Renal Replacement Therapy

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Kidney Functions

- Homeostasis: through its excretory function to get rid of endogenous metabolic substances :e.g. urea and creatinine or exogenous , e.g. drugs.
It regulates water and electrolytes concentration (sodium, potassium, chloride, calcium, phosphorus, magnesium, sulfate).
- Acid Base balance.
- Blood pressure control (via aldosterone)
- Part of the endocrine system: produces erythropoietin, calcitriol, renin.

Renal Replacement Therapy

It replaces the normal blood- filtering function of the kidneys. It is used when the kidneys are not working well as in renal failure, acute kidney injury and chronic kidney disease.

Dialysis is the artificial mechanism by which the fluid and toxic solutes are moved from the circulation when the kidneys cannot do so sufficiently.

Dialysis is an imperfect treatment to replace kidney function because it does not correct the compromised endocrine functions of the kidney.
Dialysis treatment replace some of these functions through diffusion (waste removal) and ultrafiltration (fluid removal).

The two major methods of dialyzing a patient are:

1-Hemodialysis.

2-Peritoneal dialysis.

In all form of diyalsis ;

1-dialysate (solution resembling human plasma)

2- semipermeable membrane

Settings in which dialysis is considered:

a. CKD—CKD = Stage 5 = GFR <15

Asymptomatic patients with eGFR 5 to 15 mL/min/1.73 m^2 – closely follow such but do not initiate dialysis in the absence of signs or symptoms.

Patients with eGFR 5 to 15 mL/min/1.73 m^2 with signs or symptoms that could be due to ESKD:

1-Acidosis; significant , intractable metabolic acidosis (pH <7.1)

2-Electrolytes ; sever hyperkalemia refractory to medial therapy

3-Intoxication; methanol, ethylene, aspirin , lithium, glycol

4-Overload ; hypervolemia refractory to diuretics

5-Uremia(sever); based on clinical not laboratory values(encephalopathy , pericarditis)

Patients with eGFR <5 mL/min/1.73 m^2: We initiate dialysis for most patients regardless of the absence or presence of ESKD-related signs or symptoms.

- **B. AKI—dialysis is often required as a temporary measure until the patient's renal function improves.**

Hemodialysis apparatus

The apparatus used to conduct hemodialysis consists of the following components:

- Dialyzer
- Dialysis solution (dialysate)
- Tubing for transport of blood and dialysis solution
- Machine to power and mechanically monitor the procedure

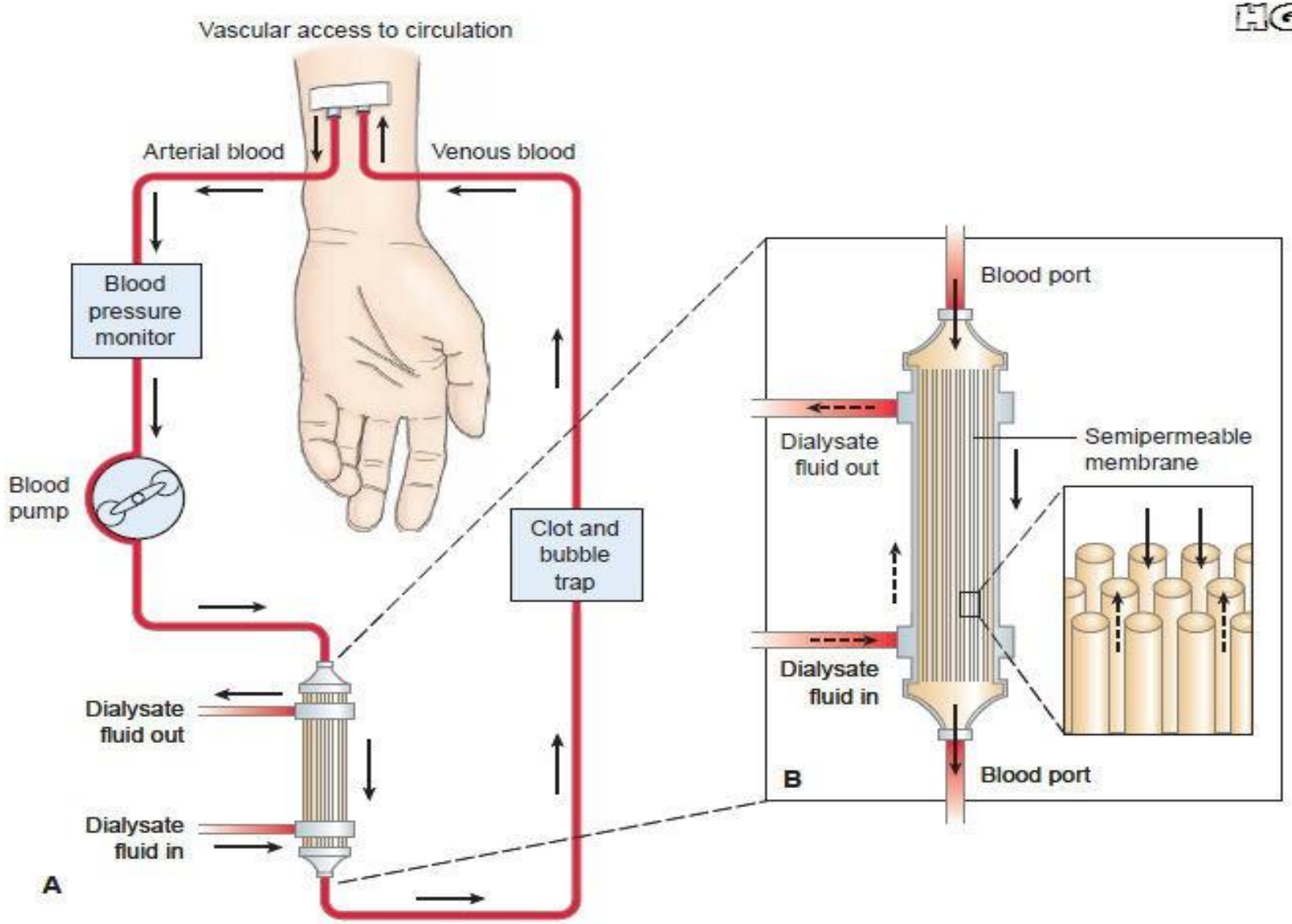
- Dialyzers are composed of a polyurethane capsule or shell within which hollow fibers or parallel membrane plates are suspended in dialysate. The fibers or plates function as a semipermeable membrane across which blood and dialysate flow in opposite directions.
- Blood flows by one side of a semi-permeable membrane and a dialysate, or special dialysis fluid, flows by the opposite side.
- By crossing this membrane, solutes and water move between a patient's intravascular compartment and the dialysis fluid contained within the dialyzer. Smaller solutes and fluid pass through the membrane, but the membrane blocks the passage of larger substances (for example, red blood cells, large proteins).

Dialysate

- Highly purified water
- Sodium
- Potassium
- Calcium
- Magnesium
- Chloride
- Bicarbonate
- Dextrose

- Dialysis tubing consists of synthetic tubing designated as the "arterial" line, which carries blood from the arteriovenous access to the dialyzer, where blood and dialysate interface at the membrane, and the "venous" line, which carries dialyzed blood back to the patient.
- The dialysis machine must include a blood pump to move blood between patient and the dialyzer, a delivery system to transport dialysis solution, and monitoring devices.

How does hemodialysis work?



HEMODIALYSIS SYSTEM . **A,** Blood from an artery is pumped into **(B)** a dialyzer where it flows through the cellophane tubes, which act as the semipermeable membrane (*inset*). The dialysate, which has the same chemical composition as the blood except for urea and waste products, flows in around the tubules. The waste products in the blood diffuse through the semipermeable membrane into the dialysate.

Hemodialysis Process

The patient's blood is pumped by an artificial pump outside of the body through the dialyzer, which typically consists of fine capillary networks of semipermeable membranes.

a. The dialysate flows on the outside of these networks,

and fluid and solutes diffuse across the membrane.

b. The patient's blood must be heparinized to prevent clotting in the dialyzer.

