NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Renal Revolt:

A Deeper Understanding of Nephron Anatomy and Urine Formation

by
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Part I – The Workout

It was a hot day in August when Noah and Jacob met to work out in preparation for their off-season fitness testing for the university lacrosse team. The two athletes were getting ready to run hill sprints when Jacob noticed that Noah seemed really tired, even though they had just begun.

"If you're tired already, you're going to fail this fitness test," said Jacob.

"Listen, Jacob, I've been putting in extra work this week trying to prepare. I know it's gonna be tough, but I really want to impress Coach. There's a lot of pressure on us this year."

Jacob shook his head. "Well, you can't make up for slacking off for three months in just one week."

"I know," said Noah, "but I have to at least try to be in shape before our testing."

"Are your legs still acting up?" Jacob asked.

"Yeah, I've been icing, but they're still super sore and they've started to swell." Noah reached down and gave them a gentle rub.

Jacob looked at his friend with concern. "I warned you about taking rest days! Man, your legs look pretty bad, did you sprain something?"

"No, I haven't injured them at all," replied Noah. "I'm sure they'll be back to normal in a few days."

Jacob wasn't convinced. "Well, in my anatomy class we've been learning about how hydrostatic and colloid osmotic pressure control the movement of fluid during capillary exchange. Less fluid is brought back into the blood vessels than was taken out, but usually that excess fluid gets picked up by the lymphatic vessels. If something goes wrong in this process, it can lead to tissue swelling."

"You and your anatomy facts," said Noah, shaking his head. "Look, I'll be fine. Let's just get to the workout!"

Questions

1. List three of Noah's symptoms.

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2. Which of the following correctly describes colloid osmotic pressure (also known as oncotic pressure)?
   a. Pressure exerted by the blood on a vessel's walls.
   b. Pressure exerted by large proteins in the plasma that draws fluid into vessels.
   c. Pressure exerted by the vessel walls on the blood.
   d. The minimum mean arterial pressure (MAP) in arteries between heart beats.

3. Which of the following correctly describes hydrostatic pressure?
   a. Pressure exerted by the blood on a vessel's walls.
   b. Pressure exerted by large proteins in the plasma, that draws fluid into vessels.
   c. Pressure exerted by the vessel walls on the blood.
   d. The maximum mean arterial pressure (MAP) in arteries between heart beats.

4. The concentration of which of the following greatly influences colloid osmotic pressure?
   a. Erythrocytes b. Leukocytes c. Platelets d. Plasma proteins

5. Complete Table 1.

   Table 1. Pressures impacting capillary exchange.

	Hydrostatic Pressure	*Colloid Osmotic Pressure*
Pressure Direction: Does this pressure push fluid out of the capillary bed or draw fluid into the capillary bed?		
Factors Influencing Pressure: List variables that alter each type of pressure. Be sure to describe the relationship between the factor and the pressure.		

6. Edema is swelling due to excessive fluid moving into the interstitial fluid or less fluid being removed from the interstitial space (e.g., blocked lymphatic vessels). Determine if each of the following is a potential cause of edema.
   a. Yes / No Increased (excessive) hydrostatic pressure.
   b. Yes / No Decreased (physiologically low) colloid osmotic pressure.
   c. Yes / No Liver failure causing reduced albumin.

Part II – Off to See the Athletic Trainer

Noah and Jacob began their workout, but not far into their sprints, Noah started to have trouble moving his legs. He soon grew nauseous, and felt like his heart was going to beat out of his chest. Jacob, concerned about Noah's condition, cautioned Noah that he should probably go see Zahra, their school's athletic trainer.

"You don't look so good, Noah, we should really stop and get you seen."

Noah, painting heavily, just managed to say, "I-I'm fine, Jacob. Just need to catch my breath."

"No, you're not fine. Look at you, man. Something is seriously wrong. We need to go see the athletic trainer."

"I've pushed myself hard before, this is just a rough patch. I'll be okay." Noah managed a few steps forward before pulling up again.

"No, this isn't like before. You're not even able to stand properly. Come on, let's go before it gets worse."

