Principles of Renal Replacement Therapy

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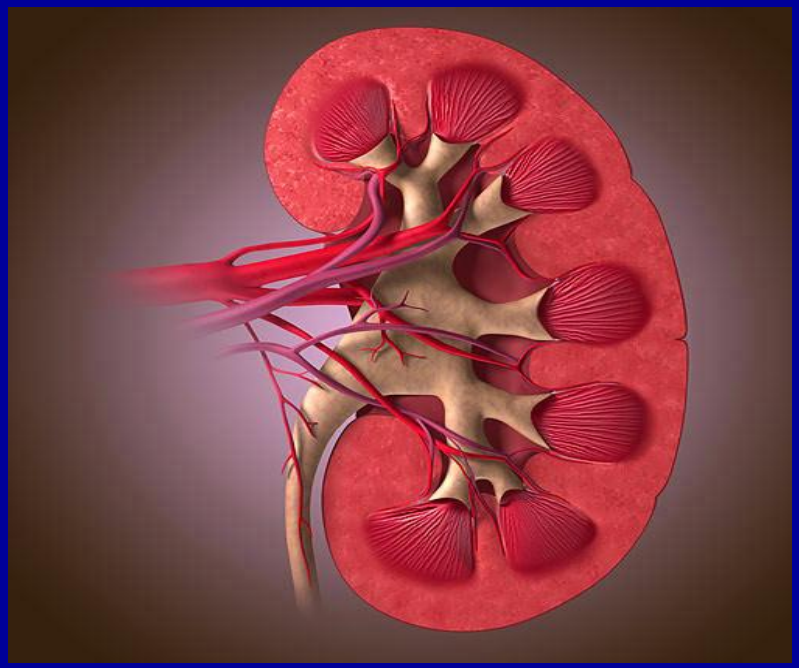


Objectives

- Review principles of chronic renal replacement therapy
  - Hemodialysis (HD)
  - Peritoneal dialysis (PD)
- Discuss considerations for drug dosing with chronic renal replacement therapy
- Review continuous renal replacement therapy (CRRT)

Chronic Renal replacement Therapy

- Hemodialysis (HD) –defined by characteristics of dialyzer filter
  - Conventional
  - High Efficiency
  - **High Flux**
- Peritoneal Dialysis (PD)

Goals of dialysis

- Replace diffusive functions of the kidney (solute removal)
- Replace convective functions of the kidney (remove excess free water)
- Dialysis *cannot* replace metabolic functions or hormone production
- Dialysis *cannot* perform active transport