Principles of dialysis

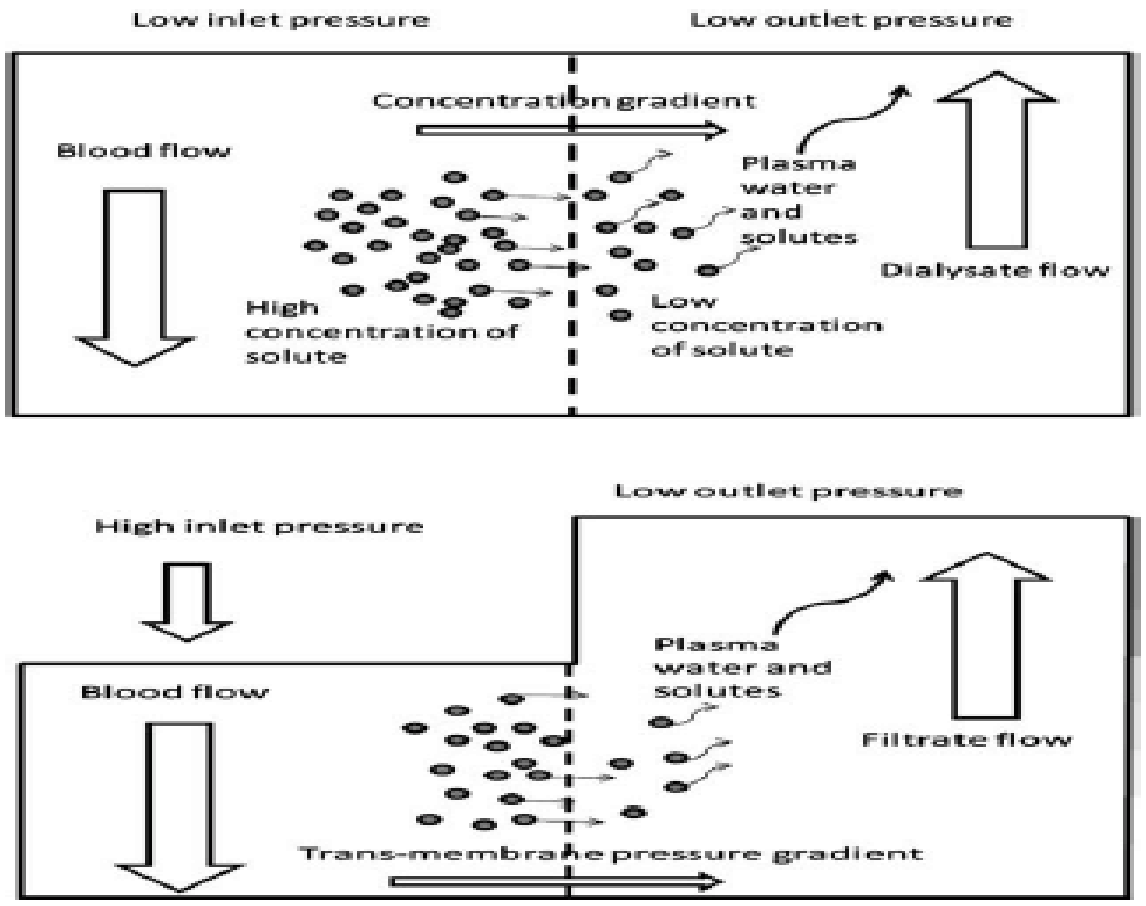


Figure 1 Principles of dialysis (top panel) and filtration (lower panel).

Diffusion passive movement of solutes across a semi- permeable membrane down concentration gradient.move from area of high to low concentration

Ultrafiltration process for removing excess fluid from the blood through the dialysis membrane by means of pressure

Convection is movement of molecules through a semipermeable membrane associated with the fluid being removed during ultrafiltration. solute molecule is swept through a membrane by a moving stream of ultrafiltrate.

Access

- Hemodialysis catheters usually have 2 main lumens attached to 2 ports (blue and red).The red= arterial lumen (draws blood from the body. The blue port= venous lumen (return of blood from the dialysis machine to the patient.

- The lumen of a dialysis catheter has a larger diameter in order to provide a high rate of flow, essential in the dialysis process.

- **Types of access:**

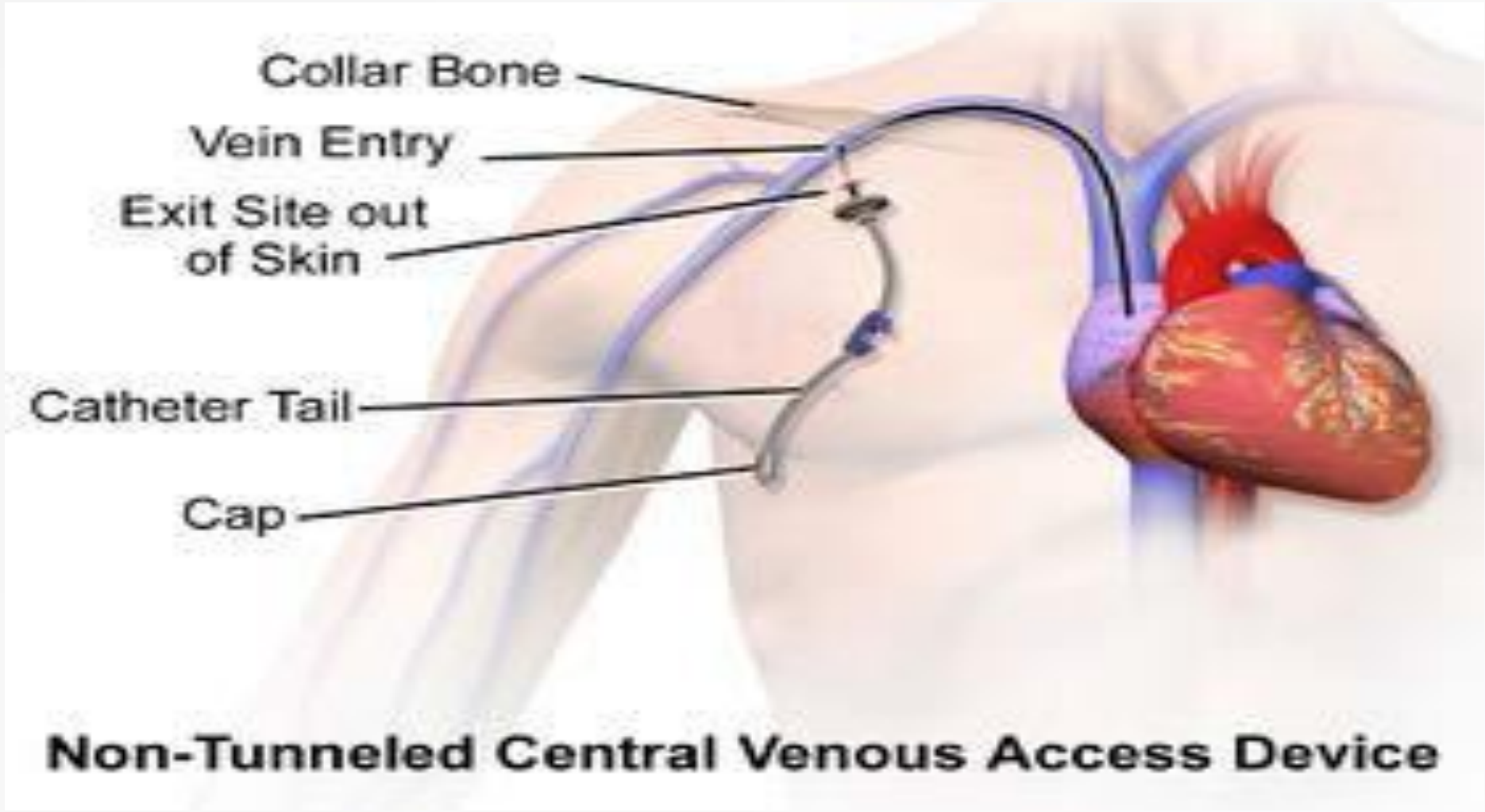
  Temporary: Central venous catheter

  Permanent: AV access

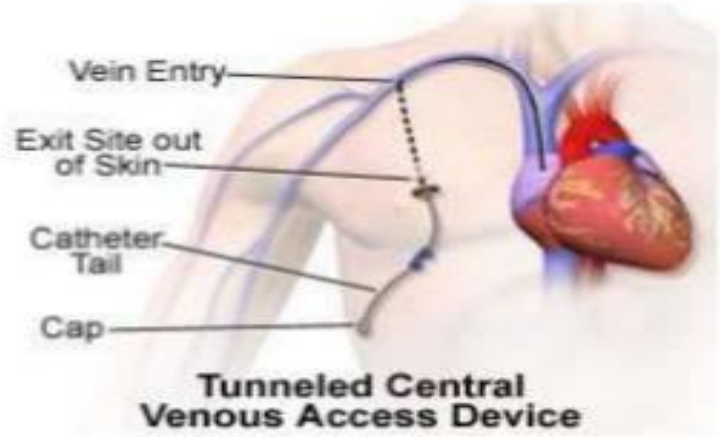
Central Venous Catheter

- **Non tunneled central line:**
- Type of short term IV catheter
- Placed in the subclavian vein or internal jugular vein or femoral vein for temporary access.

- **Tunneled central line**:
- thin flexible hollow tube that is tunneled under the skin before entering a large vein
- Placed into the internal jugular vein and extends down to a larger vein just above the heart


Collar Bone
Vein Entry
Exit Site out of Skin
Catheter Tail
Cap
Non-Tunneled Central Venous Access Device

Tunneled Central Venous Catheters



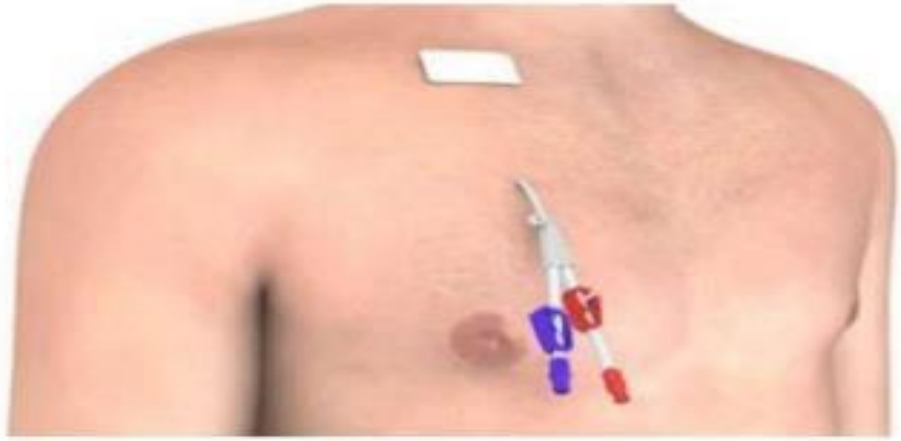


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PHOTO REFERENCE: http://images.ddocdn.com/cg/images/en141690.jpg

CHARTWELL
Care of Experts... Comfort of Home

Risks of CVC

- **Infections** (risk is lower for tunneled catheters)
- **Misplacement/ malposition** (U/S guidance to prevent this)
- **Bleeding** (perforation of vasculature =life threatening)
- **Central vein thrombosis** (turbulent blood flow and repeated catheterization)

