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18 /MHS01 /383
MBBS 300LVL
PHYSIOLOGY ASSIGNMENT

QUESTION 1: Discuss the pathophysiological process involved in renal failure

Renal failure refers to failure of excretory functions of kidney. It is usually, characterized by decrease in glomerular filtration rate (GFR). So GFR is considered as the best index of renal failure. However, decrease in GFR is not affected much during the initial stages of renal failure. If 50% of the nephrons are affected, GFR decreases only by 20% to 30%. It is because of the compensatory mechanism by the unaffected nephrons. The renal failure may be either acute or chronic.

ACUTE RENAL FAILURE (ARF)

Acute renal failure (ARF) is the sudden or abrupt stoppage of renal functions. It is a syndrome characterised by rapid onset of renal dysfunction, chiefly oliguria or anuria, and sudden increase in metabolic waste-products (urea and creatinine) in the blood with consequent development of uraemia.

ETIOPATHOGENESIS.

The causes of ARF may be classified as pre-renal, intra-renal and post-renal in nature.

- Pre-renal causes: Pre-renal diseases are those which cause sudden decrease in blood now to the nephron. Renal ischemia ultimately results in functional disorders or depression of GFR (cardiac output and hypovolemia).
- Intra-renal causes: disease of renal tissue itself. These include vascular disease of the arteries and arterioles within the kidney, diseases of glomeruli, acute tubular necrosis due to ischemia, or the effect of a nephrotoxin, acute tubulointerstitial nephritis and pyelonephritis.

- Post-renal causes: caused by obstruction to the now of urine anywhere along the renal tract distal to the opening of the collecting ducts, ureter, bladder neck or urethra. It is important to note that ARF originating in pre and post-renal disease, such as by renal ischemia or renal infection, eventually leads to intra-renal disease.

CLINICAL F EATURES.

Depend on the underlying cause of ARF and on the stage of the disease at which the patient presents:

Syndrome of acute nephritis: Associated with acute streptococcal glomerulonephritis and rapidly progressive glomerulonephritis. Renal dysfunction results from extensive proliferation of epithelial cells in the glomeruli, increase in glomerular permeability and decrease in GFR. Features are: mild proteinuria, haematuria, oedema and mild hypertension.

Syndrome accompanying tubular pathology: When the ARF is caused by destruction of the tubular cells of the nephron the disease typically progresses through 3 characteristic stages from oliguria to diuresis to recovery.

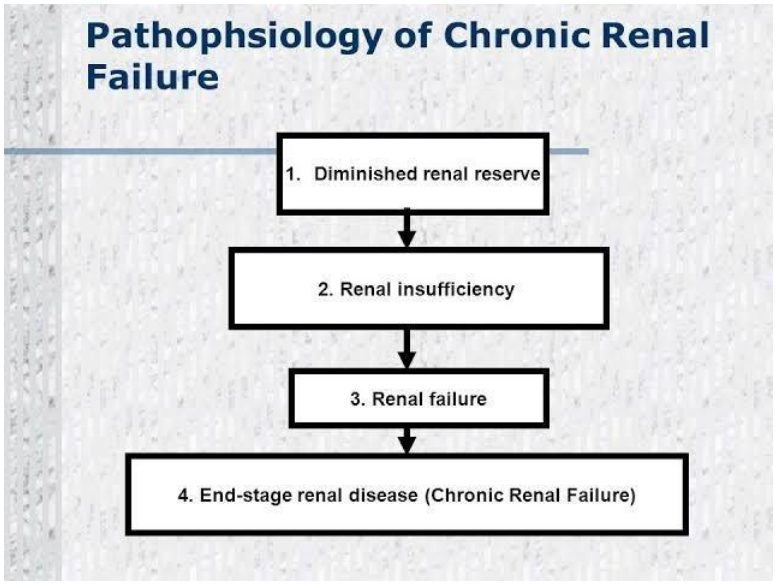
- *Oliguria phase*: The initial oliguria phase lasting on an average from 7 to 10 days with urinary output of less than 400 ml per day. Leads to accumulation of waste products of protein metabolism in the blood and resultant azotaemia, metabolic acidosis, hyperkalaemia, hypernatraemia and hypervolemia.
- *Diuretic phase*: With the onset of healing of tubules, there is improvement in urinary output. This is believed to occur due to drawing of water and sodium as they move through the nephron so as to be excreted.
- *Phase of recovery*: Full recovery with healing of tubular epithelial cells occurs in about half the cases, while others terminate in death. The process of healing may take up to one year with restoration of normal tubular function.

