4-2019

Functionality of the Kidneys

Amber Jourdan
Grand Valley State University

FUNCTIONALITY OF THE KIDNEYS

Amber Jourdan

HNR 499 – 03

I. Introduction

II. Urinary and Renal Systems

- A. Organs Involved in Urinary System
  1. Kidneys
  2. Ureters
  3. Bladder
  4. Urethra
- B. Structures in Renal System
  1. Nephron
     a) Glomerulus
     b) Loop of Henle

III. Kidney Disease

- A. What is it?
- B. Types of AKI (Acute Kidney Injury)
- C. How is it diagnosed?
- D. Current Treatments
  1. Dialysis
  2. Kidney Transplant
- E. New Therapies Being Developed
  1. Biomarkers
  2. Biocompatible Membranes

IV. Kidney Stones

- A. What are they?
- B. What happens?
- C. How common are they? How are they diagnosed?
- D. Treatment Options and Prevention
  1. Lithotripsy

V. Conclusion

INTRODUCTION

This project is an informative research paper on the role of the kidneys in the urinary system, as well as issues that arise in the kidneys. A brief introduction is given to explain the general function of the urinary system and the importance of the kidneys. Following that, a section of Acute Kidney Injury explains the disease and possible treatments. Additionally, there is a section on kidney stones, how they are formed, and how treatments are administered when a patient presents with this ailment.

This paper is not the only piece of this project. In addition, a visual aid will illustrate the information in this paper. This animation will enhance the information and allow the paper to be easily presented if desired.

URINARY SYSTEM

The urinary system consists of the kidneys and accessory structures such as the ureters, urinary bladder, and urethra. The kidneys are the organs where urine production occurs, and the ureters are hollow tubes that bring the urine to the bladder. The urinary bladder expands and fills until the reflex of urination is triggered due to the amount of pressure on the internal sphincter. At this point, the bladder contracts and sends the urine through the urethra.[15] When the urine reaches the end of the urethra, the external sphincter relaxes and expels the urine out of the body (Fig 1).

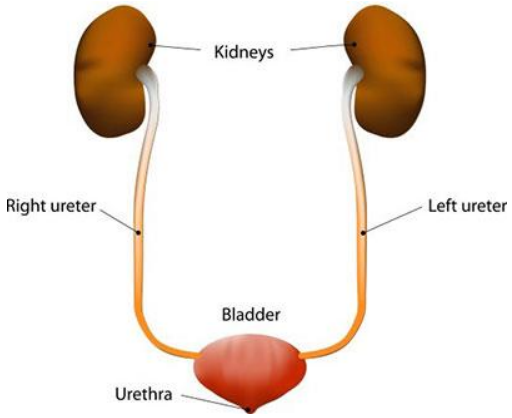

Figure 1: The structure of the urinary system.[18]

The kidneys lie on either side of the spine posterior to the eleventh and twelfth rib. Renal arteries supply the kidneys with blood, while renal veins carry blood from the kidneys to the inferior vena cava. With this connection to the circulatory system, kidneys receive 20-25% of cardiac output. This is an immense amount of output for an organ that accounts for only 0.4% of an individual's total body weight.[15] The kidneys receive high amounts of cardiac output because they play a crucial role in filtering waste products from the blood. Therefore, all the blood in the body must continually cycle through the kidneys at a rapid rate to ensure full filtration of waste products.

The kidneys achieve this filtration by using its intricate system of delicate structures. There are two layers: the cortex and the medulla. There are also tubules called nephrons, 80% of which are contained in the cortex; the other 20% dip down slightly into the medulla (Fig 2). These nephrons are an important part of the kidney and its functions. Each nephron begins with a capillary bed known as the glomerulus. It is in the glomerulus that the process of filtration of the blood is started to remove waste products. Filtrate, which consists of the waste products filtered from the blood, from the glomerulus continues down the nephron to what is known as the proximal tubule. In the proximal tubule, there is reabsorption of organic nutrients, ions, and

water. Following this, there is excretion in the proximal tubule of metabolites and xenobiotic molecules, which are foreign particles that should not be in the body. From here, the filtrate flows through the Loop of Henle, where more reabsorption of ions occurs. Then, in the distal tubule and collecting duct there is regulated reabsorption of ions and water for salt and water balance. This is important for maintaining pH homeostasis, which allows proper functioning of the body. The filtration process is complete after the filtrate passes through the collecting duct and enters the bladder to be excreted.[15]

