I.V Bolus

Example 1:

A drug has an elimination half-life of 4 hours. After the administration of a 250 mg dose, plasma concentration at zero time point was found to be 5.65 mcg/mL. What is the volume of distribution of the drug?

Example 2:

What is the concentration of drug 0, 2 and 4 hours after administration of a dose of 500 mg by I.V injection. Known pharmacokinetic parameters are apparent volume of distribution, V is 30 liter and the elimination rate constant, kel is 0.2 hr^{-1} ?

Example 3:

If Cp^2 is 4.5 mg/liter and Cp^6 hours is 3.7 mg/liter after a 400 mg IV bolus dose what are the values of kel and Vd.

Example 4:

What IV bolus dose is required to achieve a plasma concentration of 2.4 µg/ml (= 2.4 mg/L) at 6 hours after the dose is administered. The elimination rate constant, kel, is 0.17 hr- 1) and the apparent volume of distribution, V, is 25 L.

Example 5:

Procainamide is a drug that has a half-life of 3.2 h, volume of distribution of 1.8 L and minimum effective concentration of 2 µg/mL in plasma. What is the minimum dose of procainamide given intravenously as a bolus that will maintain effective plasma concentration for a period of five hours?

Example 6:

An IV dose of 500 mg of a drug was administered. A plot of plasma concentration (mg/L) versus time (hr) on a semi log paper was linear with a slope of (-0.1) and intercept of 25.

1- Estimate volume of distribution.
2- Elimination half-life.
3- Estimate the value of the initial concentration of this drug in this patient.
4- AUC0-∞
5- Half-life and volume of distribution if a dose of 1 g of drug was given.

Example 7:

When a preparation of phenytoin was administered to a patient, the volume of distribution was found to be 70 liters, and the half-life of elimination was 1.5 hours. What is the total clearance of phenytoin?

Example 8:

Single IV bolus injection containing 500 mg of cefamandole nafate (Mandol, Lilly) is given to an adult female patient (63 years, 55 kg) for a septicemic infection. The apparent volume of distribution is 0.1 L/kg and the elimination half-life is 0.75 hour. Assuming the drug is eliminated by first-order kinetics and may be described by a one-compartment model, calculate the following

1- The Cp0

2- The amount of drug in the body 3 hours after the dose is given

3- The time for the drug to decline to 0.5 μg/mL, the minimum inhibitory concentration for streptococci

Example 9:

When 250 mg of a drug is given intravenously a plasma concentration of 25 mg/L is obtained at time zero. Eight hours later the plasma concentration dropped to 6.25 mg/L.

1- Calculate the half life of this drug.
2- The plasma clearance.
3- A value of 10 mg/L is considered to be a minimum effective concentration, calculate when this concentration will be reached?

Example 10:

For a new antibiotic drug the volume of distributions is 40 L., the total body clearance is 10 L/hr., and the minimum plasma concentration needed to inhibit Neisseria gonorrhea = 6 - 12 μg/mL.

1- After 500 mg IV bolus dose of the drug, what will the plasma concentration 4 hours later.
2- At what time will the concentration drop below 8 μg/mL.
3- What dose should be given to achieve a concentration of 8 μg/mL 6 hours after the dose was given

I.V Infusion

Example 1:

An antiarrhythmic drug is administered by continuous IV infusion. A steady state plasma concentration of 9 mg/L is desired. If the clearance of this drug is 351 ml/min, calculate the infusion rate.

Example 2:

A single IV dose of 300 mg of theophylline in a patient gives an AUC0-∞ of 90 mg.hr/L. What would be the infusion rate (mg/hr) should be given to produce steady state plasma concentration of 20 mg/L?

Example 3:

An antibiotic has a volume of distribution of 10 L and a k of 0.2 hr^{-1}. A steady-state plasma concentration of 10 µg/mL is desired. Determine the infusion rate required to achieve this Css.

Example 4:

Calculate the clearance rate at steady state for a drug given by IV infusion at a rate of 30 mg/hr. The *C*ss is 20 µg/mL. If the rate of infusion were increased to 40 mg/hr, what would be the new steady-state drug concentration, *C*ss?

Example 5:

A patient was given an antibiotic ($t_{1/2}$ = 6 hr) by constant IV infusion at a rate of 2 mg/hr. At the end of 2 days, the serum drug concentration was 10 mg/L. Calculate the volume of distribution for this antibiotic.

Example 6:

A desired steady state plasma concentration of theophylline maybe 15 mg/L. The average half-life of theophylline is about 4 hr and the apparent volume of distribution is about 25 liter. What infusion rate is necessary?

Example 7:

A physician wants to administer an anesthetic agent at a rate of 2 mg/hr by IV infusion. The elimination rate constant is 0.1 hr^{-1}, and the volume of distribution (one compartment) is 10L. What loading dose should be recommended if the doctor wants the drug level to reach 2 mg/L immediately?

Example 8:

What is the concentration of a drug 6 hours after administration of a loading dose of 10mg and simultaneous infusion at 2 mg/hr (the drug has a t1/2 of 3hr and a volume of distribution of 10 L)?

Example 9:

A patient was infused for 6 hours with a drug (k = 0.01 hr–1; VD = 10L) at a rate of 2mg/hr. What is the concentration of the drug in the body 2 hours after cessation of the infusion?

