Acute Renal Failure

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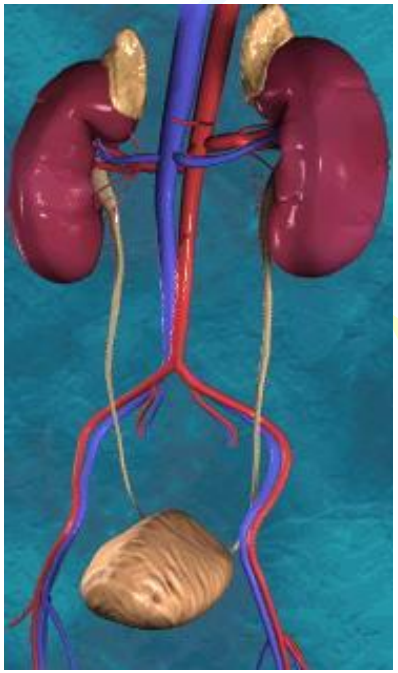


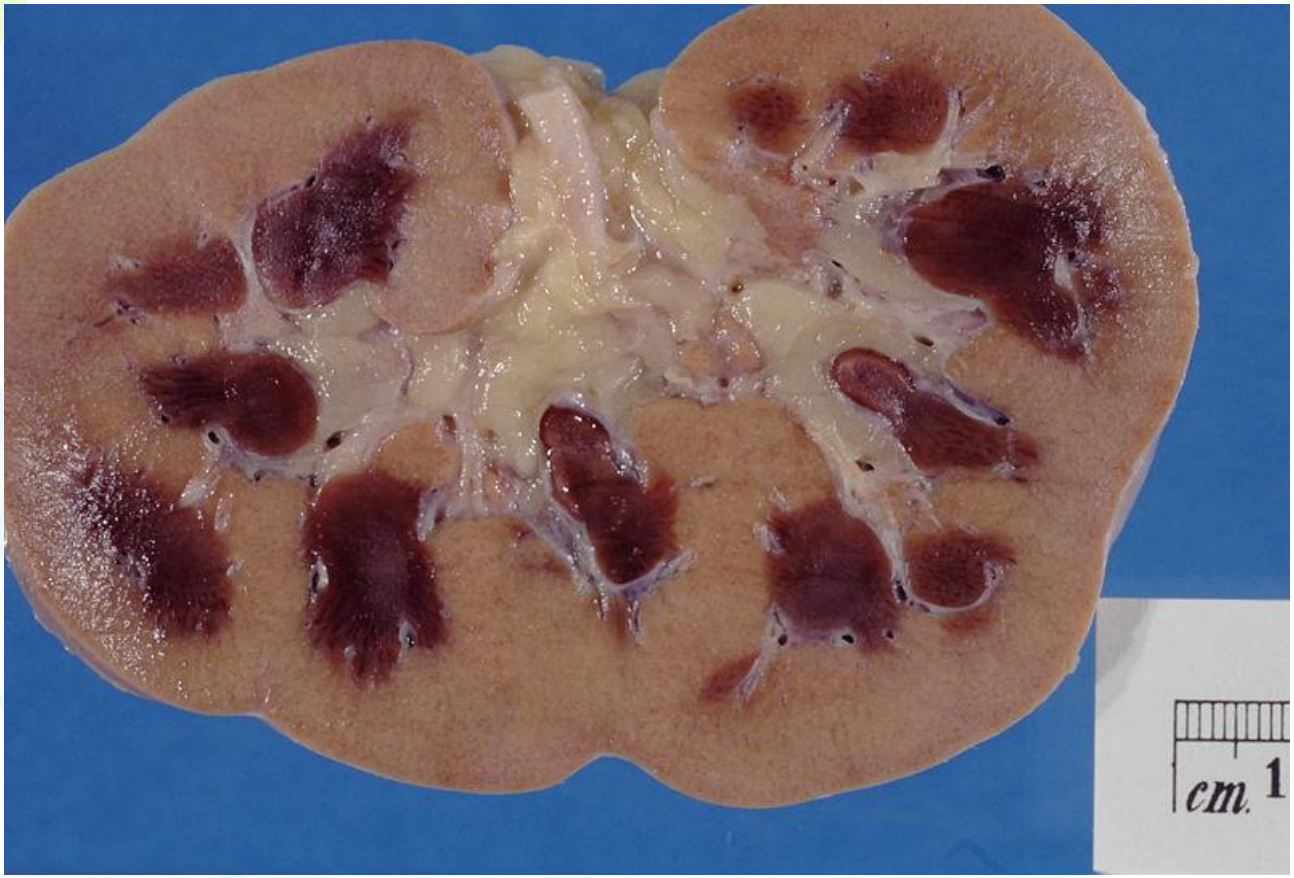


Fig:Kidney showing marked pallor of the cortex (Kidney of patient died with acute renal failure)