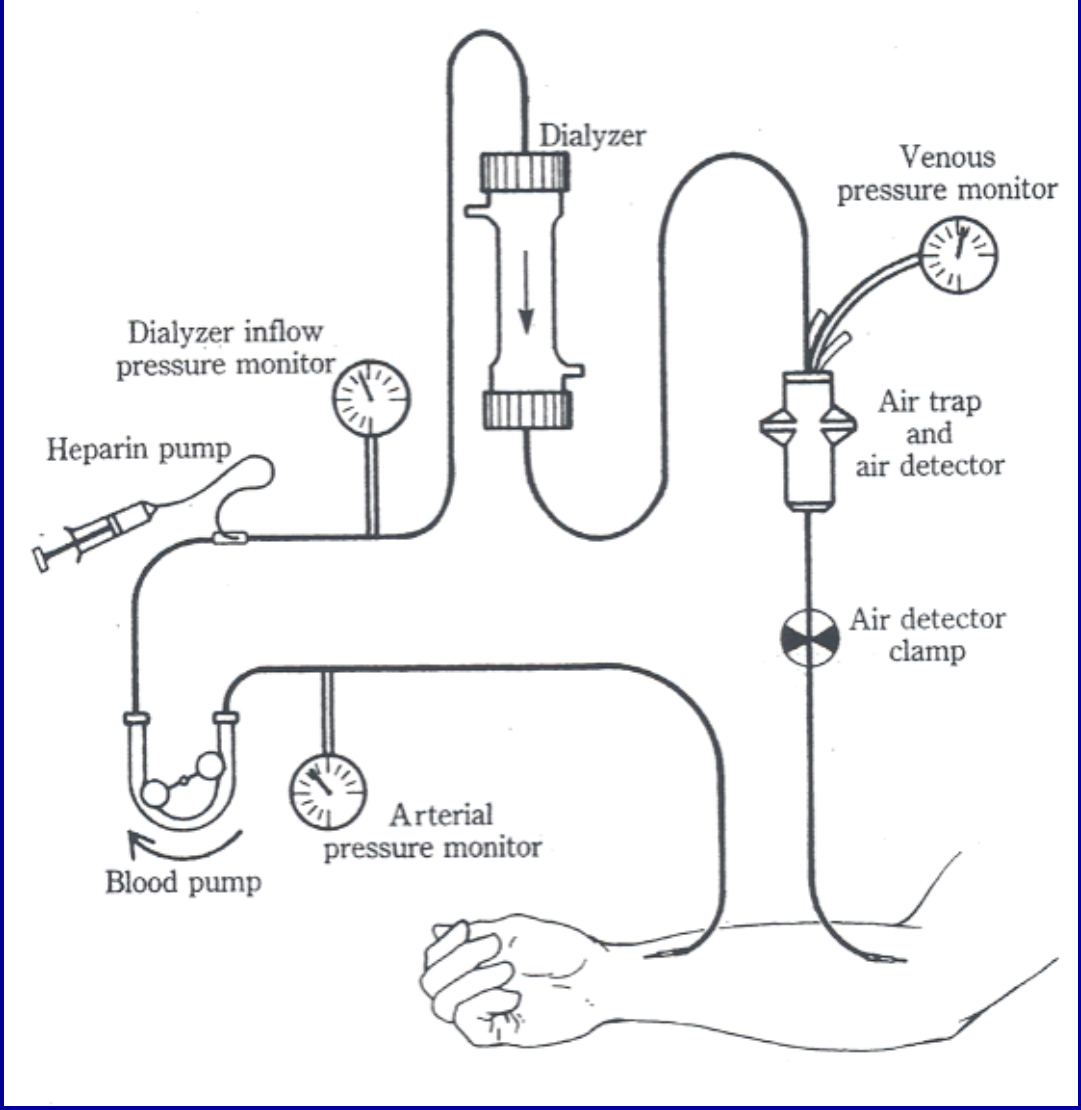
Hemodialysis classification

- Intermittent
  - Conventional or High Flux run 3-4 hours in length three times per week or more (common in the USA)
  - Long intermittent dialysis runs over 8 hours three times per week
- Daily
  - Short session:2-2.5 hours 6 to 7 days per week
  - Home nocturnal hemodialysis: 8 hours overnight 6 to 7 days per week

Intermittent Hemodialysis System Components

- Dialysis machine
- Dialyzer membrane
- Dialysate solution
- Vascular Access
  - Temporary
  - Permanent (Fistula or Graft)

The Blood Circuit - Hemodialysis



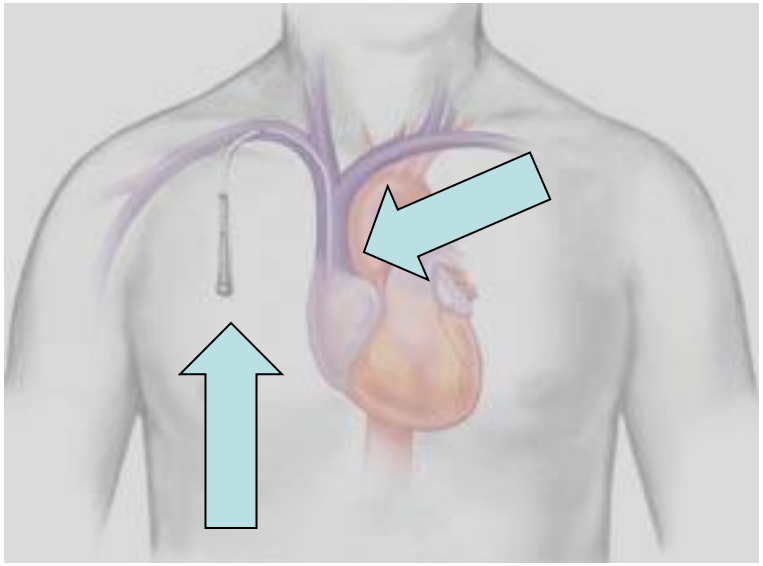
Blood Access is Primary!