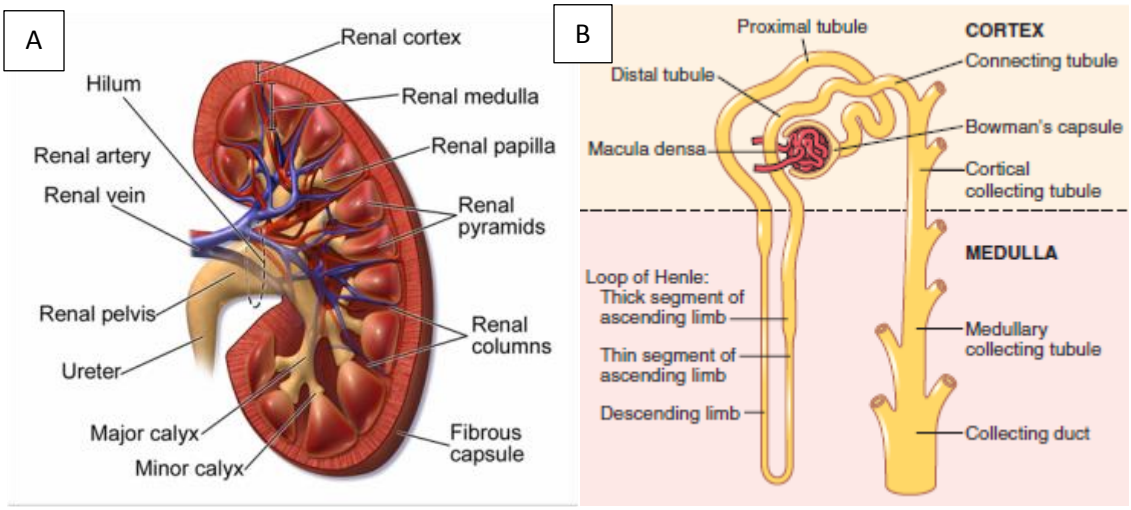

Figure 2: A) The structures that make up the kidney.[1] B) The structures of the nephron.[17]

Urinary output is the content measurement of how well the kidneys do this filtration process. The only true measure of how well the kidneys filtered is by measuring clearance from the amount of urinary output. Clearance is measured by the rate at which a solute is removed from the body by the kidneys. For example, specialists do this by comparing the load of solute filtered in the nephron with the excretion rate of the kidneys. This tells them how well the nephron did its job. If the amount of substance filtered and excreted is the same, the nephrons did their job. Problems arise when there is more of a substance in the urine than that which was put

through the filtration.[15] This indicates that all foreign particles are not being filtered from the blood, which further causes reabsorption errors in the nephron.

The urinary system is a common target for checking drug toxicity. The kidney is especially susceptible to highly toxic drugs traveling through the urinary system due to the high volume of blood the kidney receives. It works to concentrate these drugs and get rid of them, even when the drugs are needed for normal function of the patient. About 20% of cases of Acute Kidney Injury (AKI, previously known as acute renal failure) are caused by toxic drugs. Many of these drugs are administered during hospital stays, which leads to more cases of AKI in hospitalized patients compared to the general population.[9]

Essentially, the urinary system works to keep the body running smoothly, without any foreign particulates running through the circulatory system. The kidneys are the main site for this filtration, which is why it is such an important organ. Without the filtration that occurs in the nephron of the kidney, waste products would not be removed, causing the buildup of toxic waste products throughout the body. We'll see later in this paper the problems that arise when such waste products are not filtered.

ACUTE KIDNEY INJURY AND KIDNEY DAMAGE

The rapid loss of the kidney's excretory function alludes to the presence of kidney disease. There is a continuum, known as the RIFLE continuum, that explains the different stages of kidney damage. The stages are risk, injury, failure, loss, and end-stage (Fig 3).

