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Question One: Discuss the pathophysiological process involved in renal failure

 Acute kidney injury (AKI) occurs when there is a rapid decline in glomerular filtration rate, usually accompanied by impaired microcirculation, inflammation and/or tubular injury or necrosis and reduced renal blood flow. AKI is initiated by various clinical insults, including hypotensive shock, sepsis, surgery or the administration of nephrotoxic agents such as cisplatin and contrast agents (commonly used for medical imaging). Following mild kidney injury, an adaptive repair response might ensue, leading to kidney regeneration. However, with more severe injury, regeneration is incomplete and nephron mass can be replaced by scar tissue, leading to CKD. There are limited treatment options available for AKI, and its associated mortality remains high. AKI can be induced in rats by performing ischemia-reperfusion surgery or by administering toxins such as cisplatin. However, these single insults are unlikely to fully recapitulate the multiple injurious processes that have typically occurred in individuals with AKI.

CKD is an umbrella term for any renal disease that results in the progressive loss of kidney function over time. The kidney possesses only a limited capacity for regeneration, and repeated or sustained injury to the kidney results in maladaptive responses, including the deposition of excess extracellular matrix, particularly collagen, in the glomerulus and tubulointerstitium of the kidney. The pathological changes associated with CKD include glomerulosclerosis and tubulointerstitial fibrosis, which result in the loss of normal renal architecture, microvascular capillary rarefaction, hypoxia and tubular atrophy. These changes lead to the loss of renal filtrative capacity and ultimately to end-stage renal disease. Many rodent models mimic features of early CKD; however, only few exhibit features of end-stage renal disease (ESRD).

**Pathophysiology of Acute Kidney Injury (AKI)**

 This would be focusing on the phases of acute kidney injury due to acute tubular necrosis (ATN). As mentioned above, the term ATN correctly identifies the site of injury, though relatively few renal epithelial cells undergo frank necrosis. More commonly, sublethal changes in renal tubular epithelial cells are present and thus the term acute tubular injury may be more appropriate. Importantly, even sublethal changes can have a major impact on the decrement in GFR that is the hallmark of AKI.

 Clinically, ATN and the associated decrease in GFR can be divided into initiation, extension, maintenance, and recovery phases. These clinical phases directly relate to cellular events that occur during the injury and recovery process. Although a clear mechanistic explanation between tubular injury and a fall in GFR has remained elusive, afferent arteriole vasoconstriction in response to tubuloglomerular feedback, backleak of glomerular filtrate, and tubular obstruction have all been postulated as mechanisms for decreased GFR in ATN. All three of these mechanisms can be directly related to changes occurring in renal tubular epithelial cells. During the clinical phase known as maintenance, cells undergo repair, migration, apoptosis and proliferation in an attempt to reestablish and maintain cellular and tubule integrity. The GFR is stable albeit at a level determined by the severity of the initial event. This cellular repair and reorganization phase results in slowly improving cellular function and sets the stage for improvement in organ function. Blood flow returns toward normal and epithelial cells establish intracellular and intercellular homeostasis. During the recovery phase cellular differentiation continues, epithelial polarity is reestablished and normal cellular and organ function return. Thus, renal function can be directly related to the cycle of cell injury and recovery and this cell response to injury will be covered to greater extent later in this chapter.

**Pathophysiology of Chronic Kidney Disease (CKD)**

 When discussing the pathophysiology of CKD, renal structural and physiological characteristics, as well as the principles of renal tissue injury and repair should be taken into consideration.

