1. Discuss the pathophysiological process involved in renal failure?

Renal failure refers to the deterioration of renal functions resulting in a decline in glomerular filtration rate (GFR) and rise in urea and non-nitrogenous substances in the blood. It is of two types: Acute and Chronic.

**ACUTE RENAL FAILURE(ARF)**

According to Kidney Disease Improving Global Outcomes ([KDIGO](http://kdigo.org/home/guidelines/acute-kidney-injury/)), ARF is defined by one of the following 3 criteria:

* Increase in creatinine serum level of more than 0.3 mg/dl (within 48 hours).
* Increase in creatinine serum level by more than 50% (within the prior 7 days).
* Decrease in urine volume (oliguria) to less than 0.5 ml/kg body weight/hour for 6 hours.

Causes

Because of various pathophysiologic processes, kidney function can diminish rapidly. As a consequence, uremic substances accumulate and alter water, electrolyte, and acid-base balances. Usually, this loss of function is reversible, as long as the underlying cause or structural processes do not become chronic.

Types and pathophysiology

Etiologically, ARF can be subdivided into 3 types. Each type encompasses different pathophysiological processes, so understanding the type of ARF presenting in a patient is crucial to identifying the choice of treatment:

* Prerenal ARF
* Intrinsic ARF
* Postrenal ARF

**Prerenal ARF (about 60 % of all cases)**

Prerenal ARF is the result of reduced renal perfusion, with the glomerular and tubular structures initially being completely intact. It may be caused by actual hypovolemia (e.g., due to exsiccosis, [diarrhea](https://www.lecturio.com/magazine/diarrhoea/), or pancreatitis), but also relative hypovolemia stemming from e.g., [cardiac insufficiency](https://www.lecturio.com/magazine/cardiac-insufficiency-pulmonary-edema/), shock, or sepsis. Prerenal ARF may lead to a reduction in renal perfusion. Diseases that cause renal vasoconstriction may result also in prerenal failure. Hepatorenal syndrome is evident.

Through the regulation mechanisms of the [kidney](https://www.lecturio.com/magazine/kidney/), reduced perfusion activates the renin-angiotensin-aldosterone system (RAAS). At the same time, the body experiences a release of catecholamine and ADH. This reaction is vasoconstriction with simultaneous retention of sodium and water in order to compensate for the hypovolemic condition.

In the case of exsiccosis, these reactions are appropriate. However, in the presence of cardiac insufficiency, actual reduced perfusion does not involve a lack of water. Clinically, signs of hyperhydration predominate. The activation of RAAS erroneously increases the intracorporeal water concentration and hyperhydration increases. If diuretics are administered in this situation, renal perfusion will be reduced even more, increasing the risk of ischemia and intrinsic renal failure.

**Intrinsic Renal Failure (about 35 % of all cases)**

Acute damage to the glomeruli or tubular cells leads to structural damage of the kidney itself. Usually, acute tubular necrosis brought about by, e.g., different (micro- and macroangiopathic) ischemic processes such as thromboembolism or thrombotic microangiopathy will occur. Glomerulonephritides may also lead to reduced kidney function.

Toxic damage, especially iatrogenic damages, are frequent. Contrast agents or other medications play an important role here. In addition, myoglobinuria due to rhabdomyolysis, hemoglobinuria due to hemolysis, or uric acid salts due to [gout](https://www.lecturio.com/magazine/hyperuricemia-and-gout/) or tumor lysis are potential causes.

A number of frequently administered drugs can also cause damage to the kidneys, including nonsteroidal anti-inflammatory drugs, aminoglycosides, cephalosporin, vancomycin, amphotericin B, cisplatin, methotrexate, cyclosporine, diuretics, X-ray contrast agents, and angiotensin-converting-enzyme inhibitors.

The renal tubules are responsible for reabsorption. If an intrinsic renal dysfunction affects the tubules, this may cause severe polyuria as part of ARF.