The teammates gathered their belongings and slowly made their way to Zahra's office.

Noah sat down heavily in a chair. "Hey, uh…Zahra, we need your help."

"Whoa," said Zahra. "What happened? You look pale."

Jacob answered for his friend, "Noah's been feeling dizzy and his heart's racing. He can't even walk properly."

"Have you been experiencing any muscle pain or weakness recently?" asked the trainer.

"Yeah, my legs feel like jelly," replied Noah.

"Noah, I'm sorry to hear that. It sounds like you are struggling. Urine can tell us a variety of things about the health of an athlete. Have you noticed any changes in your urine?"

"Um, yeah… it's been really dark, like tea."

"Thanks for letting me know," said Zahra. "Conducting a urinalysis could provide us with information to properly diagnose you. Would you be willing to provide a urine sample?"

Questions

1. Urine formation involves three major processes. Match each process with its definition.

Process	*Definition*
___ Glomerular filtration	a. Passive or active movement of substance from the filtrate (in the nephron lumen) into the blood.
___ Reabsorption	b. Movement of substances, such as drugs or toxins, from the blood into the nephron lumen.
___ Secretion	c. Removal of the liquid portion of blood and the dissolved solutes, creating filtrate, the basis for urine

2. Urine formation occurs in the nephron; the filtrate from multiple nephrons enters into a shared collecting duct. Figure 1 below shows two types of nephrons.
   a. Figure 1 displays the *renal cortex* and *renal medulla*. Label each of these regions.
   b. Figure 1 displays the two types of nephrons: *cortical nephrons* (comprising approximately 85% of all nephrons) and a *juxtamedullary nephrons* (comprising approximately 15% of all nephrons). Label each of the shown nephrons as cortical or juxtamedullary.
   c. Review the structure of a nephron and collecting duct by labeling each of the six arrowed lines shown in Figure 1.

