the body.

In many cases of new drug development, the size of a drug dose is determined by data gathered from thousands of patients. These patients may represent diverse underlying diseases, where the goal of therapy is relief of a symptom common to all—pain relief, for example. And dosages are published in the new drug's official labeling based on the dose generally needed for an average patient experiencing the particular symptom. For some of these cases, after initial development, dosing guidelines may become tighter as the particular drug is applied to a narrower disease condition. The physical characteristics of a patient, then, may become much more important in fine tuning the proper dose building on the general dose already established during development.

Definitions

It is important in this chapter to focus first on some definitions that health practitioners often take for granted, i.e., words that are heard so often they merge into an amorphous single entity, when, in fact, they have important distinctions.

- **Dose—**Amount of drug taken by a patient for the intended medicinal (therapeutic) effect.
- **Single dose—**Amount of drug taken at one time that may be part of a continuing (perhaps over weeks or months and, possibly, irregular) dosing regimen; or, administration of only one dose of drug when only a single dose is needed to achieve the desired therapeutic effect.
- **Daily dose—**Total amount of drug taken during a 24-hour period. Sometimes, a drug dose is stated as a total amount of drug to be taken each day with further instructions to give that total daily dose as a number of divided doses during the day; for example, to give 500 mg of a drug each day as four individual (divided) doses of 125 mg each spaced during the day.
- **Total dose—**Amount of drug taken during an entire course of therapy. Some drugs have maximum cumulative doses. This is especially true for drugs with toxic effects that are related not necessarily to the size of any one dose (within bounds of propriety) but to the total time the body is exposed to the drug as well as the total amount of drug. Note that this concept may also apply as the *total daily dose* explained above for divided doses.
- **Dosage regimen—**The schedule of dosing a drug (e.g., twice daily for 14 days). Some regimens can be quite complicated, such as in the concepts of *sliding scale*. For this the size of a drug dose depends on the value of a laboratory test performed before the time for a dose (e.g., insulin). Or, for *diminishing/tapering dosing* the number of doses or the size of daily doses gradually decreases until no more doses are needed or until a baseline low chronic dose is achieved (e.g., prednisone). Note also that certain drug doses may be titrated to effect, where the size of dose varies as the response to a dose varies.
- **Usual adult dose—**Amount of drug that ordinarily produces the effect intended in adults. This is the dose established during clinical trials suitable for the typical adult patient expected to use the drug. Of course, an adult is not the only target population for drug therapy since a pediatric patient or a geriatric patient may also, in fact, be the typical patient for some drugs. Doses for these patients may require modification of the usual adult dose.

There are a number of methods used to determine drug doses. For new drugs, a dose or range of drug doses is established experimentally/statistically for inclusion in the legally required labeling (the drug package insert). If a new drug has a narrow therapeutic window (a small difference between an effective dose and a toxic dose), the labeling will often include very specific cautionary statements about physiological processes that should be monitored during a patient's therapy with the new drug. To avoid reaching a toxic dose, there may also be special dosing guidelines based on a number of factors such as a patient's age, weight, body surface area (BSA), internal organ function and, more recently, a patient's genetic composition. Speaking very generally, the progression from considering age to considering weight to considering BSA in developing drug dosing regimens can be thought of as working from the least specific to the most specific predictor of a drug's effect.