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COURSE CODE: PHS 303

**Question**

**Second assignment**

1. **Discuss the pathophysiological process involves in renal failure?**

Acute kidney injury (AKI) is defined as an abrupt or rapid decline in renal filtration function.

**Pathophysiology**

The driving force for glomerular filtration is the pressure gradient from the glomerulus to the Bowman space. Glomerular pressure depends primarily on renal blood flow (RBF) and is controlled by the combined resistances of renal afferent and efferent arterioles. Regardless of the cause of AKI, reductions in RBF represent a common pathologic pathway for decreasing glomerular filtration rate (GFR). The etiology of AKI consists of 3 main mechanisms: prerenal, intrinsic, and obstructive.

In prerenal failure, GFR is depressed by compromised renal perfusion. Tubular and glomerular function remain normal.

Intrinsic renal failure includes diseases of the kidney itself, predominantly affecting the glomerulus or tubule, which are associated with the release of renal afferent vasoconstrictors. Ischemic renal injury is the most common cause of intrinsic renal failure. Patients with chronic kidney disease may also present with

superimposed AKI from prerenal failure and obstruction, as well as intrinsic renal disease.

Obstruction of the urinary tract initially causes an increase in tubular pressure, which decreases the filtration driving force. This pressure gradient soon equalizes, and maintenance of a depressed GFR then depends on renal efferent vasoconstriction.

**Depressed renal blood flow**

Depressed RBF eventually leads to ischemia and cell death. This may happen before frank systemic hypotension is present and is referred to as normotensive ischemic AKI. The initial ischemic insult triggers a cascade of events, including production of oxygen free radicals, cytokines and enzymes; endothelial activation and leukocyte adhesion; activation of coagulation; and initiation of apoptosis. These events continue to cause cell injury even after restoration of RBF.

Tubular cellular damage results in disruption of tight junctions between cells, allowing back leak of glomerular filtrate and further depressing effective GFR. In addition, dying cells slough off into the tubules, forming obstructing casts, which further decrease GFR and lead to oliguria.

During this period of depressed RBF, the kidneys are particularly vulnerable to further insults; this is when iatrogenic renal injury is most common. The following are common combinations:

* Radiocontrast agents, aminoglycosides, or cardiovascular surgery with preexisting renal disease (eg, elderly, diabetic, jaundiced patients)
* Angiotensin-converting enzyme (ACE) inhibitors with diuretics, small- or large-vessel renal arterial disease
* NSAIDs with chronic heart failure, hypertension, or renal artery stenosis
* Acute tubular necrosis

Frank necrosis is not prominent in most human cases of ATN and tends to be patchy. Less obvious injuries include the following (see the image below):

* Loss of brush borders
* Flattening of the epithelium
* Detachment of cells
* Formation of intratubular casts
* Dilatation of the lumen

Although these changes are observed predominantly in proximal tubules, injury to the distal nephron can also be demonstrated. In addition, the distal nephron may become obstructed by desquamated cells and cellular debris. See the image above.

**Apoptosis**

In contrast to necrosis, the principal site of apoptotic cell death is the distal nephron. During the initial phase of ischemic injury, loss of integrity of the actin cytoskeleton leads to flattening of the epithelium, with loss of the brush border, loss of focal cell contacts, and subsequent disengagement of the cell from the underlying substratum.

**Inflammatory response**

Many endogenous growth factors that participate in the process of regeneration following ischemic renal injury have not been identified. However, administration of growth factors exogenously has been shown to ameliorate and hasten recovery from AKI.

Depletion of neutrophils and blockage of neutrophil adhesion reduce renal injury following ischemia, indicating that the inflammatory response is responsible, in part, for some features of ATN, especially in postischemic injury after transplant.

**Vasoconstriction**

Intrarenal vasoconstriction is the dominant mechanism for reduced GFR in patients with ATN. The mediators of this vasoconstriction are unknown, but tubular injury seems to be an important concomitant finding. Urine backflow and intratubular obstruction (from sloughed cells and debris) are causes of reduced net ultrafiltration. The importance of this mechanism is highlighted by the improvement in renal function that follows relief of such intratubular obstruction.

In addition, when obstruction is prolonged, intrarenal vasoconstriction is prominent in part due to the tubuloglomerular feedback mechanism, which is thought to be mediated by adenosine and activated when there is proximal tubular damage and the macula densa is presented with increased chloride load.

Apart from the increase in basal renal vascular tone, the stressed renal microvasculature is more sensitive to potentially vasoconstrictive drugs and otherwise-tolerated changes in systemic blood pressure. The vasculature of the injured kidney has an impaired vasodilatory response and loses its autoregulatory behavior.

This latter phenomenon has important clinical relevance because the frequent reduction in systemic pressure during intermittent hemodialysis may provoke additional damage that can delay recovery from ATN. Often, injury results in atubular glomeruli, where the glomerular function is preserved, but the lack of tubular outflow precludes its function.

**Isosthenuria**

A physiologic hallmark of ATN is a failure to maximally dilute or concentrate urine (isosthenuria). This defect is not responsive to pharmacologic doses of vasopressin. The injured kidney fails to generate and maintain a high medullary solute gradient, because the accumulation of solute in the medulla depends on normal distal nephron function.