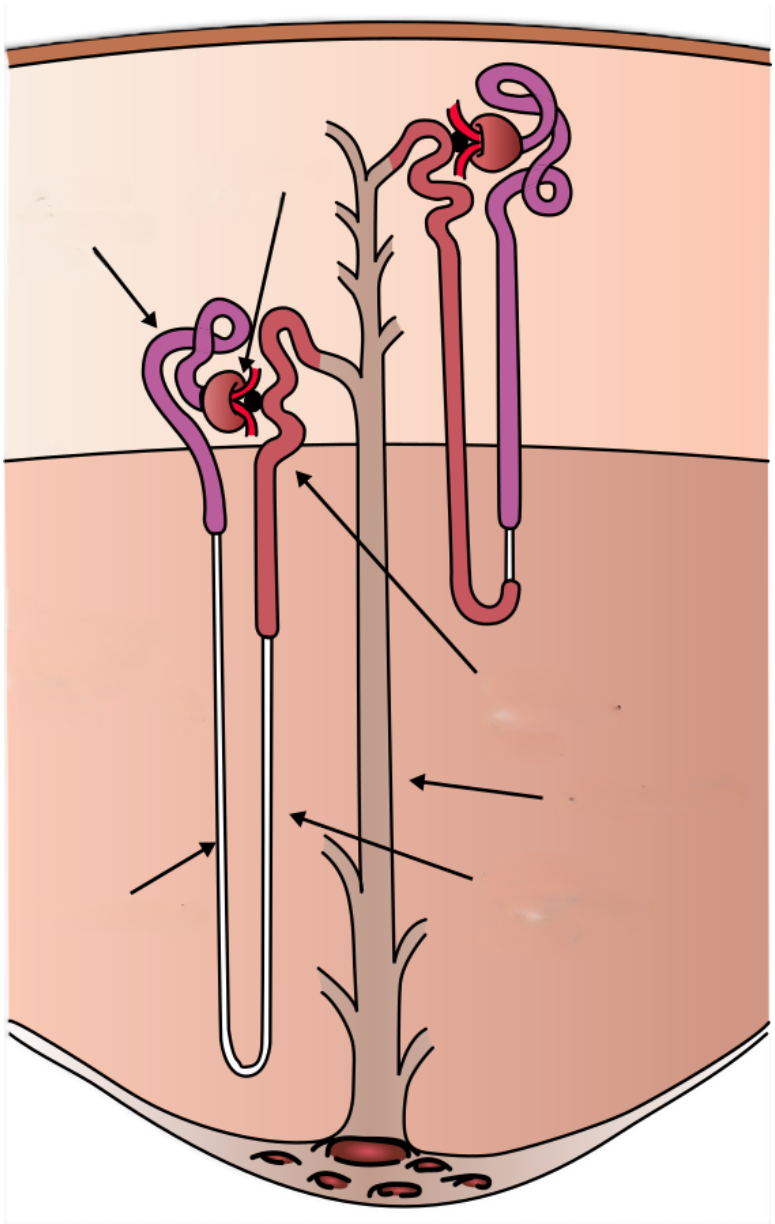


Figure 1. Nephrons. *Credit:* Holly Fischer, modified, CC BY 3.0.

3. On the cortical nephron and collecting duct in Figure 1, indicate where glomerular filtration, reabsorption, and secretion occur (note that both reabsorption and secretion occur in more than one region of the nephron). For each area, indicate what substances are filtered, reabsorbed, and secreted there. At a minimum, include the following substances: amino acids (AA), calcium ions (Ca^{2+}), glucose ($C_6H_{12}O_6$), hydrogen ions (H^+), nitrogenous waste, potassium ions (K^+), sodium ions (Na^+), and water (H_2O).

4. Which of the following are not usually part of the filtrate?
   Water Sodium Albumin Potassium RBC Glucose

5. Complete Table 2 to describe the anatomy and physiology of the renal tubule. In the function column, describe which substance(s) are being reabsorbed or secreted. Indicate if the transportation is passive or active. If you are unfamiliar with the type of epithelium or the function of each region, please consult your textbook.

Table 2. Anatomy and physiology of the renal tubule.

Part of the Renal Tubule	*Type of Epithelium*	*Function*
Proximal convoluted tubule		
Thick descending	Simple cuboidal epithelium	Water moves passively through aquaporins into the medulla.
Thin descending		Water moves passively by osmosis into the medulla.
Thin ascending	Simple squamous epithelium	
Thick ascending		Na^+, Cl^-, and K^+ are actively moved into medulla.
Distal convoluted tubule		

