PHA 5127
Case Study III
Fall 2004

Case 1:

Two pharmacy students wanted to have some fun, and bet for $20 who would have the higher creatinine clearance.
Homer J. is 25 years old and 4’9” tall. Even though he is very small, he weighs 210 lbs., due to massive donut intake.
His girlfriend Marge S. is 22 years old, and 5’9” high and a lot more athletic. She weighs 125 lbs.

a) Determine the creatinine clearance.

Homer J. 25 years, weight 210 lbs=95.5kg:
Creatinine clearance (ml/min):
(140-age)*(weight/70) = (140-25) * (95.5/70) = 156.89 ml/min

Marge S. 22 years, weight 125 lbs=56.7 kg:
Creatinine clearance (ml/min) :
(140-age)*(wight-85)=(140-22)*(56.7/85)=78.71 ml/min

b) Assume Homer J.’s serum creatinine is 1.5 mg/100ml and Marge S.’ is 1.7mg/100ml. Calculate the creatinine clearance using this data. (Cockcroft-Gault-Equation)

Homer J.: obese!
CrCl male: (140-age)*IBW / (72 * serum creatinine)
Homer J. < 5 ft. => use TBW
CrCl = (140-25)*(95.5) / (72*1.5)= 101.69 ml/min

Marge S.:
CrCl female : 0.85 *(140-age) *IBW / (72 * serum creatinine)
IBW=45.5 kg + 2.3 kg for each additional inch = 45.5+ (5*2.3) = 57 kg

CrCl=0.85*(140-22)*57 / (72 * 1.7) = 46.7 ml/min

c) What are the implications of Homer J.’s and Marge S.’s GFR?

Calculating the creatinine clearance gives us some idea about the GFR , since creatinine is cleared via glomerular filtration. GFR is 130 ml/min. Since the CrC l ‘s of Homer and Marge were so low, there might be the indication of kidney failure.

d) Why is IBW used to calculate CrCL rather than TBW. What would happen if we used TBW?

We use the IBW instead of the TBW, because creatinine is produced by muscle metabolism. If we would use the total body weight, we would overestimate the clearance and thus the GFR. Since we are relying on the GFR to calculate the dosing for drugs primarily cleared by elimination, this might lead to overdosing.

Case 2:

Researchers in industry got data from a clinical study about their new drug. The drug is supposed to be a weak base, with a pKa=9.0. The drug is non-polar when unionized. The clinical trial shows a 2 hour half-life and a VD=10L. We know that the drug is renally cleared to 50% and the fraction bound is 0.3. (urine pH =7.4)

a) What is the renal clearance,

Cltot=ke*Vd   ke= ln2 / t1/2 = 0.693 / 2 = 0.347
Cltot=0.347*10 = 3.47 l/h
Clren= Cltot*0.5 = 3.47 l/h * 0.5 = 1.74 l/h = 29 ml/min

GFR * fu = 130 ml/min * 0.7 = 91 (partial reabsorption)

b) What processes are involved in the renal clearance? Justify your answer.

Partial reabsorption of the drug.

c) How will changes in urine pH to a more acidic pH affect the renal clearance?

The drug is unionized at low pH. Hence we have more reabsobtion of the drug. By increasing the pH, more drug gets ionized and less drug gets reabsorbed.

d) What factors have to be considered when we analyze values for renal clearance? (What processes do we have to take into consideration besides glomerular filtration?)

Reabsorption and secreation.

Additional questions:

What does a renal clearance of 130ml/min tell us?

The clearance of the drug is equal to the GFR. Unlikely that active secretion or reabsoption happens.

What does a renal clearance of 0ml/min tell us?

Complete active reabsoption

What does a renal clearance > than GFR*fu tell us?

Active secretion