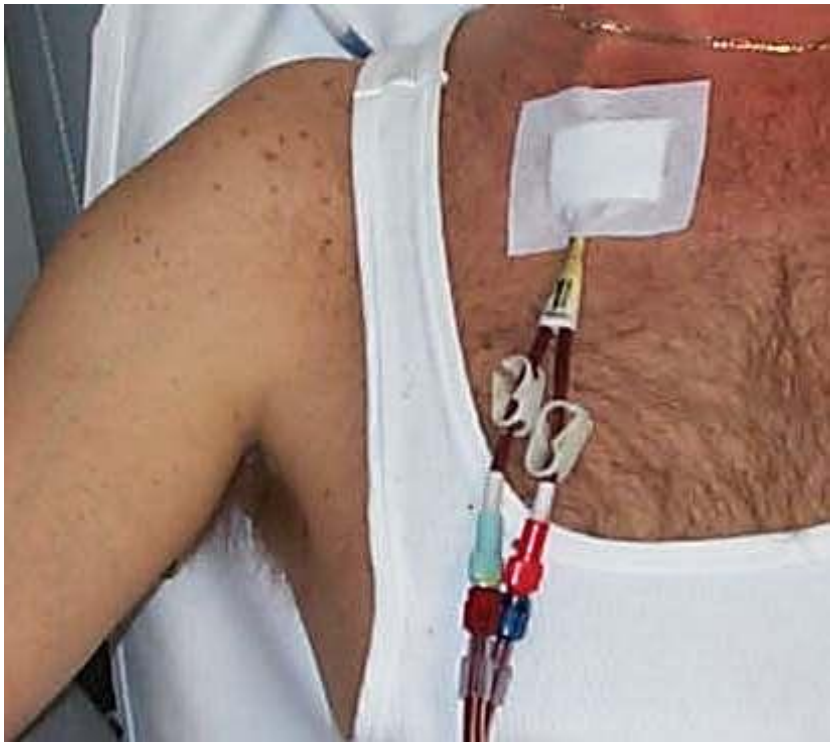
- Hemodialysis is *not possible* without access to very high blood flow rates (to allow >300ml/min through HD circuit)
- High flow access sites
  - **Temporary** catheter in a high flow vein
  - **Permanent** high-flow site surgically created

Temporary Vascular Access

- Temporary venous access: double lumen catheter (blood flows from patient through one lumen of the catheter into dialysis blood circuit and back through the second lumen into patient)
  - Subclavian vein
  - Femoral vein
  - Internal jugular vein