If sodium reabsorption is diminished because of damage to the tubular cells, the tubuloglomerular feedback mechanism causes constriction of the afferent glomerular arteriole. This, in turn, leads to a reduction in the glomerular filtration rate.

**Postrenal Failure (about 5 % of all cases)**

Any disease with the potential to impair the drainage of urine from the kidneys can lead to urinary retention with subsequent postrenal failure. Congenital malformations of the urinary tract should be excluded as a cause as should various acquired urinary obstructions including tumors, gynecological conditions, urinary catheters, outflow obstructions due to medication, prostate enlargement, and ureteric stones.

**Clinical Presentation and Symptoms of Acute Renal Failure**

The clinical manifestation of ARF is very diverse and largely depends on a persistent underlying disease. The clinical course of the disease can be divided into three stages:

1. **Initiating stage:** Before ARF manifests, it is mostly asymptomatic. Possible symptoms of an underlying disease predominate.
2. **Oliguric stage:** The preeminent symptom of ARF is oliguria or anuria. It leads to a corporeal hyperhydration with a number of complications, including [hypertension](https://www.lecturio.com/magazine/arterial-hypertension/), pulmonary edema, [pleural effusion](https://www.lecturio.com/magazine/pleural-effusion/), left ventricular heart failure, ascites, cerebral edema, and more. A consequence of urinary retention may be hyperkalemia with acidosis. However, as noted above, there are many normuric or polyuric stages.
3. **Diuretic or polyuric stage:** Usually, the glomeruli recover faster than the tubular system, which means that during recovery, reabsorption may remain disturbed while the filtration capacity of the kidney begins to function again.

Depending on what is causing the ARF, side pain, fever, fatigue, and symptoms relating to complications may also be present.

**Complications of Acute Renal Insult**

Complications are due to the above-noted pathophysiological processes. Many organ systems may be affected:

* The [lungs](https://www.lecturio.com/magazine/lung/) can be affected by hyperhydration, including [edema](https://www.lecturio.com/magazine/edemas-as-cardinal-symptoms/) and effusion. Acute respiratory distress syndrome may occur.
* Heart failure may develop due to hypertension or hyperhydration, or arrhythmias may develop due to imbalanced electrolyte concentrations.
* If heart failure occurs, there is a risk of congestion in the venous circuit causing gastritis, ulcerations, or gastrointestinal bleeding. The stress-associated release of hormones can increase the likelihood of gastrointestinal bleeding.
* Seizures may occur due to a cerebral edema or electrolyte imbalance. In addition, vigilance can be impaired.

**Treatment of Acute Renal Insult**

* **Substitution of Fluids and Electrolytes for Acute Renal Insult of Prerenal Genesis:** In prerenal ARF, kidney function can only recover when the underlying pathophysiological mechanism has been eliminated. Nephrotoxic substances should be avoided, and fluid and electrolyte balances must be thoroughly controlled and treated.The reason for the hypoperfusion must be uncovered and then treated. The administration of fluids and electrolytes is a prudent option. Loop diuretics can also be helpful in maintaining diuresis (Note that while this medication measurably increases diuresis, it does not increase glomerular filtration or have any impact on the recovery of kidney function.).

Patients with sepsis or with severe heart failure often require treatment in the intensive care unit.

* **Immunosuppressive Therapy and Revascularization for Acute Renal Failure of Intrinsic Genesis:** In intrinsic AFI, it is important to first treat the underlying disease. Immunosuppressive treatment is advisable for glomerulonephritis, and revascularization for ischemia. For raising diuresis, loop diuretics can be administered; however, the use of diuretics is controversial and therefore not generally recommended. The only absolute indication for the administration of diuretics is hyperhydration.
* **Treatment of Acute Renal Insult of Postrenal Genesis:** In cases of postrenal ARF, it is imperative to remove the urinary obstruction. If this is not immediately possible, the surgical insertion of an artificial excretory opening (percutaneous nephrostomy) is indicated.
* **Extracorporeal Treatment of Acute Renal Failure:** Extracorporeal treatment with hemodialysis or hemofiltration for electrolyte imbalances, water overloads, or acid-base imbalances can also be attempted. This type of renal replacement therapy should be considered only as a temporary measure and limited accordingly. If kidney function cannot be restored sufficiently, permanent dialysis may become necessary. This type of renal replacement therapy should be considered only as a temporary measure which must be limited accordingly. If the kidney function cannot be restored sufficiently, permanent dialysis might become necessary.

