Lesson 4: Calculations used to determine patient-specific doses "The right dose"

General Dosing Information

Dosing is one of the most common calculation functions that you will perform during your career. Dosing involves a series of steps, each of which will potentially contain some calculations for you to do. It starts with some guidelines, usually a *dosing range* and from that calculating what amount of drug the patient should receive for each dose, and how much total drug you will thus need to fill the patient's prescription. Let's look at each step.

1. Locate dosing guidelines. You decide that you need to calculate a patient-specific dose. You must first locate some dosing guidelines. You will find these guidelines in many common texts, and later on in your pharmaceutics, pharmacology, and therapeutics courses. Dosing guidelines will usually give you a range to choose from. Some of these ranges will be total daily doses. For instance the pediatric guidelines for dosing amoxicillin, an antibiotic, for an ear infection, are 30-50 mg/kg/day, with the total daily dose given as three separate doses during the day. Other ranges will be per-dose. The adult dosing guidelines for gentamicin (an antibiotic), for instance are 1.5-2.0 mg/kg/dose with doses commonly given every 8 hours. Cyclophosphamide, a medication given to cancer patients, can be dosed at 400-600 mg/m^2 , using body surface area to create a patient-specific dose. The list could go on, but hopefully you get the idea.

2. Obtain patient variable data, such as weight. After locating the dosing guidelines, you need to determine the value of the variable that the dose is dependent on: most commonly the patient's weight, age, height, or kidney function. Determining this may involve some detective work - you may have to ask the patient for his or her weight, for instance, or you may need to obtain a blood concentration of a substance (creatinine, a muscle breakdown product) in order to determine kidney function.

3. Determine the patient-specific daily dosing range. Once you have your dosing guidelines and the value, you will likely have to multiply one by the other in order to get the dosing range for that individual patient. For instance, if you have a 20 kg child who is to receive amoxicillin, and you know that the dosing guidelines are 30-50 mg/kg/day, it is a simple matter to determine that this patient should receive between 600 and 1000 mg of amoxicillin daily.

4. Calculate the range for each patient-specific dose. If you have a daily dosing guideline, and the patient is to receive more than one dose per day, you will need to divide the total daily dose by the number of doses/day. For instance, the patient who is to receive between 600 and 1000mg of amoxicillin per day is to have this medication divided evenly into three doses/day. This means that the patient should receive 200mg to 333mg in each dose.

What do you do when you have no choice but to round up or down *out* of the dosing range? In general, with an antibiotic it is better to round up than down. With all other medications it may be better to round down, rather than up, although if you're just rounding up a little bit (10% or less), then you're probably OK rounding up.

5. Determine an appropriate dosage form for the patient. Sometimes you will be given a dose of a drug that a patient is receiving in one form and will be asked to convert it to the dose a patient should receive in another form. For example, if a patient is receiving a drug intravenously, he or she may need to have an oral dose calculated in order to be eligible for discharge from the hospital. You will need to find some dose equivalency information in order to do this.

At other time, you may initiate a change of dosage form yourself. Physicians may write for oral suspensions for children, but some children will prefer to take tablets. If the patient is a child older than 5 years of age, it is best to ask him or her whether or not he or she can swallow a tablet or would prefer liquid. Likewise, a physician may write a prescription for a particularly large dosage form for an elderly adult. If that patient has an impaired ability to swallow, for example if they've had a stroke, then he or she may need an alternative dosage form. Let the patient or caregiver guide you in your choice of dosage form whenever possible.

6. Choose an appropriate strength or concentration. Once you know the range for each dose, it is simply a matter of examining the strengths that a drug is available in and choosing one that is as simple as possible for the patient to use. For example, amoxicillin comes in a concentration of 250mg/5ml and 125mg/5ml. Since 250mg is

between 200mg and 333mg, it would be easiest to have the parents administer 5ml (one teaspoonful) three times a day to the child.

What do you do if you calculate a specific strength or concentration and the drug is not available in that dose? In that case, you need think carefully about the drug, the usual dosing methods, and the patient. Did the calculation you made come close to the toxic range? If so, then choosing a lower dosage form may be the safest way to go. Or perhaps the drug can be dosed either once or twice daily and you find the dose you calculated can be easily split into two doses. If the drug can be dosed two or three times daily, would the patient be likely to miss that middle-of-the-day dose? These are only a few of several possible considerations that will depend upon the drug, the dose, the calculation, and the patient. Generally speaking, if a dosage form is available that is within 10% of your calculated dose, then you're likely going to be fine with that dosage form.

7. Calculate the total amount needed to fill the prescription. You will find that just because a prescriber writes the amount to be dispensed on a prescription, that does not mean that this is the amount that you will end up dispensing. Insurance plans may specify a maximum number of days of medication that a patient can get, requiring you to adjust the total amount of drug you fill. At other times the prescriber may not specify the total amount of drug to dispense (probably fed up with trying to second-guess insurance stipulations!) This should not be a problem for you. When you know the exact amount of the drug that will be given per dose, you can calculate the amount with which to fill the prescription. Most antibiotics are given for a finite period of time (e.g. 10 days), so you should supply enough medication for the entire course of therapy. For our example above, the patient is to receive a 10 days' supply, so you will make sure the patient receives at least 150ml of amoxicillin suspension (5ml/dose x 3 doses/day x 10 days = 150ml). For most suspensions and other liquid products, you may want to supply a small additional amount to account for spillage and for the suspension that clings to the side of the bottle and won't come out. In general, giving enough for one extra day of therapy is usually sufficient.

Dosing by weight - an example
A 10-year-old, 80-pound child is prescribed clindamycin, dose per weight x 10 days, for treatment of a skin abscess. Facts and Comparisons recommends 8-16mg/kg/day divided into 3 or 4 equal doses. You know that you should dose on the higher end to provide adequate penetration of an abscess. You carry clindamycin 150mg and 300mg capsules in your pharmacy. what strength, quantity, and directions will you dispense?

Clindamycin _____mg, #_____capsules

Take _____capsule(s) _____ times a day.

8-16 <u>mg/kg</u> x <u>1 day</u> x 80 lb x <u>1 kg</u> = 97-194mg po TID *or* 73-145mg po QID
day 3-4 doses 2.2 lb.

Clindamycin 150mg, #30 capsules

Take 1 capsule 3 times a day.

Important advice: dosage forms are made the size they are to facilitate use by the patient. If your calculated dose ends up being 75 tablets or 250ml of liquid, or perhaps 0.005 tablets or 0.002 milliliters of a liquid, you can safely assume that you did something wrong somewhere. With some exceptions, patients will usually take 1-2 tablets or capsules, or 1-2 teaspoonfuls, for each dose. Anything more or less than this, especially a lot more or a lot less, should alert you that you goofed.

Another pearl: you *cannot* cut capsules in half. You *can* cut tablets in half, but that's a pain for the patient. Please use full dosage forms for tablets and capsules whenever possible.

Body weight considerations

You are probably quite deft by now at converting pounds to kilograms and back again. Congratulations! You are now ready to consider some additional concepts regarding medication dosing that is done by weight.

