Acute Kidney Injury & Chronic Kidney Disease

Review Renal Anatomy & Physiology The kidneys filter the blood to remove wastes and balance fluid, electrolytes, minerals, and acids and bases in the body. The kidneys are also responsible for production of renin and erythropoietin, and activation of Vitamin D. Impairment of these functions can lead to systemic problems, even death.

Key Terms:

Azotemia is increased blood urea nitrogen (BUN), creatinine, and other nitrogenous waste products in the blood (azot = nitrogen, emia = blood). Azotemia occurs in both acute kidney injury and chronic kidney disease, which are characterized by reduced renal filtering. **Uremia**: Azotemia can lead to uremia, which is a clinical syndrome characterized by a cluster of signs/symptoms in various body systems, including the cardiac and nervous systems. Uremia can occur in acute kidney injury but is more common in chronic disease. **Acute kidney injury (AKI)** is characterized by a rapid decrease in renal function over days or weeks; it is associated with azotemia and, sometimes, uremia. Acute kidney injury was formerly called acute kidney failure; this new terminology includes, but is not limited to, kidney failure. **Chronic kidney disease (CKD)** is characterized by a gradual, progressive loss of renal function and declining GFR (less than 60 ml/min/1.73 mt2 lasting for 3+ months). We can break the progression of CKD into 5 stages with decreasing renal functioning, increasing accumulation of toxins, and worsening uremia. CKD was previously called "chronic kidney failure"; new terminology includes, but is not limited, to kidney failure. **End-stage renal disease (ESRD)** is the terminal stage of kidney disease; GFR is less than 5% of normal. **Renal failure** is the result of excess retention of nitrogenous waste products and electrolyte disturbances that produce a variety of signs and symptoms. **MAD HUNGER** signs and symptoms of Renal Failure:

- Metabolic acidosis

- Dyslipidemia

- Hyperkalemia

- Uremia

- Na+ and H2O retention (with resulting heart failure, pulmonary edema, and hypertension)

- Growth retardation and developmental delay

- Erythropoietin deficiency (anemia)

- Renal osteodystrophy

ACUTE KIDNEY INJURY

AKI is characterized by increased creatinine and decreased urine volume.

- Specifically: an increase in creatinine (Cr) higher than 0.3 mg/dl (26.5 umol/L) in 48 hours, a rise of creatine greater than 1.5 times the baseline ((occurring within the last seven days) and a decrease of urine volume of equal to or lesser than 0.5 ml/kg/h (2012 Kidney Disease: Improving Global Outcomes)).

"Pre-renal" etiologies affect renal perfusion at the renal artery (which is a "pre-renal" vessel, anatomically). "Intrinsic" or 'intrarenal" etiologies affect the renal medulla, which includes the vasculature, interstitium, or the nephrons, themselves. "Post-renal" etiologies affect the ureter or bladder, which are distal to the kidney (anatomically "post-renal"). **Pre-Renal**

