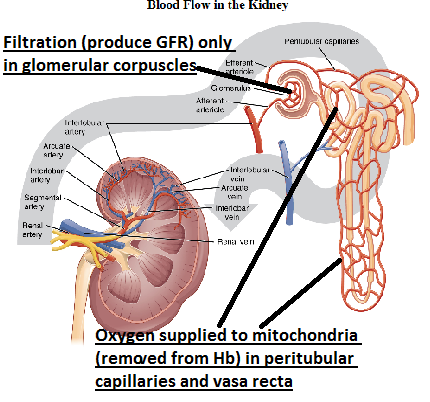
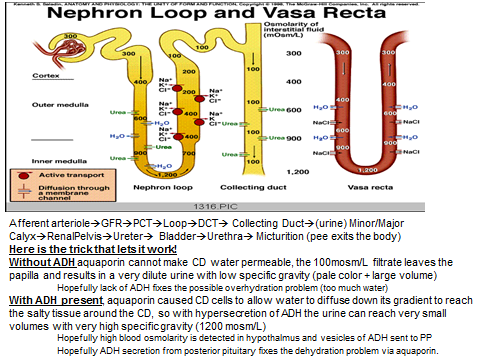
**Kidney Function Assignment: 10 points**

**Work in groups if you like, each person hands in separate *answer at the D2L drop box***

1) **Draw** the path that blood takes moving from renal artery to vena cava with perfusion of cortex and medulla. Indicate where blood in capillaries is filtered and where oxygen is removed from capillaries for use by mitochondria. (10+ items)



2) **Draw t**he path that filtrate/urine takes from a glomerular corpuscle to the urethra . Indicate the osmolarity of the filtrate in the PCT, short or long Loops of Henle, DCT and collecting duct in **presence** OR **absence** of ADH. (10+ items)



3) **Compare and contrast** Glomerular Filtration Rate (GFR), Urine Formation Rate (UFR) and Renal Blood Flow (RBF). Compare and contrast the causes and effects of Diabetes mellitus (type 1) vs Diabetes Insipidus 20-30 words each). What are the two different reasons the urine has a low specific gravity in these diseases? Discuss these hormones with respect to the dehydration each disease can create: ADH, Angiotensin II, and Aldosterone.

**GFR: Glomerular Filtration Rate**- This represents the volume of fluid (ml/minute-about 125 or liters/day-about 180) that is filtered out of the capillaries that are fed from the afferent arterioles into the glomerular capsule. GFR was plasma in the blood.

**RBF: Renal Blood Flow**- This represents the volume of blood traveling into the kidney per minute, about 1.2 L/minute at rest or about 20% of cardiac output at rest.

**RPF: Renal Plasma Flow**- This represents the amount of plasma delivered to the kidney per minute. For instance if the hematocript was 50% and 1.2 L/min of blood were delivered to the kidney, then 600 would be plasma. Because GFR represent volume removed from blood, the hematocrit in the efferent arteriole will be higher than it was in the afferent arteriole prior to filtration. Filtration Fraction is 130ml/min / 600ml/min X 100 = 22%

Diabetes mellitus (type 1) results from an inability of beta-cells of pancreas to secrete insulin into the blood, therefore glucose cannot move from the blood into insulin sensitive tissues (i.e. liver, adipose, skeletal muscle). Therefore, after a meal the plasma glucose levels (i.e. 250 mg/dl) exceed the ability of the proximal convoluted tubule to reabsorb the glucose found in the filtrate. The glucose not removed in PCT stays in the filtrate and appears in urine (also feeds bacteria ledign to urinary tract infection). The large glucose sphere of hydration causes polyuria and massive dehydration. Glucose is present in urine as disease hallmark. (Contrast: type 2 D.M. occurs if tissues are insulin insensitive)

Diabetes Insipidus results when the antidiuretic hormone (ADH) is unable to be secreted into the blood from the posterior pituitary. Often this is associated with a tumor that puts pressure on the stalk of the pituitary so vesicle cannot reach endings in posterior pituitary (no ADH secretion). Lack of ADH means aquaporin is not present on plasma membrane of cells lining the collecting duct and water is not removed from the urine, but glucose is not present in the urine.

In either case the dehydration results in the three As attempting to conserve water losses at the same time that blood volume could decrease, hematocrit would increase and blood pressure would decrease, perhaps even below 70 mmHg when GFR would quickly stop completely.

Aldosterone-secretion from adrenal cortex would increase Na+ reabsorption from DCT and collecting duct for both diseases.

Antidiuretic Hormone- secretion from PP would increase for of Diabetes mellitus, but lack of secretion is the hallmark of Diabetes Insipidus.

Angiotensin II- dehydration could result in low blood pressure and increases in renin secretion leading to Angiotensin II formation via ACE in lung. Angiotensin II effects include an intense sense of thirst, increased aldosterone secretion/Na+ reabsorption, and if needed constriction of arteries.

