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DEPARTMENT: MEDICINE AND SURGERY

ASSIGNMENT

1. Discuss the pathophysiological process involved in renal failure

Acute Renal Failure

The causes of acute renal failure can be divided into three main categories:

1. Acute renal failure resulting from decreased blood supply to the kidneys; this condition is often referred to as *prerenal acute renal failure* to reflect the fact that the abnormality occurs as a result of an abnormality originating outside the kidneys. For example, prerenal acute renal failure can be a consequence of heart failure with reduced cardiac output and low blood pressure or conditions associated with diminished blood volume and low blood pressure, such as severe hemorrhage.
2. *Intrarenal acute renal failure* resulting from abnormalities within the kidney itself, including those that affect the blood vessels, glomeruli, or tubules.
3. *Postrenal acute renal failure*, resulting from obstruction of the urinary collecting system anywhere from the calyces to the outflow from the bladder. The most common causes of obstruction of the urinary tract outside the kidney are kidney stones, caused by precipitation of calcium, urate, or cystine.

Prerenal Acute Renal Failure Caused by Decreased Blood Flow to the Kidney

The kidneys normally receive an abundant blood supply of about 1100 ml/min, or about 20 to 25 percent of the cardiac output. The main purpose of this high blood flow to the kidneys is to provide enough plasma for the high rates of glomerular filtration needed for effective regulation of body fluid volumes and solute concentrations. Therefore, decreased renal blood flow is usually accompanied by decreased GFR and decreased urine output of water and solutes. Consequently, conditions that acutely diminish blood flow to the kidneys usually cause *oliguria*, which refers to diminished urine output below the level of intake of water and solutes. This causes accumulation of water and solutes in the body fluids. If renal blood flow is markedly reduced, total cessation of urine output can occur, a condition referred to as *anuria*.

As long as renal blood flow does not fall below about 20 to 25 percent of normal, acute renal failure can usually be reversed if the cause of the ischemia is corrected before damage to the renal cells has occurred. Unlike some tissues, the kidney can endure a relatively large reduction in blood flow before actual damage to the renal cells occurs. The reason for this is that as renal blood flow is reduced, the GFR and the amount of sodium chloride filtered by the glomeruli (as well as the filtration rate of water and other electrolytes) are reduced. This decreases the amount of sodium chloride that must be reabsorbed by the tubules, which use most of the energy and oxygen consumed by the normal kidney. Therefore, as renal blood flow and GFR fall, the requirement for renal oxygen consumption is also

reduced. As the GFR approaches zero, oxygen consumption of the kidney approaches the rate that is required to keep the renal tubular cells alive even when they are not reabsorbing sodium. When blood flow is reduced below this basal requirement, which is usually less than 20 to 25 percent of the normal renal blood flow, the renal cells start to become hypoxic, and further decreases in renal blood flow, if prolonged, will cause damage or even death of the renal cells, especially the tubular epithelial cells.

If the cause of prerenal acute renal failure is not corrected and ischemia of the kidney persists longer than a few hours, this type of renal failure can evolve into intrarenal acute renal failure, as discussed later. Acute reduction of renal blood flow is a common cause of acute renal failure in hospitalized patients, especially those who have suffered severe injuries. Table 31-2 shows some of the common causes of decreased renal blood flow and prerenal acute renal failure.

Table 31-2 Some Causes of Prerenal Acute Renal Failure

Intravascular Volume Depletion
Hemorrhage (trauma, surgery, postpartum, gastrointestinal)
Diarrhea or vomiting
Burns
Cardiac Failure
Myocardial infarction
Valvular damage
Peripheral Vasodilation and Resultant Hypotension
Anaphylactic shock
Anesthesia
Sepsis, severe infections
Primary renal hemodynamic abnormalities
Renal artery stenosis, embolism, or thrombosis of renal artery or vein

Intrarenal Acute Renal Failure Caused by Abnormalities Within the Kidney

Abnormalities that originate within the kidney and that abruptly diminish urine output fall into the general category of *intrarenal acute renal failure*. This category of acute renal failure can be further divided into (1) conditions that injure the glomerular capillaries or other small renal vessels, (2) conditions that damage the renal tubular epithelium, and (3) conditions that cause damage to the renal interstitium. This type of classification refers to the primary site of injury, but because the renal vasculature and tubular system are functionally interdependent, damage to the renal blood vessels can lead to tubular damage, and primary tubular damage can lead to damage of the renal blood vessels. Some causes of intrarenal acute renal failure are listed in Table 31-3.