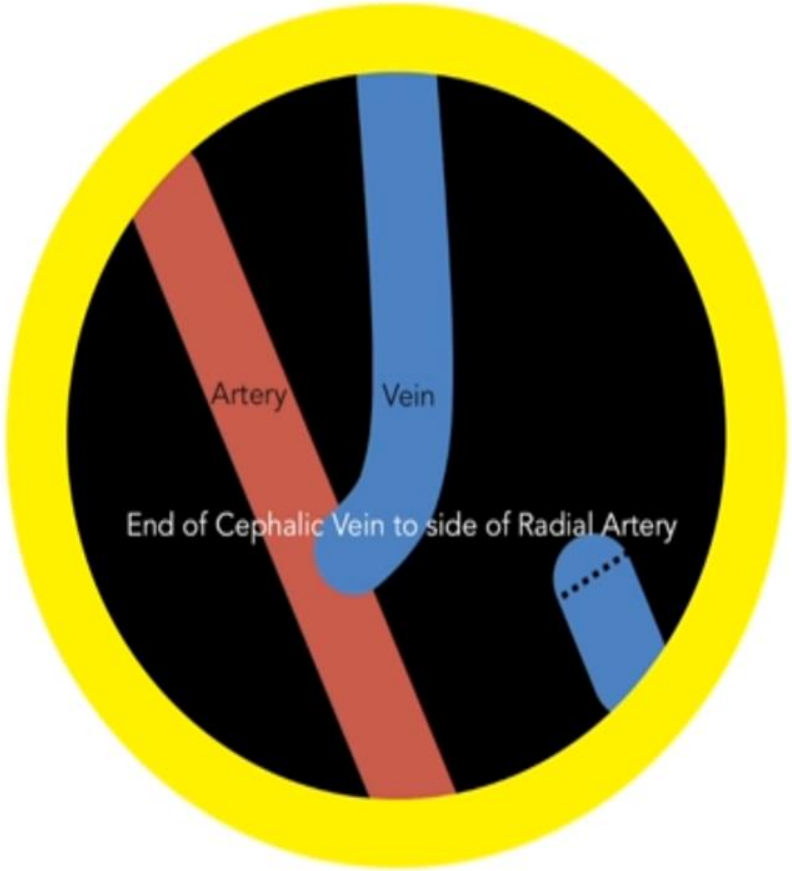
AV access

- 1) Arteriovenous fistula
- 2) AV grafts

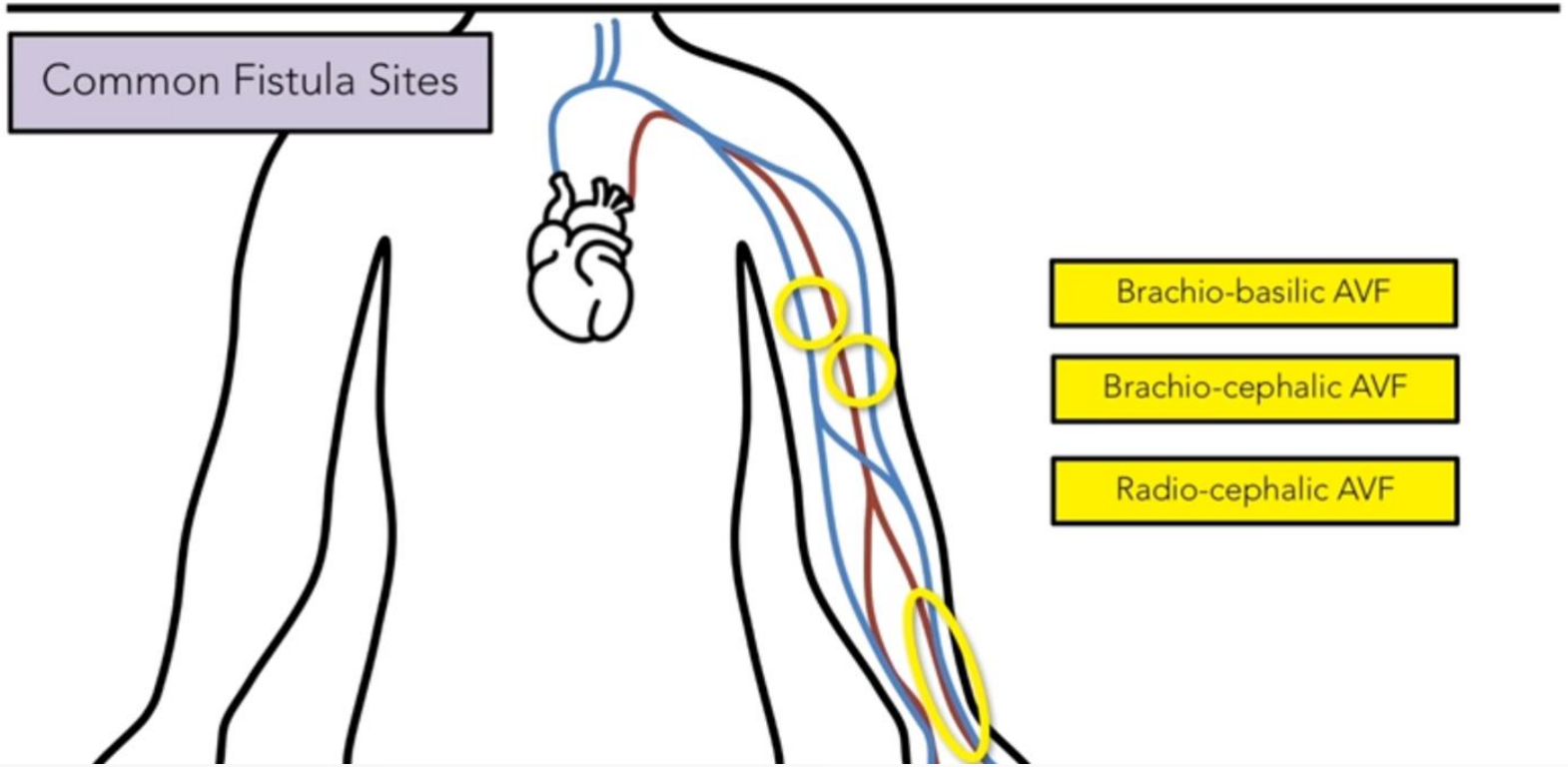
AV fistula

- It is a surgical connection where the artery connects directly to the vein
- Requires vascular surgery
- Av fistulas will need time to heal and mature completely before they can be used as a dialysis access (3-4 months)
- Considered the best option due to decrease risk of infection