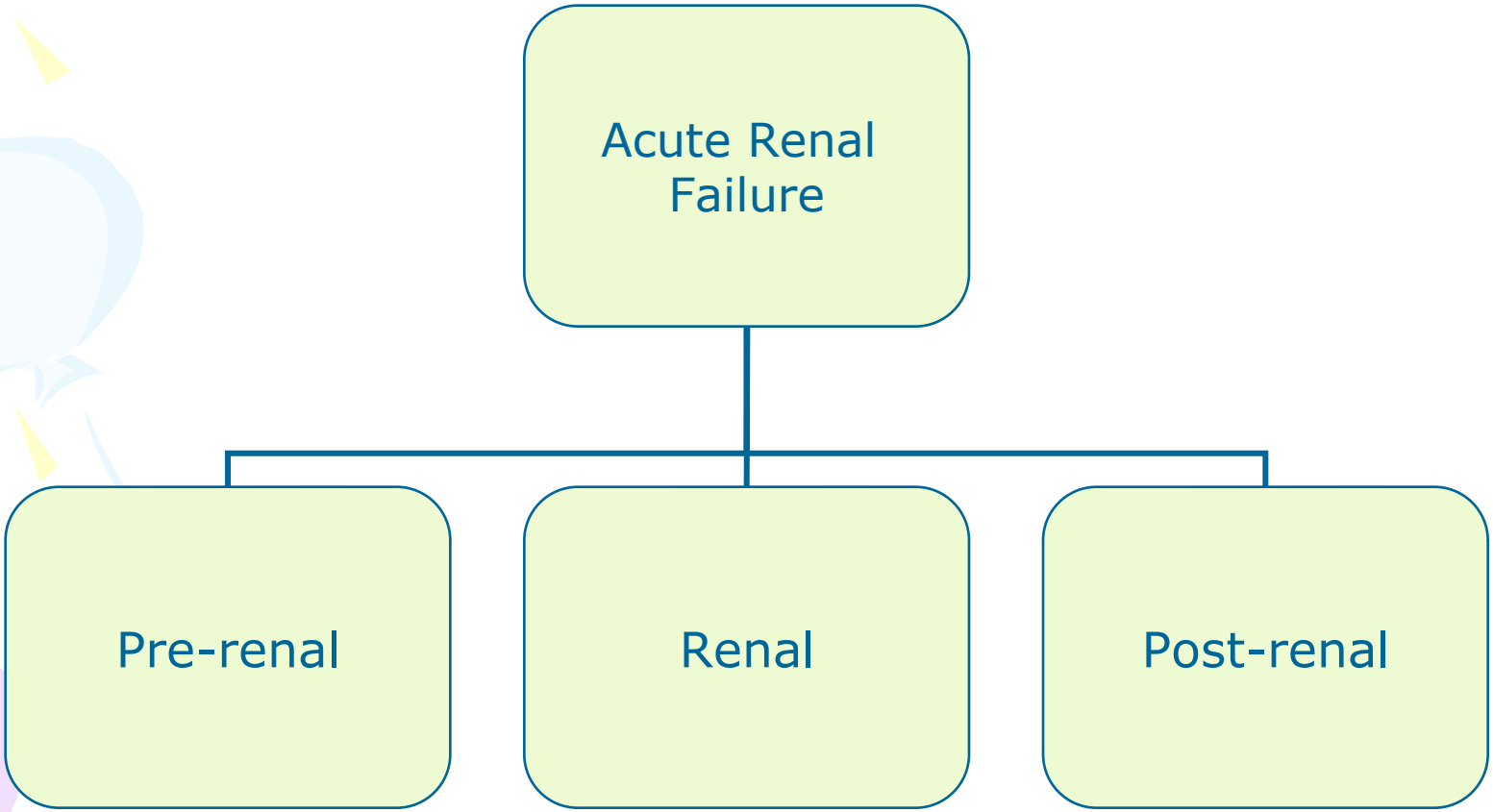
Introduction

- Acute renal failure (ARF), also known as acute kidney failure or acute kidney injury, is a rapid loss of renal function due to damage to the kidneys, resulting in retention of nitrogenous (urea and creatinine) and non-nitrogenous waste products that are normally excreted by the kidney.
- It can be characterised by oliguria or anuria (decrease or cessation of urine production), although *nonoliguric ARF* may occur.
- It is a serious disease and treated as a medical emergency.

Epidemiology

- ARF is a common condition in the general population, with an annual incidence of approximately 200 cases per million population per year.
- The incidence rate is higher in hospitalized patients.
- ARF develops in 2-25% of patients in intensive care units.
- More common in advanced age.
- Men and women are affected equally.

Types of ARF



Etiology

❖Pre-renal (causes in the blood supply):

- hypovolemia (decreased blood volume), usually from shock or dehydration and fluid loss or excessive diuretics use.
- hepatorenal syndrome in which renal perfusion is compromised in liver failure
- vascular problems, such as atheroembolic disease and renal vein thrombosis (which can occur as a complication of the nephrotic syndrome)
- infection usually sepsis, systemic inflammation due to infection

- Renal (damage to the kidney itself):
  - toxins or medication (e.g. some NSAIDs, aminoglycoside antibiotics, iodinated contrast, lithium, phosphate nephropathy due to bowel preparation for colonoscopy with sodium phosphates)
  - rhabdomyolysis (breakdown of muscle tissue) - the resultant release of myoglobin in the blood affects the kidney; it can be caused by injury (especially crush injury and extensive blunt trauma), statins, stimulants and some other drugs
  - hemolysis (breakdown of red blood cells) - the hemoglobin damages the tubules; it may be caused by various conditions such as sickle-cell disease, and lupus erythematosus
  - multiple myeloma, either due to hypercalcemia or "cast nephropathy" (multiple myeloma can also cause chronic renal failure by a different mechanism)
  - acute glomerulonephritis which may be due to a variety of causes, such as anti glomerular basement membrane disease/Goodpasture's syndrome, Wegener's granulomatosis or acute lupus nephritis with systemic lupus erythematosus

- Post-renal (obstructive causes in the urinary tract) due to:
  - medication interfering with normal bladder emptying (e.g. anticholinergics).
  - benign prostatic hypertrophy or prostate cancer.
  - kidney stones.
  - due to abdominal malignancy (e.g. ovarian cancer, colorectal cancer).
  - obstructed urinary catheter.