AKI Pre-renal etiologies are those that induce changes to renal hemodynamics and perfusion. Because renal blood flow is reduced, so is the glomerular filtration rate. As a result, less fluid and solutes are filtered from the blood. Thus, some indicators of pre-renal AKI include reduced sodium urine levels, less than 20 mEq/L, and less than 1% fractional excretion of sodium. Also note that, upon fluid administration, patients with pre-renal AKI will show reduction in serum creatinine. Etiologies are numerous, since any event that alters systemic circulation or renal perfusion can impact GFR, including: Intravascular volume depletion and hypotension, bilateral renal stenosis, heart failure, and use of ACE inhibitors or Angiotensin II receptor blockers (ARBs). Recall that, in healthy individuals, GFR is maintained by autoregulatory mechanisms, but those mechanisms are overwhelmed in renal disease. **Intrinsic/intrarenal** acute kidney injury is associated with urine sodium above 40 mEq/L, and fractional excretion of sodium greater than 2 percent. This form of AKI can be further divided into four groups, based on the renal structures primarily involved: *Vascular causes*, which include vasculitis, Hemolytic uremic syndrome (HUS), malignant hypertension, and thrombotic thrombocytopenia purpura (TTP). *Glomerular damage*, which can be further divided into Nephrotic or Nephritic disorders, based on which solutes erroneously pass through the membrane. Nephrotic syndrome occurs when proteins leak out of the capillaries and into the ultrafiltrate; this occurs in focal segmental glomerulosclerosis, membranous nephropathy, and minimal change disease. Nephrotic syndrome (aka nephrosis) is characterized by a group of signs/symptoms resulting from the loss of protein in the urine: proteinuria, hypoalbuminemia, edema, hyperlipidemia, with puffy eyelids and edema, foamy urine, fatigue, and loss of appetite. Nephritic syndrome occurs when blood cells leak into the ultrafiltrate, and is associated with infection associated glomerulonephritis, IgA nephropathy, and anti-glomerular basement membrane antibody disease. Signs and symptoms of nephritic syndrome include hematuria, hypertension, edema, and oliguria, with red blood cells and their casts and WBC in urine; proteinuria is not uncommon, but to a lesser degree than in nephrotic syndrome. *Tubular damage*, which is usually caused by acute tubular necrosis (ATN), and is the most common cause of AKI overall (especially in hospitalized patients). This is associated with high morbidity and mortality. Acute tubular necrosis is characterized by patchy injury to the nephron tubule, often caused by ischemia (so etiologies of pre-renal AKI can also cause acute tubular necrosis) or toxic substances (medicines, hemoglobin/myoglobin, lead, etc.). Renal tubular cell damage and death impair tubular function, and the debris that obstructs tubules with backflow leads to reduced GFR. Urine analysis shows muddy brown casts, and tubular cells. *Acute interstitial nephritis* (AIN), which is usually caused by medicines, esp. antibiotics and NSAIDs, but can also be caused by autoimmune disorders and infections. Notable signs and symptoms include skin rash, fever, and eosinophilia, with white blood cells and their casts in urine. **Post-renal** AKI is the result of urine obstruction. Bladder outlet obstruction is the most common cause of post-renal AKI. In these patients, urine is trapped in the bladder and can backflow into the ureters, which increases pressure in the renal system and results in lowered GFR. Important obstructive causes include tumors (including prostrate tumors), kidney stones, infections that cause swelling or compression, and congenital anomalies (such as renal dysplasia). Note that unilateral renal obstruction is less often associated with AKI because the non-obstructed structure can typically compensate.

CHRONIC KIDNEY DISEASE

Top causes:
Diabetes Hypertensive nephrosclerosis Glomerular disorders Autosomal dominant polycystic kidney disease Be aware that episodes of Acute Kidney Injury put patients at higher risk of developing chronic kidney disease.
Uremia:
As mentioned earlier, uremia is more common in chronic kidney disease. The following signs and symptoms of uremia are due to the metabolic disturbances caused by renal impairment:

- Anorexia, with nausea and vomiting

- Anemia and fatigue

- Pruritus (itching), edema, and uremic "frost" (deposition of urea crystals on the skin that are left behind when sweat evaporates)

- Muscle cramping and twitching

Peripheral neuropathies, mental status changes, and seizures As mentioned earlier, chronic kidney disease is a gradual, progressive disease that is clinically divided into 5 stages. In the early stages, patients experience few signs or symptoms, and early detection can help prevent progression to renal failure.

BOARD REVIEW

ACUTE KIDNEY INJURY
Getting ready for boards? Review these concise, bulleted high yield reviews for your exam.
USMLE & COMLEX-USA
USMLE Step 1 / COMLEX-USA Level 1 USMLE Step 2 / COMLEX-USA Level 2 USMLE Step 3 / COMLEX-USA Level 3

NURSE PRACTITIONER (NP)
Nurse Practitioner Licensing Exam
PHYSICIAN ASSISTANT (PA)
Physician Assistant Licensing Exam
INTERNAL MEDICINE (ABIM)
American Board of Internal Medicine (ABIM) Exam
CHRONIC KIDNEY DISEASE

USMLE & COMLEX-USA
USMLE Step 1 / COMLEX-USA Level 1 USMLE Step 2 / COMLEX-USA Level 2 USMLE Step 3 / COMLEX-USA Level 3

NURSE PRACTITIONER (NP)
Nurse Practitioner Licensing Exam
PHYSICIAN ASSISTANT (PA)
Physician Assistant Licensing Exam
INTERNAL MEDICINE (ABIM)
American Board of Internal Medicine (ABIM) Exam

REFERENCES

• "Acute Kidney Injury (AKI) – KDIGO." Accessed August 10, 2022. https://kdigo.org/guidelines/acute-kidney-injury/.