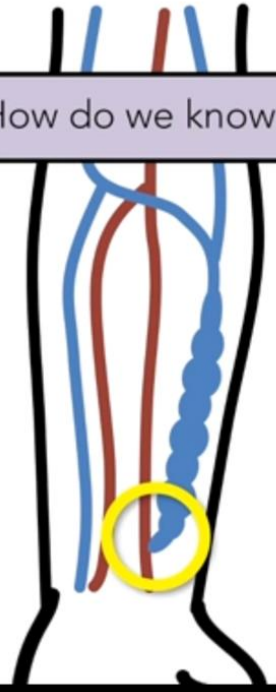
The Basics of AV Access



Vascular Anatomy & AV Access



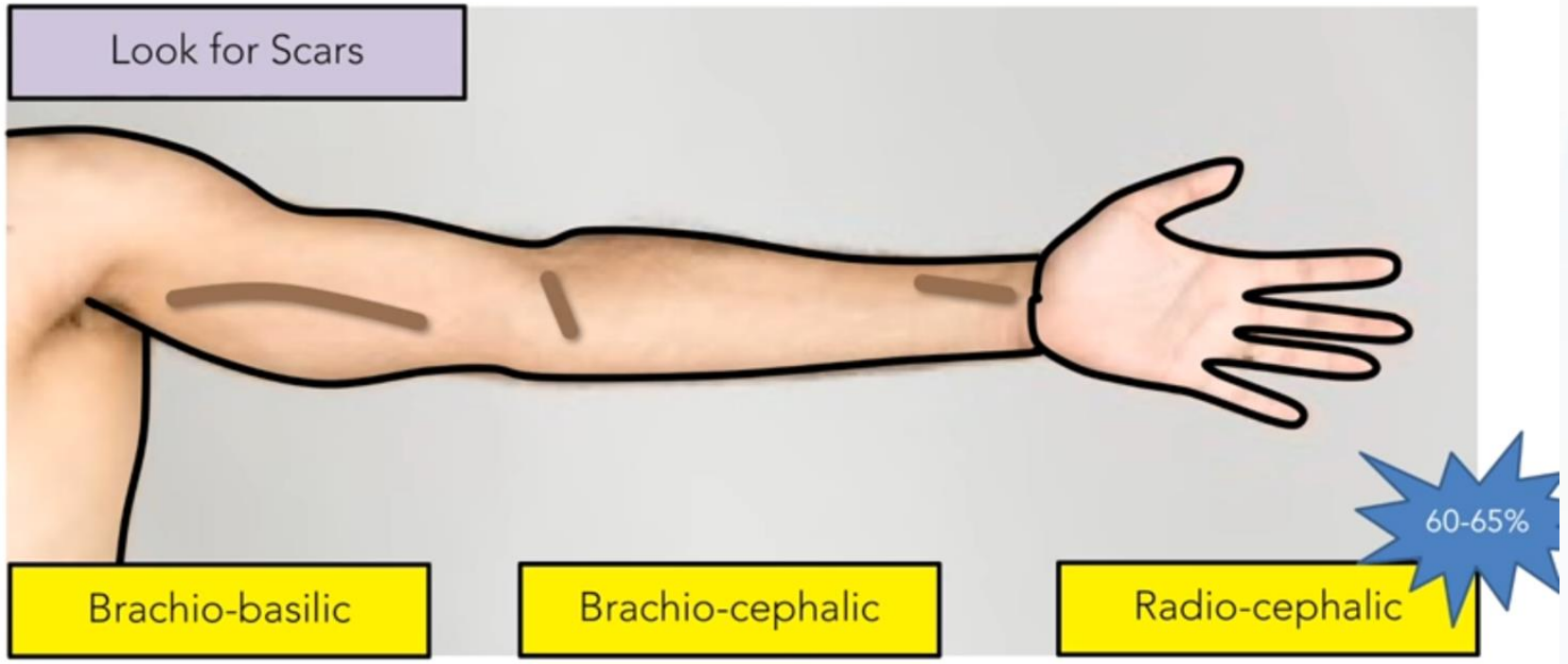
The Basics of AV Access

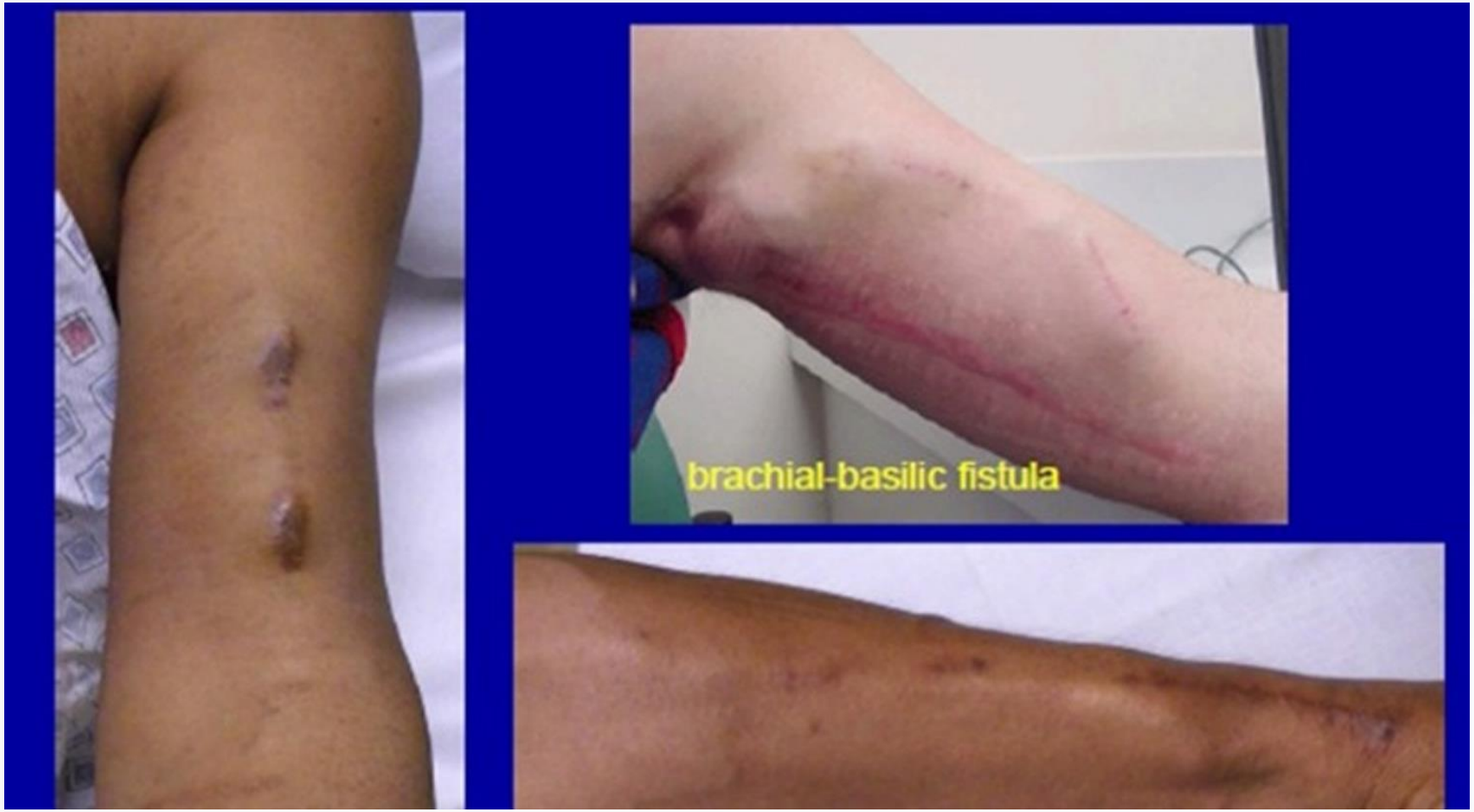


How do we know when the fistula is ready to be used?

- At least 0.6cm in width
- 0.6cm or less from the surface
- Flow of at least 600ml/min by 6 weeks post fistula creation
- Linear segment of at least 6 cm (ideally 10 cm)

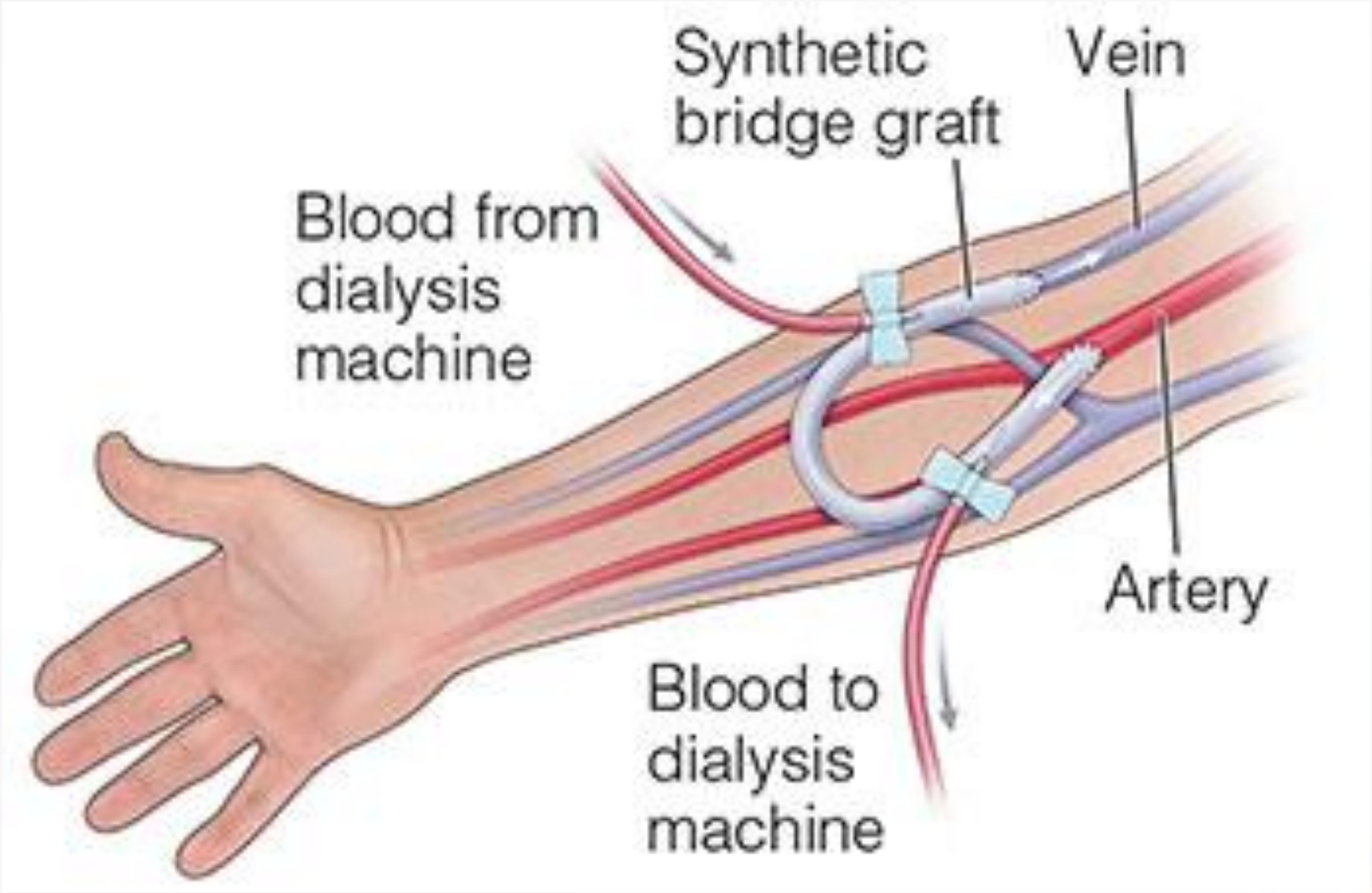
Vascular Anatomy & AV Access




brachial-basilic fistula

AV graft

- Connection of a vein and an artery utilizing a hollow, synthetic tube ”graft”
- This connection results in blood flowing from the high pressure artery to low pressure vein providing a flow rate for adequate hemodialysis treatment

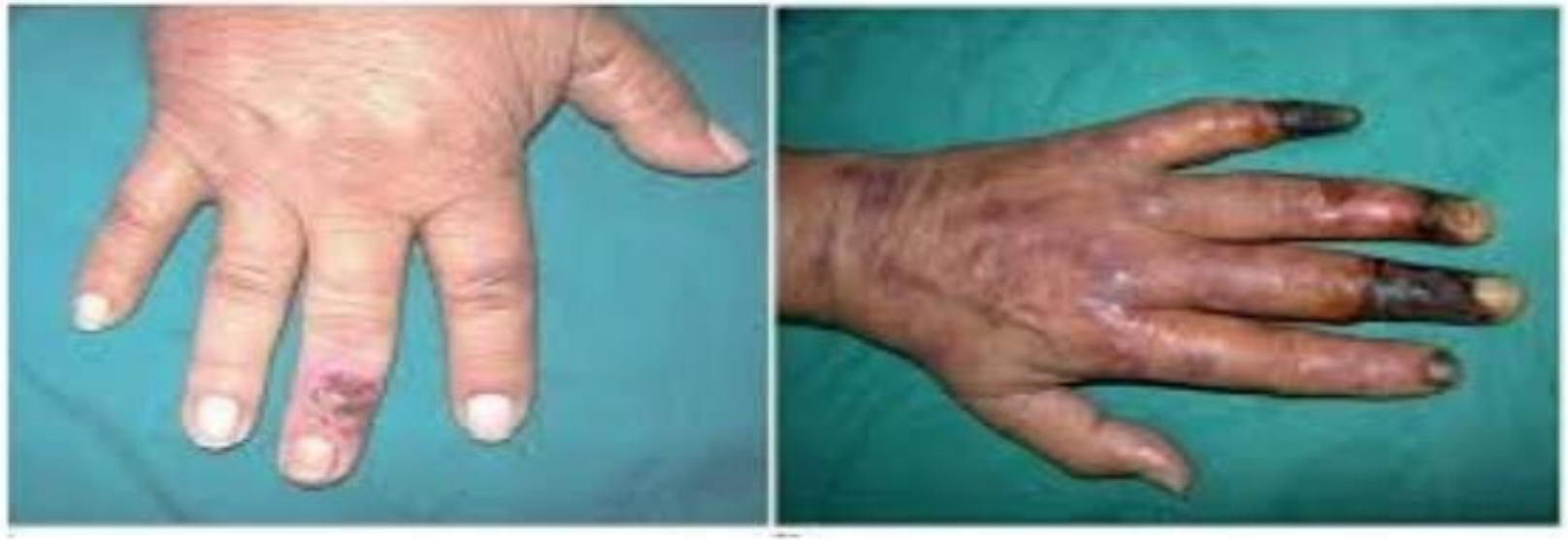

Synthetic bridge graft
Vein
Blood from dialysis machine
Artery
Blood to dialysis machine