Table 31-3 Some Causes of Intrarenal Acute Renal Failure

Small Vessel and /or Glomerular Injury
Vasculitis (polyarteritis nodosa)
Cholesterol emboli
Malignant hypertension
Acute glomerulonephritis
Tubular Epithelial Injury (Tubular Necrosis)

Acute tubular necrosis due to ischemia
Acute tubular necrosis due to toxins (heavy metals, ethylene glycol, insecticides, poison mushrooms, carbon tetrachloride)
Renal Interstitial Injury
Acute pyelonephritis
Acute allergic interstitial nephritis

Acute Renal Failure Caused by Glomerulonephritis

Acute glomerulonephritis is a type of *intrarenal* acute renal failure usually caused by an abnormal immune reaction that damages the glomeruli. In about 95 percent of the patients with this disease, damage to the glomeruli occurs 1 to 3 weeks after an infection elsewhere in the body, usually caused by certain types of group A beta streptococci. The infection may have been a streptococcal sore throat, streptococcal tonsillitis, or even streptococcal infection of the skin. It is not the infection itself that damages the kidneys. Instead, over a few weeks, as antibodies develop against the streptococcal antigen, the antibodies and antigen react with each other to form an insoluble immune complex that becomes entrapped in the glomeruli, especially in the basement membrane portion of the glomeruli.

Once the immune complex has deposited in the glomeruli, many of the cells of the glomeruli begin to proliferate, but mainly the mesangial cells that lie between the endothelium and the epithelium. In addition, large numbers of white blood cells become entrapped in the glomeruli. Many of the glomeruli become blocked by this inflammatory reaction, and those that are not blocked usually become excessively permeable, allowing both protein and red blood cells to leak from the blood of the glomerular capillaries into the glomerular filtrate. In severe cases, either total or almost complete renal shutdown occurs.

The acute inflammation of the glomeruli usually subsides in about 2 weeks and, in most patients, the kidneys return to almost normal function within the next few weeks to few months. Sometimes, however, many of the glomeruli are destroyed beyond repair, and in a small percentage of patients, progressive renal deterioration continues indefinitely, leading to *chronic renal failure*, as described in a subsequent section of this chapter.

Tubular Necrosis as a Cause of Acute Renal Failure

Another cause of intrarenal acute renal failure is *tubular necrosis*, which means destruction of epithelial cells in the tubules. Some common causes of tubular necrosis are (1) severe ischemia and inadequate supply of oxygen and nutrients to the tubular epithelial cells and (2) poisons, toxins, or medications that destroy the tubular epithelial cells.

Acute Tubular Necrosis Caused by Severe Renal Ischemia

Severe ischemia of the kidney can result from circulatory shock or any other disturbance that severely impairs the blood supply to the kidney. If the ischemia is severe enough to seriously impair the delivery of nutrients and oxygen to the renal tubular epithelial cells, and if the insult is prolonged, damage or eventual destruction of the epithelial cells can occur. When this happens, tubular cells “slough off” and plug many of the nephrons, so that there is no urine output from the blocked nephrons; the affected nephrons often fail to excrete urine even when renal blood flow is restored to normal, as long as the tubules remain plugged. The most common causes of ischemic damage to the tubular epithelium are the

prerenal causes of acute renal failure associated with circulatory shock, as discussed earlier in this chapter.

Acute Tubular Necrosis Caused by Toxins or Medications

There is a long list of renal poisons and medications that can damage the tubular epithelium and cause acute renal failure. Some of these are *carbon tetrachloride*, *heavy metals* (such as mercury and lead), *ethylene glycol* (which is a major component in antifreeze), various *insecticides*, some *medications* (such as tetracyclines) used as antibiotics, and *cis-platinum*, which is used in treating certain cancers. Each of these substances has a specific toxic action on the renal tubular epithelial cells, causing death of many of them. As a result, the epithelial cells slough away from the basement membrane and plug the tubules. In some instances, the basement membrane also is destroyed. If the basement membrane remains intact, new tubular epithelial cells can grow along the surface of the membrane, so the tubule may repair itself within 10 to 20 days.