 Firstly, the rate of renal blood flow of approximately 400 ml/100g of tissue per minute is much greater than that observed in other well perfused vascular beds such as heart, liver and brain. As a consequence, renal tissue might be exposed to a significant quantity of any potentially harmful circulating agents or substances. Secondly, glomerular filtration is dependent on rather high intra- and transglomerular pressure (even under physiologic conditions), rendering the glomerular capillaries vulnerable to hemodynamic injury, in contrast to other capillary beds. In line with this, Brenner and coworkers identified glomerular hypertension and hyperfiltration as major contributors to the progression of chronic renal disease. Thirdly, glomerular filtration membrane has negatively charged molecules which serve as a barrier retarding anionic macromolecules. With disruption in this electrostatic barrier, as is the case in many forms of glomerular injury, plasma protein gains access to the glomerular filtrate. Fourthly, the sequential organization of nephron’s microvasculature (glomerular convolute and the peritubular capillary network) and the downstream position of the tubuli with respect to glomeruli, not only maintains the glomerulo-tubular balance but also facilitates the spreading of glomerular injury to tubulointerstitial compartment in disease, exposing tubular epithelial cells to abnormal ultrafiltrate. As peritubular vasculature underlies glomerular circulation, some mediators of glomerular inflammatory reaction may overflow into the peritubular circulation contributing to the interstitial inflammatory reaction frequently recorded in glomerular disease. Moreover, any decrease in preglomerular or glomerular perfusion leads to decrease in peritubular blood flow, which, depending on the degree of hypoxia, entails tubulointerstitial injury and tissue remodeling. Thus, the concept of the nephron as a functional unit applies not only to renal physiology, but also to the pathophysiology of renal diseases. In the fifth place, the glomerulus itself should also be regarded as a functional unit with each of its individual constituents, i.e. endothothelial, mesangial, visceral and parietal epithelial cells - podocytes, and their extracellular matrix representing an integral part of the normal function. Damage to one will in part affect the other through different mechanisms, direct cell-cell connections (e.g., gap junctions), soluble mediators such as chemokines, cytokines, growth factors, and changes in matrix and basement membrane composition.

The main causes of renal injury are based on immunologic reactions (initiated by immune complexes or immune cells), tissue hypoxia and ischaemia, exogenic agents like drugs, endogenous substances like glucose or paraproteins and others, and genetic defects. Irrespective of the underlying cause glomerulosclerosis and tubulointerstitial fibrosis are common to CKD. An overview of the pathophysiology of CKD should give special consideration to mechanisms of glomerular, tubular and vascular injury.

Mechanism of Glomerular Impairment

 **Hereditary defects** account for a minority of glomerular disease. A prototype of an inherited glomerular disease is the Alport’s syndrome or hereditary nephritis, usually transmitted as an X-linked dominant trait although autosomal dominant and recessive forms have been reported as well. In its classical X-linked form there is a mutation in the COL4A5 gene that encodes the α5 chain of type IV collagen located on the X chromosome. As a consequence, GBM is irregular with longitudinal layering, splitting or thickening, and the patient develops progressive glomerulosclerosis and renal failure. Other types of inherited glomerular disease are thin membrane syndrome, nail-patella syndrome, partial lipodystrophy, and familial lecithin-cholesterol acyltranferase deficiency.

Most **acquired glomerular disease** is triggered by immune mediated injury, metabolic and mechanical stress. From a pathological and pathogenetic point of view glomerular diseases can broadly be divided into three groups:

* nonproliferative (without cell proliferation) glomerular diseases without glomerular inflammation and without deposition of immunoglobulins (minimal change disease, idiopathic focal, and segmental glomerulosclerosis [FSGS]) or with deposition of immunoglobulins, but without glomerular inflammation, most likely because of subepithelial localization of immunoglobulins (e.g., membranous nephropathy)
* proliferative glomerular diseases with deposition of immunoglobulins leading to increased cellularity (proliferative glomerulonephrites, e.g., lupus nephritis, IgA nephropathy, anti-GBM, postinfectious GN), or with severe glomerular injury and inflammation, but without deposition of immunoglobulins (e.g., pauci-immune glomerulonephritis).
* heterogenous group of glomerular diseases in systemic diseases like glomerular disease in diabetes, amyloidosis and paraproteinemia.

The podocyte seems to occupy the central role in the pathogenesis of the first group of glomerular diseases as well as in diabetic nephropathy. This topic will be elaborated separately.

In the second group of glomerular diseases with cell proliferation, either deposition of immune complexes from the circulation or formed in situ lead to activation of intrinsic renal cells (via Fc receptors and complement cascade activation), resulting in inflammatory cell recruitment. Futhermore, severe glomerular injury and inflammation can occur without discernible immune complexes in the glomeruli, as in ANCA (antineutrophil cytoplasmic antibodies) positive glomerulonephritis. The offending etiologic agents are mainly unknown, with the rare exception of ß hemolytic streptococci in poststreptococcal glomerulonephritis, and hepatitis C virus in type 1 cryoglobulinemic membranoproliferative glomerulonephritis. Most antibody-mediated glomerulonephrites are initiated by the reactivity of circulatory antibodies and glomerular antigens, whereby antigens might be the components of normal glomerular parenchyma as in anti-GBM antibody disease (Goodpasture’ syndrome), or the antigens are planted from the circulation within the glomeruli as in poststreptococcal glomerulonephritis (the in situ formation of immune complexes). The immune complexes formed in systemic circulation can be deposited and trapped in glomeruli (in cryoglobulinemic glomerulonephritis). Additional mechanism of antibody-mediated glomerular injury, but without immune complexes in the glomeruli, is represented by circulating autoantibody against neutrophil cytoplasmatic antigens (ANCA). Reactive oxygen species, protease, cytokines, chemokines and other inflammatory mediators originating from recruited and resident inflammatory cells play the key pathogenic roles.