Complications

- **The most common complications of AV fistulas and AV grafts include:**

- Thrombosis.
- infection.
- Access-related hand ischemia (vascular steal syndrome).
- Aneurysmal dilation
- venous hypertension.
- Seroma.
- heart failure.
- local bleeding.

Steal Syndrome



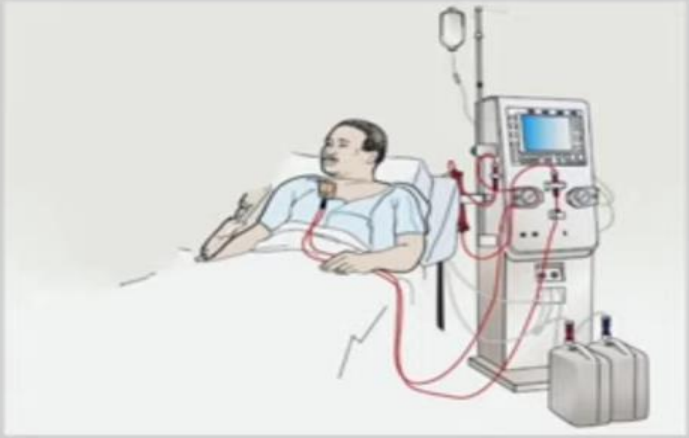
Complications cont’d

❖ **Complications associated with hemodialysis.**

- Hypotension—may result in myocardial ischemia, fatigue, and so on.
- “First-use syndrome”—chest pain, back pain, and rarely, anaphylaxis may occur immediately after a patient uses a new dialysis machine
- Complications associated with anticoagulation—hemorrhage, hematoma, etc.
- Infection of vascular access site—may lead to sepsis

Dialysis Disequilibrium Syndrome (DDS)

- It is characterized by **neurological symptoms caused by rapid removal of urea during hemodialysis**. It develops primarily from an osmotic gradient that develops between the brain and the plasma as a result of rapid hemodialysis.



Rapid Removal of Urea(Small molecule)

Urea
Low conc. in blood

Vs

Urea
High conc. in brain

Water move

Brain

Cerebral oedema

Reverse Urea effect

Etiology of DDS

- Elderly and pediatric patients
- Patients with pre existing CNS lesions (head trauma pr recent strokes)
- Severe metabolic acidosis
- High pre dialysis BUN

Symptoms

Mild

- Headache, restlessness

Modertae

- Nausea, vomiting, hypertension

Severe

Seizures, coma, death

Medical Nutrition Therapy Objectives in Dialysis

- Prevent dehydration or fluid overload
- Maintain normal potassium and sodium blood levels
- Maintain acceptable serum phosphorus and calcium levels

Supplementation

- Calcitriol.
- Erythropoietin.
- Iron.
- Phosphorus binders.
- B-complex vitamens and folic acid.
- Vitamin E.

The Adequacy of hemodialysis

- The adequacy of hemodialysis refers to how well toxins and waste products are removed from the patient's blood.

- normally once a month

❑ Two methods are generally used to assess dialysis adequacy, URR and Kt/V:

- 1- URR stands for urea reduction ratio.
- 2- KT/V (also known as single-pool Kt/V)

URR

- **Example:**
- If the initial, or pre-dialysis, urea level was 50 mg/dL
- And the post-dialysis urea level was 15 mg/dL, the amount of urea removed was 35 mg/dL.
- 50 mg/dL - 15 mg/dL = 35 mg/dL
- The amount of urea removed (35 mg/dL) is expressed as a percentage of the predialysis urea level (50 mg/dL).
- 35/50 = 70/100 = 70%

- ***** some experts recommend a minimum URR of 65 percent.**

Single-pool Kt/V

- represents the number of times the entire body's urea distribution volume (close to the volume of total body water) gets cleared of urea in the dialysis treatment.

- K represents dialyzer clearance
- T duration of dialysis
- V urea distribution volume

Single-pool Kt/V

- **Example:** If the dialyzer's clearance is 300 mL/min and a dialysis session lasts for 180 minutes (3 hours), Kt will be 300 mL/min multiplied by 180 minutes. The result comes to 54,000 mL, or 54 liters.
- Kt = 300 mL/min multiplied by 180 minutes
  Kt = 54,000 mL = 54 liters
- The body is about 60 percent water by weight. If a patient weighs 70 kilograms (kg), or 154 pounds (lbs), V will be 42 liters.
- V = 70 kg multiplied by .60 = 42 liters
- So the ratio—K multiplied by t to V, or Kt/V—compares the amount of fluid that passes through the dialyzer with the amount of fluid in the patient's body. The Kt/V for this patient would be 1.3.
- Kt/V = 54/42 = 1.3
- ***These guidelines recommend a target single-pool Kt/V of 1.2 to 1.4 per session

Peritoneal Dialysis

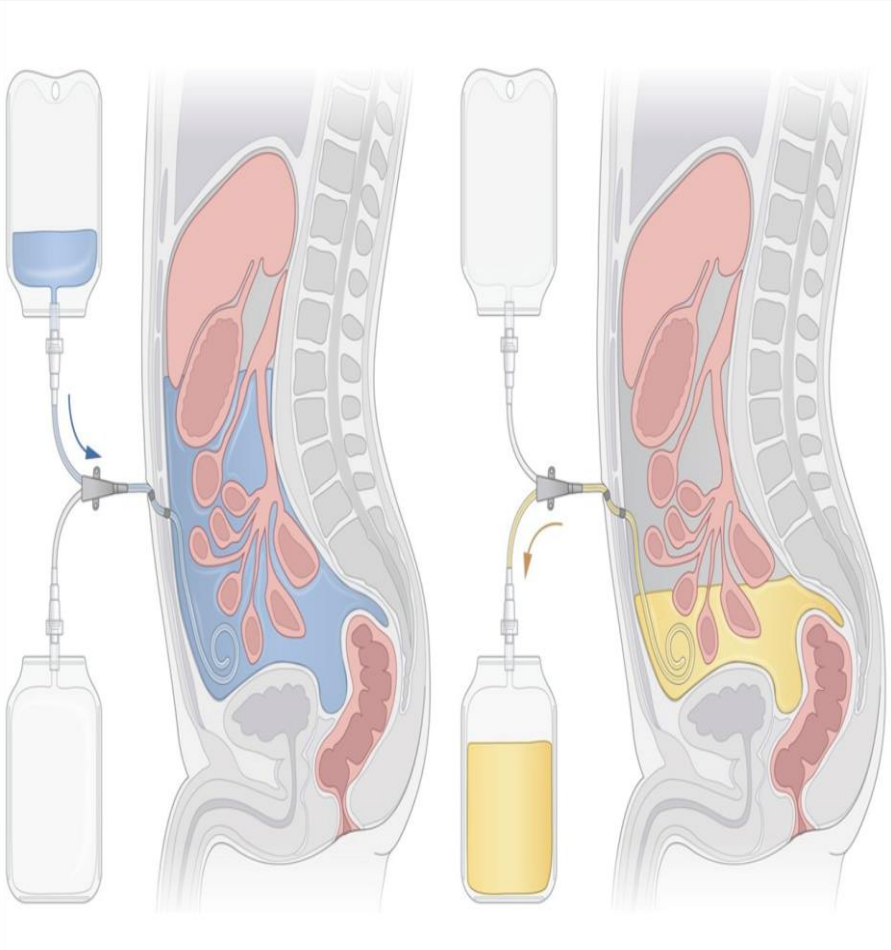
Process

- The peritoneal membrane serves as the semipermeable membrane.
- Dialysate fluid is infused into the peritoneal cavity, causing solutes (urea, creatinine, potassium) from the peritoneal capillaries move into the dialysate fluid via **diffusion**. This process is known as “Clearance”.
- A hyperosmolar (high-glucose) solution is used as the dialysate to create an osmotic gradient, causing excess water to be removed from the blood via **osmosis**. This process is known as “Ultrafiltration”.
- The fluid is then drained from the abdomen.