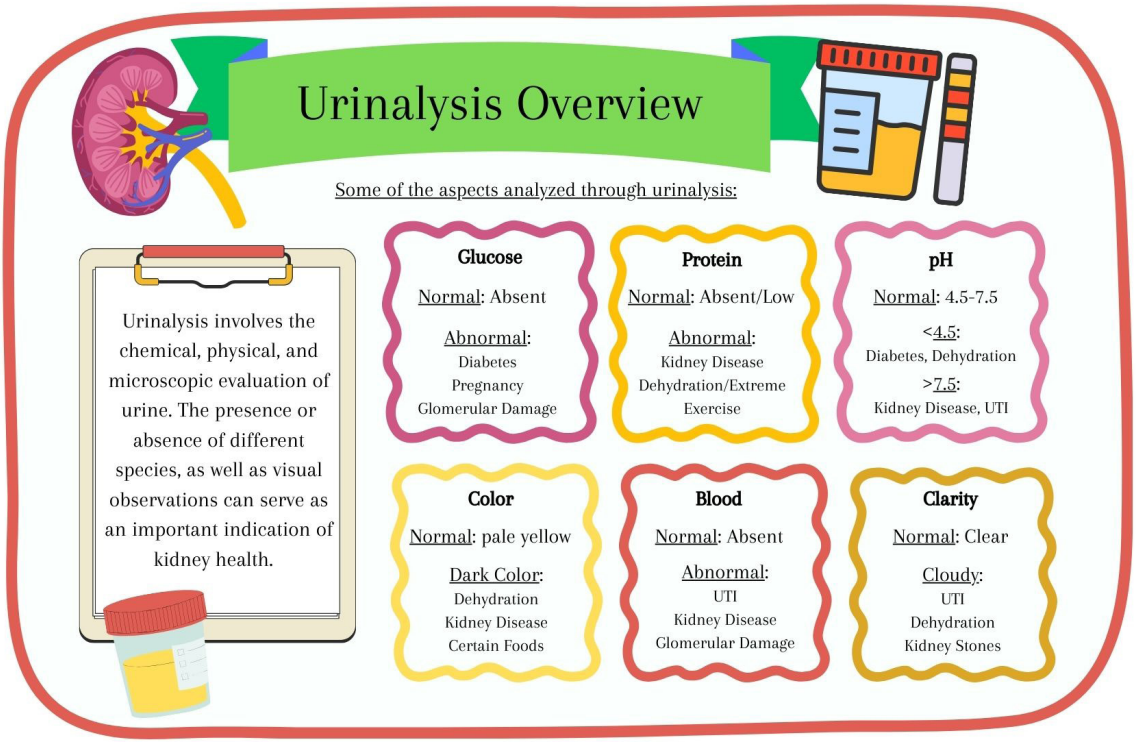


Figure 2. Urinalysis overview. *Credit:* Julia G. Primak.

6. Analyze the results of Noah's urinalysis (Table 3 below). For each abnormality, state which part of the nephron would usually prevent that substance from being in the urine or provide a hypothesis for the abnormality. One example has been provided for you. More information regarding expected results can be seen in Figure 2.

Table 3. Noah's urinalysis results.

Test	*Urinalysis Results for Noah (PT 21 yrs)*	*Normal Urinalysis Results*	*Region of Tubule Responsible*
Color	Dark red/brown (due to the presence of myoglobin in Noah's urine)*	Pale yellow	
Clarity	Clear	Clear	
pH	4.0	4.5–7.5	
Glucose (+/-)	+	–	Most glucose is actively reabsorbed in the proximal convoluted tubule.
Protein (+/-)	+	–	
Blood* (+/–)	+	–	
*A dipstick urinalysis does not directly test for the presence of myoglobin or blood.			

Part III – To the ER We Go

The urinalysis results raised concerns for Zahra. "Noah, I don't want to alarm you, but the abnormal color of your urine could be a sign of something needing medical attention. I'ld like to accompany you to the emergency room." Zahra believed Noah might have rhabdomyolysis, a condition involving the breakdown of muscle fibers. As the muscle fibers break down, a muscle protein, myoglobin, enters the urine, giving it a dark color. Zahra knew that rapid treatment of rhabdomyolysis was crucial for long-term kidney health.

Noah, Jacob, and Zahra arrived at the ER, and Dr. Lily was assigned their case. Through conversation she learned of Noah's muscle weakness, muscle pain, and abnormal urinalysis. Dr. Lily confirmed Zahra's suspicion.

"Noah, based on the information you have provided, I believe you have a condition known as rhabdomyolysis. I would like to conduct a blood test and urinalysis." Dr. Lily continued to explain to Noah what rhabdomyolysis is and why it was important to assess his blood and urine to determine the best course of treatment.

Noah's blood work and urinalysis confirmed Dr. Lily's suspicion. Dr. Lily diagnosed Noah with rhabdomyolysis.

Please read the following article to learn about rhabdomyolysis and then answer the questions below.

- Stanley, M., V. Chippa, & R. Adigun. (2024). Rhabdomyolysis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. <https://pubmed.ncbi.nlm.nih.gov/28846335/>

Questions

1. In one or two sentences, describe rhabdomyolysis.

2. What most likely caused Noah to develop rhabdomyolysis?

3. List several common signs and symptoms seen in rhabdomyolysis.

Part IV –Struggling Kidneys

A while later Dr. Lily returned to explain how Noah's blood results provided information about the impact of rhabdomyolysis on his kidney function. Noah's blood serum creatine kinase (CK), creatinine, and myoglobin levels were elevated. The doctor explained that due to the extra work Noah had put in while trying to catch up for the off season fitness test, he did not give his muscles enough time to heal. As his muscle fibers (cells) were depleted of energy, they died, releasing their contents, including creatine, creatine kinase (CK), creatinine, and myoglobin.

