# **LAB 10: RENAL FUNCTION**

## **Pre-Lab Reading**

Some of the functions of the kidneys include (1) filtration of the blood plasma, (2) reabsorption back into the blood of water, ions and reusable molecules (e.g., glucose) and (3) secretion and elimination of waste products that were not removed during the initial filtration process. The final products of kidney function are eliminated in the urine during the process of micturition.

The processes by which the kidneys perform these functions are extremely complex. Within each 24-hour period 180 liters of filtrate is processed from the blood passing through the kidneys. This equates to the total plasma volume being filtered approximately **60 times** per day.

**Filtration**:

The kidneys filter the blood plasma. The blood components that are not filtered are RBCs, WBCs, platelets and most plasma proteins. Filtration occurs at the renal corpuscle. Fluid and small substances move from the glomerulus to the Bowman’s capsule to form the ultrafiltrate.

**Reabsorption**:

Many plasma components that are filtered in the kidneys are still useful for body functions, and, thus, are reabsorbed back into the vascular system. Some of the components of plasma that are reabsorbed are ions (Na+, K+, Ca++), water, glucose, amino acids, etc.

**Secretion**:

All blood plasma is not filtered during a single passage through the kidneys, yet, certain waste products in the blood may still be eliminated from the blood by selective secretion into the kidney tubules. Some products that are secreted are urea, creatinine and hydrogen ions.

**Erythropoiesis**:

This function is not demonstrated in this lab. The kidneys produce a hormone, **erythropoietin**, which stimulates the production of red blood cells in the bone marrow. For example, when an individual goes from sea level to a higher altitude erythropoietin production increases, due to the decreased pO2, to stimulate increased RBC production for greater oxygen carrying capacity of the blood.

The efficiency of kidney function may be determined by an analysis of the products of kidney function. Analysis of the production and composition of urine is known as urinalysis. There are several compounds that may be administered to a subject to determine the efficiency of filtration, reabsorption and secretion. For example, inulin is a plant product that is filtered by the kidney but is neither reabsorbed nor secreted. By measuring the amount of inulin that appears in the urine after injecting inulin into a person’s bloodstream, one can determine the amount of plasma that is filtered per unit time. This amount is known as the glomerular filtration rate (GFR). A normal GFR is 125 ml/min. Some of the analysis methods are beyond the capabilities of this lab, however, considerable information is available from more basic techniques.

The functional units of the kidneys are the nephrons.

* **Proximal Convoluted Tubule:**

This initial portion of the nephron is comprised of Brush Border Cells – Simple Cuboidal with LOTS of microvilli on the apical (luminal) membrane and a folded basolateral membrane. They have lots of mitochondria because they need tons of ATP to power the transporters on the membranes. This is the location of the majority of reabsorption

**What is a Transport Maximum (TM)?**

The limiting factor on the reabsorption of substances is how many and how fast the types of transporters can work. For example: Diabetes Mellitus. One of the key symptoms of this disease is the excretion of glucose in the urine. Normally glucose is reabsorbed in the proximal convoluted tubule. However, since this disease impedes cells’ ability to take in glucose the blood glucose levels are abnormally high. Because there is so much glucose from the blood that gets filtered that all the glucose transporters working as fast as they can go can’t work fast enough to reabsorb it all so you excrete it because you’ve exceeded your transport maximum!

* **Descending Loop of Henle:**

This location in the nephron is comprised of Simple Squamous Epithelium, with no microvilli. There are not many transporters of any kind (besides the basic leaks and pumps) but it allows the water to flow out of the tubule and down its concentration gradient (which is made by the ascending Loop of Henle), but the solutes can’t move so this is where there is a great increase in the concentration of filtrate in the tubule

*What is the Countercurrent Multiplier?*

This is a physiological example of countercurrent exchange and is another name for the loop of Henle. The Descending Loop is only permeable to water the ascending Loop actively transports solutes out. The bottom of the Loop is around 1200 mOsm whereas the top (cortex) is only around normal body osmolarity: 300-330 mOsm

*How* does this differ from the Vasa Recta?