	GFR criteria	Urine output criteria
Risk	1·5-fold increase in S_{creat} or GFR decrease >25%	UO <0·5 mL/kg/h for 6 h
Injury	Two-fold increase in S_{creat} or GFR decrease >50%	UO <0·5 mL/kg/h for 12 h
Failure	Three-fold increase in S_{creat}, GFR decrease >75%, S_{creat} ≥4 mg/dL, or acute rise in S_{creat} ≥0·5 mg/dL	UO <0·3 mL/kg/h for 24 h or anuria for 12 h
Loss	Complete loss of kidney function >4 weeks	
ESKD	End-stage kidney disease (>3 months)	

Figure 3: The differences between the levels in the RIFLE continuum[3]

Acute Kidney Injury (AKI) is the precursor to end-stage renal failure. It is essentially the first step in identifying a patient with kidney disease. AKI is typically diagnosed by the accumulation of the waste products urea and creatinine in the blood, which come from nitrogen metabolism. Along with this, a decrease in urine output can be used to diagnose AKI. This being said, AKI is usually asymptomatic until there has been an extreme loss in kidney function, making it difficult to diagnose. Consequently, kidney injury is noticed when scanning for other problems. For example, diagnosis occurs when acute loss of another organ system is diagnosed (Fig 4).[3]

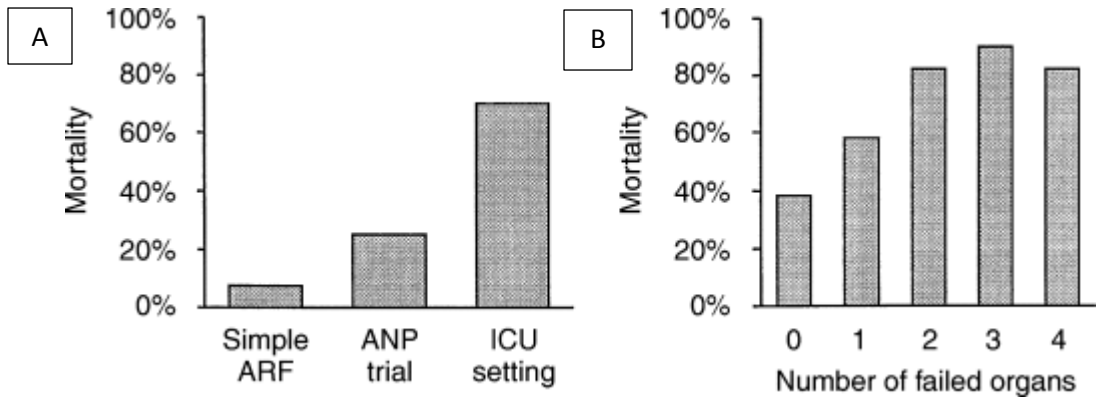

Figure 4: A) The relationship between increased mortality rates and the stage of renal failure of the patient.[16] B) A comparison between mortality rate and the number of failed organs.[16]

There are two types of Acute Kidney Injury. The first is pre-renal, which occurs due to intrarenal vasoconstriction caused by pharmaceutical drugs, systemic vasodilation caused by sepsis, and volume depletion caused by vomiting or diarrhea (Fig 5).[11] A patient diagnosed with pre-renal AKI has kidneys that can return to normal with the correction of the causative injury that led to AKI in the first place. This type of kidney injury is common in community and hospital settings. The other type is post-renal AKI. This type is readily diagnosed. The therapy for this type is straightforward: remove the obstruction. This type is common in community settings.[12]

Table 2. Causes of Acute Kidney Injury

Cause	Processes/Subgroup	Examples
Prerenal	Intrarenal vasoconstriction	Drugs: antihypertensives, cyclosporine, diuretics, laxatives, NSAIDs, tacrolimus, vasoconstrictors
	Systemic vasodilation	Sepsis, neurogenic shock
	Volume depletion	Diuretic overuse, osmotic diuresis, vomiting, diarrhea, burns, sweating, blood loss
Intrinsic	Glomerular	Drugs: allopurinol, chlorpropamide, dapsone, gold, halothane, hydralazine, levamisole, NSAIDs, penicillamine, penicillin, probenecid, procainamide, psoralen, quinidine, rifampicin, thiazides, tolbutamide
	Interstitial	Drugs: acyclovir, allopurinol, aminosalicylates, bumetanide, cephalosporins, cimetidine, cotrimoxazole, furosemide, gold, interferon, isoniazid, lithium, NSAIDs, penicillin analogues, phenytoin, PPIs, quinolones, rifampicin, thiazides Infections: bacterial, fungal, or viral Systemic disease: sarcoidosis, lupus
	Tubular	Ischemic: prolonged hypotension Nephrotoxic: exogenous toxins including acyclovir, aminoglycosides, amphotericin, cisplatin, contrast media, cyclosporine, ethylene glycol, foscarnet, ifosfamide, lithium, mannitol, NSAIDs, paracetamol, tacrolimus, vancomycin Endogenous toxins such as hemolysis, rhabdomyolysis, tumor lysis syndrome, myeloma
	Vascular	Renal vein thrombosis, malignant hypertension, scleroderma renal crisis, renal atherothrombotic disease, renal infarction
Postrenal	Ureteral/bladder	Prostate hypertrophy, neurogenic bladder, retroperitoneal fibrosis, cancer of bladder, prostate, or cervix
	Pelvic	Transitional cell carcinoma, pelvic malignancy leading to extrinsic compression of ureters, inflammatory aortic aneurysm
	Intrarenal obstruction	Stones, crystals (acyclovir, indinavir), clots, tumors, paraproteins