Actual Body Weight (ABW). This is a patient's real weight. It is also called total body weight (TBW)

Ideal Body Weight (IBW). This is the weight of our lean body mass (LBM): the weight we would all really like to be in our heart of hearts, and the weight goal that fills gyms and aerobic classes each January with New Year's resoluteers. You need to know about this because many medications are dosed based on a patient's IBW. Why? These are medications that do not distribute well into fat (i.e., hydrophilic drugs), and if you dosed an overweight patient for a such a medication using ABW, you would end up overdosing the patient. The common equation used for calculating IBW is:

male: 50kg + (2.3kg)(each inch > 5 ft) = IBW in kg

female: 45kg + (2.3kg)(each inch > 5ft) = IBW in kg

The sooner you memorize these equations, the better. You will use them a lot in practice.

If you know the patient's height in centimeters, you could use the following equation:

male: 50kg + (0.9kg)(each cm > 152 cm) = IBW in kg

female: 45kg + (0.9kg)(each cm > 152 cm) = IBW in kg

IBW is also called lean body mass (LBM) or lean body weight (LBW).

What do you do if a patient is shorter than five feet tall? There are no published guidelines that I am aware of. Many clinicians will subtract 2.3kg for each inch under five feet. However, if you divide the baseline weight of 45kg or 50kg for a woman or man (respectively) by 60 inches in height (5 feet), you will end up with 0.75 kg/inch for women and 0.83 kg/inch for men. Taking 2.3 kg off for each inch under five feet in height may be too much. It is probably better to take off 0.75 kg/each inch under 60 inches for women, and 0.83 kg/each inch under 60 inches for men.

Adjusted Body Weight. There are some medications where you will be asked to use an adjusted version of IBW. The main reason this is done is because many people believe that some of the tissue on an overweight person may be muscle tissue. Pharmacokinetic studies for some medications have supported the concept that larger people have a slightly larger muscle mass compared to someone at IBW.

Adjusted body weight will most commonly start with IBW and add a fraction of the difference between ABW and IBW—usually 10%, 20%, or 25%. Common equations for adjusted body weight are thus:

a) adjusted body weight = IBW + (0.1)(ABW-IBW)
b) adjusted body weight = IBW + (0.2)(ABW-IBW)
c) adjusted body weight = IBW + (0.25)(ABW-IBW)

with the choice of degree of adjustment usually dependent upon the drug and the clinician's judgement.

Please do not abbreviate this as ABW because most health care professionals will think "actual body weight" when they see ABW. If you had to abbreviate, the most accurate way would probably be IBW_{adj}

Calculating IBW for a patient with an amputation. If your patient has had a significant portion of a limb removed, then this will affect your IBW calculations. Figure 1 on the next page will provide you with some guidance in the percentage of body weight you will need to remove from the IBW after you have calculated it.

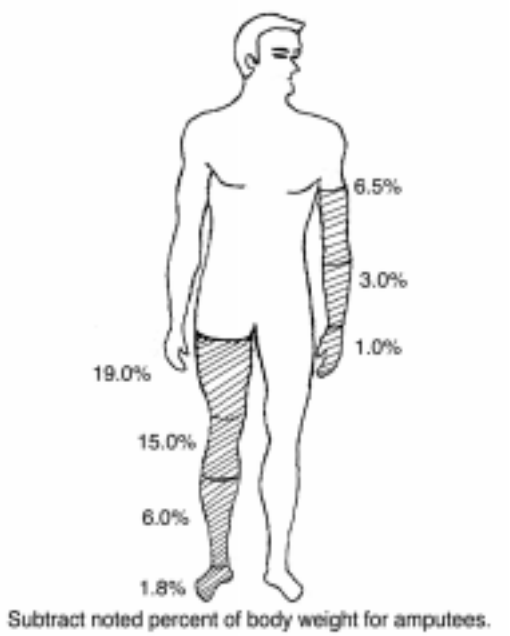


Figure 1. As indicated, you will subtract the noted percent of body weight for the portion of a limb missing from the amuptee. For example, if a patient has a below-the-knee amputation (BKA), you will subtract 6% of the body weight. If an above-the-knee amputation (AKA), you would subtract 15%. If the entire leg has been amputated then 19% of IBW would be subtracted.

Doses for patients with decreased kidney function

Many drugs are cleared by the kidney (i.e. cleared "renally"). In order to dose medications cleared by the kidney in patients whose kidneys are not working well, you will need to first figure out how well their kidneys are working, then apply that estimation of function to dosing. The most commonly-used measurement method for determining kidney function utilizes an endogenous compound called "creatinine," which is a by-product of muscle breakdown. Serum creatinine is measured using blood drawn out of a patient. You will need to identify the patient's weight and gender. You will use all of this information to determine a patient's "creatinine clearance" (CrCl). CrCl units are milliliters/minute

Cockroft-Gault equation

$$CrCl = \frac{(140 - age)\,(IBW)}{(\text{gender factor})(S_{cr})}$$ **Memorize this equation.**

where

- age = age in years
- IBW in kg; ABW can be used when the patient is less than 110% of IBW
- gender factor = 72 for males, 85 for females
- S_{cr} = the patient's serum creatinine in mg/dL

Note: Canceling the units will *not* work with this equation (you'll go nuts if you try to make them cancel), so this is the exception to the rule of always being sure that your units cross out.

Now that you know how to determine creatinine clearance, you can use it to follow any given renal dosing guidelines.

example: A 62yo, 160lb, 5'6" female patient with pneumonia is admitted to hospital and the decision is made to begin therapy with piperacillin, an antibiotic. Her measured serum creatinine is 1.4 mg/dL. Standard dosing for patient with good kidneys is 4g IV q6h. This is decreased to 4g IV q8h for patients with CrCl between 20 and

40ml/min, and 4g IV q12h for patients with CrCl < 20ml/min. Please determine the dosing frequency you will recommend for this patient.

CrCl = $\frac{(140 - age)\,(IBW)}{(85)(S_{cr})}$ = $\frac{(140 - 62)\,(59)}{(85)(1.4)}$ = 39 ml/min

Recommendation: 4g IV q8h

Notice that this patient's IBW was used, rather than her ABW, since her ABW was more than 20% over her IBW. Also notice that the calculated creatinine clearance was rounded off to the nearest whole number.

There is one other equation for calculating creatinine clearance that deserves mention. The Salazar-Corcoran method of calculating creatinine clearance has been found to be more accurate in groups of obese[1] and cardiac[2] patients, compared to Cockroft-Gault. Bear in mind, however, that the accuracy in groups may not translate to individuals (for example, if half the group has a higher and half the group a lower predicted creatinine clearance compared to the real creatinine clearance, then the average might be pretty close to the real creatinine clearance, but that doesn't mean that it would be accurate in an individual patient). In case you should wish to use this method of calculating creatinine clearance, the equations are included here.

Salazar-Corcoran equations

Men: $\frac{[(137-age)(0.28)(wt)] + (12.1)(ht^2)}{(51)(S_{Cr})}$ Women: $\frac{[(146-age)(0.287)(wt)] + (9.74)(ht^2)}{(60)(S_{Cr})}$

where:
d) weight: ABW in kg
e) height: meters (divide inches by 2.54 to convert to cm, then divide by 100 to convert to meters)
f) 1.0 is used for serum creatinine concentration if actual serum creatinine is below 1.0 mg/dL
These equations are far too complex to memorize for the infrequent times you will use them.

