PHA 5127 Dose Optimization I, Fall 2012, Case Study V

If you have any questions regarding this case study, do not hesitate to contact Benjamin Weber (benjaminweber@ufl.edu). Please remember that attendance of the case study lecture is mandatory.

Problem 1

For the following situations, indicate whether the drug is: filtered, reabsorbed (if fully or if reabsorbed through transporters), or actively secrete. Assume that the GFR is 130mL/min and that the urine flow is 1.5mL/min.

1. Drug with f_u= 0.3 and a Cl_{ren}=39mL/min
2. Drug with f_u=0.6 and a Cl_{ren}=30mL/min
3. Drug with f_u=0.05 and a Cl_{ren}=15mL/min
4. Drug with f_u=0.2 and a Cl_{ren}=0.3mL/min
5. Drug with f_u=0.8 and a Cl_{ren}=0.3mL/min

Problem 2

T.T. (male, 6'3'' tall, 111 kg, 24 years old) shows a serum creatinine level of 1.3 mg/dL.

a) Use the Cockcroft-Gault-Equation to calculate his creatinine clearance and glomerular filtration rate (GFR). Comment on the renal function of T.T.?
b) Why do we use the creatinine clearance to estimate the GFR?
c) Drug A shows a plasma protein binding and tissue protein binding of 10% and 95%, respectively. Drug A is eliminated by hepatic (80%) and renal processes (20%). Calculate the total systemic clearance of drug A (in L/h) when administered to T.T.Assume that the drug is neither actively secreted nor reabsorbed.
d) Graph the plasma-concentration time profile for the first 24 hours when 1000mg of drug A are administered to T.T. via an IV bolus injection. Assume that the drug is immediately distributed throughout the body, crosses membranes easily, and that all elimination processes are first-order processes.

Problem 3

Which properties does a drug need to have in order to demonstrate the following? Explain briefly.

a) Active tubular secretion
b) Glomerula secretion
c) Passive tubular reabsorption

Problem 4

TRUE (T) or FALSE (F)

For a high extraction drug, liver blood flow is important to both hepatic clearance and oral bioavailability.

T F

For low extraction drug, f_u (fraction of unbound drug in plasma) is important to both hepatic clearance and oral bioavailability.

T F

Basic drugs that are polar in their unionized form, the extent of re-absorption depends on the degree of its ionization.

T F

Secretion is indicated when renal clearance is larger than GFR*f_u.

T F

It is possible for renal clearance to be close to the kidney blood flow.

T F

Assuming no plasma protein binding, the renal clearance equals the urine flow when full reabsorption occurs.

T F