Postrenal Acute Renal Failure Caused by Abnormalities of the Lower Urinary Tract

Multiple abnormalities in the lower urinary tract can block or partially block urine flow and therefore lead to acute renal failure even when the kidneys' blood supply and other functions are initially normal. If the urine output of only one kidney is diminished, no major change in body fluid composition will occur because the contralateral kidney can increase its urine output sufficiently to maintain relatively normal levels of extracellular electrolytes and solutes, as well as normal extracellular fluid volume. With this type of renal failure, normal kidney function can be restored if the basic cause of the problem is corrected within a few hours. But chronic obstruction of the urinary tract, lasting for several days or weeks, can lead to irreversible kidney damage. Some of the causes of postrenal acute failure include (1) bilateral obstruction of the ureters or renal pelvises caused by large stones or blood clots, (2) bladder obstruction, and (3) obstruction of the urethra.

Physiologic Effects of Acute Renal Failure

A major physiologic effect of acute renal failure is retention in the blood and extracellular fluid of water, waste products of metabolism, and electrolytes. This can lead to water and salt overload, which, in turn, can lead to edema and hypertension. Excessive retention of potassium, however, is often a more serious threat to patients with acute renal failure because increases in plasma potassium concentration (hyperkalemia) above 8 mEq/L (only twice normal) can be fatal. Because the kidneys are also unable to excrete sufficient hydrogen ions, patients with acute renal failure develop metabolic acidosis, which in itself can be lethal or can aggravate the hyperkalemia.

In the most severe cases of acute renal failure, complete anuria occurs. The patient will die in 8 to 14 days unless kidney function is restored or unless an artificial kidney is used to rid the body of the excessive retained water, electrolytes, and waste products of metabolism. Other effects of diminished urine output, as well as treatment with an artificial kidney, are discussed in the next section in relation to chronic renal failure.

Chronic Renal Failure: An Irreversible Decrease in the Number of Functional Nephrons

Chronic renal failure results from progressive and irreversible loss of large numbers of functioning nephrons. Serious clinical symptoms often do not occur until the number of functional nephrons falls to at least 70 to 75 percent below normal. In fact, relatively normal blood concentrations of most electrolytes and normal body fluid volumes can still be maintained until the number of functioning nephrons decreases below 20 to 25 percent of normal.

Table 31-4 gives some of the most important causes of chronic renal failure. In general, chronic renal failure, like acute renal failure, can occur because of disorders of the blood vessels, glomeruli, tubules, renal interstitium, and lower urinary tract. Despite the wide variety of diseases that can lead to chronic renal failure, the end result is essentially the same—a decrease in the number of functional nephrons.

Table 31-4 Some Causes of Chronic Renal Failure

Metabolic Disorders
Diabetes mellitus
Obesity
Amyloidosis
Hypertension
Renal Vascular Disorders
Atherosclerosis
Nephrosclerosis-hypertension
Immunologic Disorders
Glomerulonephritis
Polyarteritis nodosa
Lupus erythematosus
Infections
Pyelonephritis
Tuberculosis
Primary Tubular Disorders
Nephrotoxins (analgesics, heavy metals)
Urinary Tract Obstruction
Renal calculi
Hypertrophy of prostate
Urethral constriction
Congenital Disorders
Polycystic disease
Congenital absence of kidney tissue (renal hypoplasia)

Vicious Cycle of Chronic Renal Failure Leading to End-Stage Renal Disease

In many cases, an initial insult to the kidney leads to progressive deterioration of kidney function and further loss of nephrons to the point where the person must be placed on dialysis treatment or transplanted with a functional kidney to survive. This condition is referred to as *end-stage renal disease (ESRD)*.

Studies in laboratory animals have shown that surgical removal of large portions of the kidney initially causes adaptive changes in the remaining nephrons that lead to increased blood flow, increased GFR, and increased urine output in the surviving nephrons. The exact mechanisms responsible for these changes are not well understood but involve hypertrophy (growth of the various structures of the surviving nephrons), as well as functional changes that decrease vascular resistance and tubular reabsorption in the surviving nephrons. These adaptive changes permit a person to excrete normal amounts of water and solutes even when kidney mass is reduced to 20 to 25 percent of normal. Over a period of several years, however, these renal adaptive changes may lead to further injury of the remaining nephrons, particularly to the glomeruli of these nephrons.