Pre-renal syndrome: Secondary to disorders in which neither the glomerulus nor the tubules are damaged, results in pre-renal syndrome. Typically, this is seen in ischemia caused by renal arterial obstruction, hypovolaemia, hypotension or cardiac insufficiency. Due to depressed renal blood flow, there is decrease in GFR causing oliguria, azotaemia (elevation of BUN and creatinine) and possible fluid retention and oedema. Since the tubular cells are functioning normally, the nephron retains its ability to concentrate the glomerular filtrate according to the adaptive needs.

CHRONIC RENAL FAILURE (CRF)

Chronic renal failure is the progressive, long standing and irreversible impairment of renal functions. It is a syndrome characterised by progressive and irreversible deterioration of renal function. Slow destruction of renal parenchyma, eventually terminating in death when sufficient number of nephrons have been damaged. Acidosis is the major problem in CRF with development of biochemical azotaemia and clinical uraemia syndrome.

ETIOPATHOGENESIS



Regardless of the initiating cause, CRF evolves progressively through 4 stages:

1. *Decreased renal reserve*: At this stage, damage to renal parenchyma is marginal and the kidneys remain functional. The GFR is about 50% of normal, BUN and creatinine values are normal and the patients are usually asymptomatic except at times of stress.
2. *Renal in sufficiency*: At this stage, about 75% of functional renal parenchyma has been destroyed. The GFR is about 25% of normal accompanied by elevation in BUN and serum creatinine. Polyuria and nocturia occurs.
3. *Renal failure*: At this stage, about 90% of functional renal tissue has been destroyed. The GFR is approximately 10% of normal. Tubular cells are essentially non-functional. As a result, the regulation of sodium and water is lost resulting in oedema, metabolic acidosis, hypocalcaemia, and signs and symptoms of uraemia.
4. *Chronic renal failure*

All chronic nephropathies can lead to CRF. The diseases leading to CRF can generally be classified into two major groups:

>Those causing glomerular pathology.

>Those causing tubulointerstitial pathology.

Though this classification is useful to facilitate study. The disease merely remains confined to either glomeruli or tubulointerstitial tissue alone. In the final stage of CRF, all parts of the nephron are involved.

1. Diseases Causing Glomerular Pathology.

A number of glomerular diseases associated with CRF have their pathogenesis in immune mechanisms. Glomerular destruction results in changes in filtration process and leads to development of the nephritic syndrome characterised by proteinuria, hypoalbuminaemia and oedema. The important examples of chronic glomerular diseases causing CRF are covered under two headings: primary and systemic.

I. *Primary glomerular pathology*: The major cause of CRF is chronic glomerulonephritis, initiated by glomerulo-nephritis, membrano proliferative glomerulonephritis, lipoid nephritis (minimal change disease) and anti-glomerular basement membrane nephritis.

II. *Systemic glomerular pathology*: Certain conditions originate outside the renal system but induce changes in the nephrons secondarily. Major examples of this type are systemic lupus erythematous, serum sickness nephritis and diabetic nephropathy.

2. Diseases Causing Tubulointerstitial Pathology.

Damage to tubulointerstitial tissues results in alterations in reabsorption and secretion of important constituents leading to excretion of large volumes of dilute urine. Tubulointerstitial diseases can be categorised according to initiating aetiology into 4 groups namely;

I. *Vascular causes*: Long-standing primary or essential hypertension produces characteristic changes in renal arteries and arterioles referred to as nephrosclerosis.

II. *Infectious causes*: A good example of chronic renal infection causing CRF is chronic pyelonephritis. The chronicity of process results in progressive damage to increasing Number of nephrons leading to CRF.

III. *Toxic causes*: The most common example is intake of high doses of analgesics such as aspirin and acetaminophen (chronic analgesic nephritis). Other substances that can cause CRF after prolonged exposure are lead, cadmium and uranium.

IV. *Obstructive causes*: Chronic obstruction in the urinary tract leads to progressive damage to the nephron due to fluid backpressure. The examples of this type of chronic injury are stones, blood clots, tumours, strictures and enlarged prostate.

CLINICAL FEATURES.

Clinical manifestation of full blown CRF culminating in uremic syndrome are described under 2 main headings; Primary (renal) uremic manifestation and Secondary (systemic or extra-renal) uremic manifestations.