NSAID: nonsteroidal anti-inflammatory drug; PPI: proton pump inhibitor.
Source: References 13-17.

Figure 5: Explanation of causes of Acute Kidney Injury.[11]

Currently, there are no specific therapies for treating Acute Kidney Injury, so any treatment options available to the patient are merely supportive.[3] Dialysis is one treatment option that aims to replace the function of a failed kidney. Today, about 2.0 million patients utilize this

treatment method. These patients are most likely on dietary restrictions to reduce the load of potassium, phosphate, sodium, and water in the kidney, which can all cause further damage. Unfortunately, dialysis can only partially compensate for the deficiencies that are caused by Acute Kidney Injury and kidney disease. Even with dialysis, a patient's full kidney function will not return after treatments.[6]

Kidney transplantation is the other major therapy for patients with Acute Kidney Injury. This is the most successful and most common type of organ transplant surgery.[14] The standard procedure is to insert the donor kidney into the pelvis with vascular anastomosis, which is the connection of blood vessels, into the vessels of the groin. In doing this, the kidney is able to establish a direct filtration system while being in close proximity with the bladder to allow for a short connection between the transplanted kidney and the bladder, so urinary drainage into the recipient's bladder can occur.[7] If this is achieved, the surgery is a success.

There is a new diagnostic technique as well as a new treatment method still being developed. One of these is the use of biomarkers to diagnose a patient before the harsh symptoms of kidney damage present themselves. Biomarkers act as a notification to specialists that there is something abnormal going on in the body. Most often, these biomarkers signal that an organ system is failing (Fig 6). For the kidneys, the biomarkers that specialists can look for in the urine are cystatin C, neutrophil gelatinase-associated lipocalin, interleukin-18, kidney injury molecule-1, and urinary growth factor. The biomarkers from the serum that specialists can look for are cystatin C, neutrophil gelatinase-associate lipocalin, interleukin-18, and fibroblast growth factor-2.[12] The main issue with biomarkers is that they are non-specific and lack sensitivity, which has been the primary difficulty in developing them as an effective diagnostic tool.[10] This

causes specialists to steer away from using these biomarkers as diagnostic tools because they may not truly indicate the disease present in the patient.