Signs & symptoms

Symptoms

- Outpatient:
  - Change in urinary habits, weight gain, or flank pain
- Inpatient:
  - Typically ARF is noticed by clinicians before it is noticed by the patient

Signs

- Patient may have edema
- Urine may be colored or foamy
- Vital signs may indicate orthostatic hypotension in volume depleted patients
- Urine and blood chemistries may determine prerenal cause
- Serum creatinine >1 mg/dL
- Urine microscopy may reveal casts, WBCs, RBCs, and eosinophils

Laboratory Test	Prerenal Azotemia	Acute Intrinsic Renal Failure	Postrenal Obstruction
Urine sediment	Normal	Casts, cellular debris	Cellular debris
Urinary RBC	None	2 – 4+	Variable
Urinary WBC	None	2 – 4+	1+
Urine sodium	<20	>40	>40
FE_{Na} (%)	<1	>2	Variable
Urine/serum osmolality	>1.5	<1.3	<1.5
Urine/serum creatinine	>40:1	<20:1	<20:1
BUN/S_{Cr}	>20	15	15

Table. Laboratory parameters for differential diagnosis of ARF

Pharmacotherapy

Goals of therapy

1. To prevent ARF, but if ARF develops,

2. Avoid or minimize further renal insults that would delay recovery,

3. To provide supportive measures until kidney function returns.

Prevention of ARF

- Infusions of 0.9% NaCl prior to radiocontrast dye infusion is helpful in preventing ARF.
- Hemofiltration provided prior to and 24 hours after dye administration significantly reduces mortality rates and a reduced need for dialysis.
- The nephrotoxic potential of amphotericin B deoxycholate can be reduced significantly by slowing the infusion rate from a standard 4-hour infusion to a slower 24-hour infusion of the same dose.

Loop diuretics

- Loop diuretics in addition to producing diuresis, reduce renal tubular cell metabolic demands and increase renal blood flow stimulating the release of renal prostaglandins.
- Diuretic therapy should only be initiated after the circulating volume has been restored (if not diuresis produce might produce a negative fluid balance and precipitate or exacerbate a prerenal state.
- Dose: 1-2 g of furosemide in 24 hrs by continuous i.v infusion at a rate of 4 mg/min.

Mannitol

- The tubular debris causes mechanical intrarenal obstruction and the use of an osmotic diuretic will wash it out.
- A dose of 0.5-1.0 g/kg as a 10-20% infusion is used.

Dopamine

- Low doses of dopamine (≤2 μg/kg per minute) increase renal blood flow and might be expected to increase GFR.
- Theoretically, this might be considered beneficial, as an enhanced GFR might flush nephrotoxins from the tubules, minimizing their toxicity.
- But controlled studies concluded that low-dose dopamine does not prevent ARF and its use could not be justified.
- In spite of that, low-dose dopamine continues to be commonly used for the prevention of ARF.

Fenoldopam

- Fenoldopam is a selective dopamine-1 receptor agonist that has been investigated for its ability to prevent radiocontrast dye nephropathy.
- A large, multicenter, randomized, placebo-controlled trial of fenoldopam use to prevent radiocontrast dye nephropathy in patients with chronic kidney disease (CKD) found that fenoldopam provided no benefit!

Acetylcysteine

- Pre-treatment with oral acetylcysteine, 600 mg twice daily on the day before and the day of radiocontrast dye administration has been documented to lower the rate of ARF in patients with pre-existing CKD.
- The mechanism for acetylcysteine's ability to reduce the incidence of radiocontrast dye nephrotoxicity is not fully elucidated, but likely is due to its antioxidant effects.
- Acetylcysteine should be given to all patients at risk for radiocontrast dye nephrotoxicity.

Intervention	Evidence for Prevention of Nephrotoxicity	Situations in Which Intervention Documented to be Effective
Hydration (sodium loading)	Y	Prior to amphotericin or contrast dye administration; tumor lysis syndrome prevention
Mannitol	N	
Loop diuretics	N	
Dopamine	N	
Calcium channel blockers	+/−	Recipient should receive drug prior to transplantation and when kidney is stored in solution containing drug. Not useful for preventing contrast dye nephropathy.
Theophylline	Y	Prior to contrast dye administration
Acetylcysteine	Y	Prior to contrast dye administration
Fenoldopam	N	
Insulin (to maintain serum glucose of 80–110 mg/dL)	Y	Critically ill patients

Y, some evidence exists for benefit; +/−, evidence equivocal; N, evidence suggests no benefit.

Treatment of established ARF

- Renal replacement therapies (RRT) are the most common nonpharmacologic treatment that patients with ARF receive.
- Renal replacement therapies come in two different forms, intermittent therapies like hemodialysis, and continuous RRTs like continuous hemofiltration or peritoneal dialysis.

Hemodialysis

- In hemodialysis, blood is heparinized and diverted of a large central venous cannula line and actively pumped through the lumen of an artificial kidney (dialyser) returning to the patient by a venous line.
- The dialyser consists of a cartridge comprised of either a bundle hollow tubes or a series of parallel flat plates made of a synthetic semi-permeable membrane.
- Hemodialysis involves diffusion of solutes across a semi-permeable membrane.
- Dialysis fluid is perfused around the membrane in a countercurrent to the flow of blood in order to maximize diffusion gradients.
- Hemodialysis can be performed in either intermittent or continuous schedules.