The cause of this additional injury is not known, but some investigators believe that it may be related in part to increased pressure or stretch of the remaining glomeruli, which occurs as a result of functional vasodilation or increased blood pressure; the chronic increase in pressure and stretch of the small arterioles and glomeruli are believed to cause injury and sclerosis of these vessels (replacement of normal tissue with connective tissue). These sclerotic lesions can eventually obliterate the glomerulus, leading to further reduction in kidney function, further adaptive changes in the remaining nephrons, and a slowly progressing vicious cycle that eventually terminates in ESRD (Figure 31-2). The only proven method of slowing down this progressive loss of kidney function is to lower arterial pressure and glomerular hydrostatic pressure, especially by using drugs such as angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists.

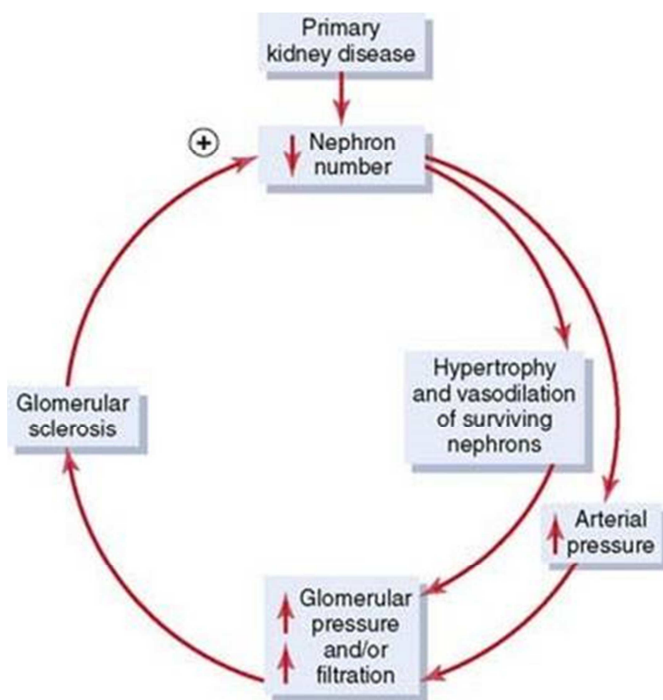


Figure 31-2 Vicious circle that can occur with primary kidney disease. Loss of nephrons because of disease may increase pressure and flow in the surviving glomerular capillaries, which in turn may eventually injure these “normal” capillaries as well, thus causing progressive sclerosis and eventual loss of these glomeruli.

2. With the aid of suitable diagrams, discuss the types of dialysis you know

In medicine, **dialysis** is the process of removing excess water, solutes, and toxins from the blood in people whose kidneys can no longer perform these functions naturally. This is referred to as renal replacement therapy.