"Based upon the color of your urine and other signs, it appears that the myoglobin (a protein responsible for oxygen-delivery to your skeletal muscles) was released during the breakdown of your muscle tissue. This is limiting your kidney's ability to properly produce urine," said Dr. Lily. She continued to explain that creatine, CK, and creatinine are part of a metabolic pathway associated with ATP production. Noah had elevated levels of CK-MM, a variation of the CK found specifically in skeletal muscles. "Creatinine is a waste product of muscle metabolism. Usually your kidneys remove creatinine from the blood and eliminate it in the urine. High levels of creatinine in your blood can be a marker of reduced glomerular filtration rate or GFR, indicating reduced kidney function."

Dr. Lily paused a moment to make sure that Noah was following before continuing. "Glomerular filtration rate provides us information on the rate at which a person's kidneys are filtering his blood. We want individuals to have a GFR of 90 mL/minute or greater. A decrease in GFR indicates the kidneys are filtering the blood too slowly and allowing dangerous waste products to build up."

After the physician left the room, Noah turned to Jacob. "Man, I'm too tired to understand all this. The doctor said that my serum creatinine levels would tell us about my GFR. What even is GFR?"

A decline in GFR indicates a decrease in kidney function. GFR is proportional to the net filtration pressure, surface area of the glomerulus capillaries, and the permeability of the glomerulus capillaries. Answer the following questions to determine what factors influence each of these variables so that you can help Jacob explain GFR to Noah.

Questions

1. What is glomerular filtration rate (GFR)?
   a. The volume of urine produced over a period of time.
   b. The amount of fluid filtered by the glomerular capillaries over a unit of time.
   c. The change in sodium concentration over time.
   d. The speed that filtrate moves through the loop of Henle.

2. Net filtration pressure (NFP) is the total of the pressures that promote and oppose filtration. Using your knowledge of the four Starling forces (glomerular colloid osmotic pressure, glomerular hydrostatic pressure, Bowman's capsule colloid osmotic pressure, and Bowman's capsule hydrostatic pressure) complete Figure 3 (next page) to create an equation for the net filtration rate. Each force should be used only once. NFP is proportional to GFR; if NFP increases, GFR increases; if NFP decreases, GFR decreases. If you need to review Starling forces, consult the following video which discusses them from time stamp 2:19 min to 4:10 min:
   - Byte Size Med. (2020). Glomerular filtration. <https://youtu.be/wxaEd8p2EQM>

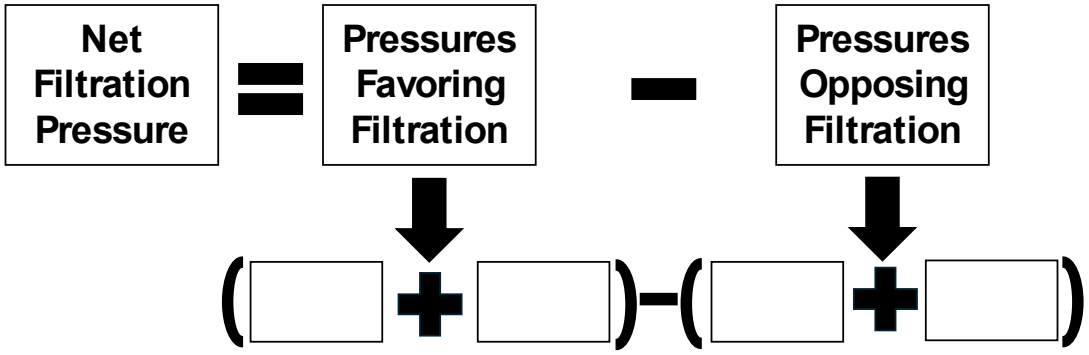


Figure 3. Net filtration rate.

3. On Figure 4 below, use the word bank to do the following:
   a. Label each of the listed structures.
   b. Indicate the location of each of the four Starling forces. For each force, draw an arrow indicating whether it favors filtration (moving substances from the glomerulus capillary into Bowman's space) or opposes filtration.