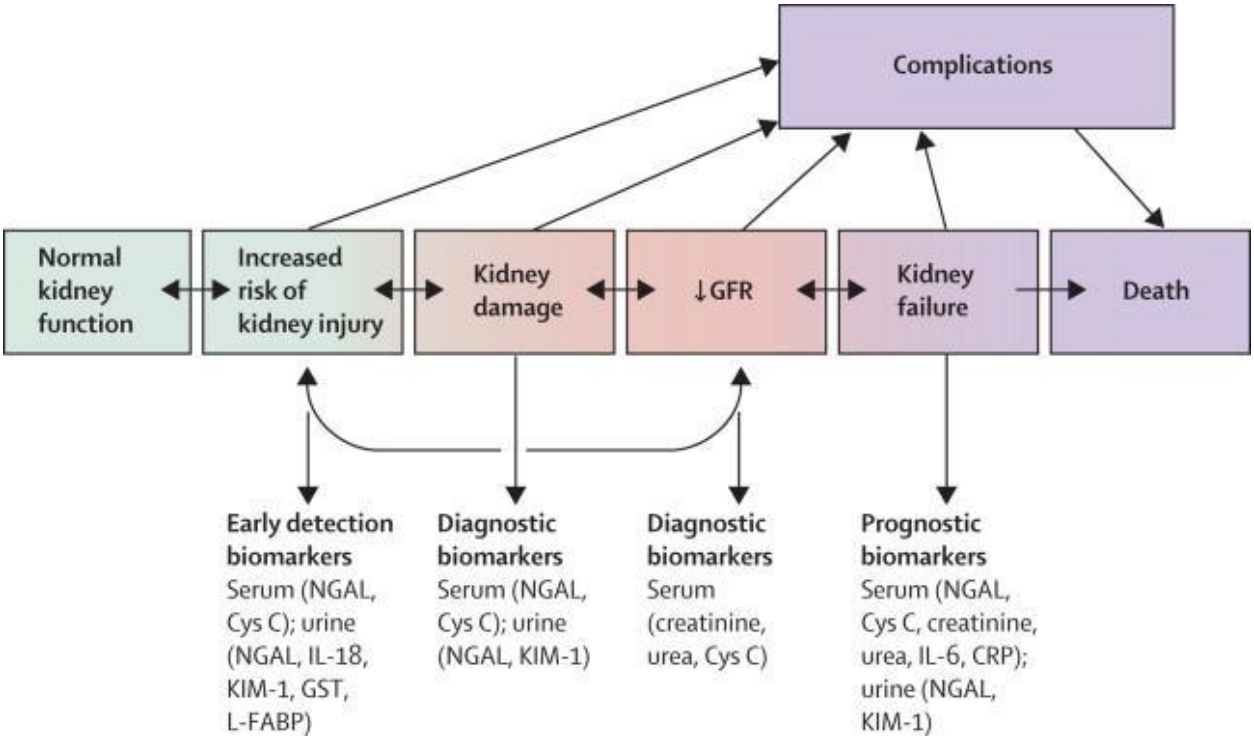

Figure 6: The use of biomarkers for diagnosis at each stage of kidney disease.[10]

As explained before, dialysis is a treatment method for patients with a damaged kidney. There are two ways dialysis can be done. The first is by hemodialysis, which involved circulating the blood through a disposable dialyzer 3-5 times a week for 3-5 hours each session. The other method is peritoneal dialysis, which uses the peritoneum as the dialysis membrane. Biocompatible membranes and advancement being explored in cases of hemodialysis. These membranes would be in the dialyzer while a patient receives dialysis. These membranes would allow for less complement activation due to the interactions of the blood with the membrane surface. This would mean the biocompatible membrane helps to reduce inflammation by removing inflammatory mediators from the blood circulation. By reducing the risk of inflammation, the risk of developing pre-renal acute kidney injury is reduced because there is

less risk of systemic vasodilation (Fig 5). Several studies have shown the survival rate to be higher in patients who receive dialysis with a biocompatible membrane in the dialyzer as opposed to a synthetic membrane. The major downside of using biocompatible membranes is in the cost. These membranes are more expensive; however, they do not decrease the recovery time needed for patients suffering from Acute Kidney Injury or other kidney damage.[13]

In essence, Acute Kidney Injury is the precursor to kidney disease that specialist look for when problems within the urinary system arise. AKI is difficult to diagnose, so it is essential that specialists catch it early, before other organ failure occurs. This is why the use of biomarkers would be beneficial, however, with the nonspecific nature of the biomarkers, it is difficult to make a clear diagnosis based on the presence of biomarkers. While dialysis is effective and works well for the 2.0 million patients who are reliant on it, it could be improved with the biocompatible membrane. This being said, the high price does not justify the switch, especially when the biocompatible membranes do not shorten the amount of time the patient must rely on dialysis. There is still much research to be done in order to use the symptoms associated with AKI to treat kidney disease before it has truly begun.

KIDNEY STONES

A kidney stone is a solid accumulation of material that forms in the tubular system of the kidney. Kidney stones cause problems when they block the flow of urine through or out of the kidney. This blockage can result in pressure build up in the kidneys and cause the kidneys to swell. If this occurs for an extended period of time, the delicate structure of the kidney will be damaged. With kidney stones come severe pain. This pain is felt as the kidney stone passes

through the ureter, which is the tube connecting the kidney to the bladder. Most stones are small enough that the kidney is able to maintain its normal function (Fig 7).[5]