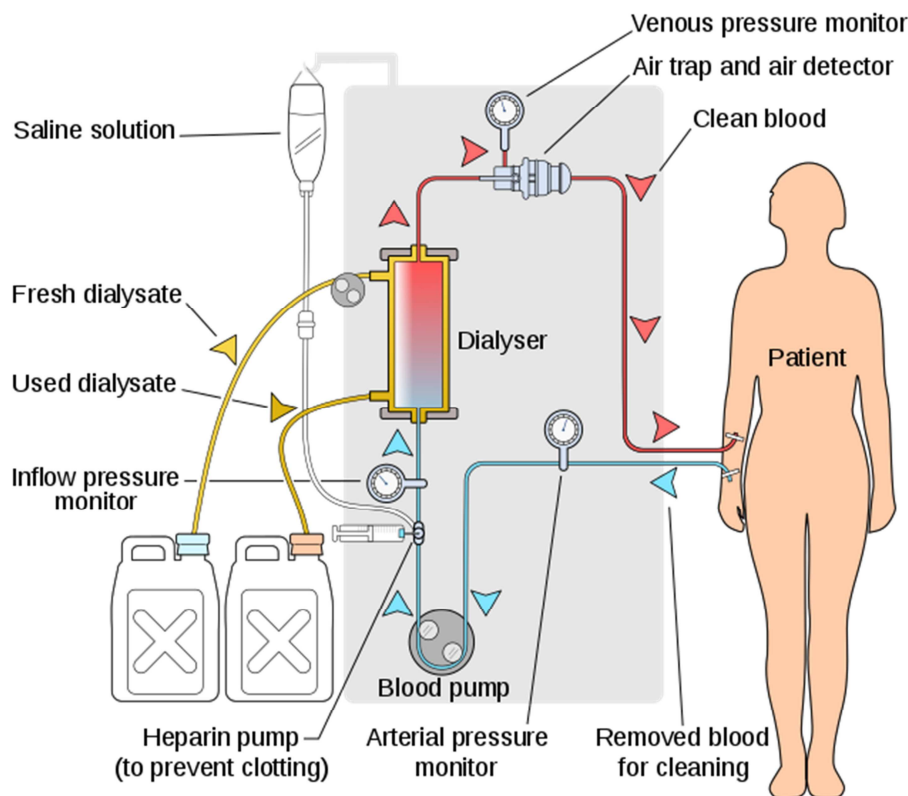
Dialysis is used in patients with rapidly developing loss of kidney function, called acute kidney injury (previously called acute renal failure), or slowly worsening kidney function, called Stage 5 chronic kidney disease (previously called chronic kidney failure, end-stage renal disease, and end-stage kidney disease).

Dialysis is used as a temporary measure in either acute kidney injury or in those awaiting kidney transplant and as a permanent measure in those for whom a transplant is not indicated or not possible.

Types

There are two types of dialysis: peritoneal and hemodialysis. There are three primary and two secondary types of dialysis: hemodialysis (primary), peritoneal dialysis (primary), hemofiltration (primary), hemodiafiltration (secondary) and intestinal dialysis (secondary).

Hemodialysis

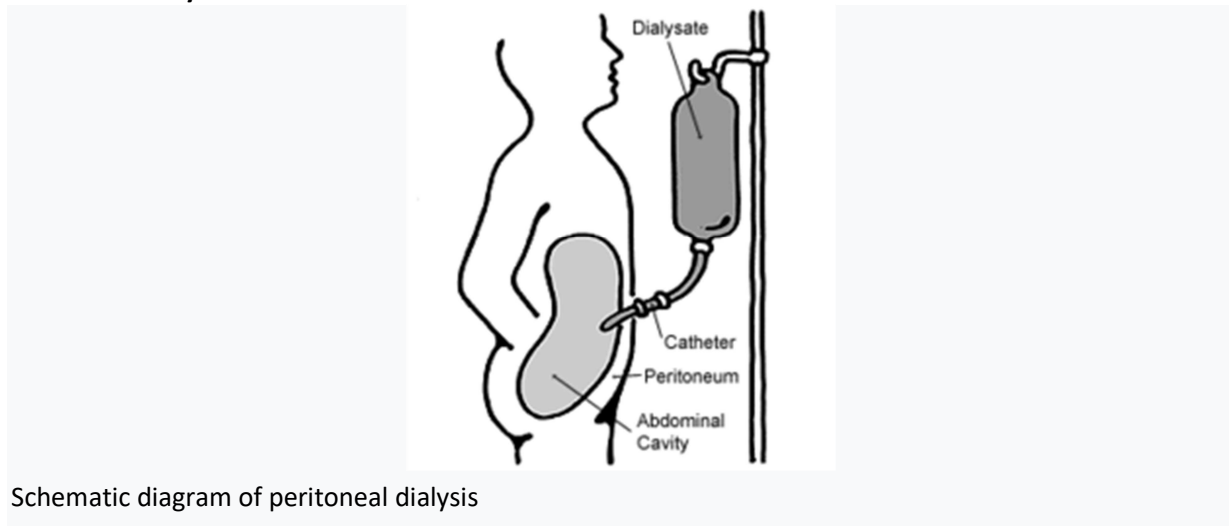


In hemodialysis, the patient's blood is pumped through the blood compartment of a dialyzer, exposing it to a partially permeable membrane. The dialyzer is composed of thousands of tiny hollow synthetic fibers. The fiber wall acts as the semipermeable membrane. Blood flows through the fibers, dialysis