4) **Consider the ball-park factors (mmHg) that alter GFR.** Positive net=> you made GFR Negative or 0 = no GFR possible

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| Normal GFR and Blood 120mmHg/80mmHg🡪 PulsePressure = 40mmHg  MeanArtPress (MAP) = 93.3 mmHg  MAP in afferent artery is about 60 | Hypotension: a patient’s blood pressure is very low 90/60  MAP= 70mmHg and MAP in afferent arteriole is only 30 mmHg | Patients Ureter is partly blocked: drainage of capsule is poor so hydrostatic pressure in capsule backs up (45mmHg) | Proteinuria: patient has a urinary track infection so oncotic pressure in capsule is not “0 mmHg” but 10 mmHg due to protein that is located in capsule. |
| *Hydrostatic pressure in capillary= 60mmHg (out of capillary)*  Hydrostatic pressure in capsule= 20 mmHg (into capillary)  Oncotic pressure in plasma= 28mmHg (into capillary)  Oncotic pressure in filtrate=0mmHg  What is the net pressure? Show Math: 60out-20in-28in+0= +22 out | *Hydrostatic pressure in capillary= 30mmHg*  Hydrostatic pressure in capsule= 20mmHg  Oncotic pressure in plasma= 28mmHg into capillary  Oncotic pressure in filtrate=0mmHg  What is the net pressure? Show Math: 30out-20in-28in+0= -18 in | Hydrostatic pressure in capillary= 60mmHg  *Hydrostatic pressure in capsule= 45mmHg*  Oncotic pressure in plasma= 28mmHg  Oncotic pressure in filtrate= 0mmHg  What is the net pressure?  Show Math:  60out-45 in-28in+0= -13 in | Hydrostatic pressure in capillary= 60mmHg  Hydrostatic pressure in capsule= 20mmHg  Oncotic pressure in plasma= 28mmHg  *Oncotic pressure in filtrate= 10mmHg (Protein in Filtrate pulls fluid into GFR)*  What is the net pressure?  Show Math:  60out-28in-20in+10 out=32out |
| Net mmHg In or Out?\_net22out\_\_\_  **+ out**, so fluid leaves as GFR\_\_\_\_\_  Why would urine formation change?\_\_\_Urine formation changes if the % reabsorption of GFR changes\_\_ | Net mmHg In or Out?\_\_NO GFR\_\_  More or less urine? \_NO Urine if no GFR\_\_\_\_\_  Why would urine formation change?\_\_\_No GFR to reabsorb\_\_ | Net mmHg In or Out?\_\_NO GFR\_\_  More or less urine? \_No Urine if No GFR\_\_\_\_\_  Why would urine formation change?\_No GFR to reabsorb\_\_ | Net mmHg In or Out?\_\_\_net32 out\_  More or less urine? More GFR than normal, so “potential” for more urine if reabsorption % not increased\_\_\_\_\_\_  Why would urine formation change?\_Urine formation might go up, but if reabsorption doesn’t go up\_\_\_\_ |
| **How do does vasodilation/vasoconstriction of the afferent arterioles, and efferent arterioles work to conserve GFR as long as MAP is maintained at between 70-150mmHg?** This is the healthy range where blood pressure normally is located at rest and during exercise. This the range where one wants GFR to be relatively constant. If blood pressure was a bit high (i.e. 130 mmHg) high GFR might be too high, so you could reduce GFR (maintained at 130ml/min) if the afferent arteriole constricted, efferent arteriole dilate or both. If blood pressure was a bit low (i.e. 80mmHg) filtration pressure in the glomerular corpuscles might also be low causing a low GFR, JG Apparatus would help cause the afferent arteriole to dilate or cause the efferent arteriole to constrict or both.  **Why it is best to “lose” GFR below a 70 mmHg MAP and have increased GFR above about 150mmHg?**  Simple reason for GFR to come to a grinding halt if MAP is below 70mmHg, if blood volume is low enough to result in a blood pressure this low, you might not have enough blood pressure to supply oxygen to your brain and vital organs. At this point slow accumulation of nitrogenous waste is the “least of your bodies worries” and conserving any remaining fluid is the most important concern, hence GFR puts all water loss via the kidney to ZERO. | | | |

**5) How do these factors alter our GFR values? (look in the book, try google or look in the notes)**

a) Age- young, middle aged, old? As we grow older we lose GFR capacity

b) Sex- male vs female? Women tend to start with lower age matched GFR values relative to men

c) Race- Black vs white? Persons who are black high higher rates of diabetes and hypertension, both of these factors are associated with reduced GFR and kidney disease (lowered GFR)

d) Why does a low GFR serve as a risk factor for kidney failure? If you lose the ability to form GFR you also tend to lose the ability to regular blood volume which may increase the tendency for hypertension/heart disease, which (positive feedback) tends to increase the risk for kidney failure.

e) Why might hypertension lead to kidney failure which leads to ever more hypertension and death from heart disease? (*Classic insipid Positive Feedback Loop-*) Each increase in blood pressure results in greater losses in functional nephrons and a further erosion of one’s ability to reduce blood volume and blood pressure, this puts ever greater strain on the few nephrons left resulting in ever greater losses in ability to create GFR. Add in diabetes and infection (due to glucose in urine) and loss of nephrons is even greater.