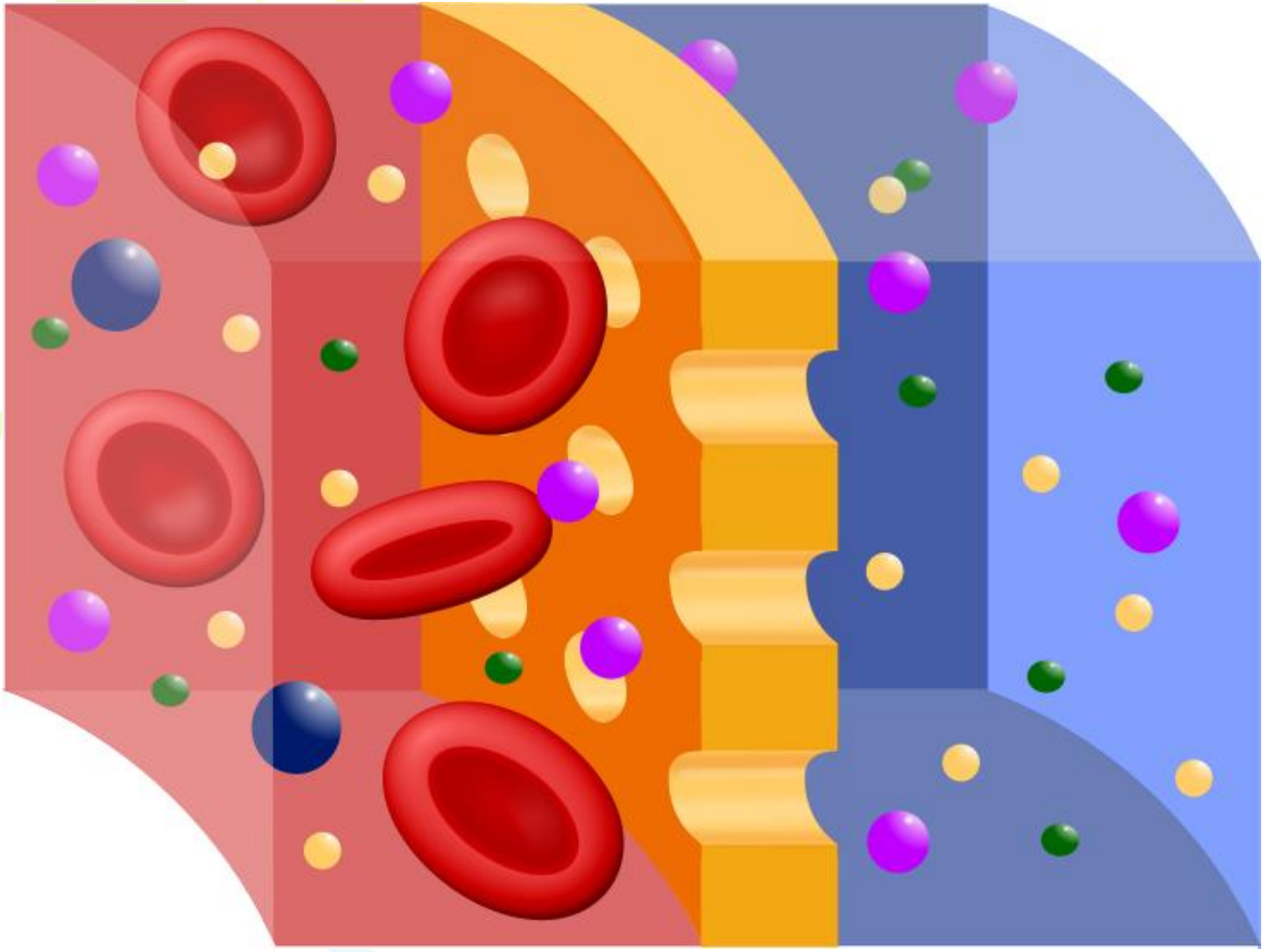
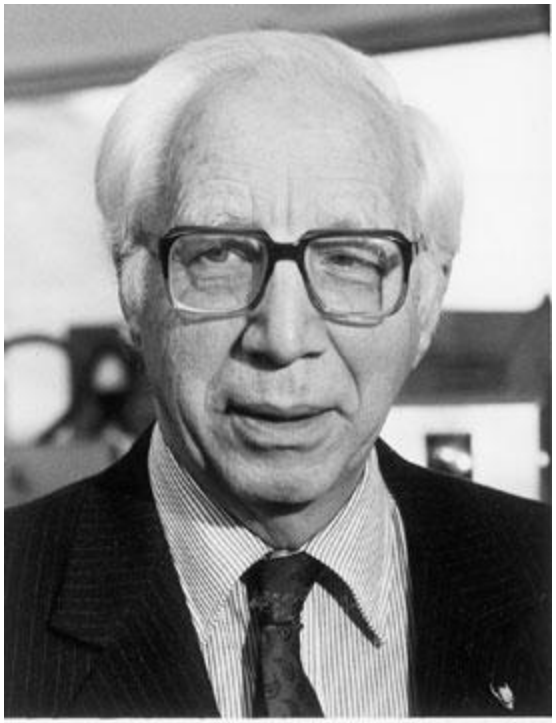