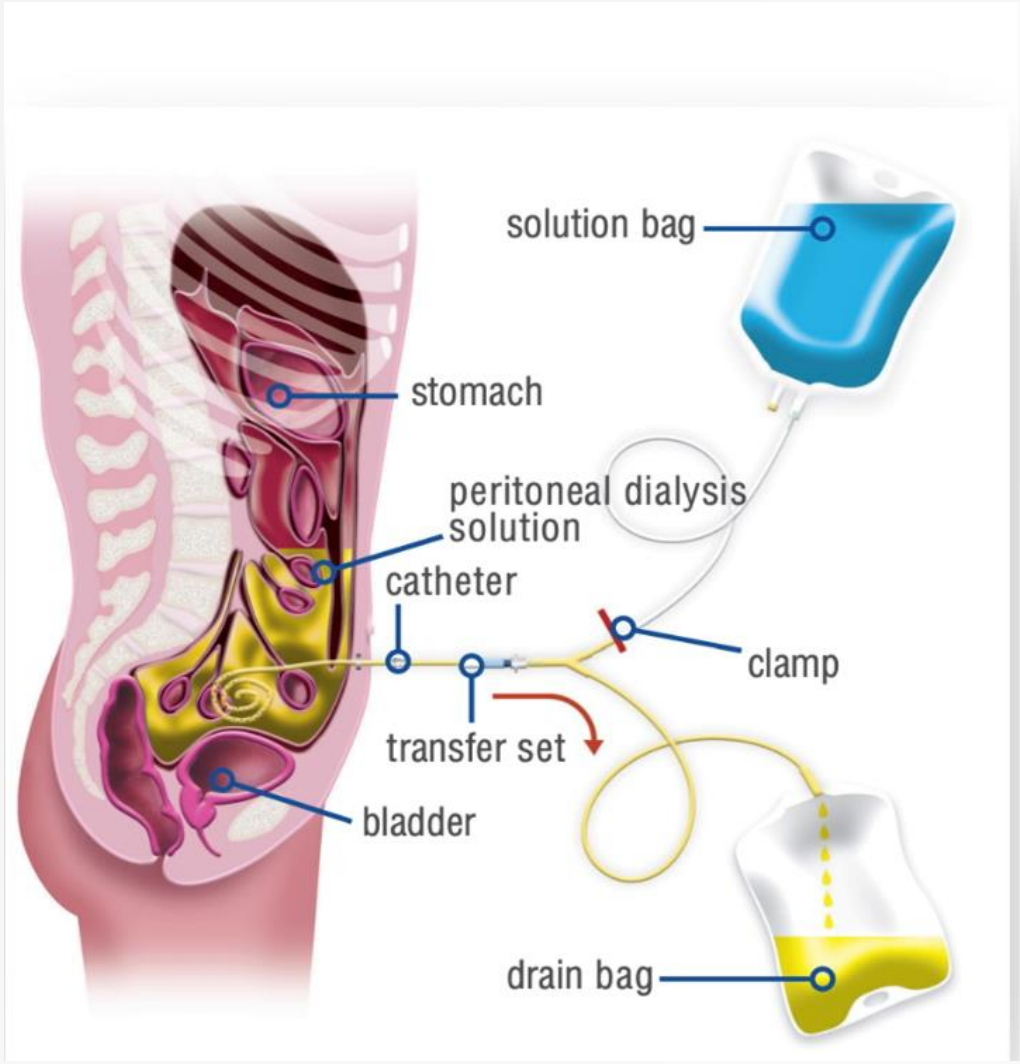
Access

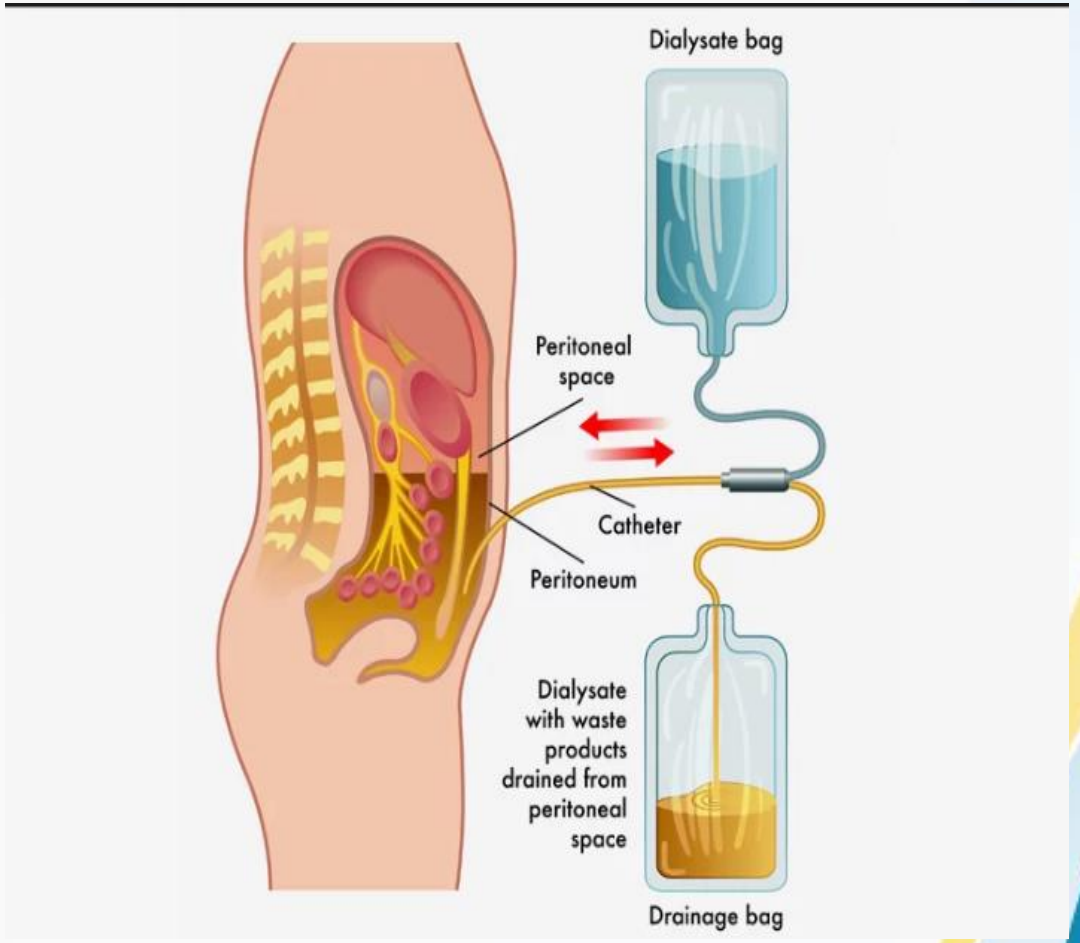
- A soft catheter is placed through a skin tunnel into the peritoneal cavity through the midline of the anterior abdominal wall .
  - Dialysate is infused into the peritoneal fluid via the implanted catheter.
  - A temporary catheter is used for acute peritoneal dialysis.

dialysate is inserted into the intraperitoneal space through a surgically placed catheter. The dialysate is left in the abdominal cavity for a period of time (the dwell time). During the dwell time, fluid and molecules in the blood travel across the peritoneum into the dialysate via various sized pores.



The dialysate is removed from the peritoneal cavity. The process of inserting dialysate, the dwell time, and dialysate removal is called an exchange and peritoneal dialysis involves multiple exchanges each day.


solution bag
stomach
peritoneal dialysis solution
catheter
clamp
transfer set
bladder
drain bag


Dialysate bag
Peritoneal space
Catheter
Peritoneum
Dialysate with waste products drained from peritoneal space
Drainage bag

Types of peritoneal dialysis

There are 2 types of PD:

- Continuous Ambulatory Peritoneal Dialysis (CAPD)
  CAPD: A machine is not needed. The peritoneal cavity is **manually** filled with dialysate
- Assisted Peritoneal Dialysis (APD)
  APD:A simple exchange machine performing continuous low- volume exchanges each night while the patient is asleep.

Continuous Ambulatory Peritoneal Dialysis (CAPD)

- In continuous ambulatory peritoneal dialysis (CAPD), about 2 litres of sterile, isotonic dialysis fluid are introduced and left in place for approximately 4–6 hours. Metabolic waste products diffuse from peritoneal capillaries into the dialysis fluid down a concentration gradient.
- The fluid is then drained and fresh dialysis fluid introduced, in a continuous four-times-daily cycle. The inflow fluid is rendered hyperosmolar by the addition of glucose or glucose polymer; this results in net removal of fluid from the patient during each cycle, due to diffusion of water from the blood through the peritoneal membrane down an osmotic gradient (ultrafiltration). The patient is mobile and able to undertake normal daily activities.

Continuous Ambulatory Peritoneal Dialysis (CAPD)

- CAPD is particularly useful in children, as a first treatment in adults with residual renal function, and as a treatment for elderly patients with cardiovascular instability. The long-term use of peritoneal dialysis may be limited by episodes of bacterial peritonitis and damage to the peritoneal membrane, including sclerosing peritonitis

Assisted Peritoneal Dialysis (APD)

- Assisted peritoneal dialysis (APD) is similar to CAPD but uses a mechanical device to perform the fluid exchanges during the night, leaving the patient free.
- It includes the same number of exchanges as CAPD, but shorter dwell times. Fluid exchanges are all done at night, leaving the daytime free.

Frequency

- Dialysate fluid is drained and replaced
- **Once a day** in APD (Assisted peritoneal Dialysis)
- **Every 4 to 6 hours** in CAPD (Continuous ambulatory peritoneal dialysis).

Advantages

- The patient is able to perform dialysis on their own.
- It mimics the physiology of normal kidney function more closely than hemodialysis in that it **is more continuous**.
- Less expensive
- Less restrictive diet

Disadvantages

- The patients must be highly motivated to self-administer it.
- Cosmetic—there is increased abdominal girth due to dialysate fluid.
- Catheter kinks/infection.

Complications

- Bacterial peritonitis, presenting as fever, abdominal pain and a cloudy peritoneal dialysate fluid.
- Catheter exit site infections may progress to skin tunnel infections and peritonitis.
- Hyperglycemia—especially with diabetic patients.
- Protein malnutrition.