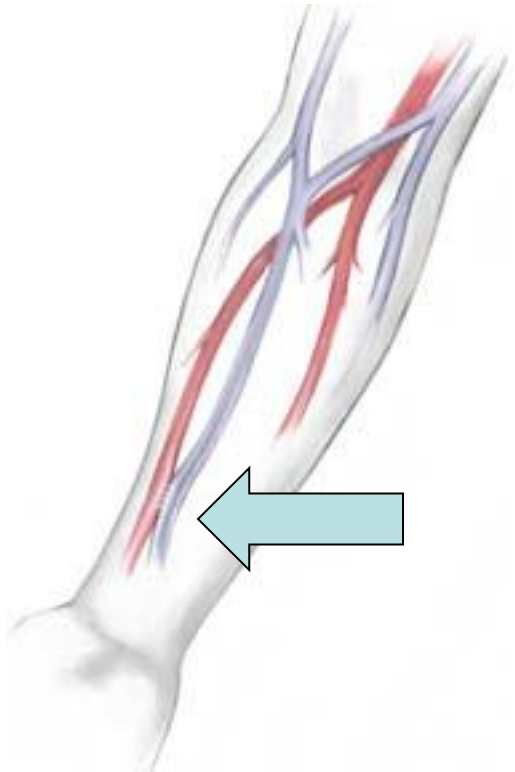
Double Lumen Subclavian catheter



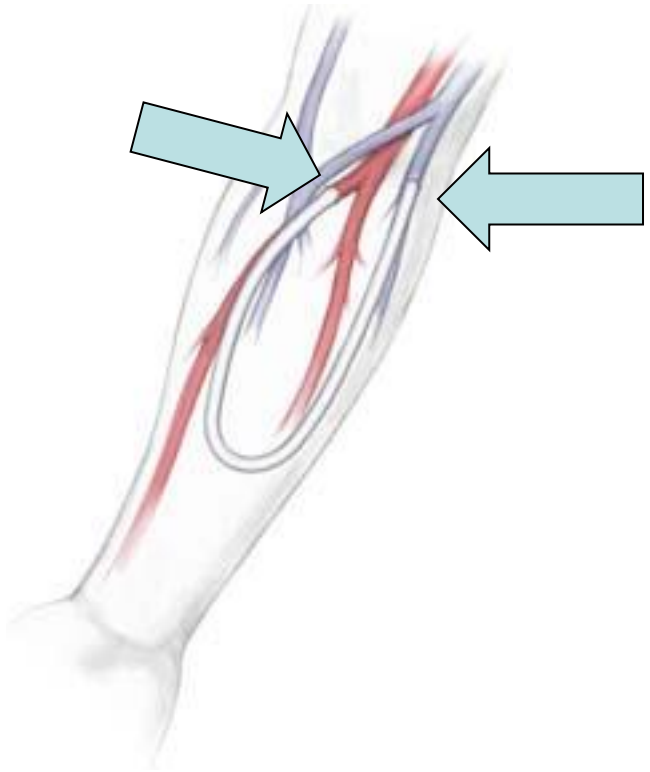


Gold Standard: Permanent Access

- Arteriovenous Fistula



- Arteriovenous Graft