***Primary uraemic (renal) manifestations*:** Primary symptoms of uraemia develop when there is slow and progressive deterioration of renal function. The resulting imbalances came the following manifestations:

I. *Metabolic acidosis:* As a result of renal dysfunction, acid base balance is progressively lost and excess of hydrogen ions occurs, while bicarbonate level declines in the blood resulting in metabolic acidosis. The clinical symptoms of metabolic acidosis include: compensatory breathing. Hyperkalaemia and hypocalcaemia.

II. *Hyperkalaemia*: A decreased GFR results in excessive accumulation of potassium in the blood since potassium is normally excreted mainly in the urine. The clinical features of hyperkalaemia are: cardiac arrhythmia, weakness, names, intestinal colic, diarrhoea, muscular irritability and flaccid paralysis.

III. *Sodium and water imbalance*: As GFR declines, sodium and water cannot pass sufficiently into Bowman‘s capsule leading to their retention. Release of renin from juxtaglomemlar apparatus further aggravates sodium and water retention.

IV. *Hyperuricaemia*: Decreased GFR results in excessive accumulation of uric acid in the blood. Uric acid crystals may be deposited in joints and soft tissues resulting in gout.

V. *Azotaemia:* The waste-products of protein metabolism fail to be excreted resulting in elevation in the blood level of urea, creatinine, phenols and guanidine causing biochemical abnormality, azotaemia.

***Secondary uraemic (extra-renal) manifestations*:** A number of extra-renal systemic manifestations develop secondarily following fluid-electrolyte and acid-base imbalances. These include the following:

I. *Anaemia*: Decreased production of erythropoietin by diseased kidney results in decline in erythropoiesis and anaemia. Besides, gastrointestinal bleeding may further aggravate anaemia.

II. *Integumentary system*: Deposit of urinary pigment such as urochrome in the skin causes sallow-yellow colour. The urea content in the sweat as well as in the plasma rises. On evaporation of the perspiration, urea remains on the facial skin as powdery 'uraemic frost'

III. *Cardiovascular system*: Fluid retention secondarily causes cardiovascular symptoms such as increased workload 0n the heart due to the hypervolemia and eventually congestive heart failure.

IV. *Respiratory system*: Hypervolemia and heart failure cause pulmonary congestion and pulmonary oedema due to back pressure. Radiologically, uremic pneumonitis shows characteristic central, butterfly-pattern of oedema and congestion in the Chest radiograph.

V. *Digestive system*: Azotaemia directly induces mucosa ulcerations in the lining of the stomach and intestines. Subsequent bleeding can aggravate the existing anaemia. Gastrointestinal irritation may cause nausea, vomiting and diarrhoea.

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

Dialysis is the procedure to remove waste materials and toxic substances and restore normal volume and composition of body fluid in severe renal failure. Dialysis works on the principles of the diffusion of solutes and ultrafiltration of fluid across a semi-permeable membrane. Diffusion is a property of substances in water; substances in water tend to move from an area of high concentration to an area of low concentration. Blood flows by one side of a semi-permeable membrane, and a dialysate, or special dialysis fluid, flows by the opposite side. A semipermeable membrane is a thin layer of material that contains holes of

various sizes, or pores. Smaller solutes and fluid pass through the membrane, but the membrane blocks the passage of larger substances (for example, red blood cells and large proteins). This replicates the filtering process that takes place in the kidneys when the blood enters the kidneys and the larger substances are separated from the smaller ones in the glomerulus.

There are three primary and two secondary types of dialysis:

1. Primary: which include

- Hemodialysis
- Peritoneal dialysis
- Hemofiltration

2. Secondary: which include

- Hemodiafiltration
- Intestinal dialysis

Hemodialysis

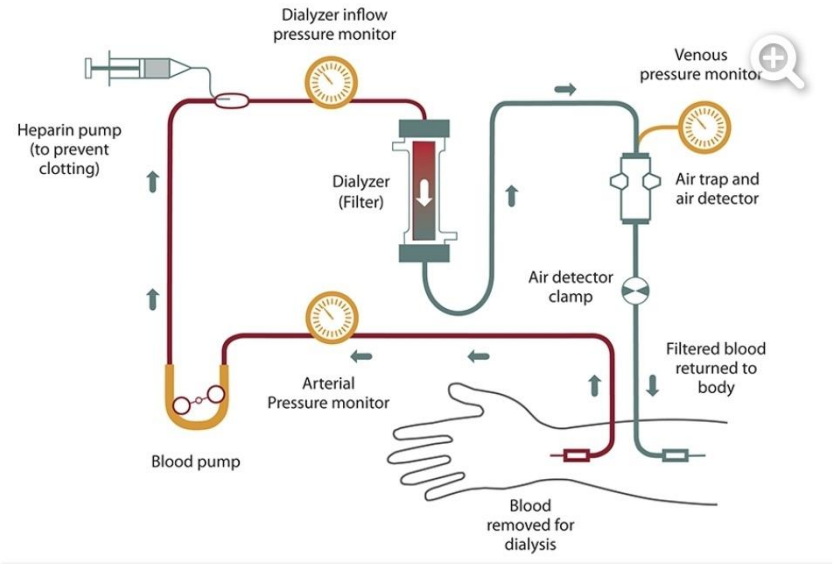
Hemodialysis is the most common type of dialysis. This process uses an artificial kidney (hemodialyzer) to remove waste and extra fluid from the blood. The blood is removed from the body and filtered through the artificial kidney. The filtered blood is then returned to the body with the help of a dialysis machine. To get the blood to flow to the artificial kidney, surgery to create an entrance point (vascular access) into your blood vessels is performed. 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.

Process of hemodialysis



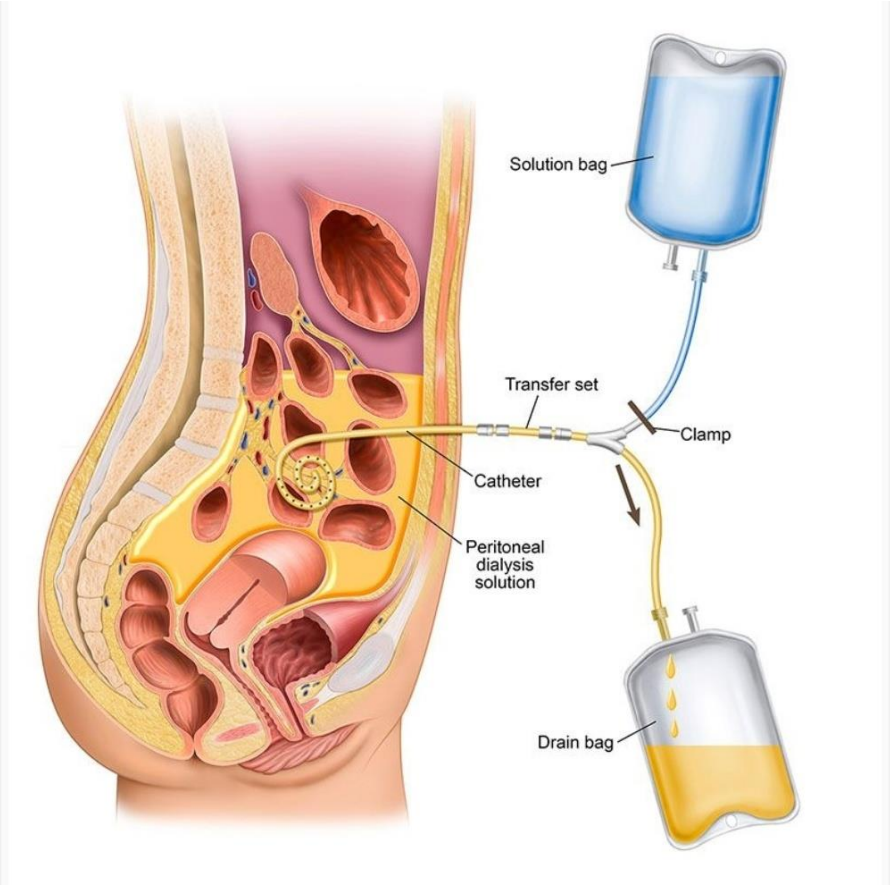
In hemodialysis, the patient's blood is pumped through the blood compartment of a dialyzer, exposing it to a partially permeable membrane. The dialyzer is composed of thousands of tiny hollow synthetic fibers. The fiber wall acts as the semipermeable membrane. Blood flows through the fibers, dialysis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

Peritoneal dialysis

Peritoneal dialysis involves surgery to implant a peritoneal dialysis (PD) catheter into the abdomen. The catheter helps filter blood through the peritoneum, the 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 the 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 sleeping or awake.