Fig: Semi permeable membrane



Dr. Willem Kolff

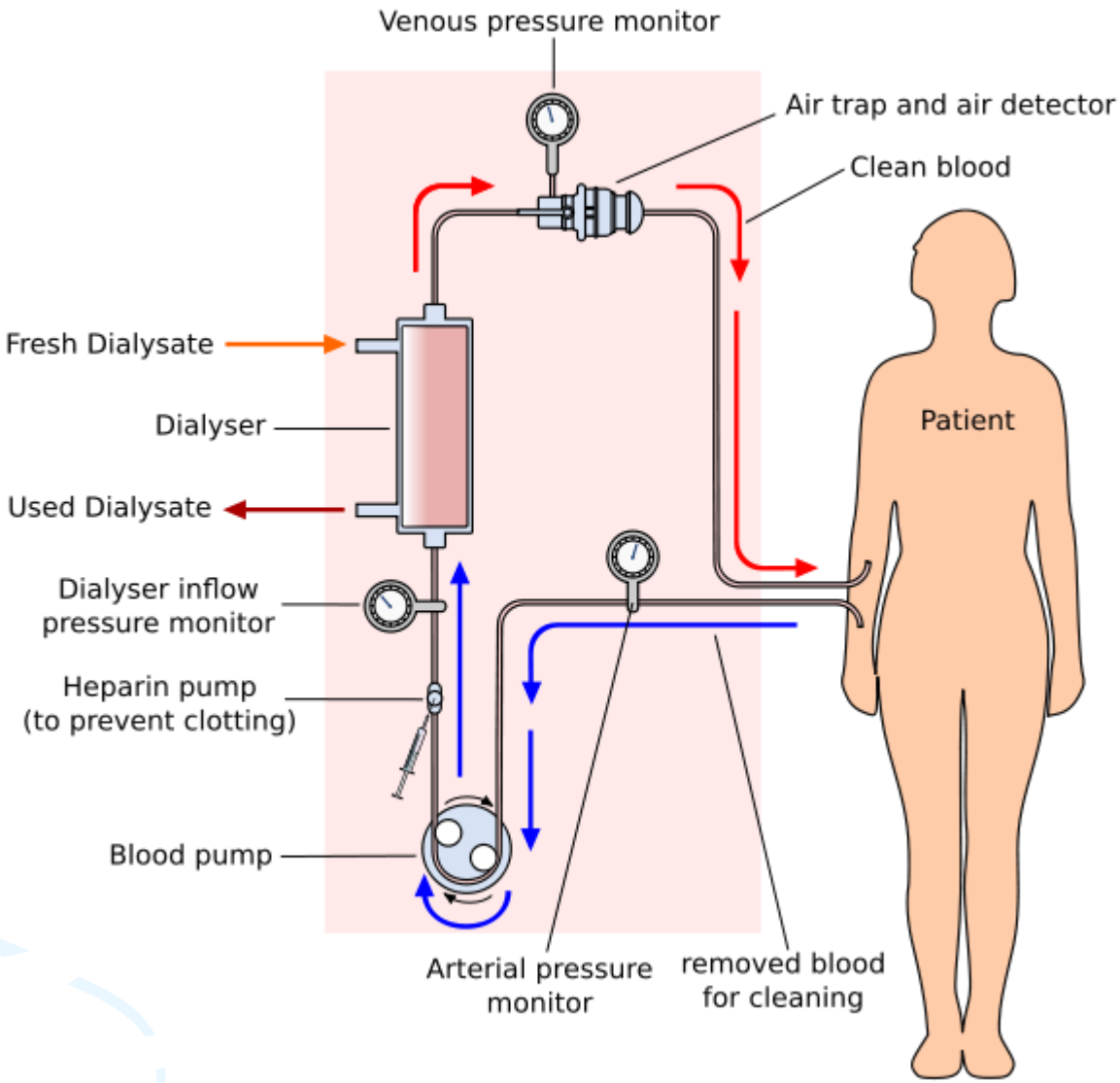
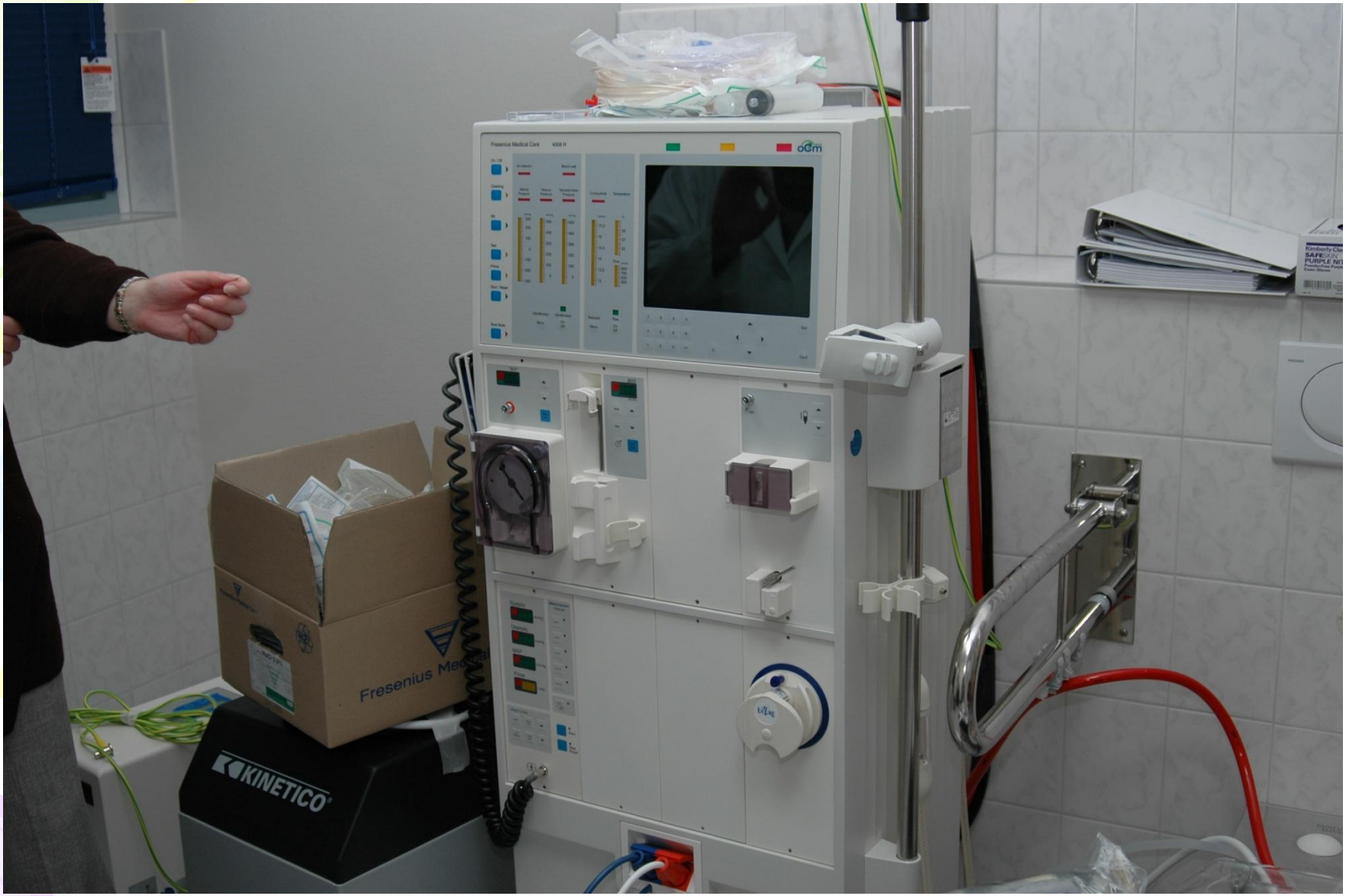