**CHRONIC RENAL FAILURE**

Chronic renal failure is defined as an irreversible decrease of not only glomerular and tubular function but also endocrine renal function. This damage has to have been exhibited for longer than 3 months.

**The Pathophysiological Processes of Chronic Kidney Disease**

Chronic renal failure is caused by a progressive decline of all kidney functions, ending end with terminal kidney damage. During this time, there is modulation and adaptation in the still-functional glomeruli, which keeps the kidneys functioning normally for as long as possible. The remaining glomeruli, therefore, experience a rise in pressure through hyperfiltration.

The release of various cytokines and growth factors leads to hypertrophy and hyperplasia. At the same time, the function of the glomeruli suffers due to the excessive demands on them, leading to increased permeability and proteinuria. Increased protein concentrations in the proximal tube system are direct nephrotoxins and can further impair kidney function.

There are four phases of chronic renal failure:

**1. Reduction in Excretory Function**

Breakdown of excretory function is the consequence of an accumulation of endogenous and extraneous substances. This leads to changes in pharmacokinetics and an increase in the concentration of various medications. Breakdown occurs when the remaining glomeruli are confronted by a surplus of waste products, leading to osmotic diuresis. There is a reduction in the maximal concentrating capacity of the kidney. In order to filter the physiological quantity of dissolved substances, the nephrons produce between 3 and 4 times as much urine during renal failure, resulting in an accumulation of waste substances.

**2. Reduction in Incretory Renal Function**

Because the kidney plays a part in the regulation of many important hormonal cycles, chronic renal failure also has endocrinal consequences. Through a shortage of erythropoietin, there is a reduction in erythrocyte synthesis, which leads to renal anemia; uremia then leads to a reduction of functional erythrocytes due to hemolysis or hemorrhages.

Vitamin D production is also impaired, and phosphate excretion is reduced. Secondary hyperparathyroidism and the associated renal osteopathy (‘high-turnover’ osteopathy) develop as a result of hyperphosphatemia. Parallel to this, other pathomechanisms lead to a disruption in bone metabolism: osteomalacia occurs due to a disruption of mineralization, and adynamic [bone](https://www.lecturio.com/magazine/bones-fundamentals-of-anatomy/) disease occurs due to a reduction in bone cell activity (particularly in dialysis patients).

**3. Over-hydration and the Disruption of Electrolyte Balance**

As long as the glomeruli can manage to compensate, diuresis and fractional sodium excretion rise. If the glomerular filtration rate noticeably drops, then the ability to compensate is exhausted, leading to increased retention of water and electrolytes.

Hypertension, pulmonary edema, and peripheral edema result from overhydration. Water and salt excretion are thereby inextricably linked. Diuretics can aid in water and salt excretion where critical glomerular damage is present. Early loss of salts as a result of the disturbance in the resorption process can actually be made worse by the use of diuretics.

Thus, as the glomeruli adapt to compensate, the tubular transport mechanisms also adapt in order to prevent hyperkalemia through increased potassium secretion. Hyperkalemia only develops as a result of hyperstimulation of the resorption capacity. As many patients are treated with calcium-sparing diuretics due to previous conditions, it is vital to refer to patient’s medication history and adapt the treatment plan accordingly.

Acidosis also rises alongside hyperkalemia. The kidneys can no longer sufficiently eliminate accumulating protons due to a strongly reduced glomerular filtration rate. This metabolic acidosis leads to increased bone calcium release and strengthening renal osteopathy, an increase in gastrointestinal problems, and the impairment of protein metabolism.