Checking doses

I cannot overemphasize the value of checking the dose of every drug in every prescription that you receive. As you develop experience in practice, you will learn to recognize usual doses, but you will also need to think about each medication dose in relationship to the patient. How is each patient likely to respond to the "usual" dose? Consider each patient's size, history of response to medications, and ability to excrete the medication. For example, if you receive a prescription for acetaminophen 325mg and codeine 30mg per tablet, and the prescriber has written directions of "1-2 tabs po q4h prn pain," and the patient is a small woman, you may want to caution her to start with a low dose, particularly if she has a history of being sensitive to the effects of medications. It is fine to have her start with a half-tablet and wait for 45 minutes or an hour to determine the effect of the medication. If she is still experiencing an unsatisfactory amount of pain and is not too sedated, then she can always take the second half of the tablet at that point. Because the medication can produce anywhere from mild to profound sedation, however, this is an easy way for her to avoid the excess sedation that might result from taking two tablets in a single dose, since that is what the directions state she can do. This is not to say that you will encourage patients to increase or decrease a prescribed dose of a drug willy-nilly. It means that for some drugs which may have undesirable side effects at too high a dose, it is fine for the patient to start with a low first dose to see how the drug affects them, and then move to the prescribed dose. If the patient cannot tolerate the prescribed dose, then that patient should contact you and you can discuss with the prescriber what to do.

You should always check the dose of medications for patients who have disease states that may predispose them to altered excretion of a drug. For example, a patient with diabetes will be at risk of decreased kidney function in comparison to a patient without diabetes. A patient with liver failure will not quickly get rid of drugs that are normally changed to inactive forms by the liver. In both cases you will need access to a patients laboratory results to see if you need to adjust the doses of their medications. Ask the patient to obtain a copy of these for you, so that you can check their drug doses, or else call the prescriber's office and ask the nurse for the laboratory results you need.

Checking doses is crucial when you get a prescription for a child. Although most prescribers do an excellent job determining doses of medications for children, every now and again you will find a dose that may be too high and you will need to contact the prescriber. Never dispense a dose that you think might be potentially toxic to a child (or an adult, for that matter). Remember that a prescription is a request to fill, not a command, and you do not legally have to fill a prescription if you think that the dose might endanger the patient. Keep a pediatric dosing reference manual in your pharmacy so that you can check doses.

Infusion rate dosing calculations.

Many medications in a hospital are given to a patient intravenously in a continuous fashion, i.e. the patient will be hooked up to a bag 24 hours/day. (You may have visited a hospital and seen patients roaming the halls steering a pole on wheels which holds an IV bag with attached tubing that disappears somewhere under the billows of those beautiful hospital gowns—this patient is receiving a continuous IV infusion.) Nurses have to calculate the infusion rate in per-minute or per-hour increments and then program an infusion pump to give the medication at the correct rate. They will often call the pharmacy if they end up having to infuse an unfamiliar medication, so you will need to be able to calculate an infusion rate. When this happens to you, you will need to know the solution concentration and the desired infusion rate (in amount of drug to be infused per unit time). You can then calculate the solution volume to be infused per unit time.

e.g., A physician wishes to infuse lidocaine into a patient at the rate of 2 mg/min. Your pharmacy stocks a pre-mixed lidocaine drip that contains 2g of lidocaine in 500ml D5W. The nurse will want to program the pump to infuse the drug in ml/hour.

$$\text{x ml/min} = \frac{2\ \text{mg}}{\text{min}} \times \frac{500\ \text{ml}}{2\ \text{g}} \times \frac{1\text{g}}{1000\text{mg}} \times \frac{60\ \text{min}}{\text{hr}} = \frac{30\ \text{ml}}{\text{hr}}$$

e.g., A physician has ordered a bag of dopamine to infuse at 10μg/kg/minute. You already calculated and mixed your pharmacy's "standard" dopamine drip (400mg in 250ml of D5W) You guestimate the patient to be about 180 pounds.

$$\frac{250\text{ml}}{400\text{mg}} \times \frac{10\mu\text{g}}{\text{kg/minute}} \times \frac{1\text{mg}}{1000\mu\text{g}} \times 180\ \text{lbs} \times \frac{\text{kg}}{2.2\ \text{lb}} = \frac{0.5\ \text{ml}}{\text{minute}}\ \text{(approx)}$$

rate to program pump to run

Standard units for infusion rates are either ml/minute or ml/hour.

Easing patients into and out of doses: tapering and desensitization

There are times when you not want to start the patient on a full dose of a drug right away, or you will not want to discontinue a medication dose abruptly. In these situations, you will want to ease the patient into or out of a certain medication dose.

The most common drug that is tapered from a high dose down to a low dose (or off the medication) is prednisone. Prednisone is a commonly-used member of a group of drugs called corticosteroids. These drugs are given to patients to help suppress the immune response; rheumatoid arthritis and asthma are two examples of diseases that may require treatment with corticosteroids. Because the adrenal gland in the human body produces natural corticosteroids, giving patients exogenous corticosteroids (meaning they come from a source outside the body) causes the patient's adrenal glands to stop secreting the patient's own corticosteroids. If the patient has been on a corticosteroid long enough for it to shut down the adrenal gland (two weeks or longer), then abruptly discontinuing the drug will leave the patient without any source of corticosteroid, precipitating an aptly-named adrenal crisis. It is thus important to slowly decrease the dose of the prednisone, so that the adrenal gland can slowly start producing its own corticosteroids again. This slow decrease is often called a "pred taper." You will need to figure out which strength of medication to give the patient for the taper, how many tablets that patient will need for each dose, and how many total tablets the patient should receive for the prescription. You will want to choose a medication strength that minimizes the number of times that a patient will need to cut a tablet in half (in fact, you would prefer that the patient not cut any tablets in half, whenever possible).

For example: a patient brings in a prescription for a prednisone taper as follows:
prednisone 30mg po tonight
20mg po BID tomorrow and day 3
10mg po BID day 4 and day 5
10mg po qd day 6 and 7
5mg po qd day 8 and 9
then off

You have prednisone available in 1mg, 5mg, 10mg, 20mg, and 50mg tablets in your pharmacy. What strength and quantity will you dispense?

Here it would be easiest for the patient if you dispensed 5mg tablets, since all doses that patient will take will be in some multiple of 5mg.

I will dispense # 36 tablets of the 5 mg strength.

The directions you will give to the patient are to:

day 1: 6 tablets tonight
day 2: 4 tablets twice daily
day 3: 4 tablets twice daily
day 4: 2 tablets twice daily
day 5: 2 tablets twice daily
day 6: 2 tablets once daily
day 7: 2 tablets once daily
day 8: 1 tablet daily
day 9: 1 tablet daily
day 10: off (stop taking tablets)

You will encounter two major challenges in these problems: figuring out the correct number of tablets to give to the patient and (the biggest challenge) getting the directions onto the label in the small amount of space given you by the computer.

Sometimes you will want to ease a patient into a dose of a medication. This is done commonly for many medications over a matter of weeks, and usually does not require any calculations—you just check to see if a particular dose seems to be working and if it isn't, then increase the dose to the next higher strength (and monitor to see if it has the desired effect or if it causes any unwanted side effects). Occasionally, you will escalate a dose of a medication faster than once a week or once a month. This typically occurs when a patient has had an immune reaction to a medication, but that patient needs the medication because there are no optimal alternatives. In this case the physician will start with tiny doses of the drug and increase the dose rapidly in an attempt to tie up the immune system and develop tolerance to the immune response caused by the drug. This process is called desensitization, and will involve some pretty heavy-duty calculations on your part.