Radiocephalic AV Fistula

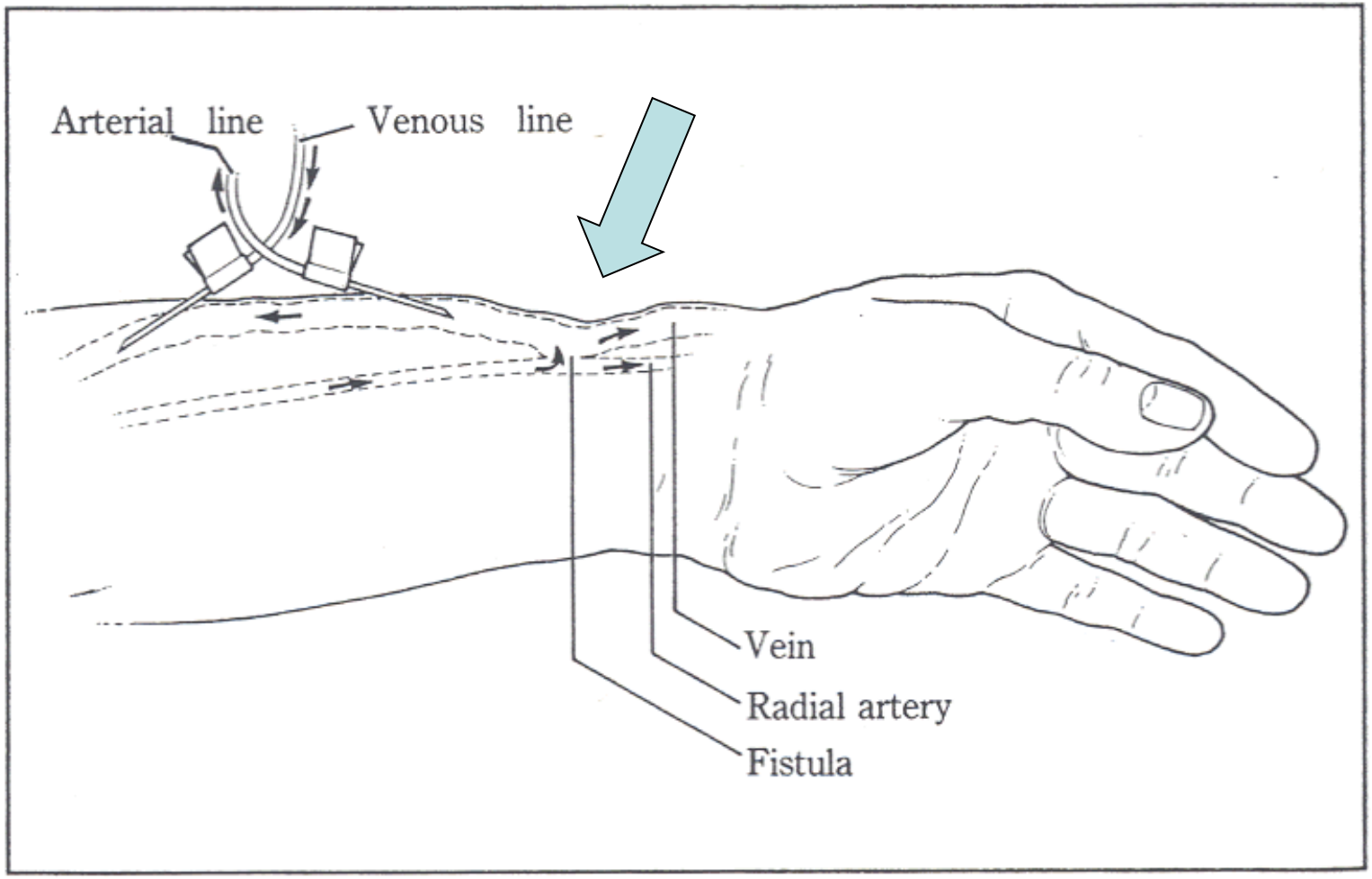
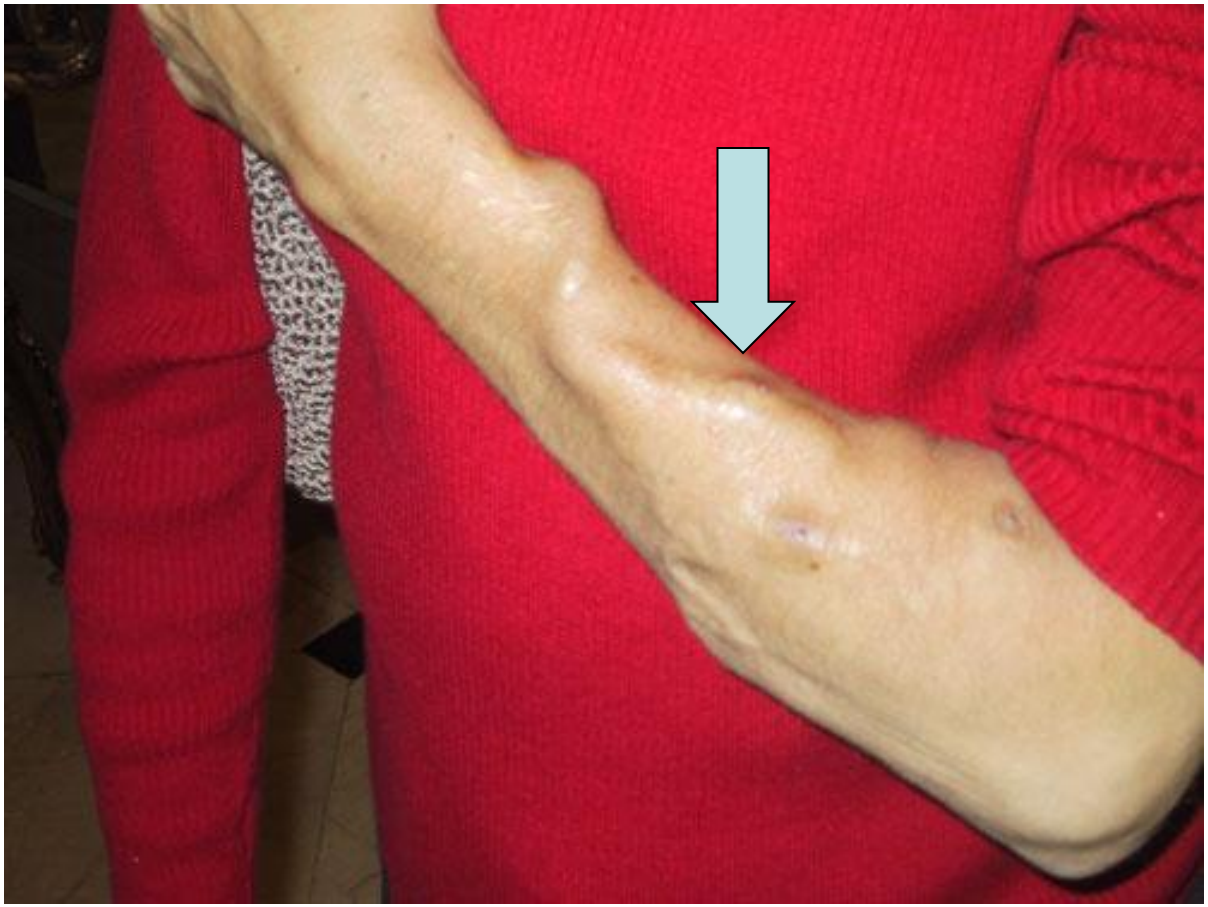


Fig. 4-4. The radiocephalic AV fistula, showing blood flow and the usual position of the access needles.

