PHA5127
Case Study #4
Fall 2005

1. Jonathan Weasley is put on aminoglycoside therapy and given an i.v. bolus injection of 10mg of drug A, which has a clearance rate equal to the creatinine clearance and a volume of distribution of 26 L. This 34 year old man had a serum creatinine level of 0.6 mg/dL. Jonathan is 5'9'' and weighs 220 lbs.
    a. What is his creatinine clearance?
    b. What is the k_e?
    c. What is the half-life, $t_{1/2}$?
    d. What is the C_{max}?
    e. What is the AUC_∞?

2. Six other patients are also put on similar therapy and given the same treatment (an i.v. bolus injection of 10 mg of drug A). Please consider the following cases and answer their corresponding questions (*Hint. Use the PK simulations for one compartment i.v. bolus models. Also note, that Jonathan had a fu of 0.1, fu_T of 0.17, and CL_i of 140 L/h*):

    Patient 1: Has the same V_d as Jonathan but has double the clearance rate. Has the following parameters increased, decreased, or stayed the same: i) C_{max}, ii) k_e, iii) $t_{1/2}$, and iv) AUC_∞?

    Patient 2: Has the same clearance rate as Jonathan but twice the V_d. Has the following parameters increased, decreased, or stayed the same: i) C_{max}, ii) k_e, iii) $t_{1/2}$, and iv) AUC_∞?

    Patient 3: Has the half the clearance rate and V_d as Jonathan. Has the following parameters increased, decreased, or stayed the same: i) C_{max}, ii) k_e, iii) $t_{1/2}$, and iv) AUC_∞?

    Patient 4: Is given drug B instead which has half the fraction of drug bound in plasma (in comparison to drug A) but the fraction of drug bound in tissue and the intrinsic clearance is the same. Has the following parameters increased, decreased, or stayed the same: i) C_{max}, ii) k_e, iii) V_d, iv) CL, v) $t_{1/2}$, vi) E, vii) F, and viii) AUC_∞? Drug B is eliminated by liver only.

    Patient 5: Is given drug C instead which has twice the intrinsic clearance as drug A (The fraction bound in plasma and tissue is the same as Jonathan's). Has the following parameters increased, decreased, or stayed the same: i) C_{max}, ii) k_e, iii) V_d, iv) CL, v) $t_{1/2}$, vi) E, vii) F, and viii) AUC_∞? Drug C is eliminated by the liver only.

    Patient 6: Is given drug D instead. The drug is eliminated by the kidney only (Note: no tubular reabsorption or secretion occurs). If the fraction of drug unbound in tissue is actually twice than expected, does the following parameters increase, decrease, or stay

the same: i) C_{max}, ii) k_e, iii) V_d, iv) CL, v) $t_{1/2}$, and vi) AUC_∞? Note: the patient has a fu and initial fu_T of 0.1 and the clearance is equal to the maximum possible for this drug.