Here is an example where a physician has ordered a desensitization regimen where he has instructed the pharmacist to prepare oral doses of penicillin starting at 100 units and doubling the dose every 15 minutes, until the patient is at a dose of 400,000 units, then switching over to injectable penicillin SC at 50,000 units and doubling the dose until a dose of 400,000 units IV is reached. After this point, the physician will begin giving full doses of the penicillin, intravenously. Here is what the regimen would look like:

Oral Desensitization

- Reconstitute oral penicillin VK 250mg/5ml (400,000units/5ml) suspension. This will be considered **concentration A: 80,000 units/ml**.
- Measure 2ml of concentration A and dilute with 18ml of distilled water. This will give you **concentration B: 8000 unit/ml**.

- Measure 2ml of concentration B and add 18ml of water. This will give you **concentration C: 800 units/ml**.
- Measure 1 ml of concentration C and add 7ml of water. This will give you **concentration D: 100 units/ml**.

Begin administration as follows:

Time	**volume**	**concentration**	**strength received**
0	1.0 ml	"D"	100 units
15 minutes	2.0 ml	"D"	200 units
30 minutes	4.0 ml	"D"	400 units
45 minutes	1.0 ml	"C"	800 units
60 minutes	2.0 ml	"C"	1600 units
1 hour, 15 minutes	4.0 ml	"C"	3200 units
1 hour, 30 minutes	8.0 ml	"C"	6400 units
1 hour, 45 minutes	1.6 ml	"B"	12,800 units
2 hours	3.2 ml	"B"	25,600 units
2 hours, 15 minutes	6.4 ml	"B"	51,200 units
2 hours, 30 minutes	1.25 ml	"A"	100,000 units
2 hours, 45 minutes	2.5 ml	"A"	200,000 units
3 hours	5.0 ml	"A"	400,000 units

Parenteral desensitization

- In a sterile field, prepare penicillin G to **concentration E: 1,000,000 u/ml**.
- Mix 1.0ml of concentration E with 1.5ml of water to make **concentration F: 400,000 units/ml**.

Give oral desensitization regimen, then begin the parenteral desensitization:

Time	**volume**	**concentration**	**route**	**strength received**
3 hours, 15 minutes	0.125 ml	"F"	SC	50,000 units
3 hours, 30 minutes	0.25 ml	"F"	SC	100,000 units
3 hours, 45 minutes	0.5ml	"F"	SC	200,000 units
4 hours	0.4 ml	"E"	SC	400,000 units
4 hours, 15 minutes	0.8 ml	"E"	SC	800,000 units
4 hours, 30 minutes	1.0 ml	"E"	IM	1,000,000 units
4 hours, 45 minutes	0.25 ml	"F"	IV	100,000 units
5 hours	0.5 ml	"F"	IV	200,000 units
5 hours, 15 minutes	1.0 ml	"F"	IV	400,000 units

Pharmacokinetic dosing calculations

Pharmacokinetics is a fancy term that refers to the study and characterization of drug disposition in the body. Pharmacokinetics basically came about because of the desire to individualize drug doses. It involves the study of drug absorption, distribution, and elimination, and the relationship of these processes to the intensity of pharmacologic and toxicologic effects. Most dosing calculations that utilize pharmacokinetic concepts are what I call "plug and play." You will be given or have access to a master equation. You will also be given some patient-specific information and/or general population information. You will need to plug this information into the equation in the correct order. Your main challenge will involve getting all the units lined up correctly - just make sure the units cancel out, leaving you with only your desired units. I will use two important concepts, volume and clearance, to illustrate how this works.

Volume. Volume, as you know, refers in general to the capacity of a three-dimensional object. In pharmacokinetics, volume is used to describe a specific three-dimensional object: the human body. Now, if you look around at all your friends and loved ones, you can easily see that volume is not the same for everyone. A tiny female will have a smaller volume than a large male football player. If you use the analogy of a bucket, then you can envision the people you see as large buckets, small buckets, and in-between buckets. Like the volume of many buckets, pharmacokinetic volume units are usually liters (L), and are sometimes normalized to body weight: L/kg.

Volume is more often and correctly called "volume of distribution" and abbreviated V_d, but I will continue to call it "volume" since it will be less confusing this way.

The premise of volume, in pharmacokinetics, is that you need to give a patient a certain amount of drug in order to reach a concentration that will produce the desired pharmacologic effect. In essence, you need to "fill the bucket" (the patient) with the right amount of drug. If the bucket is too empty, then your desired pharmacologic effect will not occur. If the bucket is too full, then toxicity could occur (i.e., overdose). You will use the concentration of the drug in the blood or serum as a surrogate measure of how full the bucket (body) is. Hope this seems pretty straightforward.

The concept of volume is most often used with the initial dose of a needed medication. This first dose is called the *loading dose* or sometimes a *bolus*, and refers to the amount of drug needed to "load" or "fill" the body with the right amount of drug. In order to calculate a loading dose, you will need to know two things: the volume of the drug you want to use, and the desired serum concentration.(How much drug do you need to "fill the bucket?")

$LD = (V)(C_p)$, where V = volume of distribution for the drug and C_p = desired plasma concentration of the drug, and the loading dose involves a drug given intravenously (IV).

For example, you are the pharmacist on an emergency room drama (nominated for a prestigious award for its progressive practice of having a pharmacist in the emergency room to ensure proper dosing and patient medication education!). In this particular episode, the paramedics have brought in a male patient who has been found "down." The docs hook the patient up to an EKG (electrocardiogram - this machine is the one that traces out the electrical conductance of the heart) which shows that he is experiencing a very irregular heart rate. The doctor first attempts to "shock" the patient, which regulates the heart rate for a few minutes, but then the heart rate begins acting irregular again. The doctor decides to use a drug, lidocaine, to control the heart rate. You know that:

- the volume of distribution is about 1.3 L/kg in patients with otherwise healthy hearts,
- the patient weighs around 190 lbs (your estimate)
- irregular heart rates are usually controlled when the serum concentration is between 1 and 4 mg/L, but that toxic effects are more likely to occur if the serum concentration exceeds 5 mg/L. You choose 2 mg/L as your desired serum concentration, since it is within the therapeutic range of 1 - 4 mg/L. There is no magic in this number choice: you just need to choose *one number* within the desired concentration range.
- you have lidocaine 1% and 2% pre-filled syringes in your drug cart. Both syringes contain 10ml of solution

Which one will you use and how much of the solution will you administer to the patient as a loading dose to control his irregular heart rate? (Network ratings are depending on you!)

$LD = (V)(C_p)$

$$\textbf{LD} = 1.3\ \frac{\text{L}}{\text{kg}} \times 2\ \frac{\text{mg}}{\text{L}} \times 190\ \text{lbs} \times \frac{1\ \text{kg}}{2.2\ \text{lbs}} = 224\ \text{mg}$$

A 1%, 10ml syringe of lidocaine contains 100mg lidocaine and a 2% 10ml syringe contains 200mg of lidocaine (please double check these calculations for me if you have any questions about how I calculated these numbers). I would administer one 2% syringe to this patient, since I tend to round down on any medication that is not an antibiotic.