AV Fistula

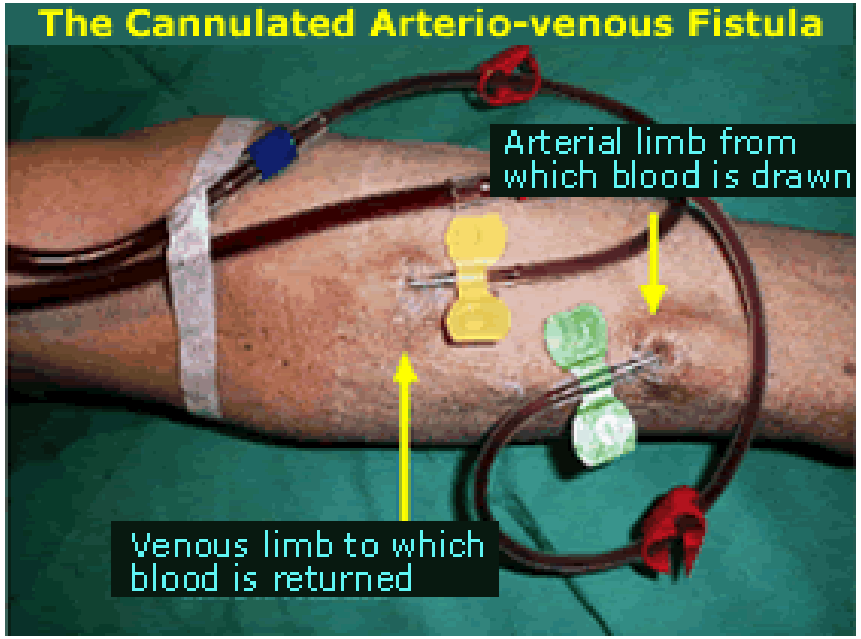
- The fistula is created 2 to 6 months prior to initiation of dialysis
- The fistula matures over 2 months – cannot be used before mature
- Connects the radial artery to the cephalic vein in the non-dominant arm
- The venous limb of the fistula dilates and thickens permitting repeated insertion of the dialysis needles three times weekly
- Lasts for years (3 yr fistula survival rate 65-75%)
- Blood flow is 1-2L/min(20-30% of cardiac output) – can cause "steal syndrome" (distal ischemia).

