



1.4. Renal Drug Dosing

Important Equations

Dosage adjustment factor (Q)

$$Q = 1 - [f_e \times (1 - KF)]$$

Where f_e is the fraction of the dose excreted unchanged in the urine for a drug,

$$KF = \frac{CrCl_r}{CrCl_n}$$

$CrCl_r$ is the patient's creatinine clearance that is reduced due to renal dysfunction, and $CrCl_n$ is normal creatinine clearance—assumed to be 120 mL/min.

Adjusting Dose or Interval Using Q

To adjust interval only:

$$\tau_r = \frac{\tau_n}{Q}$$

To adjust dose only:

$$D_r = D_n \times Q$$

To adjust both dose and interval:

$$D_r = \frac{[D_n \times \tau_r \times Q]}{\tau_n}$$

Where τ_n and D_n are the interval and dose used in normal renal function and τ_r and D_r are the interval or dose that is altered to be used in the reduced renal function.

Self-Assessment Problems

- The usual dose of cefazolin in patients with normal renal function (120 mL/min) is 1 g every 8 hours. What dose (in exact mg) should be given every 12 hours to patients with an estimated creatinine clearance of 20 mL/min? Use $f_e = 0.85$ (range is reported to be 0.75 to 0.95).
- A patient inadvertently received a digoxin overdose and has a post-distribution digoxin concentration reported as 4 ng/mL. Hemodialysis was initiated for 3 hours and the digoxin concentration was 2.5 ng/mL at the end of dialysis. Two hours later the concentration is again measured and reported as 3.4 ng/mL. What is the explanation for this phenomenon?
- Rate the following in terms of the need to adjust dose based on the creatinine clearances shown (assume normal renal function is a CrCl of 120 mL/min). Calculate Q and compare the results.

Drug	f_e	CrCl (mL/min)
Cidofovir	0.9	50
Glyburide	0.5	30
Itraconazole	0.35	10

- If the usual recommended dose of gabapentin (Neurontin) is 600 mg every 8 hours in patients with normal renal function (i.e., 120 mL/min), use the dosage adjustment in renal dysfunction equation to determine the *closest available dose* to be given every 12 hours for a patient who has a creatinine clearance of 30 mL/min. Neurontin (gabapentin) is available in 100-, 300-, and 400-mg capsules and 600- and 800-mg tablets. Combinations may be used. Gabapentin $f_e = 0.9$.

- Indicate whether the following would tend to increase or decrease either the potential for a drug to be dialyzed or the efficiency of the dialysis procedure:
 - Lower molecular weight drug
Increase Decrease
 - Higher protein binding of drug
Increase Decrease
 - Greater dwell time (i.e., the same dialysate stays in contact with the blood longer)
Increase Decrease
 - High fat solubility of drug
Increase Decrease
- If the normal dose of cimetidine ($f_e = 0.6$; range 0.5 to 0.7) in patients with active duodenal ulcer is 800 mg twice daily or 400 mg four times daily, what dose and schedule would you recommend for a patient with a creatinine clearance of 30 mL/min for dosing intervals of every 8 and every 12 hours?
- Design a dosing nomogram for cefoxitin at 20 mL/min CrCl intervals (i.e., what mg of normal dose [use 1 g every 8 hours for the normal dose] should be used at 80, 60, 40, and 20 mL/min, using the intervals below). Calculate the exact dose from the formula and then round to the nearest 250 mg for the doses in the nomogram (i.e., 250 mg, 500 mg, 750 mg, 1000 mg). Only fill in space where there are underlined blanks. Cefoxitin $f_e = 0.8$.

Cefoxitin Renal Dosing Nomogram

CrCl (mL/min)	Dose every 8 hr	Dose every 12 hr	Dose every 24 hr
80	_____	X	X
60	_____	_____	X
40	_____	_____	X
20	X	_____	_____