**4. Toxic Organ Damage as a Result of Retention of Urinary Excreted Metabolites**

Toxic organ damage can be explained under the umbrella term ‘uremic syndrome.’ The rise in urinary excreted metabolites in the blood is called azotemia. These metabolites include urea, creatinine, beta-2 microglobulin, parathyroid hormone, among others. Uremic syndrome (uremia) principally describes a systemic disruption of all organ functions, especially the circulatory system, central nervous system, blood, and membranes.

Clinically, many symptoms of chronic renal failure can be detected via the [skin](https://www.lecturio.com/magazine/skin/). Patients often have macules (‘café au lait’ spots), are conspicuously pale, and have a gray, dirty-looking complexion. They often complain of pruritus. Internal membranes are also affected, leading to pericarditis, peritonitis, and pleurisy.

Uremia can also lead to hemolysis with anemia. Simultaneously, thrombocyte and leukocyte dysfunctions or deficiencies can arise.

People with chronic renal failure have a generally increased risk of atherosclerosis with an elevated cardiovascular risk. This leads to media calcification caused by calcium phosphate and to intima calcification through inflammatory factors and cholesterol plaques. Hypertension is common, along with edemas and pulmonary congestion.

Impairments of the central nervous system are indicated by a reduction in vigilance, from general drowsiness to uremic coma. Seizures can occur. Uremia also causes polyneuropathy with paresthesia.

**Symptoms of Chronic Kidney Disease**

Chronic renal failure often begins with generalized symptoms such as tiredness, loss of appetite, and headaches. Further early indicators are polyuria, newly emerging or worsening hypertension, or peripheral edemas. Depending on the etiology, there can also be flank pain or fever.

As the disease progresses, increased tiredness, paleness, headaches, visual disturbances, and a severe loss of renal capacity become noticeable. Uremic gastroenteropathy leads to a loss of appetite and nausea. Pruritus occurs and muscle fibrillations become apparent.

In the final stages, renal failure leads to oliguria or anuria, dyspnea, vomiting, uremic encephalopathy with a severe reduction in vigilance, and increased susceptibility to bleeding.

**TREATMENT**

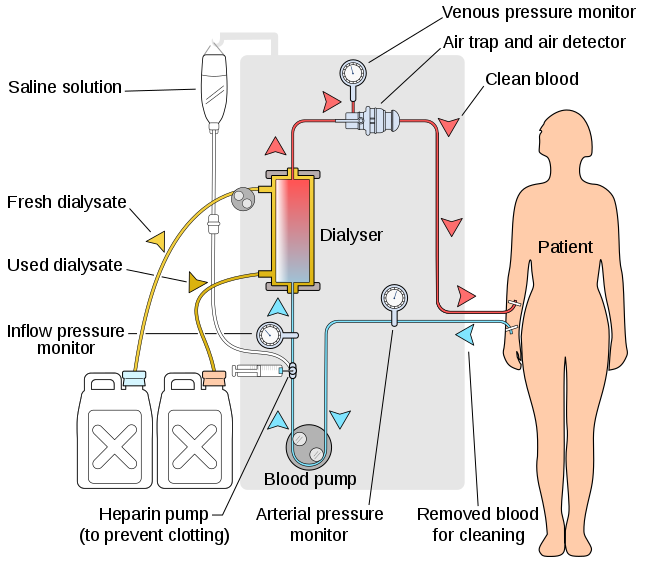
* Loop diuretics are recommended for more advanced renal failure. If over time, the diuretic effect begins to weaken, diuretic resistance may be present; this can be overcome by sequential nephron blockade in which loop diuretics are combined with thiazide. The resultant loss of electrolytes must be closely monitored and replaced, however.
* Symptoms of hyperkalemia should be monitored. A low-potassium diet is recommended and potassium-sparing diuretics should not be prescribed. If renal acidosis occurs, serum bicarbonate values of < 22 mmol/L can be counterbalanced by the administration of bicarbonate.
* Adequate regulation of blood pressure can often be achieved by undertaking combined antihypertensive therapy, during which angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers should be avoided due to their nephroprotective properties.
* As renal failure is accompanied by a change in pharmacokinetics, appropriate medication adjustments must be made in order to avoid intoxication.
* Renal anemia can be improved with synthetic erythropoietin. Depending on the blood parameters, iron supplements can also be necessary, particularly if dialysis is underway and blood loss is occurring, as this is often accompanied by iron deficiency.
* If it is not possible to stop or slow the progress of renal failure via conservative therapies, then renal replacement therapy is essential. There is a range of different extra or intracorporeal dialysis treatments available.
* The treatment of choice for terminal renal failure is kidney transplant. Kidney transplant is far preferable to long-term dialysis, despite the operative procedure and immunosuppressive therapy necessary.