Word Bank

Structures	Glomerulus	Bowman's capsule	Afferent arteriole	Efferent arteriole
Starling Forces	Glomerular hydrostatic pressure	Bowman's capsule colloid osmotic pressure	Bowman's capsule hydrostatic pressure	Glomerular colloid osmotic pressure

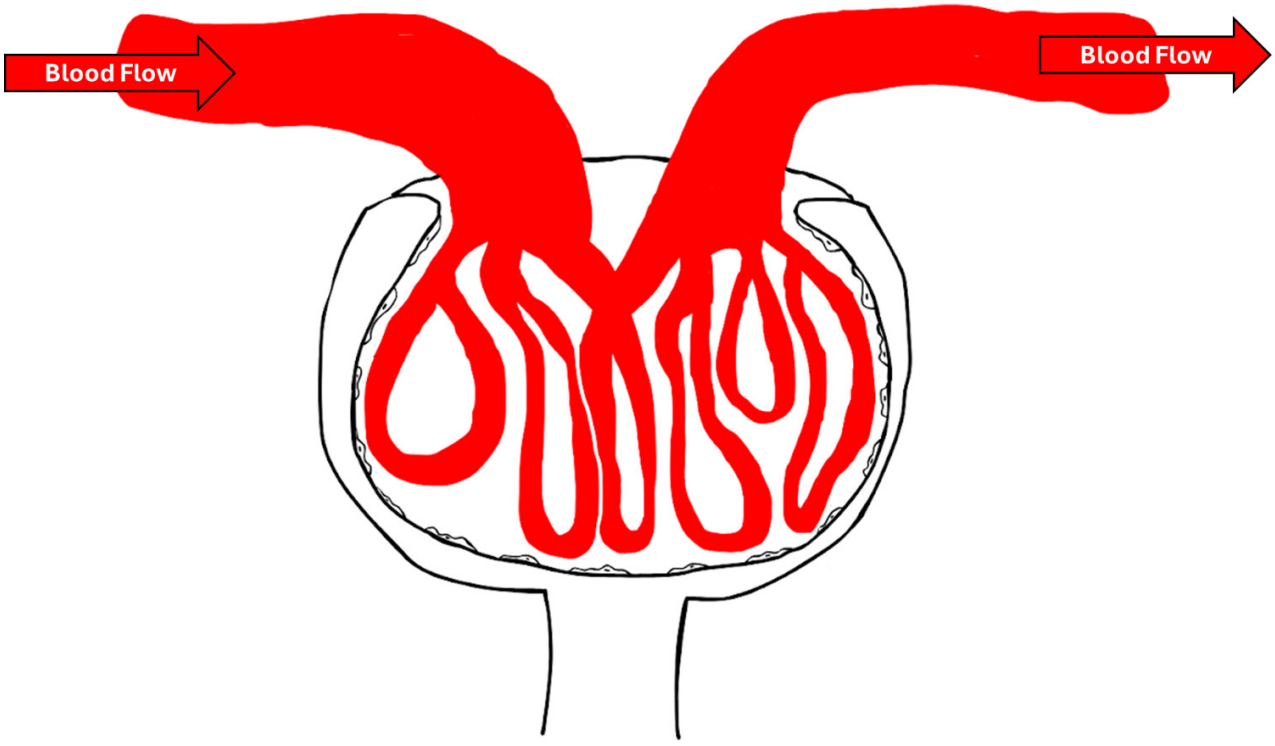
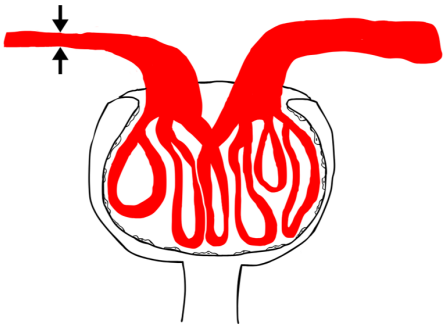
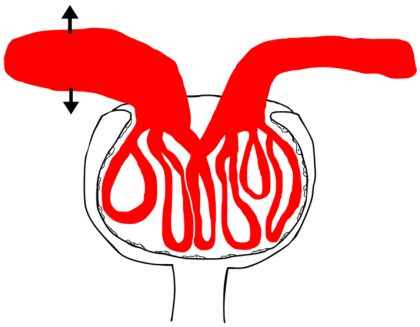
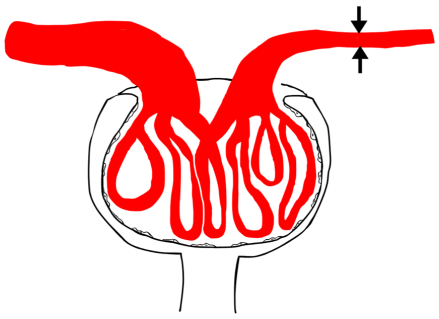
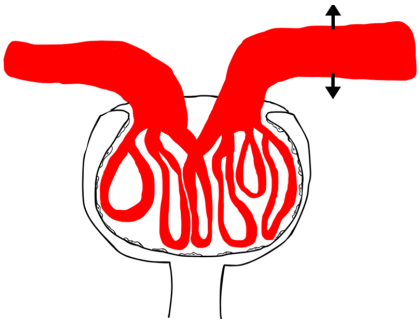