Fig: Hemodialysis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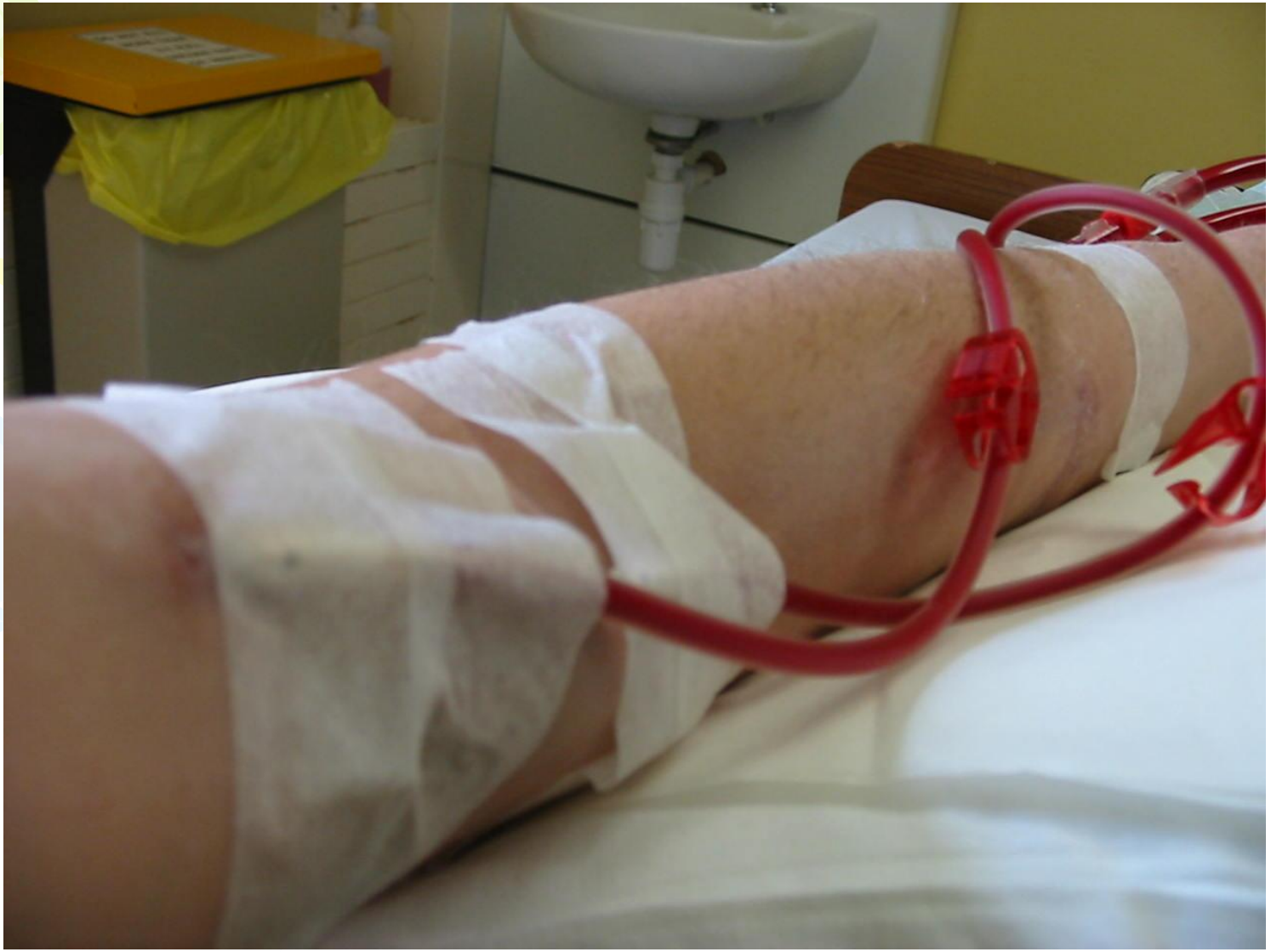
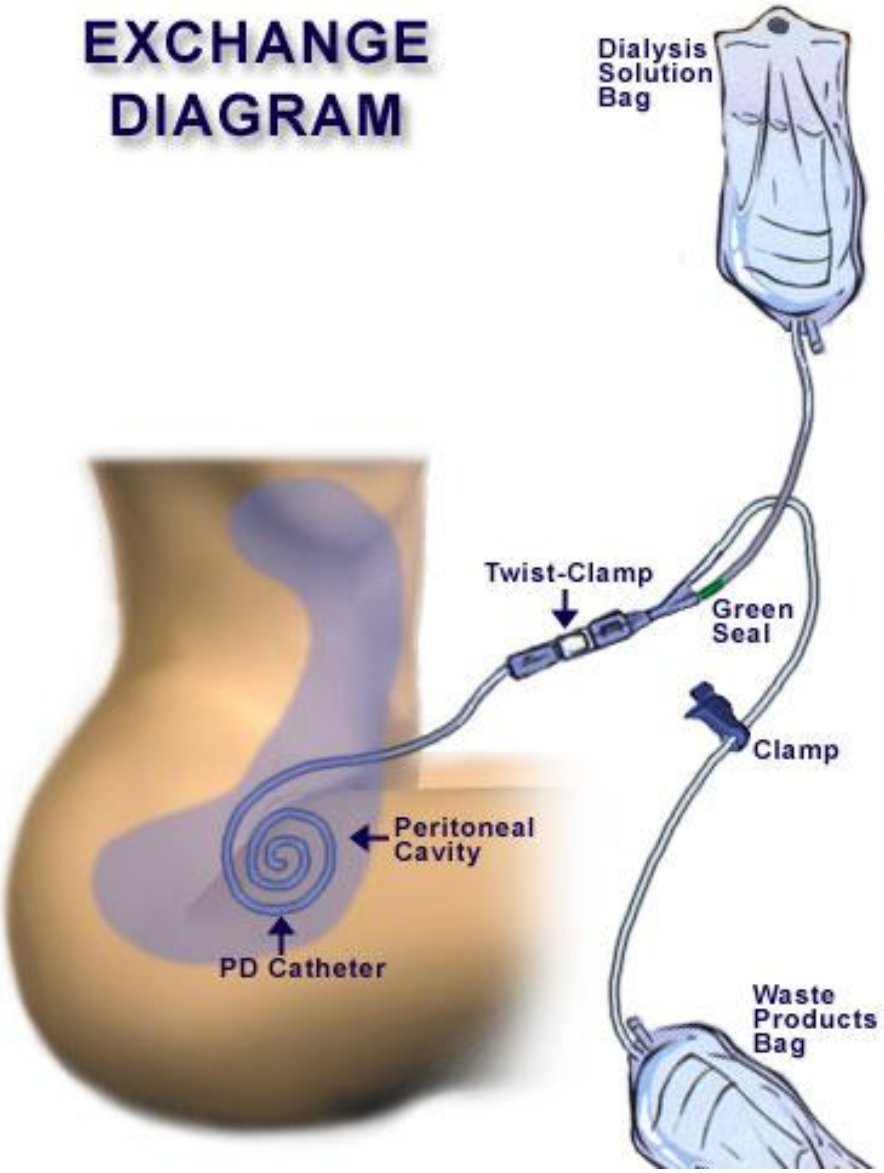