Complications

- Constipation may impair flow of dialysate in and out of the pelvis.
- Abdominal/inguinal Hernias are caused by raised intra-abdominal pressure ,and dialysate ‘leaks’ into the pleural cavity or scrotum
- Sclerosing peritonitis is a potentially fatal complication of CAPD, where long- term patients develop progressive thickening of the peritoneal membrane. This occurs in association with adhesions and strictures, turning the small bowel into a mass of matted loops and causing repeated episodes of small bowel obstruction.

Complications

17.33 Problems with continuous ambulatory peritoneal dialysis

Problem	Clinical features	Cause	Treatment
Peritonitis	Cloudy drainage fluid; abdominal pain and systemic sepsis are variable	Usually entry of skin contaminants via catheter; bowel organisms less common	Culture of peritoneal dialysis fluid Intraperitoneal antibiotics, tobramycin, vancomycin Catheter removal sometimes required
Catheter exit site infection	Erythema and pus around exit site	Usually skin organisms	Antibiotics; sometimes surgical drainage
Ultrafiltration failure	Fluid overload	Damage to peritoneal membrane, leading to rapid transport of glucose and loss of osmotic gradient	Replace glucose with synthetic, poorly absorbed polymers for some exchanges (icodextrin)
Peritoneal membrane failure	Inadequate clearance of urea etc.	Scarring/damage to peritoneal membrane	Increase exchange volumes; consider automated peritoneal dialysis or switch to haemodialysis
Sclerosing peritonitis	Intermittent bowel obstruction Malnutrition	Unknown; typically occurs after many years	Switch to haemodialysis (may still progress) Surgery and tamoxifen may be used

Comparison between Hemodialysis and Peritoneal Dialysis

Haemodialysis	Peritoneal dialysis
Efficient; 4 hrs three times per wk is usually adequate	Less efficient; 4 exchanges per day are usually required, each taking 30–60 mins (continuous ambulatory peritoneal dialysis) or 8–10 hrs each night (automated peritoneal dialysis)
2–3 days between treatments	A few hours between treatments
Requires visits to hospital (although home treatment is possible for some patients)	Performed at home
Requires adequate venous circulation for vascular access	Requires an intact peritoneal cavity without major scarring from previous surgery
Careful compliance with diet and fluid restrictions required between treatments	Diet and fluid less restricted
Fluid removal compressed into treatment periods; may cause symptoms and haemodynamic instability	Slow continuous fluid removal, usually asymptomatic
Infections related to vascular access may occur	Peritonitis and catheter-related infections may occur
Patients are usually dependent on others	Patients can take full responsibility for their treatment

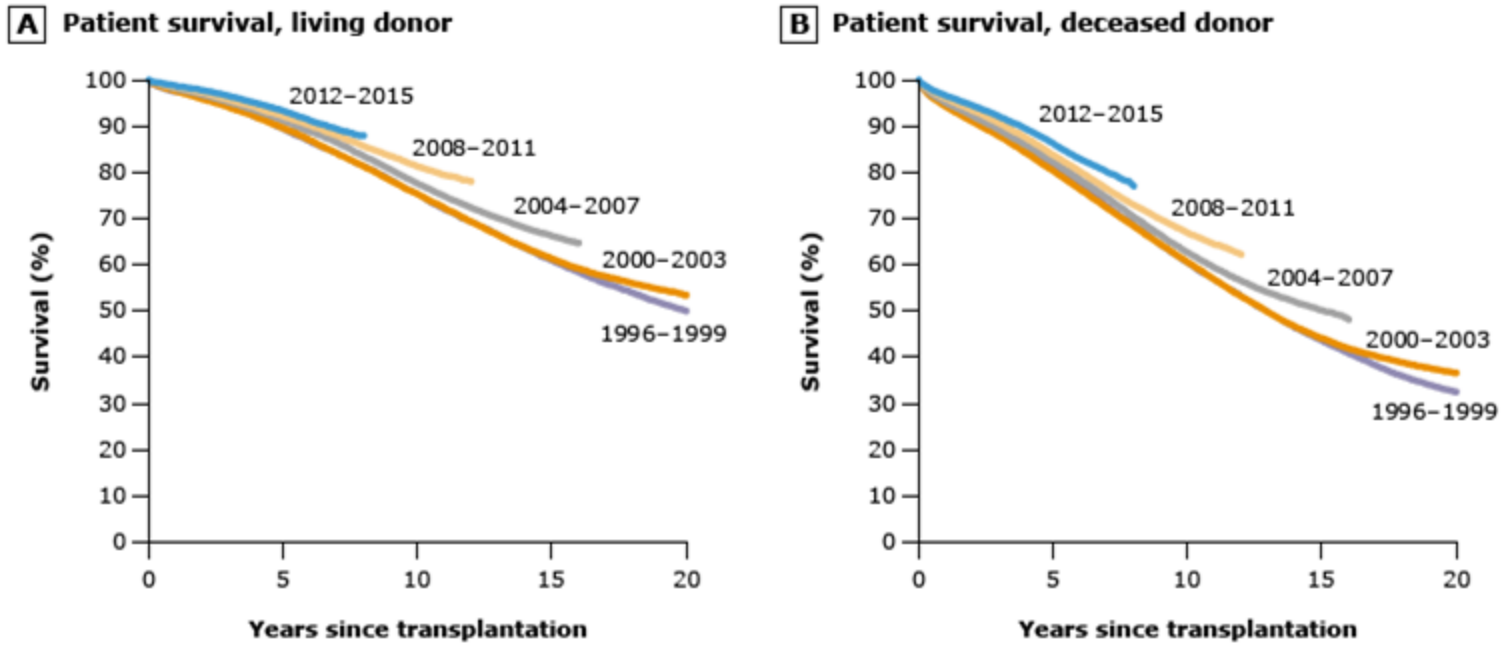
Renal Transplantation

- A kidney transplant is a surgery to place a healthy kidney from a **living or deceased** donor into a person whose kidneys no longer function properly.

- Best way to restore normal kidney function and reverse all the metabolic and uremic abnormalities of CKD.

- When compared to dialysis:
  - Better quality of life
  - Lower risk of death
  - Fewer dietary restrictions
  - Lower treatment cost

Graft and patient survival after kidney transplantation in the United States



Renal donation sources:-

1-Living donors

Nonvital organs and tissues (e.g., kidney or bone marrow) can be acquired from living donors.

Advantages

- Donor is usually healthy, which reduces the risk of complications for both donor and recipient.
- Preoperative and perioperative immunomodulation is possible in the recipient.
- Short cold ischemia time
- Minimal waiting time

Disadvantages: increased risk of morbidity and mortality in the donor

2-Deceased and dying donors

When treating a dying patient, it is therefore important to initiate conversations with the patient and their family about the potential for organ donation. Due to the ethical concerns associated with organ donation, there are

- The transplantation of cells, tissues, and organs between individuals of different species is referred to as xenotransplantation.
- **Sources of xenografts** – The most favored sources of xenografts are pigs genetically engineered to limit the impact of innate immunity and to overcome inherent incompatibility of major physiologic systems such as coagulation.
- The biggest barrier remains the immunologic response of the recipient against the graft.

- Early transplantation (within 1 year of dialysis initiation) yields best results.
- Living donor kidney outcomes are superior to deceased donor kidney outcomes.
- Refer for transplant evaluation when eGFR=/< 20 ml/mn/1.73 m2.

Prerequisites for organ matching

1-Cross-matching (transplantation)

Recipient serum is examined for preformed antibodies (donor-specific antibodies) against donor T and B lymphocytes

A negative cross-match against T and B cells indicates a lower risk of rejection reactions; therefore, transplantation may be performed.

A negative cross-match against T cells but a positive cross-match against B cells indicates a higher risk of acute rejection, but transplantation may still be performed with a high level of caution.

A positive cross-match against donor T and B lymphocytes indicates a high risk of hyperacute rejection; therefore, the transplantation must not be performed.

2-ABO compatibility

ABO compatibility is preferred but incompatibility can be tolerated.

Solid organ transplantation: ABO compatibility is required.

Rh compatibility is not required for solid organ transplantation. Both Rh compatibility and ABO compatibility are not essential for hematopoietic stem cell transplantation..

3-Histocompatibility:-The degree of matching for major histocompatibility antigens influences the incidence of rejection.MHC matching at the HLA-DR, HLA-A, and HLA-B loci

Matching of HLA-C, HLA-DP, and HLA-DQ is preferred but not always required.

4-Infectious screening:-

Screen both the donor and recipient for infections, including (at a minimum):

A-HIV, human T-cell lymphotropic virus,Herpes simplex virus, varicella zoster virus

Epstein-Barr virus, cytomegalovirus,Viral hepatitis panel,Rapid plasma reagin,Toxoplasma gondii antibody ,Tuberculin skin test or interferon-γ release assay ,Consider serological screening for endemic infections, e.g., Leishmania, Trypanosoma cruzi

Ensure immunization schedule is completed.