Figure 4. Starling forces. *Credit:* Julia Primak.

4. To regulate glomerular filtration rate (GFR), the human body can alter the diameter of the afferent and efferent arterioles. Changing the diameter of these vessels alters glomerular hydrostatic pressure and therefore, alters GFR. Use Table 4 below to summarize how changes in vascular diameter impacts GFR. Using the figures, determine whether vasoconstriction or vasodilation is displayed; then indicate the term that describes the associated changes to glomerular hydrostatic pressure and GFR.

Table 4: Relationship between arteriole changes and GFR. The vessel left of the glomerulus represents the afferent arteriole and the vessel on the glomerulus represents the afferent arteriole.

Diameter change of afferent arteriole:	Vasoconstriction or vasodilation?	Vasoconstriction or vasodilation?
		
Impact on glomerular hydrostatic pressure:	Increase or decrease?	Increase or decrease?
Effect on GFR:	Increase or decrease?	Increase or decrease?
Diameter change of efferent arteriole:	Vasoconstriction or vasodilation?	Vasoconstriction or vasodilation?
		
Impact on glomerular hydrostatic pressure:	Increase or decrease?	Increase or decrease?
Effect on GFR:	Increase or decrease?	Increase or decrease?

5. True or false? As the permeability of the glomerulus capillary bed increases, GFR increases.

6. Changes in any one of the Starling forces or permeability of the glomerulus alters GFR. Read about each of the clinical situations and determine if they would cause an increase or a decrease in GFR. Provide an explanation for your conclusion.
   a. Diabetic nephropathy occurs as a result of hyperglycemia (high blood glucose levels). Substances are deposited on the walls of the glomerular capillaries.

   b. Glomerulonephritis, a condition marked by increased porosity of the glomerular basement membrane and excessive loss of proteins into the urine.

   c. Multiple myoma, a form of cancer due to excess plasma cells, associated with an increase of blood proteins.

   d. Renal calculi, commonly referred to as kidney stones, lodge in the nephron loop.

7. The majority of creatinine is usually freely filtered by the glomerulus and a small percentage is secreted into the distal convoluted tubule. Explain how elevated serum (blood) creatinine levels indicate kidney damage or failure. Include the terms filtration, reabsorption, and excretion.

Part V – Treatment (Dialysis for the Win)

Dr. Lily tells Noah that he is being diagnosed with Acute Kidney Injury, a sudden decrease in glomerular filtration rate, caused by rhabdomyolysis. His decreased GFR combined with the presence of protein detected in his urinalysis, CK presence, and increased serum creatinine levels found from his blood draw led to this diagnosis.