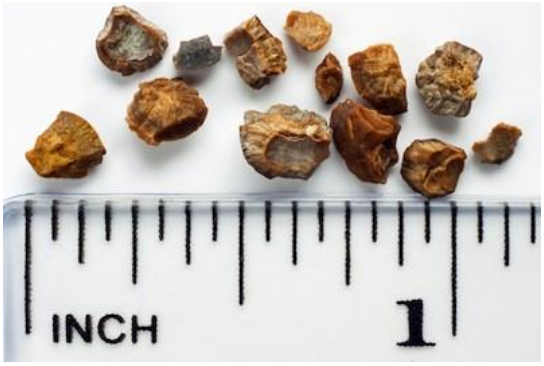

Figure 7: Image is of kidney stones with ruler for reference to the average size of the stones.[8]

About 10% of the population gets kidney stones. The most common victims of these stones are Caucasians, males, people over 30 years of age, people who have previously had kidney stones, and people who have relatives who have had kidney stones. In general, 80% of the stones are made of calcium and phosphate or calcium and oxalate, determined by polarization microscopy. Using this method, calcium phosphate and calcium oxalate stones are black, grey, or white, as opposed to the other common kidney stone made of uric acid which appear white or orange.[4] These stones can also be associated with other diseases that cause patients to have increased blood calcium levels.[5]

Unfortunately, kidney stones are not diagnosed until the stone begins to pass through the ureter and the patient complains of severe pain in the flank area, which is the area of the lower back in the space between the ribs and pelvis. Occasionally, patients notice blood in their urine before they experience any pain, which can assist with an earlier diagnosis.[5]

There are several treatment options for patients who suffer from kidney stones. The most common treatment, which is given in cases of extreme pain and discomfort, is the use of narcotic pain medications such as meperidine or morphine. Along with this, specialists often encourage

drinking large amounts of water to help the stone pass more quickly. If an individual is unable to drink due to the severity of the pain, the fluids may be delivered intravenously. In rare cases, the stone may need to be surgically removed if it appears too large to pass on the ultrasound.[5]

There is a treatment method that is used in some cases. This treatment involves crushing the stone through the use of shock waves. This method is called lithotripsy (Fig 8).[5] The shock waves from the machine are specifically focused on the kidneys using ultrasound and X-ray imaging.[2]

Figure 8: The machine used for lithotripsy.[2]

The goal of this treatment method is to break the stone into small enough fragments so they can pass naturally.[5] This technique works best when the stone is located in the upper ureter and is between 4mm and 2cm in diameter because they are easier to access for focusing (Fig 9).[2]

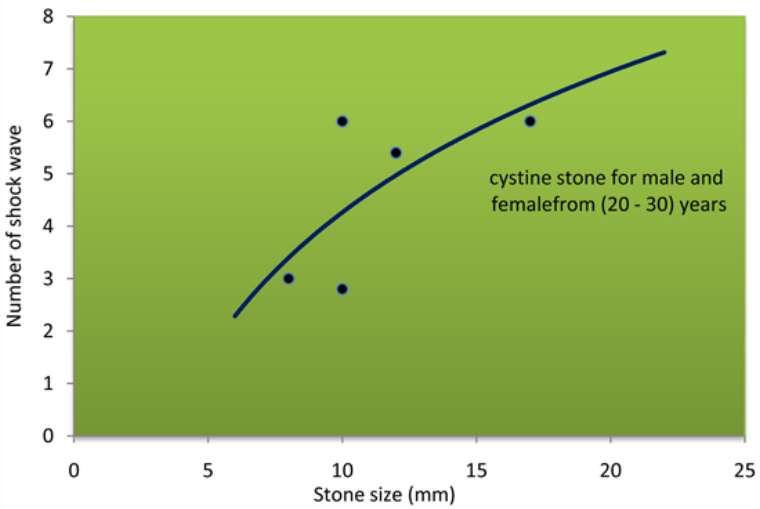

Figure 9: Relationship between stone size and the number of shock waves administered to the patient before results were seen. Note that as the size of the stone increases, the number of shock waves needed increases as well.[2]

This procedure reduces the patient's recovery time in comparison to traditional surgery.[5] Additionally, the side effects from this type of treatment are insignificant, except for the rare cases of hematoma, bleeding, etc.[2]

There are a few prevention methods recommended for individuals who are predisposed to kidney stones. The primary prevention method is to increase fluid intake to several quarts of water a day. In addition, individuals are encouraged to eat less protein. This is thought to help reduce the formation of calcium oxalate stones. Individuals are also encouraged to limit consumption of foods high in oxalates such as beer, black pepper, berries, broccoli, chocolate, spinach, and tea.[5]

Kidney stones are quite painful, so the patient is usually willing to take the necessary precautions following to ensure they do not get another stone for a while. While surgery may be the quickest way to get rid of a stone, it is the least common due to its invasiveness, except in cases of large stones. Naturally passing a kidney stone is the most common, however, with the advancing technology of the lithotripsy procedure, more patients will undergo that treatment

method if their stones are small enough. Although the chances of getting a second kidney stone are higher after having a first one, many patients hope to never experience that pain again.

