Problem 1 (Digoxin; 4 points)

R.J. is a 50-year-old, 70-kg man (non-obese) and has a serum creatinine of 1.2 mg/dL. Calculate a maintenance dose at steady state that will achieve an average digoxin plasma concentration of 750 ng/L. Develop a dosing regimen assuming that digoxin is available in tablets of 125-μg and 250-μg.

You decided to give 125-μg and 250-μg tablets on alternate days for an average dose of 187.5 μg/day. Four weeks later, R.J. is started on long-term medication with quinidine sulfate tablets. Would you have to adjust his dosing regimen? If yes, calculate a new maintenance dose and recommend a new dosing regimen.

Problem 2 (Methotrexate; 3 points)

J.J. is a 25-year-old, 80-kg (non-obese), man with a serum creatinine of 1.0 mg/dL. He has osteonic sarcoma and is to receive 30g IV methotrexate (MTX) infused over 4 h. Calculate the anticipated MTX concentration (in μM) at the end of the 4h infusion, 12h after the start of the infusion, and 48h after the end of the infusion. A sketch of the expected plasma-concentration-time profile may be helpful to answer this problem.

Problem 3 (Phenytoin; 3 points)

A male patient of 113 kg in weight was administered sodium phenytoin capsules by oral route. Phenytoin (not the salt form) has a volume of distribution of 0.65 L/kg. This patient exhibited phenytoin $K_M$ of 4.7 mg/L and a $V_{\text{max}}$ of 8.2 mg/kg/day. Compute the following:

1. The loading dose required to achieve an initial phenytoin concentration of 20 mg/L
2. The daily maintenance dose to obtain the target average steady-state concentration of 15 mg/L.