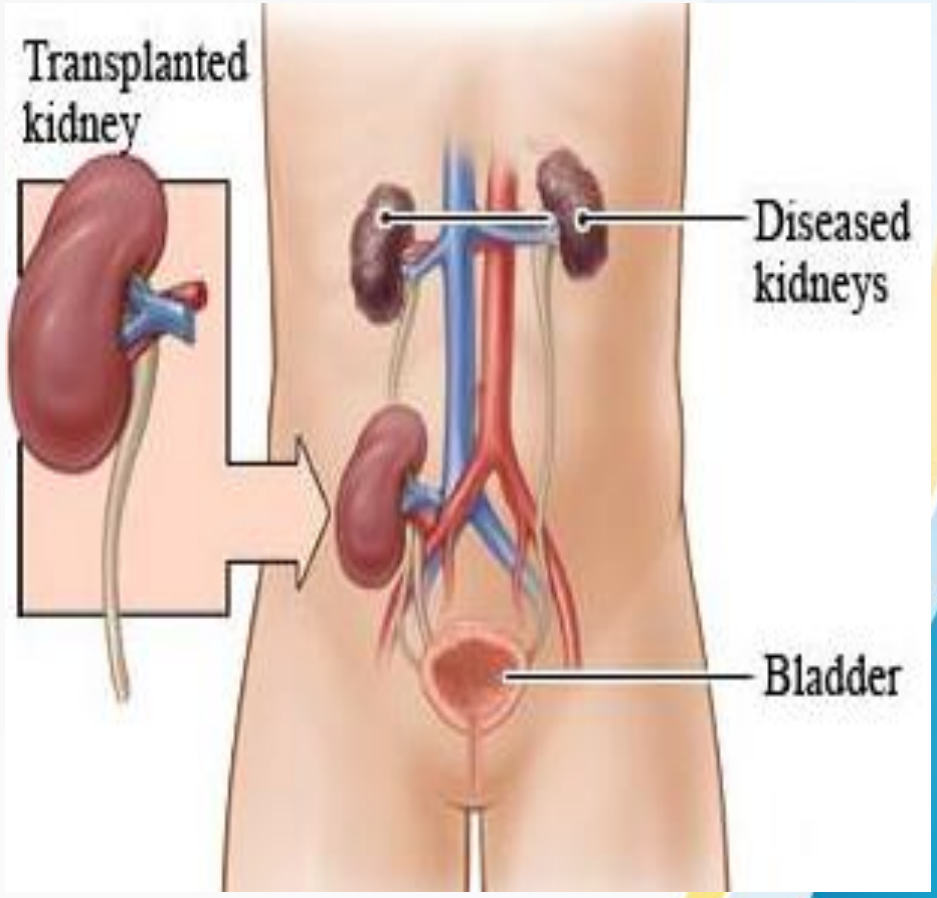
Technique

- The left kidney is preferred in living-donor kidney transplantations because it has a longer renal vein,so the longer vessel facilitates the surgical connection of the donor kidney to the recipient's vasculature.
- Kidney transplants are transplanted heterotopically in the iliac fossa since this position holds several advantages over orthotopic implantation due to:-

1-The transplanted kidney can be more easily palpated, biopsied, and evaluated via ultrasound.

2-Vascular anastomosis with the inguinal arteries is easier.

3-Distance between the ureter and bladder is shorter.



Overview of organ transplantation sites		
	Description	**Examples**
Orthotopic	• The graft is placed in the normal anatomical position. • The diseased or nonfunctional organ being replaced is removed.	• Heart transplantation • Liver transplantation
Heterotopic	• The graft is placed in a site other than the normal anatomical position. • The nonfunctional organ is usually left in place.	• Kidney transplantation • Pancreas transplantation
Paratopic	• The donor organ is placed close to the normal anatomical position.	• Pancreas transplantation

Absolute contraindications

- •Active infections
- •Active malignancy (excluding non-melanoma skin cancers)
- •Active substance use disorder (with center-specific policies on marijuana use)
- •Reversible kidney failure
- •Uncontrolled psychiatric disease
- •Documented active and ongoing treatment nonadherence

Relative contraindications

- These include malnutrition, primary oxalosis, and active systemic diseases that may limit the longevity of the transplant allograft (such as uncontrolled antineutrophil cytoplasmic antibody-associated vasculitides, systemic lupus erythematosus, or monoclonal gammopathy of renal significance). Some centers exclude patients with severe hyperparathyroidism

Post-transplant care:-

1-Serial monitoring of renal function tests (e.g., serum creatinine, urine protein)

2-To prevent Kidney Rejection:

- Intense immunosuppression in the early postoperative period (3–6 months)
- Induction immunosuppression with **IV thymoglobulin** or basiliximab, followed by maintenance oral immunosuppression with an oral immunosuppression, including **Prednisolone, Cyclosporine or Tacrolimus and Azathioprine**
- To minimize drug toxicity, use low doses of multiple drugs rather than high doses of a few drugs..

3-Universal prophylaxis

- **PCP prophylaxis with trimethoprim-sulfamethoxazole for a minimum of 6–12 months**
- **CMV prophylaxis with ganciclovir or valganciclovir for 12–14 weeks(also prevent reactivation of HSV)**

Suggested frequency of laboratory tests following kidney transplantation

Test	Frequency
Basic chemistry panel (including eGFR), magnesium, and phosphorus	Every visit
Complete blood count and differential	Every visit
Tacrolimus/cyclosporine/everolimus/sirolimus level	Every visit
Urinalysis with sediment examination	Every visit
Spot urine protein-to-creatinine ratio	Every visit
Fasting blood glucose	Weekly for the first four weeks, then at three and six months, then every year
HbA1C	Every three months or every visit if less frequent
Fasting lipid profile	Every three months or every visit if less frequent
PTH and 25-hydroxyvitamin D	Immediately posttransplant and then every 6 to 12 months
BK virus blood and/or urine PCR testing	Monthly for the first six months, and then at 9, 12, 18, and 24 months
CMV blood PCR testing (in patients not receiving CMV prophylaxis therapy)	Weekly for the first three months

eGFR: estimated glomerular filtration rate; PTH: parathyroid hormone; PCR: polymerase chain reaction; CMV: cytomegalovirus.

Courtesy of Anil Chandraker, MD.

- **Infectious issues** – Infections such as upper respiratory or urinary tract infection are common in kidney transplant recipients. Decongestants and nonsteroidal antiinflammatory agents should be avoided. Patients are also at risk for opportunistic infections including cytomegalovirus (CMV), *Pneumocystis jirovecii* (formerly carinii) pneumonia (PCP), and polyomavirus (BK and John Cunningham [JC] virus).
- **Cardiovascular disease** – CVD is the major cause of death and graft loss in diabetic kidney transplant recipients. Potentially modifiable risk factors for CVD such as hypertension, hyperlipidemia, and obesity should be addressed. Some risk factors are caused or exacerbated by immunosuppressive medications.

- posttransplant diabetes mellitus:
- Reasons for the relatively high incidence of PTDM include the following:
- ●The new kidney metabolizes and excretes insulin more efficiently than the failing native kidneys.
- ●The transplanted kidney is gluconeogenic.
- ●Immunosuppression medications, such as glucocorticoids, calcineurin inhibitors (CNIs), and mammalian (mechanistic) target of rapamycin (mTOR) inhibitors, are diabetogenic.
- ●Preexisting risk factors (eg, increased age, obesity, being African American, family history of diabetes or gestational diabetes, and hepatitis C virus infection) predispose patients to developing diabetes.

- **Malignancy** – Cancer is more common among transplant recipients than in the general population. Kidney transplant patients should have the same routine cancer screenings as those recommended for the general population, except for skin cancer screenings, which should be performed monthly by self-skin examinations, with total-body skin examinations completed every six months to yearly by expert clinicians and dermatologists.
- **Bone disease** – Bone disease is common following kidney transplantation. Patients should be regularly monitored for hyperparathyroidism, vitamin D deficiency, hypercalcemia, and hypophosphatemia. In addition, kidney transplant recipients should undergo assessment of bone mineral density pretransplant, with subsequent monitoring dependent upon whether the patient has evidence of osteoporosis.

Complications of renal transplantation

- **Any time post-transplant**
- **Post-transplant infections**
- **Graft rejection**
- **Adverse effects of immunosuppressants (e.g., calcineurin-induced nephrotoxicity)**
- **Recurrence of primary disease**

- **Acute postoperative (< 1 week)**
- **Acute tubular necrosis**
- **Urinary leakage**
- **Renal vein thrombosis (rare and serious)**

- **Early (1–12 weeks)**
- **Urinary tract obstruction (acute)**
- **Etiology: extraluminal compression (e.g., hematoma), edema, thrombus, kinking of the anastomosis**
- **Clinical features: renal colic, hematuria, oliguria**
- **Lymphocele**
- **Renal artery thrombosis**

Complications

Late (> 12 weeks)

- Renal artery stenosis: most common vascular complication
- Urinary tract obstruction (subacute or chronic)
- Post-transplant malignancy (e.g., renal cell carcinoma)

Immunosuppression medication complications:

- Diabetes
- Bone thinning and bone damage
- Increased risk of cancer, particularly skin cancer and lymphoma
- High blood pressure
- High cholesterol

Transplant rejection

TYPE OF REJECTION	ONSET	PATHOGENESIS	FEATURES
Hyperacute	Within minutes	Pre-existing recipient antibodies react to donor antigen (type II hypersensitivity reaction), activate complement	Widespread thrombosis of graft vessels (arrows within glomerulus A) → ischemia and fibrinoid necrosis Graft must be removed
Acute	Weeks to months	Cellular: CD8+ T cells and/or CD4+ T cells activated against donor MHCs (type IV hypersensitivity reaction) Humoral: similar to hyperacute, except antibodies develop after transplant (associated with C4d deposition)	Vasculitis of graft vessels with dense interstitial lymphocytic infiltrate B Prevent/reverse with immunosuppressants
Chronic	Months to years	CD4+ T cells respond to recipient APCs presenting donor peptides, including allogeneic MHC Both cellular and humoral components (type II and IV hypersensitivity reactions)	Recipient T cells react and secrete cytokines → proliferation of vascular smooth muscle, parenchymal atrophy, interstitial fibrosis Dominated by arteriosclerosis C Organ-specific examples: ▪ Chronic allograft nephropathy ▪ Bronchiolitis obliterans ▪ Accelerated atherosclerosis (heart) ▪ Vanishing bile duct syndrome
Graft-versus-host disease	Varies	Grafted immunocompetent T cells proliferate in the immunocompromised host and reject host cells with "foreign" proteins → severe organ dysfunction HLA mismatches (most importantly HLA-A, -B, and -DR antigens) ↑ the risk for GVHD Type IV hypersensitivity reaction	Maculopapular rash, jaundice, diarrhea, hepatosplenomegaly Usually in bone marrow and liver transplants (rich in lymphocytes) Potentially beneficial in bone marrow transplant for leukemia (graft-versus-tumor effect) For patients who are immunocompromised, irradiate blood products prior to transfusion to prevent GVHD

THANK YOU