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

Dialysis is a minimally invasive blood purifying treatment (removing excess [water](https://en.wikipedia.org/wiki/Water), [solutes](https://en.wikipedia.org/wiki/Solutes), and [toxins](https://en.wikipedia.org/wiki/Toxins)) given when kidney function is not optimum. This is referred to as [renal replacement therapy](https://en.wikipedia.org/wiki/Renal_replacement_therapy).

There are three major or primary types of dialysis and two secondary types. They primary types of dialysis are:

### HAEMODIALYSIS:



The most common method of dialysis is the Haemodialysis. In this method, the doctor will create a vascular access into the body, surgically. This will allow more blood to flow through the dialyzer and return back to the body after purification. The vascular access is an entrance to the 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.

Inside the dialyzer, there are thousands of tiny synthetic fibres that act as semi-permeable membrane. A dialysis solution, also known as dialysate, is used to purify the blood that runs through this membrane of fibres. A negative pressure is used to remove the water from the blood to the dialysate. The usual span for the haemodialysis process is 4 hours. Typically, a person has to undergo three haemodialysis sessions per week. However, depending on the condition, requirement or disease, haemodialysis can be done more frequently and for shorter or longer sessions.

The body size and the amount of waste in the blood determine the frequency of haemodialysis suitable for the patient. Usually the procedure is done at a doctor’s office or at a hospital or at a dialysis centre. Nowadays, with advanced technology, haemodialysis is also being offered at the patient’s home. Those, who are in need for a long-term dialysis, are recommended the at-home haemodialysis treatment.

### PERITONEAL DIALYSIS:

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This is a surgical procedure of dialysis. The doctor implants a catheter into the patient’s belly and this comes out from below the navel. A dialysate fluid is inserted into the abdomen through the catheter. This fluid draws out the waste materials and extra water from the blood, through the small blood vessels in the abdomen. Once the process is done, the waste materials and extra water from the blood along with the dialysate fluid, all get deposited into a bag through the catheter and the bag is discarded. Here it must be mentioned that there are two types of peritoneal dialysis –

* Continuous ambulatory peritoneal dialysis (CAPD)
* Continuous cycling peritoneal dialysis (CCPD)

CAPD is useful for those, who want to undergo the dialysis treatment while staying mobile or while doing other tasks. It is carried out multiple times a day. This method does not require any machine to carry out the dialysis treatment. CCPD is useful for those, who do not want any interruption throughout the day. It is done at night, while the patient is asleep.

### HEMOFILTRATION:

Hemofiltration is similar to haemodialysis except for the principle which it follows. In this process, the blood is passed via the dialyzer but the dialysate is not used. The water is passed through permeable membranes rapidly, taking along with it the dissolved substances including large molecular substances which are usually not cleared in hemodialysis. During the treatment process, water and salts that are replaced during this filtration process is infused back in the extracorporeal circuit.

**The secondary types of dialysis include:**

* **Haemodiafiltration:** This is actually a combination of hemodialysis and hemofiltration.
* **Intestinal Dialysis:** In this type of dialysis, the diet is incorporating acacia fibre, a soluble fibre, which is easily digested by the bacteria in the colon. This bacterial growth increases the nitrogen content in the digestive system which is then eliminated from the body through feaces.