Estimate GFR based on age, sex and race based on plasma creatinine standardized to the average surface area of a young adult 1.73 meter2 . This is a good online GFR calculator <http://www.qxmd.com/calculate-online/nephrology/ckd-epi-egfr> Use the MDRD GFR estimate to assess the renal health of these patients (who all have **plasma creatinine concentration of 1.2 mg/dL** and assume that a **GFR of less than 60 ml/min-1.73 m2**indicatives kidney disease and increased cardiovascular disease risk in your renal status assessment. ***Rank best to worst and why.***

What is kidney failure? Take a look at this website: http://nkdep.nih.gov/learn/testing/understand-gfr.shtml

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| Why Study the Kidney? These are the faces of the real people who may need kidney consultation from you someday.  Tyga (Rapper) Dr Wilson(not-so-famous) Chris Rock(comedian) Demi Moore(actress) Barbara Bush (Ex 1st lady) | | | | |
|  |  |  |  |  |
| 26 yrs, black, male | 53 yrs, white, male | 53 yrs, black, male | 53 yrs white female | 92 yrs white female |
| GFR \_\_\_62.3\_ml/min-1.73 m2 | GFR \_51.6\_ml/min-1.73 m2 | GFR \_59.8\_\_ml/min-1.73 m2 | GFR 51.6\_ ml/min-1.73 m2 | GFR\_ 44.6\_\_ ml/min-1.73 m2 |
| Renal Status? **Why?**  **Healthy above 60** | Renal Status? **Why?**  **Healthy above 60** | Renal Status? **Why**  **Healthier than Dr Wilson above 60** | Renal Status? **Why?**  **Higher risk of kidney/heart disease, below 60** | Renal Status? **Why?**  **Far high risk of kidney/heart disease, far below 60** |
| ***V.I.P. How can a 1.2 mg/dL plasma creatinine be associated with so MANY different GFR values and health outcomes?***  *Because our organs grow old, sex is linked to baseline GFR value, and because ethnicity is a predictor of diabetes, hypertension, and heart disease. Remember these are all “healthy” people, but once a disease kicks in (i.e. hypertension and kidney failure🡪 rapid loss of GFR) then all bets are off regarding the use of these standard GFR calculators…hence your patient might have a GFR that is MUCH worse than your predicted value, especially if they are an African-American male.* | | | | |

**Black Americans and Chronic Kidney Disease: *Due to high rates of diabetes, high blood pressure and heart disease, black Americans have an increased risk of developing kidney failure. Black Americans need to be aware of these risk factors and visit their doctor or clinic regularly to check their blood sugar, blood pressure, urine protein and kidney function.***

🡪 ***A GFR that looks good today, can rapidly go bad in a few short years as a result of hypertension and damager to the glomeruli….this is what they call a “PARADOX”.***

Black Americans suffer from end stage renal disease (ESRD) disproportionately and develop kidney failure at a significantly higher rate than whites. The incidence of kidney failure is more than 3 times higher in black Americans than white Americans.

Black Americans constitute more than 32% of all patients in the U.S. receiving dialysis for kidney failure, but represent 13% of U.S. population.

Diabetes is the leading cause of kidney failure in black Americans. Black Americans are twice as likely to be diagnosed with diabetes as non-Hispanic white Americans. Approximately 4.9 million black Americans over 20 years of age live with either diagnosed or undiagnosed diabetes.

Additionally, 12.6% percent of all non-Hispanic black Americans over 20 years of age have diagnosed diabetes, compared with 7.1% of non-Hispanic white Americans.

***The most common type of diabetes in black Americans is type 2 diabetes*.** Risk factors for diabetes include: family history, impaired glucose tolerance, diabetes during pregnancy, hyperinsulinemia and insulin resistance, obesity and physical inactivity. Black Americans with diabetes are more likely to develop complications of diabetes and to have greater disability from these complications than white Americans. Black Americans are also more likely to develop serious complications such as heart disease and strokes.

***High blood pressure is the second leading cause of kidney failure among black Americans, and remains the leading cause of death overall in black Americans due to its link with heart attacks and strokes.***

From: <https://www.kidney.org/news/newsroom/factsheets/African-Americans-and-CKD.cfm>

**Women and Chronic Kidney Disease: *Women tend to have a lower GFR than men on average when matched to age.*** All persons tend to lose GFR as they grow older, this is an event called “organ senescence”. If a woman starts with a lower GFR they will reach the 60 value more rapidly than a male. Add factors like diabetes, hypertension and a woman should reach a GFR associated with chronic kidney disease or kidney failure more rapidly. <http://www.kidney.org/professionals/kdoqi/guidelines_ckd/p4_class_g1.htm>