Peritoneal dialysis

- Abdominal cavity, which is covered by a thin membrane, containing many small blood vessels. This membrane, called the peritoneum, is like a big bag that contains much of the intestines, helping to keep them in place.
- The waste products move from the blood into the dialysis fluid; means that the peritoneum works as a dialysis filter.
- A semi-rigid catheter is inserted into the abdominal cavity.
- Warmed sterile peritoneal dialysis fluid is instilled into the abdomen, left for a period of about 30 minutes and then drained into a drain bag.

EXCHANGE DIAGRAM



Hemofiltration

- In hemofiltration hydrostatic pressure of the blood drives water and solutes across the filter membrane from the blood compartment to the filtrate compartment, from which it is drained.
- Solute clearance occurs by convection rather than by diffusion.
- Dialysis fluid is not used.
- An isotonic replacement fluid is added to the blood to replace fluid volume and electrolytes.

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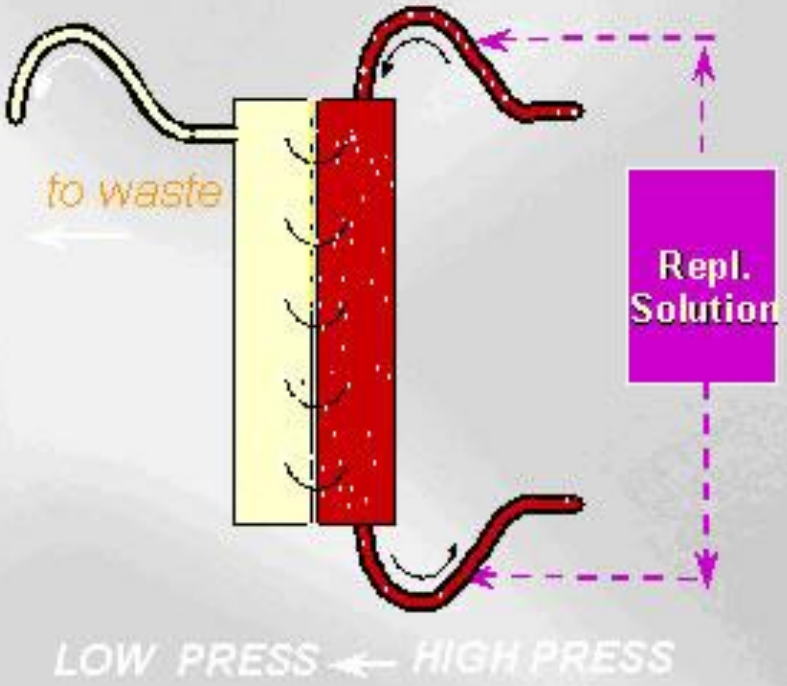
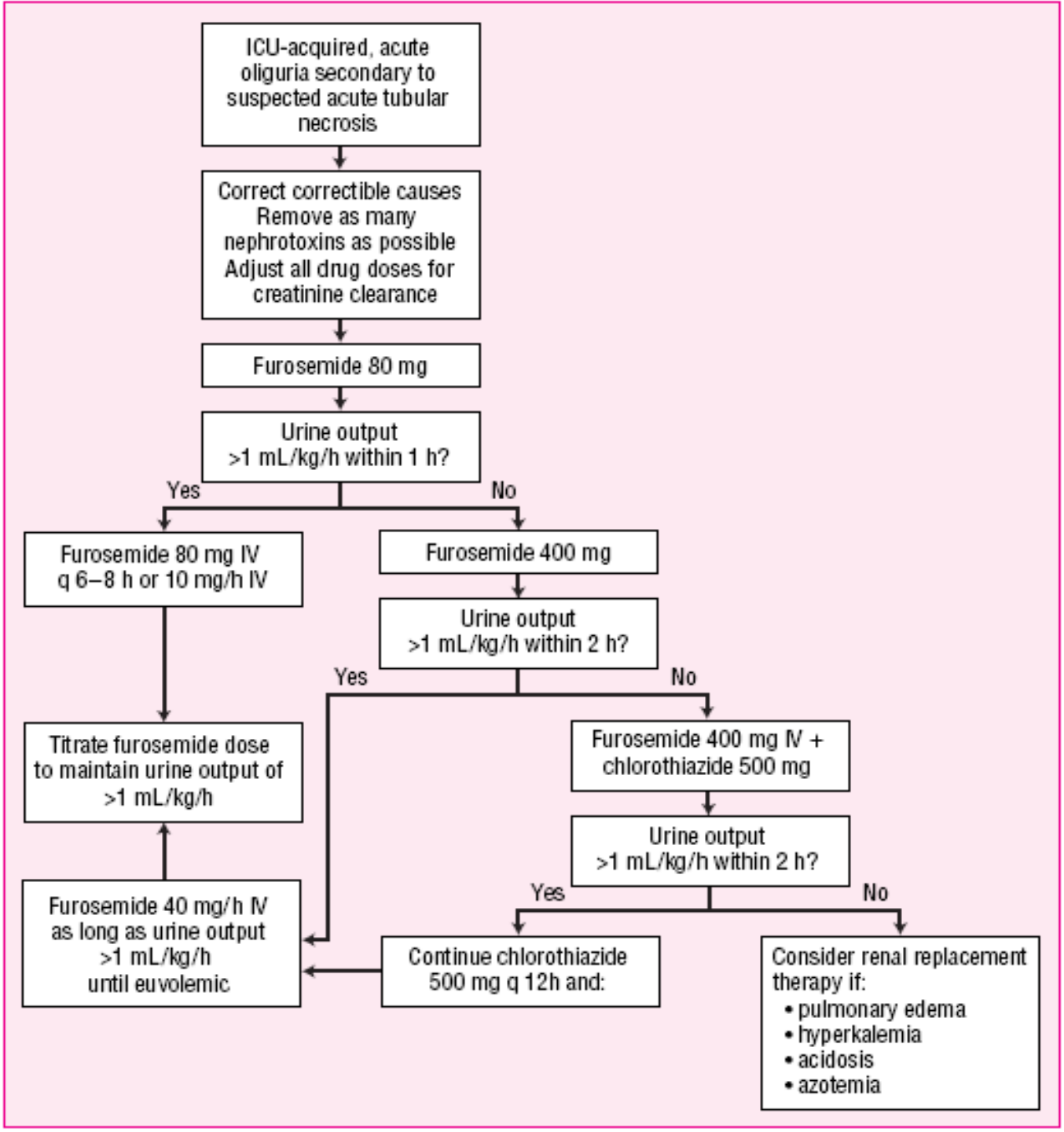
Hemofiltration

Removal of relatively large volumes of fluid by ultrafiltration, resulting in removal of solutes through convection.



GAMBRO Renal Products


ICU-acquired, acute oliguria secondary to suspected acute tubular necrosis
Correct correctible causes
Remove as many nephrotoxins as possible
Adjust all drug doses for creatinine clearance
Furosemide 80 mg
Urine output >1 mL/kg/h within 1 h?
Yes
No
Furosemide 80 mg IV q 6–8 h or 10 mg/h IV