Oral absorption

Example 1

A single oral dose (100 mg) of an antibiotic was given to an adult male patient (43 years, 72 kg). From the literature, the pharmacokinetics of this drug fit a one-compartment open model. The equation that best fits the pharmacokinetics of the drug is

$$\boldsymbol{Cp = 45\ (e^{-0.17t}\ -\ e^{-1.5\,t})}$$

From the equation above, calculate K, Ka, $t_{1/2}$, C_{max}, T_{max} for the drug in this patient. Assume C p is in µg/mL and the first-order rate constants are in hours^{-1}

Example 2

Two drugs, A and B, have the following pharmacokinetic parameters after a single oral dose of 500 mg:

Drug	Ka (hr^{-1})	K (hr^{-1})	Vd (ml)
A	**1.0**	**0.2**	**10.000**
B	**0.2**	**1.0**	**20.000**

Both drugs follow a one-compartment pharmacokinetic model and are 100% bioavailable.

a. Calculate the t max for each drug.

b. Calculate the C max for each drug

Example 3

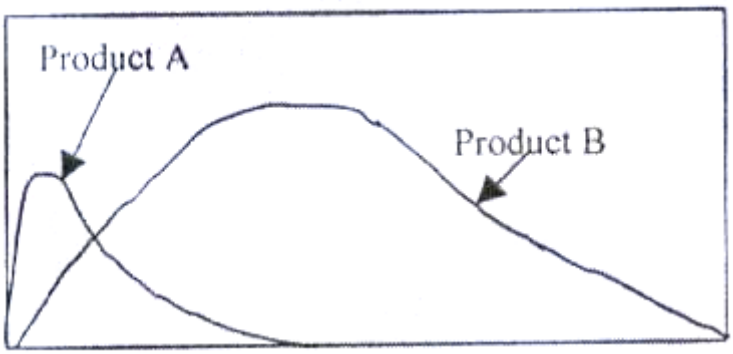
Drug a with elimination rate constant of 0.11 hr^{-1}, absorption rate constant of 0.8 hr^{-1}, volume of distribution of 35 L and bioavailability of 100 %.

What will be the plasma concentration at 6 hours after single oral dose of 520 mg?

What will be the plasma concentration at 6 hours after a single oral dose of 520 mg if the absorption rate constant was 2 hr^{-1}?

Example 4

Two different oral drug products that contain the same amount of the active ingredient were administered to the same patient. The following conc-time plots were obtained



Which drug product has faster absorption?

Which drug product achieves higher C_{max}?

Which drug product has better bioavailability?

Example 5

Plasma samples from a patient were collected after an oral bolus dose of 10 mg of a new benzodiazepine solution as follows:

Time (hr.)	0.25	0.5	0.75	1	2	4	6	10	14	20
Con. (ng/ml)	2.85	5.43	7.75	9.84	16.20	22.15	23.01	19.09	13.9	7.97

1- Determine the equation that describes the plasma drug concentration of the new benzodiazepine if y intercept was observed to be 60 ng/ml, K = 0.1 hr^{-1} and Ka = 0.3 hr^{-1}
2- Determine elimination and absorption half-life
3- Determine peak drug concentration and time of peak drug concentration
4- Determine the volume of distribution of the patient

Multiple dosage regimen (I.V bolus)

Problem 1

Gentamicin has an average elimination half-life of approximately 2 hours and an apparent volume of distribution of 20% of body weight. It is necessary to give gentamicin, 1 mg/kg every 8 hours by multiple IV injections, to a 50-kg woman with normal renal function. Calculate:

a. C_{max}

b. C_{min}

c. C_{av}.

Problem 2

A physician wants to give theophylline to a young male asthmatic patient (age 29, 80 kg). According to the literature, the elimination half-life for theophylline is 5 hours and the apparent V_D is equal to 40 L. The plasma level of theophylline required to provide adequate airway ventilation is approximately 10 µg/mL.

a. The physician wants the patient to take medication every 6 hours around the clock. What dose of theophylline would you recommend (assume theophylline is 100% bioavailable)?

b. If you were to find that theophylline is available to you only in 225-mg capsules, what dosage regimen would you recommend?

Problem 3

What is the loading dose for an antibiotic ($t_{½}$ = 3 hr) with a maintenance dose of 200 mg every 3 hours?

Problem 4

Tetracycline hydrochloride (Achromycin V, Lederle) is prescribed for a young adult male patient (28 years old, 78 kg) suffering from gonorrhea. According to the literature, tetracycline HCl is 77% orally absorbed, is 65% bound to plasma proteins, has an apparent volume of distribution of 0.5 L/kg, has an elimination half-life of 10.6 hr, and is 58% excreted unchanged in the urine. The minimum inhibitory drug concentration (MIC) for gonorrhea is 25–30 μg/mL.

a. Calculate an *exact* maintenance dose for this patient to be given every 6 hours around the clock.

b. Achromycin V is available in 250-mg and 500-mg capsules. How many capsules (state dose) should the patient take every 6 hours?

c. What loading dose using the above capsules would you recommend for this patient?

Problem 5:

Adrug has an elimination half-life of 2 hours and a volume of distribution of 40 L. The drug is given at a dose of 200 mg every 4 hours by multiple IV bolus injections. Predict the plasma drug concentration at 1 hour after the third dose.

Multiple dosage regimen (Oral)

Example 1:

An adult male patient (46 years old, 81 kg) was given orally 250 mg of tetracycline hydrochloride every 8 hours for 2 weeks. From the literature, tetracycline hydrochloride is about 75% bioavailable and has an apparent volume of distribution of 1.5 L/kg. The elimination half-life is about 10 hours. The absorption rate constant is 0.9 hr^{-1}. From this information, calculate **(a)** C_{max} after the first dose, **(b)** C_{min} after the first dose, **(c)** plasma drug concentration C_p at 4 hours after the 7th dose, **(d)** maximum plasma drug concentration at steady-state C^{∞}_{max}, **(e)** minimum plasma drug concentration at steady-state C^{∞}_{min}, and **(f)** average plasma drug concentration at steady-state C^{∞}_{av}.