Immune complexes can be deposited in the mesangium (as in IgA nephropathy, Henoch Schonlein purpura, lupus nephritis class II, postinfectious GN), in subendothelial (lupus nephritis class III, membranoproliferative GN), or subepithelial area (idiopatic membranous nephropathy or class V lupus nephritis, postinfectious GN), or along GBM (as in anti-GBM disease). The site of antibody deposition defines the response to injury and clinicopathological presentation. A strong inflammatory reaction occurs only when circulating inflammatory cells can be activated by contact with immunoglobulins or soluble products released by intrinsic renal cells. Thereby, the deposition of antibodies in the subendothelial area, mesangium or membrane elicits a nephritic response, as the position of immune complexes enables activation of endothelial or mesangial cells which release soluble products and rapidly recruit leukocytes and platelets from the blood. Leukocyte-derived products, such as cytokines, lysosomal enzymes, reactive oxygen species, complement components and other, damage the vascular wall and filtration barrier and attract more leukocytes from the circulation. The subepithelial position of immune complexes (as in membranous nephropathy) leads to nephrotic response, as GBM precludes the contact between immune complexes and inflammatory cells from the circulation. Another reason for this kind of response is that large fluid flow from vascular lumen to Bowman’s space does not permit inflammatory mediators formed in the subepithelium to diffuse retrogradely from epithelial to the endothelial layer and vascular lumen.

Tissue injury after IC deposition is mediated through complement activation resulting in the formation of C5-9 membrane attack complex which appears to be the major effector of glomerular injury through release of chemotactic C5a and C3a. C5-9-activated cells release chemokines and oxidant proteases, and upregulate adhesion molecules.

T-cells also act as mediators of glomerular injury and as modulators of the production of nephrite/ogenic antibodies, especially in pauci-immune GN. They interact through their surface receptor/CD3 complex with antigens presented in the clefts of MHC molecules of endothelial, mesangial and epithelial glomerular cells. This process is facilitated by the cell-cell adhesion and costimulatory molecules. Once activated, T-cells release cytokines and other mediators of inflammatory reaction, cytotoxicity and fibrogenesis. Soluble factors from T cells have been implicated in the pathogenesis of minimal change disease and focal and segmental glomerulosclerosis, but their identity has yet to be determined.

TGF-ß and connective tissue growth factor (CTGF) are important in glomerular fibrogenesis, as they stimulate glomerular cells to produce extracellular matrix (ECM), a key event in the progression of kidney disease, inhibiting the synthesis of tissue protease, mostly matrix metalloproteinase, which otherwise degradates matrix proteins.

Glomerular inflammation can either completely recover or resolve with a variable degree of fibrosis. The resolution process requires cessation of further antibodies production and immune complex formation, degradation and removal of deposited and circulating immune complexes, cessation of recruitment and clearing of inflammatory cells, dispersing of inflammatory mediators, normalization of endothelial adhesiveness, permeability and vascular tone, and clearance of proliferating resident glomerular cells.

**Nonimmunologic glomerular injury**. Hemodynamic, metabolic and toxic injuries can induce glomerular impairment alone or in conjunction with immunological processes.

**Systemic hypertension** translated to glomeruli and glomerular hypertension resulting from local changes in glomerular hemodynamics may cause glomerular injury. The kidney is normally protected from systemic hypertension by autoregulation which can be overwhelmed by high blood pressure, meaning that systemic hypertension is translated directly to glomerular filtration barrier causing glomerular injury. Chronic hypertension leads to arteriolar vasoconstriction and sclerosis with consequent secondary sclerosis and glomerular and tubulointerstitial atrophy. Different growth factors like angiotensin II, EGF, PDGF, and CSGF, TGF-ß cytokine, activation of stretch-activated ion channels and early response gene are involved in coupling high blood pressure to myointimal proliferation and vessel wall sclerosis.

**Glomerular hypertension** is normally an adaptive mechanism in remaining nephrons to increased workload resulting from nephron loss, whatever the cause. This sustained intraglomerular hypertension increases mesangial matrix production and leads to glomerulosclerosis by ECM accumulation. The process is mediated by TGF-ß in the first place, with a contribution of angiotensin II, PDGF, CSGF and endothelins.