solution flows around the outside of the fibers, and water and wastes move between these two solutions. The cleansed blood is then returned via the circuit back to the body. Ultrafiltration occurs by increasing the hydrostatic pressure across the dialyzer membrane. This usually is done by applying a negative pressure to the dialysate compartment of the dialyzer. This pressure gradient causes water and dissolved solutes to move from blood to dialysate and allows the removal of several litres of excess fluid during a typical 4-hour treatment. In the United States, hemodialysis treatments are typically given in a dialysis center three times per week (due in the United States to Medicare reimbursement rules); however, as of 2005 over 2,500 people in the United States are dialyzing at home more frequently for various treatment lengths. Studies have demonstrated the clinical benefits of dialyzing 5 to 7 times a week, for 6 to 8 hours. This type of hemodialysis is usually called *nocturnal daily hemodialysis*, which a study has shown it provides a significant improvement in both small and large molecular weight clearance and decreases the need for phosphate binders. These frequent long treatments are often done at home while sleeping, but home dialysis is a flexible modality and schedules can be changed day to day, week to week. In general, studies show that both increased treatment length and frequency are clinically beneficial.

Hemo-dialysis was one of the most common procedures performed in U.S. hospitals in 2011, occurring in 909,000 stays (a rate of 29 stays per 10,000 population).

Peritoneal dialysis

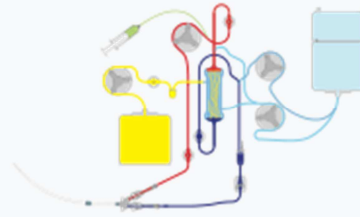


Schematic diagram of peritoneal dialysis

In peritoneal dialysis, a sterile solution containing glucose (called dialysate) is run through a tube into the peritoneal cavity, the abdominal body cavity around the intestine, where the peritoneal membrane acts as a partially permeable membrane.

This exchange is repeated 4–5 times per day; automatic systems can run more frequent exchange cycles overnight. Peritoneal dialysis is less efficient than hemodialysis, but because it is carried out for a longer period of time the net effect in terms of removal of waste products and of salt and water are similar to hemodialysis. Peritoneal dialysis is carried out at home by the patient, often without help. This frees patients from the routine of having to go to a dialysis clinic on a fixed schedule multiple times per week. Peritoneal dialysis can be performed with little to no specialized equipment (other than bags of fresh dialysate).

Hemofiltration



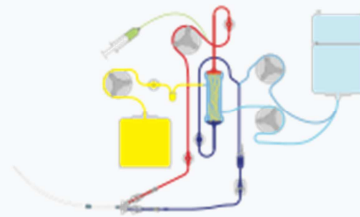
Continuous veno-venous haemofiltration with pre- and post-dilution (CVVH)

Hemofiltration is a similar treatment to hemodialysis, but it makes use of a different principle. The blood is pumped through a dialyzer or "hemofilter" as in dialysis, but no dialysate is used. A pressure gradient is applied; as a result, water moves across the very permeable membrane rapidly, "dragging" along with it many dissolved substances, including ones with large molecular weights, which are not cleared as well by hemodialysis. Salts and water lost from the blood during this process are replaced with a "substitution fluid" that is infused into the extracorporeal circuit during the treatment.

Hemodiafiltration

Hemodiafiltration is a combination of hemodialysis and hemofiltration, thus used to purify the blood from toxins when the kidney is not working normally and also used to treat acute kidney injury (AKI).

Intestinal dialysis



Continuous veno-venous haemodiafiltration (CVVHDF)

In intestinal dialysis, the diet is supplemented with soluble fibres such as acacia fibre, which is digested by bacteria in the colon. This bacterial growth increases the amount of nitrogen that is eliminated in fecal waste. An alternative approach utilizes the ingestion of 1 to 1.5 liters of non-absorbable solutions of polyethylene glycol or mannitol every fourth hour.

Indications

The decision to initiate dialysis or hemofiltration in patients with kidney failure depends on several factors. These can be divided into acute or chronic indications.