If a drug is given orally and is metabolized by the liver, you will need to account for the amount of drug that is inactivated by the liver in your calculations. The amount of drug that gets past the liver and into the rest of the body will be a certain fraction of the total dose given, is called "bioavailability," and is referred to in calculations as "F." You will divide your oral doses by your "F" in order to account for the drug lost in the liver; mathematically, the LD of an oral drug = $(V)(C_p)/F$

Clearance. Another really important concept that you will learn when you take your pharmacokinetics courses is the concept of clearance. Clearance involves the disappearance of drug over time and specifically refers to the amount of blood or serum (in ml or L) that is "cleared" of drug in a certain time period (either minutes or hours). There are two major ways in which drug is cleared from the body: hydrophilic drugs are primarily *excreted* by the kidney and lipophilic (hydrophobic) drugs are primarily eliminated by the liver. The liver *metabolizes* lipophilic drugs into more

hydrophilic compounds in various ways (e.g., adding hydroxyl groups, removing methyl groups) and these metabolites are then excreted by the kidney or gut.

The premise of clearance, in pharmacokinetics, is that you need to replace drug cleared from the body in order to maintain a "level" (i.e., constant) drug concentration that will produce the desired pharmacologic effect. If you go back to the bucket analogy, you can represent clearance by making a hole in the bottom of the bucket. In order to keep the bucket (or body) filled with the same amount of drug, you will need to either continuously or periodically replace what is lost. If you don't replace enough of the drug, then your desired pharmacologic effect will not occur. If you replace too much of the drug, then toxicity could occur (i.e., overdose). As with volume, you can use the concentration of the drug in the blood or serum as a surrogate measure of how full the bucket (body) is. Hope this seems pretty straightforward.

Clearance units are most commonly ml/min or L/hr, and can be normalized to weight: L/hr/kg. The concept of clearance is most often used with doses of a needed medication which come *after* the loading dose. These subsequent doses are called the *maintenance dose*. Maintenance dose (MD) utilizes drug clearance in order to maintain a desired serum concentration (i.e., How much drug will you have to replace for that lost out the hole in the bottom of the bucket in order to keep the bucket full?)

MD = (Cl) (C_p) where Cl = clearance of the drug and C_p = the desired plasma concentration

e.g., Your lidocaine loading dose works, but you know that lidocaine very quickly disappears from the body, with an average clearance of 10 ml/min/kg (you can get this number from a reference book). You will need to quickly prepare a maintenance intravenous infusion (i.e. the patient will constantly have lidocaine being delivered to his veins at the same rate in which it is disappearing from his body) in order to maintain your desired therapeutic effect (i.e. a heart beating with a normal rhythm). You have a premixed bag in your drug cart which contains lidocaine 2g in 500ml D5W. While the nurse hooks the medication up to the pump, please calculate the infusion rate that the IV pump will need to be programmed to deliver. The nurse wants to know the infusion rate in ml/hr. Again, your target serum concentration will be 2 mg/L

MD = (Cl) (C_p)

MD = 10 ml x 60 min x 190 lb x 1 kg x 2 mg x 500ml x 1 L x 1g = 26 ml/hr
min/kg 1 hr 2.2 lb L 2g 1000ml 1000mg

If the drug is given orally and is metabolized by the liver, you will need to account for the amount of drug that is inactivated by the liver in your calculations. The amount of drug that gets past the liver and into the rest of the body will be a certain fraction of the total dose given, is called "bioavailability," and is referred to in calculations as "F." You will divide your oral doses by your "F" in order to account for the drug lost in the liver, i.e., MD of an oral drug = (Cl)(C_p)/F

There are all sorts of factors which can affect volume and clearance, which I will not get into at this time. You will be taught pharmacokinetic concepts in other courses in your curriculum, so will learn what you need to know then. My primary purpose in addressing this information at this time is to let you work through some of the calculations that you will see in subsequent pharmacokinetics courses so that you can dazzle the professors with your dexterous mathematical manipulations. You do *not* need to memorize any of these equations at this time.

As you can see, pharmacokinetic calculations are generally pretty easy - you just plug the numbers into the correct places in the master question. The hard part for you will be to include all the numbers that you need to include. The *only* way that you will be able to do this with any accuracy is to *write out all of your units and then make sure that they cancel out., leaving only those units you desire in your final answer.* I cannot adequately emphasize the importance of this concept, but the calculation immediately above should serve as an illustration of how complex these dosing equations can be. How can you get all of the variables in the right order if you don't write out the units?

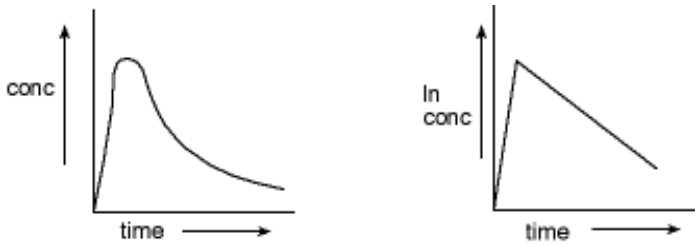
Beyond plug and play

Pharmacokinetics also involves using calculus to determine rates of change in drug concentration over time, and this is why we make you suffer through it as a prerequisite to pharmacy school admission. I will illustrate the use of

calculus in pharmacokinetics by introducing you to the ubiquitous concentration versus time graph. This may well be the first time you have seen one of these, but believe me you will be *dreaming* about these things before you finish your pharmacy program.

Figure 2 below shows two ways of visually representing changes in drug concentration over time. Time will always be placed on the x-axis and concentration on the y-axis. This is true of graphs in general. The *independent* variable is placed on the x-axis and the *dependent* variable on the y axis. In this case, concentration is dependent on time i.e. it changes with time. Time, however, is independent of drug concentration. Time marches forth regardless of what happens to drug concentration.

Figure 2. Each graph shows concentration (the dependent variable) on the y-axis and time (the independent variable) on the x-axis. The first graph shows what it would look like if you took a single dose of a medication and measured serum concentrations at multiple times after taking the dose. The second graph shows time on the x-axis and the natural logarithm of the serum concentrations (ln conc) on the y-axis.



Let's say that you give a patient a drug, and obtain a series of serum drug concentrations over a certain period of time. If you graph them out, your result will look somewhat like the graph on the left in Figure 2. You would be interested in knowing how fast the drug disappeared from your body and so would want to know the slope of the line after the peak (highest point of concentration in the blood). You will, however, notice that the slope of the line on the left-side graph is curved and so it is not easy to measure. If you take the natural logarithms of the concentrations, your graph will change to look more like the graph on the right. This is a graph you can work with, because you can determine the slope of the line corresponding to drug disappearance from the body. It's a straight line.

There are a couple of things that you will need to know in order to determine the rate of disappearance for a given drug in a given patient. The first thing is K, which is called an *elimination rate constant.* This is basically the slope of the downsloping line on the right-hand graph of figure 2.The other thing you will want to know is a serum drug concentration, let's say the initial one (C_0: the concentration at time 0) determined right after the dose was given to the patient. Once you have these pieces of information, you can use calculus to represent the rate of change in the body such that you can calculate the serum concentration for any time, t (i.e., C_t), like this:

$\ln C_t = \ln C_0 - Kt$ in English, this means that the natural log of the serum concentration at any time, t, will be equal to the natural log of the initial serum concentration minus the drug eliminated up to that time.