Noah is admitted to the hospital and has an IV placed to replace his fluids and help balance his electrolytes. As Noah is getting fluids and resting in the hospital, Dr. Wilson, his nephrologist (a physician specializing in kidney care) comes in to talk to him about the next steps for treatment. Dr. Wilson tells Noah that he will need to start dialysis to assist his kidneys in filtering out the myoglobin that was released from his muscles as they were damaged. "The exact time you will need to be on dialysis will depend on how quickly your kidneys recover and the presence of creatinine in your blood. We will monitor your GFR and blood metabolites to determine when to stop your dialysis. Do you have any questions?"

Read the following article and then answer the questions below.

- NKF Patient Education Team (2023, January 2). Dialysis. National Kidney Foundation. Accessed October 31, 2024 from <https://www.kidney.org/kidney-topics/dialysis>

Questions

1. Pretend that you are Dr. Wilson and describe to Noah the purpose and process of dialysis.

Part VI – Back at School (Spread the Word)

A couple months later, after Noah had recovered and was back at classes, the university's athletic training staff hosted an event to educate all the athletic teams on the importance of kidney health to an athlete as well as tips on preventing rhabdomyolysis. Imagine you are part of the athletic training staff and you are to create a training protocol to inform coaches of the dangers of rhabdomyolysis. Create an infographic or four-slide presentation that includes the following:

Overview and Risk Factors

- Briefly describe rhabdomyolysis.
- List and describe common risk factors and/or behaviors that increase an individual's risk of developing rhabdomyolysis.

Normal Nephron Anatomy and Physiology

- Describe the anatomy of a human cortical nephron. Provide an accompanying graphic.
- Describe the process of urine formation, including the processes of glomerular filtration, reabsorption, and secretion. This section should include the following terms and substances: albumin, Bowman's capsule colloid osmotic pressure, Bowman's capsule hydrostatic pressure, and glomerular hydrostatic pressure, amino acids, glucose, red blood cells (RBCs), sodium (Na^+), and potassium (K^+).

Signs, Symptoms, and Diagnosis

- Describe common signs (observable by the medical provider) and symptoms (reported by the patient).
- Describe the role of urinalysis and GFR in the diagnostic process.

Treatment

- List how medical providers treat rhabdomyolysis.

Additional Requirements

- Include a minimum of two visual elements, one of which must be a visual representation of a nephron.
- Use bullet points instead of large paragraphs of text.
- Text should be written for a lay (non-scientific) audience.
- Use in-text citations or footnotes. In-text citations and end-of-text full citations should follow APA guidelines.

Part VII – Real World Examples

While Noah's story is fictional, rhabdomyolysis is a real condition observed in the world. Although it is rare, rhabdomyolysis affects around 26,000 Americans each year. Acute renal failure is more common, affecting 31% of inpatients around the world.

One example of rhabdomyolysis in the real world was observed in the Tuft University men's lacrosse team. In September of 2024, fifty players completed a voluntary workout led by an uncertified Tuft alumnus who had recently graduated from the Navy SEAL program. This voluntary workout led to nine players being hospitalized with rhabdomyolysis. Other factors contributing to this hospitalization could be caffeine, creatine, and return to workout after an off-season break. However, the extreme workout led by the Navy SEAL graduate was the ultimate reason for the rhabdomyolysis outbreak (Watson, 2024).

An additional example of rhabdomyolysis was observed in the University of Oregon State's football team. In 2017, after a rigorous "military" style workout consisting of an hour of continuous push-ups and up-downs, offensive lineman Sam Poutasi was hospitalized with rhabdomyolysis. His diagnosis was confirmed by discolored urine and elevated levels of creatine kinase. Many other players passed out as a result of the extreme exercise, and two others ended up in the hospital. The University of Oregon eventually released a statement stating that modifications were made to their program to prevent future incidents (Jussim, 2018; Lisanti, 2017).

As seen through the case study and these real world examples, the kidneys are crucial in the formation and composition of urine. This case study covered the physiology of glomerular filtration rate (GFR), reabsorption, and secretion as well as the components of urine. Understanding nephron physiology, urine composition, and GFR can allow for proper treatment of acute kidney disease. As depicted in this case study, rapid treatment of Noah's decreased GFR can allow one to fully recover from rhabdomyolysis.

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