Chávez-Iñiguez, Jonathan S, Goretty J Navarro-Gallardo, Ramón Medina-González, Luz Alcantar-Vallin, and Guillermo García-García. "Acute Kidney Injury Caused by Obstructive Nephropathy." Edited by David B. Kershaw. International Journal of Nephrology 2020 (November 29, 2020): 1–10. https://doi.org/10.1155/2020/8846622.

• Chávez-Iñiguez, Jonathan S., Goretty J. Navarro-Gallardo, Ramón Medina-González, Luz Alcantar-Vallin, and Guillermo García-García. "Acute Kidney Injury Caused by Obstructive Nephropathy." International Journal of Nephrology 2020 (November 29, 2020): e8846622. https://doi.org/10.1155/2020/8846622.

• "Clinical Manifestations and Diagnosis of Acute Interstitial Nephritis - UpToDate." Accessed August 10, 2022. https://www-uptodate-com.proxy.ulib.uits.iu.edu/contents/clinical-manifestations-and-diagnosis-of-acute-interstitial-nephritis?search=acute%20interstitial%20nephritis&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1.

• Domek, Magdalena, Jakub Gumprecht, Gregory Y. H. Lip, and Alena Shantsila. "Malignant Hypertension: Does This Still Exist?" Journal of Human Hypertension 34, no. 1 (January 2020): 1–4. https://doi.org/10.1038/s41371-019-0267-y.

• Farris, Nicholas, Rupesh Raina, Abhishek Tibrewal, Miraides Brown, Maria Colvis, Andrew Schwaderer, and Kirsten Kusumi. "Acute Kidney Injury Associated With Urinary Stone Disease in Children and Young Adults Presenting to a Pediatric Emergency Department." Frontiers in Pediatrics 8 (2020). https://www.frontiersin.org/articles/10.3389/fped.2020.591520.

• Jennette, J. Charles, and Patrick H. Nachman. "ANCA Glomerulonephritis and Vasculitis." Clinical Journal of the American Society of Nephrology 12, no. 10 (October 6, 2017): 1680–91. https://doi.org/10.2215/CJN.02500317.

• Naik, Ruchi H., and Pavan Annamaraju. "Interstitial Nephritis." In StatPearls. Treasure Island (FL): StatPearls

Publishing, 2022. http://www.ncbi.nlm.nih.gov/books/NBK564349/.

• National Institute of Diabetes and Digestive and Kidney Diseases. "Nephrotic Syndrome in Adults | NIDDK." Accessed August 10, 2022. https://www.niddk.nih.gov/health-information/kidney-disease/nephrotic-syndrome-adults.

• "Notice." Kidney International Supplements 2, no. 1 (March 2012): 1. https://doi.org/10.1038/kisup.2012.1.

• Shah, Aniruddh, and Narothama R. Aeddula. "Renal Osteodystrophy." In StatPearls. Treasure Island (FL): StatPearls Publishing, 2022. http://www.ncbi.nlm.nih.gov/books/NBK560742/.

• Tarafdar, Surjit. Nephrology: A Comprehensive Guide to Renal Medicine. John Wiley & Sons, 2020.

Tyagi, Alka, and Narothama R. Aeddula. "Azotemia." In StatPearls. Treasure Island (FL): StatPearls Publishing, 2022. http://www.ncbi.nlm.nih.gov/books/NBK538145/.

• Villacorta, Javier, Francisco Diaz-Crespo, Mercedes Acevedo, Teresa Cavero, Carmen Guerrero, Manuel Praga, and Gema Fernandez-Juarez. "Renal Vasculitis Presenting with Acute Kidney Injury." Rheumatology International 37, no. 6 (June 2017): 1035–41. https://doi.org/10.1007/s00296-017-3697-2.

• Jameson, J. Larry, ed. Harrison's Principles of Internal Medicine. Twentieth edition. New York: McGraw-Hill Education, 2018.