Since the serum concentration at time t is your goal (i.e. $C_t = x$), you can use the natural antilog of each part of the equation to get your x expressed in units you can understand:

$x = (C_0)(e^{-Kt})$

e.g., A patient receives a loading dose of lidocaine, targeted to produce a serum concentration of 2 mg/L, but the pharmacist was not able to get a maintenance infusion started for 20 minutes. What was the patient's likely lidocaine serum concentration at that time?

You don't know this patient's actual K, since it takes a lot of effort to determine, but you can find a *population* value for K (0.007 min^{-1}) in a reference book.

$$\mathbf{x = 2\ \frac{mg}{L} \times e^{-(0.007)(20)} = 2\ \frac{mg}{L} \times 0.87 = 1.74\ \frac{mg}{L}}$$

As you can see, this number is still within the recommended therapeutic range of lidocaine (1- 4 mg/L)

This will hopefully illustrate to you why you will need to be intimately familiar with how to perform logarithmic functions on your calculator.

References

1. Snider RD, Kruse JA, Bander JJ, Dunn GH. Accuracy of estimated creatinine clearance in obese patient with stable renal function in the intensive care unit. Pharmacotherapy 1995;15:747-53.

2. Spinler SA, Nawarskas JJ, Boyce EG, Conners JE, Charland SL, Goldfarb S. Predictive performance of ten equations for estimating creatinine clearance in cardiac patients. Ann Pharmacother 1998;32:1275-83.

Lesson 4 practice questions

1a. You are at home and get a call from a friend of yours who is a mom. Her 15-month-old child is running a rectal temperature of 102°F and she would like to give acetaminophen but doesn't know how much. She has a bottle of suspension at home and says that the bottle reads "80mg/half-teaspoonful" and she thinks her child weighs about 25 lbs. She has an oral syringe that is marked off at 0.2 milliliter intervals and goes up to 10ml. You remember from class that the standard dose for acetaminophen elixir is 10mg/kg. How many milliliters of acetaminophen elixir will you recommend she give the child? (round to nearest 0.2ml, e.g. 1.4, 1.6, 1.8, etc)

_____ml

1b. Mom calls back. Her child (in question 1a) is refusing the elixir, but she thinks that he might take a chewable tablet. She has some at home that are 80mg/tablet. How many tablets should she give her child? (The tablets are scored so can be broken in half easily)

_____ tablet(s)

1c. A surgeon has ordered "Tylenol with Codeine elixir, 1-2 tsp po q4-6h prn pain" for a 5-year-old, 45-pound male who has just undergone a tonsillectomy. You know that Tylenol with Codeine elixir contains 12mg of codeine in each 5ml of elixir. A pediatric drug dosing reference recommends a dosing range of 0.5 - 1.0 mg/kg/dose for codeine in children under the age of 6 years, with a maximum daily dose of 30mg. If the patient receives the maximum size and number of doses prescribed, will he be within the recommended dosing range? If not, please adjust the directions of the prescription so that the patient receives an appropriate codeine regimen.

is the prescribed regimen within the recommended dosing range?
_____yes

_____no; I would adjust the directions to read: _____tsp q_____h prn pain.

2a. A 170-pound, 5'9" patient receiving chemotherapy is to receive prednisone 60mg/m^2/day orally, days 1-10. Please calculate a daily dose for this patient using the following method of BSA calculation:

$$\text{BSA } (m^2) = \sqrt{\frac{(\text{ht in cm})(\text{wt in kg})}{3600}}$$

daily dose: _____ mg

2b. Your pharmacy carries prednisone 1mg, 5mg, 10mg, 20mg, and 50mg tablets. Which product and what quantity of it will you dispense? Please remember that you would prefer that the patient take as few tablets daily as possible.

I will dispense _____tablets of the _____mg strength. She will take _____ tablets daily on days 1-10.

3. Vecuronium is an agent used to paralyze patients fighting a ventilator. The recommended maintenance dose is a constant infusion of 0.1mg/kg/hr. The infusion bag should be used within 8 hours of mixing. Vecuronium is supplied as a vial containing 10mg of powder, and an accompanying diluent which reconstitutes the drug to a concentration of 1mg/ml. Please calculate an infusion rate in ml/hr that a 186-pound patient should receive. You will need to determine how much fluid you will mix the vecuronium in, and how much vecuronium you will use when you mix it.

vecuronium 10mg/vial - I will use _____vials to mix each bag.

I will place the drug in a 100ml 250ml 500ml bag of NS. (circle 1)

The infusion rate should be: _____ ml/hr

4a. You receive a prescription for prednisone, an oral corticosteroid which helps relieve swelling and inflammation. The directions read:

Prednisone - please give one month's supply
directions: 20mg po BID day 1 and 2
10mg po BID day 3 and 4
5mg po BID day 5 and 6
5mg po qd thereafter

On your shelf you have prednisone 5mg tablets, 10mg tablets, and 20mg tablets. All of these tablets are scored (so they can be cut in half). Please indicate the product and quantity of tablets you will use to fill this prescription. (assume that there are 30 days in a month)

I will fill this prescription with _____tablets of prednisone _____mg.

The directions will read:
Take _____ tablets _ daily for _____ days, then take __ tablets _ daily for _____ days, then take __ tablet __ _____ daily for _____ days, then take __ tablet daily thereafter.

4b. A patient who has previously exhibited a rash with allopurinol is prescribed a desensization protocol by his rheumatologist. The rheumatologist would like the patient to receive by mouth each of the following doses every

day for three days (after which the patient increases to the next higher dose): 50 µg, 100 µg, 200 µg, 500 µg, 1 mg, 5 mg, 10 mg, 25 mg, 50 mg, 100mg, which he will take daily thereafter. The lowest dose of allopurinol that you can get is a 100 mg tablet, which you will crush and place in a suspension off methylcellulose, cherry syrup, and simple syrup. You want to give the patient no more than two different strengths of oral suspension to take. Determine what the two strengths of medication you will make, and calculate the dose the patient will take each day.

You will crush and mix ___ 100mg tablets of allopurinol and mix with 1% methylcellulose, cherry syrup, and simple syrup to a volume of _____ ml which will produce a concentration of _____ mg/ml. You will withdraw from this suspension _____ ml, place it in a vial and add _____ ml of the cherry syrup and simple syrup to make a second concentration of ___mg/ml.
The patient will then take the following doses:

daily dose	**day #**	**directions**
50 µg	1-3	Take _____ ml of the _____ mg/ml suspension daily on days 1-3.
100 µg	4-6	Take _____ ml of the _____ mg/ml suspension daily on days 4-6.
200 µg	7-9	Take _____ ml of the _____ mg/ml suspension daily on days 7-9.
500 µg	10-12	Take _____ ml of the _____ mg/ml suspension daily on days 10-12.
1 mg	13-15	Take _____ ml of the _____ mg/ml suspension daily on days 13-15.
5mg	16-18	Take _____ ml of the _____ mg/ml suspension daily on days 16-18.
10 mg	19-21	Take _____ ml of the _____ mg/ml suspension daily on days 22-24.
25 mg	22-24	Take _____ ml of the _____ mg/ml suspension daily for three.
50 mg	25-27	Take 1/2 of a 100mg tablet daily for 3 days.
100 mg	28+	Take 1 tablet daily.