AV fistula - mature



AV Fistula

- Cannulated for HD session



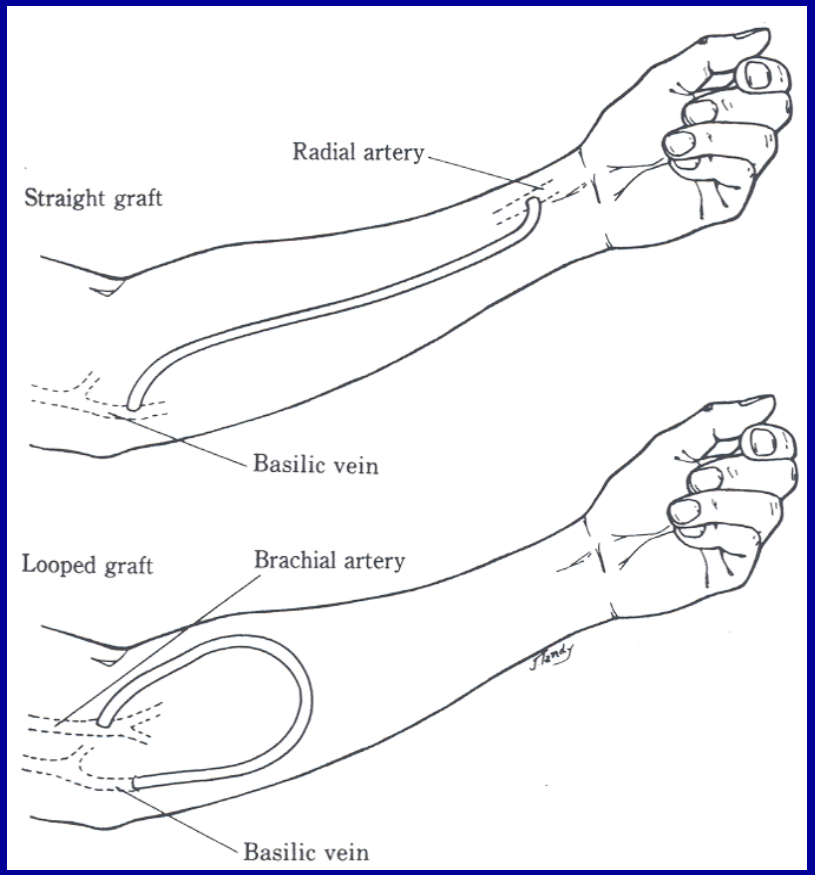
Poor Candidates for AV Fistula

- Morbidly obese
- Poor arterial flow (diabetes or severe atherosclerosis)
- Elderly
- Deep veins

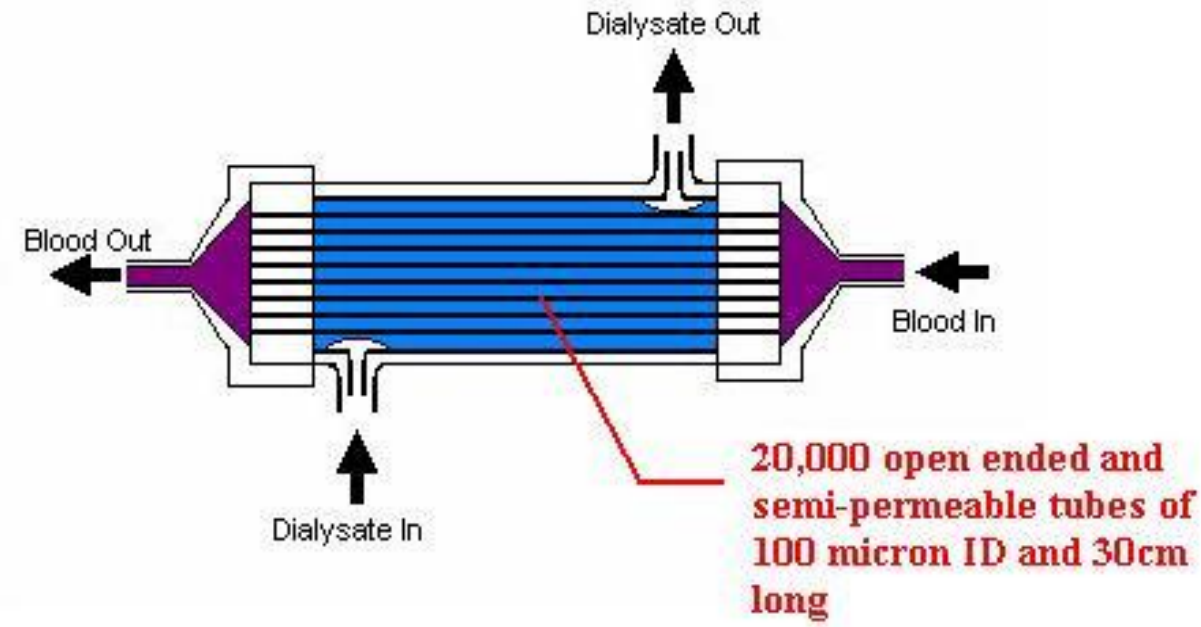
SOLUTION – USE AN AV GRAFT!

Common AV Grafts and Possible Complications

- Stenosis (narrowing) at the anastomotic site and thrombosis
- Infections (5-20% incidence) – increased incidence if graft used before sufficient healing of the subcutaneous tunnel



SCHEMATIC OF A HEMO-DIALYSIS DEVICE



source http://www.shodor.org/master/biomed/physio/dialysis/hemodialysis/fig2.jpg

Goals of Dialysis

- Attempt to normalize body chemistry and fluid status by removing uremic solutes and excess fluid.
- Although HD is twice as efficient in removing small molecules (urea) compared to functioning kidneys, it is only performed for 9-12 hours per week (overall less efficient).