## Advantages of Haemodialysis and Peritoneal Dialysis

* The main advantage of haemodialysis is that it is carried out only 3 times a week. This means that the patient has 4 dialysis free days in a week.
* With Peritoneal dialysis the main advantage is, it does not require any huge dialysis machines. Instead, it can be carried out well at home.
* If you are travelling, it is much easier to carry the portable peritoneal dialysis machine, than the Haemodialysis machine, which is huge.

## Disadvantages of Haemodialysis and Peritoneal Dialysis

* Since, haemodialysis is always carried out at a dialysis clinic; so when you are travelling, you need to find a clinic that will help you to do the procedure.
* Patients undergoing haemodialysis treatment have to maintain a very strict diet. Certain foods must be avoided and there is also a restriction on the fluid intake. Some patients cannot drink more than a cup of fluid a day.
* If you have arteriovenous fistulas or grafts, hemodialysis may fail if narrowings, called stenoses, develop in your blood vessels. Those narrowing cause poor flow, which affects the ability to efficiently dialyze the blood. The narrowings may cause additional symptoms, such as swelling of the head and arms. Without treatment, poor flow can result in clot formation, which prevents the ability to dialyze. It can even lead to permanent fistula or graft failure.
* With peritoneal dialysis, the main disadvantage is that it has to be carried out every day.
* Another upsetting matter with the peritoneal dialysis is that the catheter, almost permanently, hangs loose from the belly. Though it can be hidden under the clothes, the patient may feel uncomfortable.

Yet another disadvantage of peritoneal dialysis is that the patient has a tendency of developing peritonitis infection, along the line of the abdomen where the thin membrane of the catheter touches the abdomen. In such a case, after a few years of peritoneal dialysis, the patient has to switch to haemodialysis to avoid peritonitis. The dialysate fluid that is used for peritoneal dialysis reduces the protein level in the blood, leading to malnutrition and lack of energy. It also results in weight gain as a side effect of the dialysate fluid.

## Advantages of Hemofiltration

* Hemodialysis helps in treating heart failure while hemodialysis might worsen the condition sometimes.
* Hemofiltration can lower the rate of refractory hypertension to 1% and sometimes one might also be in a position to stop antihypertensive medicines.
* The incidence of hypotension and water and salt retention in patients undergoing hemofiltration is reduced to 5%.
* Hemofiltration, either continuous or intermittent, is actually an effective treatment of acute kidney failure.
* In case of hepatic coma, hemofiltration has shown better results as compared to hemodialysis; however, it is not as effective as blood perfusion or plasma exchange.

## Disadvantages of Hemofiltration

* Patient’s mobility is restricted in case of hemofiltration and the procedure requires a constant patient centred activity which hinders the resting and sleep times.
* The patient has to be on anticoagulant medicines except in cases where a patient has mechanical valve which regulates the effective running of pump.
* Many a times, fluid balance is open to various potential errors.

[**Dialyzable**](https://en.wiktionary.org/wiki/dialyzable) **substances (substances removable with dialysis) have these properties:**

* Low [molecular mass](https://en.wikipedia.org/wiki/Molecular_mass)
* High water solubility
* Low protein binding capacity
* Prolonged elimination (long [half-life](https://en.wikipedia.org/wiki/Half-life))
* Small volume of distribution

Substances include: [Ethylene glycol](https://en.wikipedia.org/wiki/Ethylene_glycol_poisoning), [Procainamide](https://en.wikipedia.org/wiki/Procainamide), [Methanol](https://en.wikipedia.org/wiki/Methanol), [Isopropyl alcohol](https://en.wikipedia.org/wiki/Isopropyl_alcohol), [Bromide](https://en.wikipedia.org/wiki/Potassium_bromide), [Sotalol](https://en.wikipedia.org/wiki/Sotalol), [Chloral hydrate](https://en.wikipedia.org/wiki/Chloral_hydrate), [Ethanol](https://en.wikipedia.org/wiki/Ethanol) and [Acetone](https://en.wikipedia.org/wiki/Acetone)