Drug elimination and clearance

1. Is clearance a better parameter to describe drug elimination than half-life? Why is it necessary to use both parameters in the literature?
2. What is an independent parameter in a model? Is clearance an independent parameter of the physiologic model? How is clearance related to parameters in the compartment model?
3. What is the difference between drug clearance and creatinine clearance?

Learning Questions

1. Explain why plasma protein binding will prolong the renal clearance of a drug that is excreted only by glomerular filtration but does not affect the renal clearance of a drug excreted by both glomerular filtration and active tubular secretion.

2. Explain the effect of alkalization or acidification of the urine on the renal clearance of dextroamphetaminesulfate. Dextroamphetaminesulfate is a weak base with a pK_a of 9.4.

3. Theophylline is effective in the treatment of bronchitis at a blood level of 10–20 g/mL. At therapeutic range, theophylline follows first-order kinetics. The average $t_{1/2}$ is 3.4 hours, and the range is 1.8 to 6.8 hours. The average volume of distribution is 30 L.

a. What are the average, upper, and lower clearance limits for theophylline?
b. The renal clearance of theophylline is 0.36 L/hr. What are the k_m and k_e, assuming all nonrenal clearance (Cl_{NR}) is due to metabolism?

4. A single 250-mg oral dose of an antibiotic is given to a young man (age 32 years, creatinine clearance 122 mL/min, 78 kg). From the literature, the drug is known to have an apparent V_D equal to 21% of body weight and an elimination half-life of 2 hours. The dose is normally 90% bioavailable. Urinary excretion of the unchanged drug is equal to 70% of the absorbed dose.

a. What is the total body clearance for this drug?
b. What is the renal clearance for this drug?
c. What is the probable mechanism for renal clearance of this drug?

5. A drug with an elimination half-life of 1 hour was given to a male patient (80 kg) by intravenous infusion at a rate of 300 mg/hr. At 7 hours after infusion, the plasma drug

concentration was 11 g/mL.

a. What is the total body clearance for this drug?
b. What is the apparent V_D for this drug?
c. If the drug is not metabolized and is eliminated only by renal excretion, what is the renal clearance of this drug?
d. What is the probable mechanism for renal clearance of this drug?

6. In order to rapidly estimate the renal clearance of a drug in a patient, a 2-hour postdose urine sample was collected and found to contain 200 mg of drug. A midpoint plasma sample was taken (1 hr postdose) and the drug concentration in plasma was found to be 2.5 mg%.

Estimate the renal clearance for this drug in the patient.

7. According to the manufacturer, after the antibiotic cephradine (Velosef), given by IV infusion at rate of 5.3 mg/kg per hour to 9 adult male volunteers (average weight, 71.7 kg), a

steady-state serum concentration of 17 g/mL was measured. Calculate the average total body clearance for this drug in adults.

8. Cephradine is completely excreted unchanged in the urine, and studies have shown that probenecid given concurrently causes elevation of the serum cephradine concentration. What is the probable mechanism for the interaction of probenecid with cephradine?

9. Why is clearance used as a measurement of drug elimination, rather than the excretion rate of the drug?

10. What is the advantage of using total body clearance as a measurement of drug elimination compared to using the elimination half-life of the drug?

11. A patient was given 2500 mg of a drug by IV bolus dose, and periodic urinary data was collected. **(a)** Determine the renal clearance of the drug using urinary data. **(b)** Determine total body clearance using the area method. **(c)** Is there any nonrenal clearance of the drug in this patient? What would be the nonrenal clearance, if any? How would you determine clearance using a compartmental approach and compare that with the area method?

Time (hr)	**Plasma Urinary Concentration (g/mL)**	**Urinary Volume (mL)**	**UrinaryConcentration (g/mL)**
0	250.00	100.00	0.00
1	198.63	125.00	2880.00
2	157.82	140.00	1901.20
3	125.39	100.00	2114.80
4	99.63	80.00	2100.35
5	79.16	250.00	534.01
6	62.89	170.00	623.96
7	49.97	160.00	526.74
8	39.70	90.00	744.03
9	31.55	400.00	133.01
10	25.06	240.00	176.13