Systemic and glomerular hypertension are not necessarily associated; as glomerular hypertension may precede systemic hypertension in glomerular disease.

**Metabolic injury** as that occurring in diabetes is discussed separately.

Mechanism of Tubulointerstitial Impairment

 Regardless of the etiology, chronic kidney disease is characterized by renal fibrosis - glomerulosclerosis and tubulointerstitial fibrosis. The impairment of the tubulointerstitium (tubulointerstitial fibrosis and tubular atrophy) is at least as important as that of the glomeruli (glomerulosclerosis). There is a common consensus that the severity of tubulointerstitial injury correlates closely (and better than glomerular injury) with long-term impairment of renal function. This is not surprising, considering that tubules and interstitium occupy more than 90% of the kidney volume. As very recently summarized by Fine and Norman, tubulointerstitial fibrosis encompasses a number of characteristic features including an inflammatory cell infiltrate which results from both activation of resident inflammatory cells and recruitment of circulating inflammatory cells; an increase in interstitial fibroblasts due to increased proliferation and decreased apoptosis of resident interstitial cells, as well as recruitment of cells to the tubulointerstitium; the appearance of myofibroblasts expressing the cytoskeletal protein α-smooth muscle actin, which arise by differentiation of resident interstitial fibroblasts and infiltrating cells and via transdifferentiation; accumulation of extracellular matrix (ECM) as the net result of increased synthesis of ECM components and decreased ECM degradation, mostly by specific metalloproteinases that are under the control of specific inhibitors; tubular atrophy as a consequence of apoptosis and epithelial–mesenchymal transdifferentiation (EMT); and rarefaction of peritubular capillaries. The development of fibrosis is associated with an increase in the expression of proinflammatory, vasoconstrictive and profibrotic factors.

**Renal fibrogenesis.** The initial insult leads to inflammatory response with the generation and local release of soluble mediators, an increase in local vascular permeability, activation of endothelial cells, extravasation of leukocytes along the endothelium, subsequent secretion of various mediators by infiltrating leukocytes and tubulointerstitial cells, and activation of profibrotic cells. As a consequence a vicious cycle of cell stress is initiated generating profibrotic and proinflammatory mediators, leukocyte infiltration and fibrosis.

**Induction and development of the inflammatory response.** Leukocytes migrate from the circulation through postcapillary venules and peritubular capillaries into the interstitium following gradients of chemoattractants and chemokines. All tubular cells can generate soluble mediators when stimulated by hypoxia, ischaemia, infectious agents, drugs, and endogenous toxins like lipids, high glucose, paraproteins or genetic factors as in cystic renal diseases. Glomerular disease is usually associated with a variable degree of tubulointerstitial injury and inflammation because tubular cells are exposed to proteins which are normally not filtered. The factors involved in the formation of tubulointerstitial inflammatory infiltrates are: proteinuria, immune deposits, chemokines, cytokines, calcium phosphate, metabolic acidosis, uric acid, lipids, hypoxia and reactive oxygen species.

**The inflammatory infiltrate.** Infiltrating inflammatory mononuclear cells are composed of monocytes/macrophages and lymphocytes, particularly T lymphocytes. CD4-positive T cells and CD3 T cells carrying chemokine receptors CCR5 and CxCR3 are closely associated with renal function. This inflammatory cells secrete profibrotic cytokines.

**Profibrotic cytokines.** Infiltrating inflammatory cells and resident interstitial macrophages release cytokines which stimulate fibroblasts to become myofibroblasts. The most important profibrotic factors involved in renal fibrogenesis are angiotensin II, TGF-ß1, CTGF, PDGF, FGF-2 (fibroblast growth factor -2), EGF, ET-1, tryptase mast cell. Angiotensin II induces TGF- ß synthesis in tubular epithelial cells and fibroblast. AII induces hypertrophy in tubular epithelial cells together with connective tissue growth factor (CTGF), independently of TGF- ß. It is currently assumed that TGF-ß1 is the key cytokine in renal fibrogenesis.

**Fibroblast proliferation and activation.** Fibroblasts proliferate and become active following infiltration of inflammatory cells into the tubulointerstitial space. To express α-smooth muscle actin, the fibroblasts must be activated by cytokines (mostly derived from infiltrating macrophages), change their phenotype and transit from fibroblasts to myofibroblasts. The important mitogens for renal fibroblast are PDGF, bFGF-2 and others, but no single profibrotic „master cytokine„ has been identified so far.