The vasa recta is a special set up of capillaries around the Loop of Henle – it allows the capillaries to feed the medulla of the kidney without ruining the osmotic gradient. Blood moving down the descending portion loses water, glucose and O2 to the tissues and gains NaCl and CO2. Blood moving up the ascending portion regains water by osmosis and loses NaCl – thereby maintaining the high osmolarity of the medullary tissue without a change in the osmolarity of the venous blood leaving the kidney

* **Ascending Loop of Henle and Early Distal Convoluted Tubule:**

This part of the nephron is composed of Simple Cuboidal cells with very few, small, microvilli on the luminal surface but with highly folded basolateral membranes (with lots of mitochondria and transport proteins). The luminal membrane is covered in a special glycoprotein matrix that is totally impermeable to water. This is the only place in the human body that osmosis is restricted.

* ***Juxtaglomerular Apparatus:***

This structure is the major intrinsic controller of blood flow to the nephron and is made up of two distinct cell types

* 1. The Juxtaglomerular Cells (JG Cells): Specialized smooth muscle cells surrounding the afferent arteriole. They act as baroreceptors.
	2. The Macula Dense (MD): Specialized cells that are part of the DCT and lie against the glomerular arterioles. These act as osmolarity receptors to monitor the osmolarity of the filtrate.

* **Late Distal Convoluted Tubule and Cortical Collecting Duct:**

 These two structures are both composed of simple cuboidal cells.

1. *Principle Cells:* This cell type’s permeability to water and solutes is under hormonal control:
	* 1. Aldosterone (Released through the Renin-Angiotensin-Aldosterone System or from the release of ACTH from the anterior pituitary – stimulate the reabsorption of Na+ ions and secretion of K+ ions)
		2. ADH (Released by the Hypothalamus or because of presence of Angiotensin 2 – causes insertion of Aquaporins into the cells which increases water reabsorption. Diabetes Insipidus is the Hypothalamus not releasing enough of this {central DI} or the kidneys not having the receptors to respond to this {nephrogenic DI} which causes the sufferer to produce large amounts of urine.)
		3. Atrial Natriuretic Peptide (Released by atrial myocardial cells when blood volume or blood pressure are too high – cause decrease in rate of Na+ reabsorption in the DCT, causing you to excrete Na+ in the urine, the dilation of the glomerular capillaries which causes an increase in GFR and urinary water loss and inactivation of renin, aldosterone and ADH secretion – so overall you pee more and pee more Na+ which decreases blood volume and consequentially blood pressure]

2. *Intercalated Cells:* Major responsibility to transport H+ and HCO3- to maintain acid/base balance

* **Medullary Collecting Duct**:

This structure is composed of simple cuboidal cells with less microvilli and folds of the basolateral membrane (compared to the proximal and distal tubules) This part of the nephron is mostly Principle cells so their permeability to water and other solutes (urea etc.) is regulated by hormones

**Renal Plasma Clearance**

In order to maintain homeostasis, the kidneys must maintain the ability to clear the plasma of unwanted substances.

The clearance of a substance(x) is defined as the volume of plasma that would have to be completely “cleared”( i.e. the concentration of the substance in the plasma reduced to zero) of that substance to account for the observed amount of that substance in the urine. The calculation of clearance is based on the equation that

Plasma Volume x Concentration(x) in Plasma = Urine Volume x Concentration(x) in

Urine So . . .

 The Clearance of a substance (x) is calculated as:

Urine Volume x Concentration(x) in Urine

Concentration(x) in Plasma

The clearance of a substance depends on the (1) Glomerular Filtration Rate (GFR), (2) the rate at which the substance enters the urine via secretion, and (3) the rate at which the substance leaves the urine via excretion. The GFR of a healthy individual is 120-125 ml/min and it can be estimated by the Clearance of Creatinine (CrCl). Creatinine enters the urine via filtration and is then only slightly affected by secretion and reabsorption. Thus, while almost all of the creatinine that is found in the urine is a result of filtration, sometimes this measurement can be an overestimation due to active secretion or underestimation due to reabsorption of creatinine.

A more accurate determination of GFR is made with the plant product inulin because the nephron neither secretes nor reabsorbs this substance.

Urea enters the urine by both filtration and secretion. Some urea leaves the urine by reabsorption. Under normal circumstances, about 60% of the urea that is filtered is ultimately reabsorbed. The clearance of urea can be calculated by measuring the concentration of urea in both the urine and the plasma and by measuring the volume of urine produced in a specified period of time.

Urinalysis is a quick way to evaluate the function of the kidneys. In order to determine if there is disease present, one must understand the characteristics of “normal” kidneys (kidneys in homeostasis)