Furosemide 400 mg
Urine output >1 mL/kg/h within 2 h?
Yes
No
Titrate furosemide dose to maintain urine output of >1 mL/kg/h
Furosemide 400 mg IV + chlorothiazide 500 mg
Urine output >1 mL/kg/h within 2 h?
Yes
No
Furosemide 40 mg/h IV as long as urine output >1 mL/kg/h until euvolemic
Continue chlorothiazide 500 mg q 12h and:
Consider renal replacement therapy if:
• pulmonary edema
• hyperkalemia
• acidosis
• azotemia

Parameters to be monitored

- Vigilant monitoring of patients with ARF is essential, particularly in those who are critically ill.

Parameter	Frequency
Fluid ins/outs	Every shift
Patient weight	Daily
Vital signs	Every shift
Blood cultures and sensitivities	Check for results daily; obtain more when clinical signs of infection present
Blood chemistries	
Sodium, potassium, chloride, bicarbonate, calcium, phosphate, magnesium	Daily
BUN/S_{Cr}	Daily
Albumin	Once or twice weekly
Complete blood cell count with white cell differential	Daily
Drugs and their dosing regimens	Daily
Nutritional regimen	Daily
Blood glucose	Every shift for critically ill patients
Serum concentration data for drugs	After regimen changes and after RRT has been instituted
Times of administered doses	Daily
Doses relative to administration of RRT	Daily
Urinalysis	
Calculate measured creatinine clearance	Every time measured urine collection performed
Calculate fractional excretion of sodium	Every time measured urine collection performed
Plans for renal replacement	Daily
Invasive monitoring parameters	As indicated
Swan-Ganz readings	Every shift


End