Depression and kidney failure symptoms can be similar to each other. It's important that there's an open communication in a dialysis team and the patient. Open communication will allow to give a better quality of life. Knowing the patients' needs will allow the dialysis team to provide more options like: changes in dialysis type like home dialysis for patients to be able to be more active or changes in eating habits to avoid unnecessary waste products.

Acute indications

Indications for dialysis in a patient with acute kidney injury are summarized with the vowel mnemonic of "AEIOU":

1. Acidemia from metabolic acidosis in situations in which correction with sodium bicarbonate is impractical or may result in fluid overload.
2. Electrolyte abnormality, such as severe hyperkalemia, especially when combined with AKI.
3. Intoxication, that is, acute poisoning with a dialyzable substance. These substances can be represented by the mnemonic SLIME: salicylic acid, lithium, isopropanol, magnesium-containing laxatives and ethylene glycol.
4. Overload of fluid not expected to respond to treatment with diuretics
5. Uremia complications, such as pericarditis, encephalopathy, or gastrointestinal bleeding.

Chronic indications

Chronic dialysis may be indicated when a patient has symptomatic kidney failure and low glomerular filtration rate (GFR < 15 mL/min). Between 1996 and 2008, there was a trend to initiate dialysis at progressively higher estimated GFR, eGFR. A review of the evidence shows no benefit or potential harm with early dialysis initiation, which has been defined by start of dialysis at an estimated GFR of greater than 10ml/min/1.73². Observational data from large registries of dialysis patients suggests that early start of dialysis may be harmful. The most recent published guidelines from Canada, for when to initiate dialysis, recommend an intent to defer dialysis until a patient has definite kidney failure symptoms, which may occur at an estimated GFR of 5-9ml/min/1.73².

Dialyzable substances

Characteristics

Dialyzable substances—substances removable with dialysis—have these properties:

1. Low molecular mass
2. High water solubility
3. Low protein binding capacity
4. Prolonged elimination (long half-life)
5. Small volume of distribution

Substances

- Ethylene glycol
- Procainamide
- Methanol
- Isopropyl alcohol
- Barbiturates
- Lithium
- Bromide
- Sotalol
- Chloral hydrate
- Ethanol

- Acetone
- Atenolol
- Theophylline
- Salicylates
- Baclofen

Pediatric dialysis

Over the past 20 years, children have benefited from major improvements in both technology and clinical management of dialysis. Morbidity during dialysis sessions has decreased with seizures being exceptional and hypotensive episodes rare. Pain and discomfort have been reduced with the use of chronic internal jugular venous catheters and anesthetic creams for fistula puncture. Non-invasive technologies to assess patient target dry weight and access flow can significantly reduce patient morbidity and health care costs. Mortality in paediatric and young adult patients on chronic hemodialysis is associated with multifactorial markers of nutrition, inflammation, anaemia and dialysis dose, which highlights the importance of multimodal intervention strategies besides adequate hemodialysis treatment as determined by Kt/V alone.

Biocompatible synthetic membranes, specific small size material dialyzers and new low extra-corporeal volume tubing have been developed for young infants. Arterial and venous tubing length is made of minimum length and diameter, a <80ml to <110ml volume tubing is designed for pediatric patients and a >130 to <224ml tubing are for adult patients, regardless of blood pump segment size, which can be of 6.4mm for normal dialysis or 8.0mm for high flux dialysis in all patients. All dialysis machine manufacturers design their machine to do the pediatric dialysis. In pediatric patients, the pump speed should be kept at low side, according to patient blood output capacity, and the clotting with heparin dose should be carefully monitored. The high flux dialysis (see below) is not recommended for pediatric patients.

In children, hemodialysis must be individualized and viewed as an "integrated therapy" that considers their long-term exposure to chronic renal failure treatment. Dialysis is seen only as a temporary measure for children compared with renal transplantation because this enables the best chance of rehabilitation in terms of educational and psychosocial functioning. Long-term chronic dialysis, however, the highest standards should be applied to these children to preserve their future "cardiovascular life"—which might include more dialysis time and on-line hemodiafiltration online hdf with synthetic high flux membranes with the surface area of 0.2sq.m to 0.8sq.m and blood tubing lines with the low volume yet large blood pump segment of 6.4/8.0mm, if we are able to improve on the rather restricted concept of small-solute urea dialysis clearance.