**Epithelial-mesenchymal transition.** Phenotypic conversion of epithelial cells into mesenchymal cells is known as the epithelial-mesenchymal transition. Evidence for EMT in human disease comes from utilization of mesenchymal marker proteins such as vimentin or S100A4, the human analogue of fibroblast-specific protein-1. The expression of these mesenchymal marker proteins in tubular epithelial cells was well correlated with renal function in IgA nephropathy, lupus nephritis and chronic allograft failure. TGF-ß1 is thought to be the most potent inducer of EMT, which may be induced by a variety of factors other than cytokines.

It has been shown lately that hypoxia-inducible factor-1 (HIF-1), considered to be master regulator of the adaptive response controlling expression of hundreds of genes, also stimulates EMT, which explains why hypoxia results in fibrosis and progressive renal failure. Hypoxia as a consequence of peritubular capillaries loss has been frequently observed in chronic kidney disease. It alters proximal tubular epithelial (PTE) matrix metabolism, promoting ECM accumulation, with a switch to production of interstitial collagen and suppression of matrix degradation. Exposure of PTE to hypoxia induces transition to myofibroblastic phenotype, whereas more prolonged exposure leads to mitochondrial injury and apoptosis consistent with the loss of tubular cells in vivo. In PTE, hypoxia also induces expression of fibrogenic factors. Reports from biopsies carried out in patients with diabetic nephropathy, IgA nephropathy, polycistic kidney disease, and chronic allograft nephropathy have confirmed increased expression of HIF, supporting the hypothesis that hypoxia is an important contributory factor in the pathogenesis of CKD in humans. Furthermore, changes in HIF expression correlate with the extent of tubulointerstitial injury.

**Proteinuria and tubulointerstitial damage.** Proteinuria can damage tubulointerstitium through multiple pathways including direct tubular toxicity, changes in tubular epithelial metabolism, induced cytokine and chemokine synthesis, and increased expression of adhesion molecules. (Abbate). Excess protein reabsorption in proximal tubule may exceed lysosomal processing capacity, lead to lysosomal rupture and result in direct tubular toxicity. There is a great variability in tubular toxicity induced by proteinuria. For example, patients with nephrotic range proteinuria exclusively consisting of albuminuria as in minimal change disease, rarely exhibit tubulointerstitial damage. Different experimental models have demonstrated generation of chemotactic factor for macrophages, secretion of chemokines such as monocyte chemoattractant protein-1 and RANTES, and expression of fractalkine (a chemokine promoting mononuclear cell adhesion). In addition to inducing chemokine secretion proteinuria may induce secretion of TGF-ß as well as that of adhesion intercellular adhesion molecule-1 and vascular adhesion molecule-1. In a study reporting on results from 119 renal biopsies the formation of interstitial infiltrates and the degree of tubulointerstitial fibrosis was associated with the level of expression of adhesion molecules.

Question Two: With the aid of suitable diagrams, discuss the types of dialysis you know

 Dialysis is a minimally invasive blood purifying treatment (removing excess water, solutes, and toxins) given when kidney function is not optimum. This is referred to as 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 Hemodialysis. 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 fibers 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 fibers. A negative pressure is used to remove the water from the blood to the dialysate. The usual span for the hemodialysis process is 4 hours. Typically, a person has to undergo three hemodialysis sessions per week. However, depending on the condition, requirement or disease, hemodialysis 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 hemodialysis suitable for the patient. Usually the procedure is done at a doctor’s office or at a hospital or at a dialysis center. Nowadays, with advanced technology, hemodialysis is also being offered at the patient’s home. Those, who are in need for a long-term dialysis, are recommended the at-home hemodialysis treatment.

### PERITONEAL DIALYSIS:

 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 hemodialysis 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 fiber, a soluble fiber, 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 feces.

**Advantages** of Hemodialysis and Peritoneal Dialysis

* The main advantage of hemodialysis 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 Hemodialysis machine, which is huge.

Disadvantages of Hemodialysis and Peritoneal Dialysis

* Since, hemodialysis 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 hemodialysis 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 narrowing, called stenosis, develop in your blood vessels. Those narrowing cause poor flow, which affects the ability to efficiently dialyze the blood. The narrowing 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 hemodialysis 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 centered 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 **substances (substances removable with dialysis) have these properties:**

* Low molecular mass
* High water solubility
* Low protein binding capacity
* Prolonged elimination (long half-life)
* Small volume of distribution

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