5a. A physician has ordered that a 62-year-old female patient be given ceftizoxime 1g IV q8h. You notice, upon examining the patient's labs, that her serum creatinine is 1.8 mg/dL. Upon questioning, the patient tells you that her usual weight is 122 pounds. Facts and Comparisons ® gives you the following information about ceftizoxime:

Ceftizoxime dosage in renal impairment

CrCl (ml/min)	severe infections
50-79	750mg - 1.5g IV q8h
5-49	500mg - 1g IV q12h
0-4	500mg - 1g IV q48h

What is this patient's calculated creatinine clearance?

_____ml/min

Please check the dose. Would you recommend a change?

_____ no _____ yes, I recommend _____mg IV q_____h

5b. A 68 year-old female patient has been prescribed Bactrim DS, an antibiotic, for a urinary tract infection. The physician wrote the usual directions of "Bactrim DS i po BID" on the order. You remember that patients with a creatinine clearance of 30-50ml/minute should have their dosing frequency reduced to q24h, and that patients with a creatinine clearance below 30ml/minute should receive an alternative drug. The patient tells you she weighs 120 lbs

and is 5'4". Her labs show her to have a serum creatinine of 1.2mg/dL. What is her calculated creatinine clearance? What will your recommendation (if any) be to the physician?

CrCl: _____ml/minute

recommendation:

_____continue therapy as prescribed

_____change directions to Bactrim DS i po q24h

_____use alternative antibiotic

6. Gentamicin is an antibiotic that is given intravenously for serious infections. A 52 year-old, 5'3" 120-pound female patient with a serum creatinine of 1.2 mg% is to receive this medication. Gentamicin has a volume of 0.25 L/kg, and a clearance that is the same as her calculated creatinine clearance. You would like to target a peak serum concentration of 7 mg/L.

6a. Please calculate a loading dose for this patient. (LD = (V)(C), where V = volume of distribution for the drug and C = desired plasma concentration of the drug.)

6b. You will want to give this patient another dose when her serum concentration falls below 1.0 mg/L. How many hours will it be until this happens?
($\ln C_t = \ln C° - Kt$; $K = Cl/V$)

Lesson 4 practice question answers

1a. You are at home and get a call from a friend of yours who is a mom. Her 15-month-old child is running a rectal temperature of 102°F and she would like to give acetaminophen but doesn't know how much. She has a bottle of suspension at home and says that the bottle reads "80mg/half-teaspoonful" and she thinks her child weighs about 25 lbs. She has an oral syringe that is marked off at 0.2 milliliter intervals and goes up to 10ml. You remember from class that the standard dose for acetaminophen elixir is 10mg/kg. How many milliliters of acetaminophen elixir will you recommend she give the child? (round to nearest 0.2ml, e.g. 1.4, 1.6, 1.8, etc)

__**3.6**__ ml

25 lb x $\frac{\text{1 kg}}{\text{2.2 lb}}$ x $\frac{\text{10 mg}}{\text{kg}}$ x $\frac{\text{0.5 tsp}}{\text{80 mg}}$ x $\frac{\text{5 ml}}{\text{tsp}}$ = 3.6 ml

1b. Mom calls back. Her child (in question 1a) is refusing the elixir, but she thinks that he might take a chewable tablet. She has some at home that are 80mg/tablet. How many tablets should she give her child? (The tablets are scored so can be broken in half easily)

__**1.5**___ tablet(s)

25 lb x $\frac{\text{1 kg}}{\text{2.2 lb}}$ x $\frac{\text{10 mg}}{\text{kg}}$ x $\frac{\text{1 tablet}}{\text{80 mg}}$ = 1.42 tablets ≈ 1.5 tablets

1c. A surgeon has ordered "Tylenol with Codeine elixir, 1-2 tsp po q4-6h prn pain" for a 5-year-old, 45-pound male who has just undergone a tonsillectomy. You know that Tylenol with Codeine elixir contains 12mg of codeine in each 5ml of elixir. A pediatric drug dosing reference recommends a dosing range for codeine of 0.5 - 1.0 mg/kg/dose every 4-6 hours, with a maximum daily dose of 60mg in a child this age. If the patient receives the maximum size and number of doses prescribed, will he be within the recommended dosing range? If not, please adjust the directions of the prescription so that the patient receives an appropriate codeine regimen.

is the prescribed regimen within the recommended dosing range?
_____yes

__**X**__ no; I would adjust the directions to read: __**1**__ tsp q__**6**__ h prn pain.

max prescribed dose: $\frac{\text{12mg}}{\text{5ml}}$ x $\frac{\text{5 ml}}{\text{tsp}}$ x $\frac{\text{2 tsp}}{\text{dose}}$ x $\frac{\text{6 doses}}{\text{day}}$ = 144 $\frac{\text{mg}}{\text{day}}$

this is >> 60 mg/day, so not within the recommended dosing range

desired dose: $\frac{\text{60mg}}{\text{day}}$ x $\frac{\text{1 day}}{\text{4-6 doses}}$ x $\frac{\text{5ml}}{\text{12mg}}$ x $\frac{\text{1 tsp}}{\text{5ml}}$ = 0.8 tsp q4h or 1.25 tsp q6h

It would be easiest for the patient's caregiver to measure one teaspoonful per dose.

2a. A 170-pound, 5'9" patient receiving chemotherapy is to receive prednisone 60mg/m^2/day orally, days 1-10. Please calculate a daily dose for this patient using the simplified method of BSA calculation:

BSA (m^2) = $\sqrt{\frac{(\text{ht in cm})(\text{wt in kg})}{3600}}$ = $\sqrt{\frac{(175\text{ cm})(77\text{ kg})}{3600}}$ = **1.9m^2**

daily dose: 60mg/m^2/day x 1.9m^2 = 114mg, which is close to both 110mg and 120mg

2b. Your pharmacy carries prednisone 1mg, 5mg, 10mg, 20mg, and 50mg tablets. Which product and what quantity of it will you dispense? Please remember that you would prefer that the patient take as few tablets daily as possible.

I will dispense **60** tablets of the **20** mg strength. She will take **6** tablets daily on days 1-10. **I chose this number because the patient will take the least number of tablets but still be within 10% of the calculated daily dose.**

3. Vecuronium is an agent used to paralyze patients fighting a ventilator. The recommended maintenance dose is a constant infusion of 0.1mg/kg/hr. The infusion bag should be used within 8 hours of mixing. Vecuronium is supplied as a vial containing 10mg of powder, and an accompanying diluent which reconstitutes the drug to a concentration of 1mg/ml. Please calculate an infusion rate in ml/hr that a 186-pound patient should receive. You will need to determine how much fluid you will mix the vecuronium in, and how much vecuronium you will use when you mix it.

Since the infusion needs to be used within 8 hours of mixing, I choose to make a bag that will infuse over 6 hours, rather than 8 hours, since I know that there is a lag time between when the bag is made and when the nurse will actually begin the infusion (transportation time).

$$0.1\ \frac{mg}{kg\ hr} \times \frac{6\ hrs}{bag} \times 186\ lb \times \frac{1\ kg}{2.2\ lb} = 51\ mg/bag$$

vecuronium 10mg/vial - you will use **5** vials each bag (i.e., 50mg/bag).