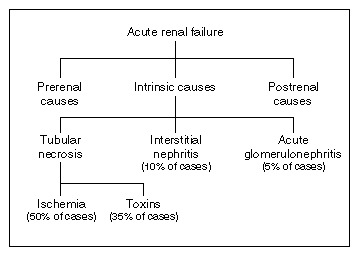
Failure to excrete concentrated urine even in the presence of oliguria is a helpful diagnostic clue in distinguishing prerenal from intrinsic renal disease. In prerenal azotemia, urine osmolality is typically more than 500 mOsm/kg, whereas in intrinsic renal disease, urine osmolality is less than 300 mOsm/kg.

**Restoration of renal blood flow and associated complications**

Recovery from AKI is first dependent upon restoration of RBF. Early RBF normalization predicts better prognosis for recovery of renal function. In prerenal failure, restoration of circulating blood volume is usually sufficient. Rapid relief of urinary obstruction in postrenal failure results in a prompt decrease of vasoconstriction. With intrinsic renal failure, removal of tubular toxins and initiation of therapy for glomerular diseases decreases renal afferent vasoconstriction.

Once RBF is restored, the remaining functional nephrons increase their filtration and eventually undergo hypertrophy. GFR recovery depends on the size of this remnant nephron pool. If the number of remaining nephrons is below a critical threshold, continued hyperfiltration results in progressive glomerular sclerosis, eventually leading to increased nephron loss.

A vicious cycle ensues; continued nephron loss causes more hyperfiltration until complete renal failure results. This has been termed the hyperfiltration theory of renal failure and explains the scenario in which progressive renal failure is frequently observed after apparent recovery from AKI.



1. **With the aid of suitable diagrams discuss the types of dialysis you know?**

You need dialysis when you develop end stage kidney failure --usually by the time you lose about 85 to 90 percent of your kidney function and have a GFR of <15.

When your kidneys fail, dialysis keeps your body in balance by:

* removing waste, salt and extra water to prevent them from building up in the body
* keeping a safe level of certain chemicals in your blood, such as potassium, sodium and bicarbonate
* helping to control blood pressure

There are three different types of dialysis.

**Hemodialysis**

Hemodialysis is the most common type of dialysis. This process uses an artificial kidney (hemodialyzer) to remove waste and extra fluid from the blood. The blood is removed from the body and filtered through the artificial kidney. The filtered blood is then returned to the body with the help of a dialysis machine.

To get the blood to flow to the artificial kidney, your doctor will perform surgery to create an entrance point (vascular access) into your blood vessels. The three types of entrance points are:

Arteriovenous (AV) fistula: This type connects an artery and a vein. It’s the preferred option.

AV graft: This type is a looped tube.

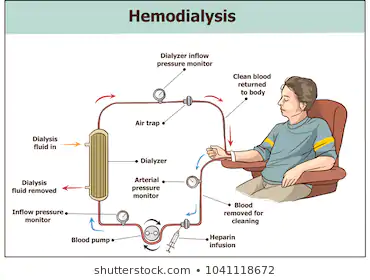
Vascular access catheter: This may be inserted into the large vein in your neck.

Both the AV fistula and AV graft are designed for long-term dialysis treatments. People who receive AV fistulas are healed and ready to begin hemodialysis two to three months after their surgery. People who receive AV grafts are ready in two to three weeks. Catheters are designed for short-term or temporary use.

Hemodialysis treatments usually last three to five hours and are performed three times per week. However, hemodialysis treatment can also be completed in shorter, more frequent sessions.

Most hemodialysis treatments are performed at a hospital, doctor’s office, or dialysis center. The length of treatment depends on your body size, the amount of waste in your body, and the current state of your health.

After you’ve been on hemodialysis for an extended period of time, your doctor may feel that you’re ready to give yourself dialysis treatments at home. This option is more common for people who need long-term treatment.



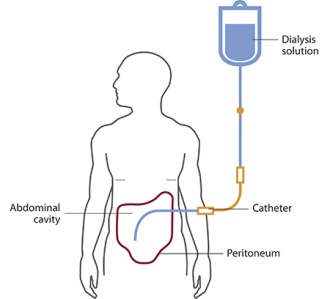
**Peritoneal dialysis**

Peritoneal dialysis involves surgery to implant a peritoneal dialysis (PD) catheter into your abdomen. The catheter helps filter your blood through the peritoneum, a membrane in your abdomen. During treatment, a special fluid called dialysate flows into the peritoneum. The dialysate absorbs waste. Once the dialysate draws waste out of the bloodstream, it’s drained from your abdomen.

This process takes a few hours and needs to be repeated four to six times per day. However, the exchange of fluids can be performed while you’re sleeping or awake.

There are numerous different types of peritoneal dialysis. The main ones are:

* Continuous ambulatory peritoneal dialysis (CAPD): In CAPD, your abdomen is filled and drained multiple times each day. This method doesn’t require a machine and must be performed while awake.
* Continuous cycling peritoneal dialysis (CCPD): CCPD uses a machine to cycle the fluid in and out of your abdomen. It’s usually done at night while you sleep.
* Intermittent peritoneal dialysis (IPD): This treatment is usually performed in the hospital, though it may be performed at home. It uses the same machine as CCPD, but the process takes longer.



**Continuous renal replacement therapy (CRRT)**

This therapy is used primarily in the intensive care unit for people with acute kidney failure. It’s also known as hemofiltration. A machine passes the blood through tubing. A filter then removes waste products and water. The blood is returned to the body, along with replacement fluid. This procedure is performed 12 to 24 hours a day, generally every day.

