Diuretics and kidney disease

Diuretics

Drugs used clinically to increase the volume of urine excreted are known as ***diuretics.*** Most of these agents act on the tubules to inhibit the reabsorption of sodium, along with chloride and/or bicarbonate, resulting in increased excretion of these ions. Because water reabsorption is dependent upon sodium reabsorption, water reabsorption is also reduced, resulting in increased water excretion.

Variety of diuretics

Classified according to the mechanism of inhibition of sodium reabsorption. For example loop diuretics such as furosemide, act on the ascending limb of the *loop of Henle* to inhibit the transport protein that mediates the first step in sodium reabsorption in this segment, cotransport of sodium and chloride (and potassium) into the cell across the luminal membrane.

Side effects of diuretics

Except for one category of diuretics, called ***potassium sparing diuretics,*** all diuretics not only increase sodium excretion but also cause increased potassium excretion, which is often an unwanted side effect. The ***potassium-sparing diuretics*** inhibit sodium reabsorption in the cortical collecting duct, and they simultaneously inhibit potassium secretion there.

Potassium-sparing diuretics either block the action of aldosterone (e.g., **spironolactone or eplerenone**) or block the epithelial sodium channel in the cortical collecting duct (e.g., **triamterine or amiloride**). This explains why they do not cause increased potassium excretion.

Osmotic diuretics such as mannitol are filtered but not reabsorbed, thus retaining water in the urine. This is the same reason that uncontrolled diabetes mellitus and its associated glucosuria can cause excessive water loss and dehydration

Uses of diuretics

- Diuretics are among the most commonly used medications. For one thing, they are used to treat diseases characterized by renal retention of salt and water. The regulation of blood pressure normally produces stability of total-body sodium mass and extracellular volume because of the close correlation between these variables.
- In contrast, in several types of disease, this correlation is disrupted and the reflexes that maintain blood pressure can cause renal retention of sodium. Sodium excretion may decrease to almost nothing despite continued sodium ingestion, leading to abnormal expansion of the extracellular fluid**(*edema*).**
- Diuretics are used to prevent or reverse this renal retention of sodium and water

Example-1: Congestive Heart Failure

- A person with a failing heart manifests a decreased GFR and increased aldosterone secretion, both of which contribute to the virtual absence of sodium in the urine. The net result is extracellular volume expansion and **edema**.
- The sodium-retaining responses are triggered by the lower cardiac output (a result of cardiac failure) and the decrease in arterial blood pressure that results directly from this decrease in cardiac output.

Example-2, Hypertension

- Another disease in which diuretics are often used is hypertension.The decrease in body sodium and water resulting from the diuretic-induced excretion of these substances brings about arteriolar dilation and a lowering of the blood pressure.
- The precise mechanism by which decreased body sodium causes arteriolar dilation is not known.

Kidney Disease

Many diseases affect kidney

Infections, allergies, congenital defects, kidney stones (accumulation of mineral deposits in nephron tubules), tumors, and toxic chemicals are some possible sources of kidney damage.

Obstruction of the urethra or a ureter may cause injury from the buildup of pressure and may predispose the kidneys to bacterial infection.

A common cause of renal failure is poorly controlled diabetes mellitus. The increase in blood glucose interferes with normal renal filtration and tubular function.

Symptoms of kidney disease

- Proteinurea

diseased renal corpuscles may become much more permeable to protein, and diseased proximal tubules may lose their ability to remove filtered protein from the tubular lumen. The result is that protein appears in the urine.

Although many diseases of the kidney are self-limited and produce no permanent damage, others worsen if untreated. The symptoms of profound renal malfunction are relatively independent of the damaging agent and are collectively known as ***uremia,*** literally, "urine in the blood."

Uremia

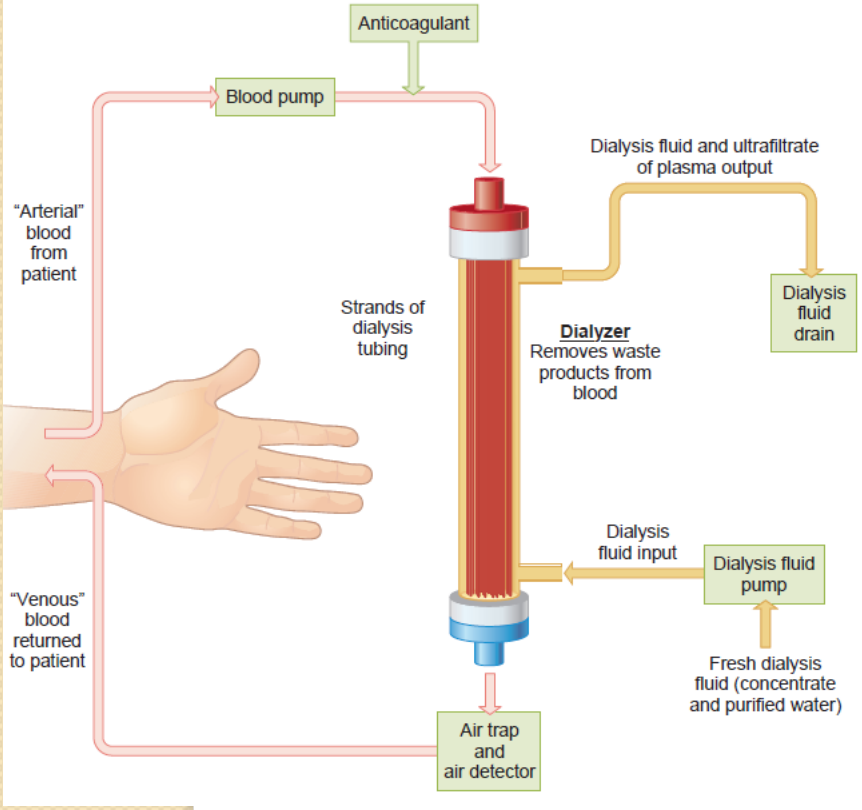
- The severity of uremia depends upon how well the impaired kidneys can preserve the constancy of the internal environment.
- Kidney destruction markedly reduces the number of functioning nephrons. Accordingly, the many substances, particularly potentially toxic waste products, that gain entry to the tubule by filtration build up in the blood.
- In addition, the excretion of potassium is impaired because there are too few nephrons capable of normal tubular secretion of this ion. The person may also develop acidosis because the reduced number of nephrons fail to add enough new bicarbonate to the blood to compensate for the daily metabolic production of nonvolatile acids.