You will place the drug in a 100ml 250ml 500ml bag of NS. (circle 1)

The infusion rate should be:

$$0.1\ \frac{mg}{kg\ hr} \times 186\ lb \times \frac{1\ kg}{2.2\ lb} = 8.5\ \frac{mg}{hr}$$

if you use a 100ml bag:

$$\frac{100ml\ NS + 50ml\ vecuronium}{50mg} \times 8.5\ \frac{mg}{hr} = 25.5\ \frac{ml}{hr}$$

if you use a 250ml bag:

$$\frac{250ml\ NS + 50ml\ vecuronium}{50mg} \times 8.5\ \frac{mg}{hr} = 51\ \frac{ml}{hr}$$

if you use a 500ml bag:

$$\frac{500ml\ NS + 50ml\ vecuronium}{50mg} \times 8.5\ \frac{mg}{hr} = 94\ \frac{ml}{hr}$$

4a. You receive a prescription for prednisone, an oral corticosteroid which helps relieve swelling and inflammation. The directions read:

Prednisone - please give one month's supply

directions: 20mg po BID day 1 and 2 (8 tabs/day x 2 days = 16 tabs)
10mg po BID day 3 and 4 (4 tabs/day x 2 days = 8 tabs)
5mg po BID day 5 and 6 (2 tabs/day x 2 days = 4 tabs)
5mg po qd thereafter (30 days – 6 days = 24 days = 24 tabs)

On your shelf you have prednisone 5mg tablets, 10mg tablets, and 20mg tablets. All of these tablets are scored (so they can be cut in half). Please indicate the product and quantity of tablets you will use to fill this prescription. (assume that there are 30 days in a month)

I will fill this prescription with **52** tablets of prednisone **5** mg.

The directions will read:

Take 4 tablets twice daily for 2 days, then take 2 tablets twice daily for 2 days, then take 1 tablet twice daily for 2 days, then take 1 tablet daily thereafter.

4b. A patient who has previously exhibited a rash with allopurinol is prescribed a desensization protocol by his rheumatologist. The rheumatologist would like the patient to receive by mouth each of the following doses every day for three days (after which the patient increases to the next higher dose): 50 µg, 100 µg, 200 µg, 500 µg, 1 mg, 5 mg, 10 mg, 25 mg, 50 mg, 100mg, which he will take daily thereafter. The lowest dose of allopurinol that you can get is a 100 mg tablet, which you will crush and place in a suspension off methylcellulose, cherry syrup, and simple syrup. You want to give the patient no more than two different strengths of oral suspension to take. Determine what the two strengths of medication you will make, and calculate the dose the patient will take each day.

You will crush and mix **2** 100mg tablets of allopurinol and mix with 1% methylcellulose, cherry syrup, and simple syrup to a volume of **100** ml which will produce a concentration of **2** mg/ml. You will withdraw from this suspension **10** ml, place it in a vial and add **100** ml of the cherry syrup and simple syrup to make a second concentration of **0.2** mg/ml.

The patient will then take the following doses:

daily dose	**day #**	**directions**
50 µg	1-3	Take **0.25** ml of the **0.2** mg/ml suspension daily on days 1-3.
100 µg	4-6	Take **0.5** ml of the **0.2** mg/ml suspension daily on days 4-6.
200 µg	7-9	Take **1** ml of the **0.2** mg/ml suspension daily on days 7-9.
500 µg	10-12	Take **2.5** ml of the **0.2** mg/ml suspension daily on days 10-12.
1 mg	13-15	Take **5** ml of the **0.2** mg/ml suspension daily on days 13-15.
5mg	16-18	Take **2.5** ml of the **2** mg/ml suspension daily on days 16-18.
10 mg	19-21	Take **5** ml of the **2** mg/ml suspension daily on days 22-24.
25 mg	22-24	Take **12.5** ml of the **2** mg/ml suspension daily for three.
50 mg	25-27	Take 1/2 of a 100mg tablet daily for 3 days.
100 mg	28+	Take 1 tablet daily.

5a. A physician has ordered that a 62-year-old female patient be given ceftizoxime 1g IV q8h. You notice, upon examining the patient's labs, that her serum creatinine is 1.8 mg/dL. Upon questioning, the patient tells you that her usual weight is 122 pounds and that she is 5'4" tall. Facts and Comparisons ® gives you the following information about ceftizoxime:

Ceftizoxime dosage in renal impairment	
CrCl (ml/min)	severe infections
50-79	750mg - 1.5g IV q8h
5-49	500mg - 1g IV q12h
0-4	500mg - 1g IV q48h

What is this patient's calculated creatinine clearance?

ABW = 122 lbs/2.2 lbs/kg = 55 kg **IBW = (2.3)(4) + 45 = 54.2 kg**

$$\textbf{CrCl} = \frac{(140 - 62)\,(55)}{(85)(1.8)} = \textbf{28 ml/min}$$

Please check the dose. Would you recommend a change?

_____ no **X** yes, I recommend **500mg IV q12h**

5b. A 68 year-old female patient has been prescribed Bactrim DS, an antibiotic, for a urinary tract infection. The physician wrote the usual directions of "Bactrim DS i po BID" on the order. You remember that patients with a creatinine clearance of 30-50ml/minute should have their dosing frequency reduced to q24h, and that patients with a creatinine clearance below 30ml/minute should receive an alternative drug. The patient tells you she weighs 120 lbs

and is 5'4". Her labs show her to have a serum creatinine of 1.2mg/dL. What is her calculated creatinine clearance? What will your recommendation (if any) be to the physician?

CrCl = (140 - 68) (55) = 28 ml/min
(85)(1.8)

CrCl: **28** ml/minute

recommendation:

_____continue therapy as prescribed

_____change directions to Bactrim DS i po q24h

X use alternative antibiotic

6. Gentamicin is an antibiotic that is given intravenously for serious infections. A 52 year-old, 5'3" 120-pound female patient with a serum creatinine of 1.2 mg% is to receive this medication. Gentamicin has a volume of 0.25 L/kg, and a clearance that is the same as her calculated creatinine clearance. You would like to target a peak serum concentration of 7 mg/L.

6a. Please calculate a loading dose for this patient. (LD = (V)(C_p), where V = volume of distribution for the drug and C_p = desired plasma concentration of the drug.) Round to the nearest multiple of 10mg.

LD = (V)(C) = (0.25 L/kg)(55 kg)(7 mg/L) = 96.25 mg ≈ 100mg

6b. You will want to give this patient another dose when her serum concentration falls below 1.0 mg/L. How many hours will it be until this happens?
($\ln C_t = \ln C° - Kt$; $K = Cl/V$)
CrCl = (140 - 52)(55) = 47 ml/min ; K = Cl = (47 ml/min)(60min/hr) = 0.205 hr^{-1}
(85)(1.2) V (0.25L/kg)(55kg)(1000ml/L)

ln1.0 mg/L = (ln 7.0 mg/L) - (0.205 hr^{-1})(t)

0 = 1.95 - (0.205)(t)

(0.205 hr^{-1})(t) = 1.95

t = 9.5 hours