CONCLUSION

This paper has outlined the structure and function of the urinary system, the diagnosis and treatment of Acute Kidney Injury, and the dangers of kidney stones. It is important to take care of this system because it is critical for filtering the blood to remove toxins from the body. Kidney disease is a hindrance to normal urinary function. Therefore, it is important to watch for signs of Acute Kidney Injury, since this is a precursor to kidney disease. Kidney stones are also dangerous to the function of the urinary system because they can damage the structures of the kidney. Taking care of the urinary system results in better kidney function, which means better filtration of toxins, and ultimately a healthier body.

References:

1 Agarwal, Anirudh. “Kidney.” *Endocrine System, Urinary System* (blog), April 11, 2018. https://www.knowyourbody.net/kidney.html.

2 Al-Hakary, Shamoo, Suzan Haji, Esraa Noory, and Sonia Issaq. “Extracorporeal Shock Wave Lithotripsy Treatment for Renal and Ureteral Stones in Duhuk City.” *Journal of Modern Physics* 7, no. 1 (January 2016): 175–84.

3 Bellomo, Rinaldo, John Kellum, and Claudio Ronco. “Acute Kidney Injury.” *The Lancet* 380, no. 9843 (August 25, 2012): 756–66.

4 Coe, Fredric, Joan Parks, and John Asplin. “The Pathogenesis and Treatment of Kidney Stones.” *The New England Journal of Medicine* 327 (October 15, 1992): 1141–52.

5 Fleming Fallon Jr., L. “Kidney Stones.” *The Gale Encyclopedia of Nursing and Allied Health* 4 (2018): 2001–4.

6 Goldsmith, David, Satish Jayawardene, and Penny Ackland. *ABC of Kidney Disease*. Second. ABC Series. John Wiley & Sons, Inc., 2013.

7 Hart, A, J.M. Smith, M.A. Skeans, S.K. Gustafson, D.E. Stewart, W.S. Cherikh, J.L. Wainright, et al. “Kidney.” *American Journal of Transplantation* 16, no. S2 (January 2016): 11–46.

8 Jackman, Michael. “On Passing a Kidney Stone.” *Detroit Metro Times*, September 15, 2015.

9 Khan, Kanwar, Gordon Hard, Xiantang Li, and Carl Alden. *Fundamentals of Toxicologic Pathology*. 3rd ed., 2018.

10 Mendoza, Jonathan. *Acute Kidney Injury: Causes, Diagnosis, and Treatments*. New York: Nova Science Publishers, Inc, 2011.

11 Panesar, Kiran. “Acute Kidney Injury: An Overview.” *US Pharmacist* 40, no. 8 (2015): HS2–6.

12 Patel, Vinood, and Victor Preedy. *Biomarkers in Kidney Disease*. Biomarkers in Disease: Methods, Discoveries, and Applications, n.d.

13 Pereira, Brian, Mohamed Sayegh, and Peter Blake. *Chronic Kidney Disease, Dialysis, and Transplantation*. 2nd ed. Philadelphia, PA: Saunders, 2005. Print.

14 Ramirez, Carlo, and Jerry McCauley. *Contemporary Kidney Transplantation*. Organ and Tissue Transplantation, n.d.

15 Silverthorn, Dee. *Human Physiology: An Integrated Approach*. Pearson Education Inc., 2016. Print.

16 Star, Robert. “Treatment of Acute Renal Failure.” *Kidney International* 54, no. 6 (1998): 1817–31.

17 “The Nephron.” *Renal Pathology* (blog), n.d. https://renalpathology.wordpress.com/portfolio/the-nephron/

18 “Urinary System Anatomy and Function.” *Cincinnati Children’s Hospital* (blog), June 2016. https://www.cincinnatichildrens.org/health/u/urinary-system.