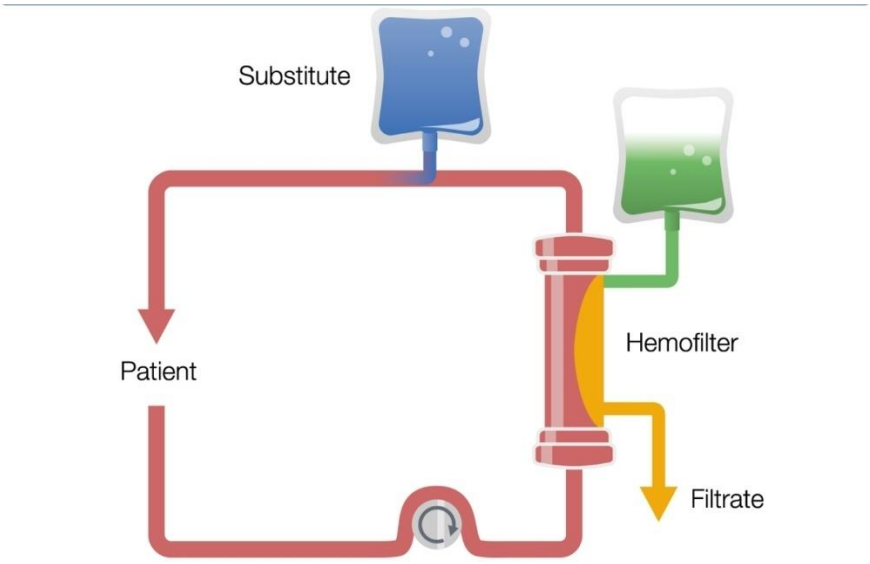
Process of peritoneal dialysis



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

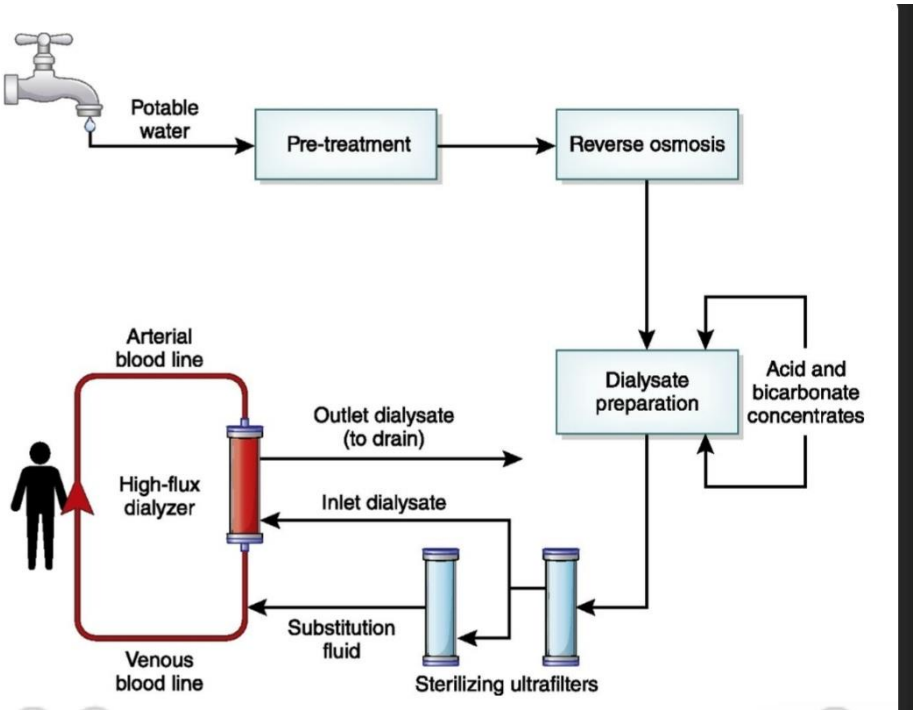
similar to hemodialysis. Peritoneal dialysis can be performed with little to no specialized equipment (other than bags of fresh dialysate).

Hemofiltration



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 (HDF) is a form of renal replacement therapy that utilizes convective in combination with diffusive clearance, which is used in standard hemodialysis. Compared with standard hemodialysis, HDF removes more middle-molecular-weight solutes.

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

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 litres of non-absorbable solutions of polyethylene glycol or mannitol every fourth hour.

REFERENCES

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