12.2.3

Acute Kidney Injury (AKI)

Watch this video on Acute Kidney Injury.

Acute kidney injury (AKI), previously known as acute renal failure (ARF), constitutes a sudden decline in kidney function, meaning low glomerular filtration rate (GFR), low urine output (oliguria), and the buildup of nitrogen–containing waste in the blood (azotemia). Chronic kidney failure is due to the destruction of nephrons within the kidney; AKIs are typically due to something decreasing GFR. There are three categories of acute kidney injury, including: prerenal, intrarenal, and postrenal.

Prerenal AKI

Prerenal AKI is the most common type of AKI. It results from a substantial decrease in blood flow to the kidneys––hence the name *prerenal*. Causes include conditions that reduce intravascular volume (hypovolemia), such as severe hemorrhage and conditions that induce dehydration, like excessive vomiting and diarrhea. With significant burns, fluid evaporates from the body faster, also leading to hypovolemia.

Prerenal AKIs may also be caused by conditions that increase vascular capacity and leakiness, such as in sepsis and anaphylaxis (i.e. types of a distributive shock). Increased vessel dilation and permeability decreases blood pressure and volume, subsequently decreasing kidney function. Cardiogenic shock, which might be secondary to decompensated heart failure or after an MI, also results in reduced blood flow reaching the kidneys.

Another cause of prerenal AKI is renal artery stenosis, where narrowed arteries supplying the kidneys decrease renal blood flow. Two main forms of stenosis include fibromuscular dysplasia, which is abnormal growth within the walls of the arteries that narrow the lumen, and atherosclerosis, characteristic of the lipid plaque buildup within the vessel wall. An embolus in the renal vasculature can also block blood flow to the kidneys.

Intrarenal AKI

An **intrarenal AKI** comes about when the internal structures of the kidneys are damaged due to ischemia, toxins, or tubular obstruction. Any of these conditions can result in acute tubular necrosis (ATN), which is characterized by necrosis (cell death) of the renal tubular cells. ATN can be caused by ischemia (lack of blood flow) from any of the causes inducing prerenal AKIs.

Other causes of ATN include exposure to exogenous, nephrotoxic compounds, such as aminoglycoside antibiotics, heavy metals (*i.e.* lead), or ethylene glycol (found in “antifreeze”). Certain endogenous substances can obstruct the tubular lumen, examples of which include myoglobin, released from damaged muscle cells, or uric acid, which come from the breakdown of purines, which make up nucleic acids. Uric acids are released in high amounts during chemotherapy because so many cells are dying. Therefore, it is important to keep well–hydrated during cancer treatment in order to reduce kidney damage. Hemoglobin, which might be found in excess amounts during a hemolytic condition, can block the filtrate flow. In multiple myeloma, excessive production of dysfunctional antibodies (especially the light–chains) can enter and block the nephron tubules.

Other causes of intrarenal AKI include interstitial nephritis and glomerulonephritis, both of which are inflammatory issues within the kidneys.

In the kidneys with ATN, there is a reduced GFR due to obstruction. Renal tubular cells die and are released into the tubular lumen, which then form a plug and partially or fully obstruct filtrate flow. The result is fluid backup proximal to the site of blockage. Consequently, there is an increased pressure inside the lumen that opposes the filtrate at the glomerulus. This explains the decreased GFR and urinary output in the setting of intrarenal AKI.

Postrenal AKI

Postrenal AKIs are due to an obstruction in the urinary tract downstream of the kidneys. The obstruction limits or blocks urine flow. The postrenal obstruction may be due to renal calculi in the ureter or urethra, or from a urethral strictures. Other causes may be expanding intraabdominal tumors that may compress the ureters, bladder, or urethra externally and obstruct urine flow. Neurogenic bladder (due to spinal cord injury) where damaged neurons to the bladder detrusor muscles may also result in obstructed urine flow and postrenal AKI.

The most common cause of postrenal AKI is benign prostatic hyperplasia (BPH), wherein the urethra is compressed by the enlarged prostate gland, and obstructs urine flow.

Whatever the cause of the postrenal blockage, a backup of fluid into the nephrons will follow, increase the tubular pressure, and reduce GFR.

Kidney Function Tests for AKI

Interpretation of the serum BUN:Creatinine ratio may be helpful in determining the type of AKI present. The normal BUN:Creatinine ratio ranges from [5 – 20] / 1. Remember that in prerenal AKI, GFR is low, and initially tubular cells are fully functional. Due to the low GFR, filtrate will flow slowly, which allows for more absorption of urea at the proximal tubule (PCT). Hence the increased BUN in prerenal AKI is attributed to two reasons: low GFR and increased reabsorption at the PCT. Creatinine goes up for only one reason: low GFR (creatinine is not reabsorbed). The result is a BUN:Creatinine ratio that is higher than normal.

As the prerenal AKI progresses, the Renin–Angiotensin–Aldosterone system (RAAS) will be activated in a negative feedback manner to increase intravascular volume, and ultimately increase renal blood flow. Recall that aldosterone will increase sodium reabsorption in the blood, so labs will show high blood sodium levels and low sodium levels in the urine in prerenal AKI. Water follows the reabsorbed sodium into the blood, leaving little in the urine. This causes the urine to be quite concentrated, and labs will show high urine osmolarity.

In intrarenal AKI, the dying tubular cells are unable to reabsorb urea; therefore, the relative levels of blood urea and creatinine remain proportional and the BUN:Creatinine ratio is typically less than 15:1 in the setting of intrarenal AKI. Water follows what urea gets filtered and dilutes the urine. Labs will accordingly show a low urine osmolarity in the setting of intrarenal AKI.

In the early course of a postrenal AKI, the BUN:Creatinine ratio is typically greater than 15:1. With gradual tubular cell damage, the BUN : Creatinine ratio falls below 15:1. Sodium levels in the urine are initially low, but begin to rise with the increased tubular damage. Urine osmolarity is initially elevated, but begins to drop as the tubular cells begin to die, and allows for water to dilute the urine. Overall, it can be said that lab findings in postrenal AKI are similar to those in a prerenal AKI, but begin to resemble lab values in an intrarenal AKI with increasing damage to the tubular cells.

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