Hemodialysis, Peritoneal Dialysis, and Transplantation

- Failing kidneys may reach a point when they can no longer excrete water and ions at rates that maintain body balances of these substances, nor can they excrete waste products as fast as they are produced. Dietary alterations can help minimize but not eliminate these problems.
- For example, lowering potassium intake reduces the amount of potassium to be excreted. The clinical techniques used to perform the kidneys' excretory functions are hemodialysis and peritoneal dialysis.

The general term *dialysis* means to separate substances using a permeable membrane.

Hemodialysis



Simplified diagram of hemodialysis.

The blood flow can be 400 ml/min, and the dialysis fluid flow rate can be 1000 ml/min! During a three- to four-hour dialysis session,
approximately 72 to 96 L of blood and 3000 to 4000 L of dialysis fluid passes through the dialyzer. The dialyzer is composed of many strands of very thin dialysis tubing. Blood flows inside each tube, and dialysis fluid bathes the outside of the dialysis tubing. This provides a large surface area for diffusion of waste products out of the blood and into the dialysis fluid.
Note that blood and dialysis fluid flow in opposite directions through the dialyzer (countercurrent).

Hemodialysis: Artificial Kidney

- The artificial kidney is an apparatus that utilizes a process termed ***hemodialysis*** to remove wastes and excess substances from the blood.
- During hemodialysis, blood is pumped from one of the patient's arteries through tubing that is surrounded by special dialysis fluid. The tubing then conducts the blood back into the patient by way of a vein.
- The dialysis tubing is generally made of cellophane that is highly permeable to most solutes but relatively impermeable to protein and completely impermeable to blood cells, characteristics quite similar to those of capillaries.

Hemodialysis: Dialysis fluid

- The dialysis fluid is a salt solution with ionic concentrations similar to or lower than those in normal plasma, and it contains no creatinine, urea, or other substances to be completely removed from the plasma.
- As blood flows through the tubing, the concentrations of non protein plasma solutes tend to reach diffusion equilibrium with those of the solutes in the bath fluid.

Hemodialysis: Dialysis fluid……..

- *For example*, if the plasma potassium concentration of the patient is above normal, potassium diffuses out of the blood across the cellophane tubing and into the dialysis fluid. Similarly, waste products and excesses of other substances also diffuse into the dialysis fluid and thus are eliminated from the body.

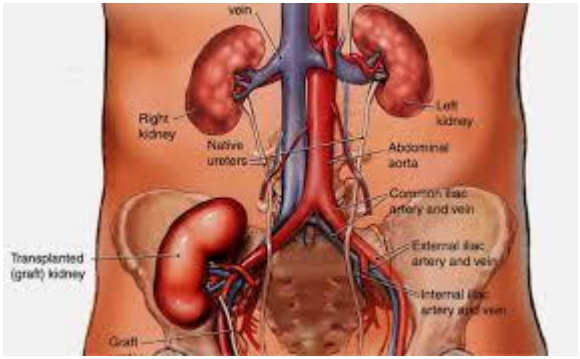
Hemodialysis: Frequency

- Patients with acute reversible renal failure may require hemodialysis for only days or weeks.
- Patients with chronic irreversible renal failure require treatment for the rest of their lives, however, unless they receive a kidney transplant. Such patients undergo hemodialysis several times a week.

Peritoneal dialysis

- Another way of removing excess substances from the blood is ***peritoneal dialysis,*** which uses the lining of the patient's own abdominal cavity (peritoneum) as a dialysis membrane.
- Fluid is injected, via a needle inserted through the abdominal wall, into this cavity and allowed to remain there for hours, during which solutes diffuse into the fluid from the person's blood. The dialysis fluid is then removed by reinserting the needle and is replaced with new fluid.
- This procedure can be performed several times daily by a patient who is simultaneously doing normal activities.

Kidney transplantation



The long-term treatment of choice for most patients with permanent renal failure is kidney transplantation. Rejection of the transplanted kidney by the recipient's body is a potential problem, but great strides have been made in reducing the frequency of rejection.

Many people who might benefit from a transplant, however, do not receive one.

Currently, the major source of kidneys for transplantation is recently deceased persons.

Improved public understanding should lead to many more individuals giving permission in frequency of rejection. Many people who might benefit from a transplant, however, do not receive one.

Kidney transplantation……..

- Currently, the major source of kidneys for transplantation is recently deceased persons. Improved public understanding should lead to many more individuals giving permission in advance to have their kidneys and other organs used following their death.
- Recently, donation from a living, related donor has become more common. Because of the large safety factor, the donor can function quite normally with one kidney.

References

Vander’s human physiology, internet (some pictures)