Physiologic Principles of Hemodialysis

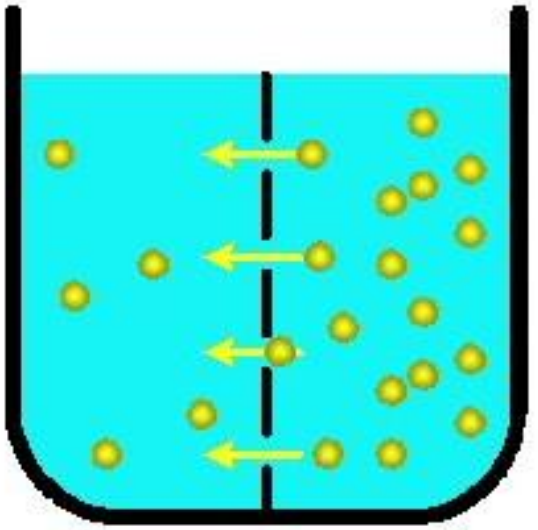
- Solute transport from plasma into the dialysate solution is accomplished primarily by diffusion (and to lesser extent convection).
- Removal of excess fluid accomplished by convection alone
  - The pressure of the plasma within the capillary tubes of the filter is higher than dialysate solution surrounding the capillary tubes.
  - This forces free water and some solutes across the membrane and into the dialysis solution

Physiologic Principles of Hemodialysis

- ***Diffusion***: solute clearance enhanced by blood flow running countercurrent to dialysate flow (maintains high concentration gradient between plasma and dialysate at all times)
- ***Ultrafiltration (convective transport)*** removes excess fluid volume (0.5L/hr) due to the hydrostatic pressure gradient between the plasma and dialysate solution; solutes small enough to pass thru membrane pores are swept along with water (solvent drag).

Principles of Dialysis

- Diffusion-movement of solutes across the membrane
- K, BUN, phosphate, creatinine move from blood to dialysate solution
- Dialysate solution solutes can move into blood to a limited extent



Diffusion

(Solvent moves by concentration gradient)

The Dialysis Prescription

- The nephrologist prescribes the dialysis session:
  - Length of session
  - Goal ultrafiltrate removal (in kg)
    - It is possible to perform dialysis without fluid removal
  - Dialysate composition – drives diffusion
    - Calcium, potassium can be prescribed for the dialysate fluid

Dialysate solution (HD)

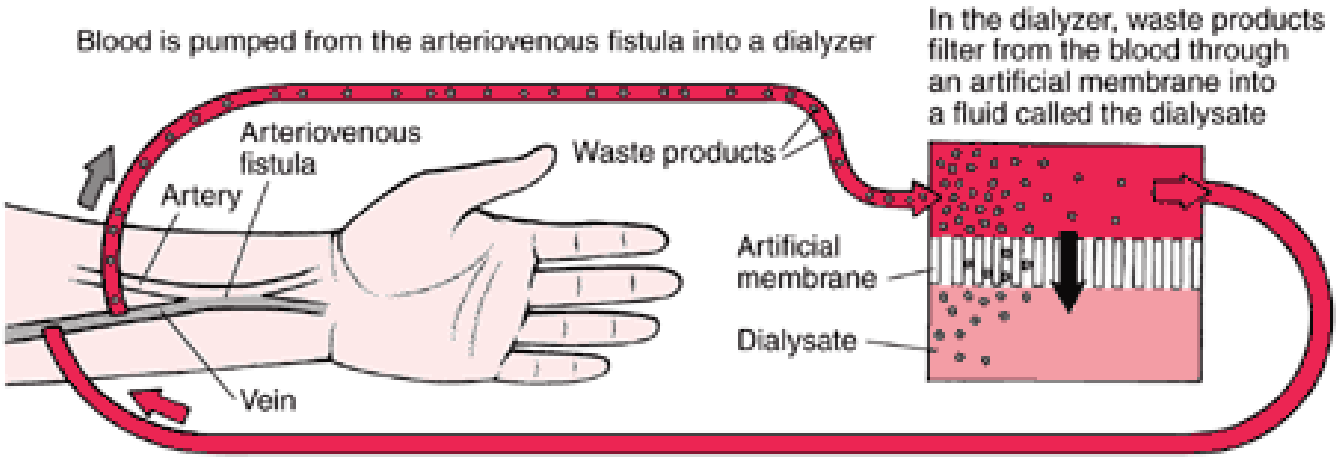
Na^+	132-145 mEq/L	No net transport. Less than 135 mEq/L in dialysate associated with leg cramps and hypotension during HD
K^+	0 – 4 mEq/L	Net movement from blood into dialysate
Cl^-	103-110mEq/L	No net transport
$HCO3^-$	0 – 40mEq/L	buffer
(Acetate)	2 – 37	buffer
Ca^{++}	0 – 3.5 mEq/L	Variable
Mg^{++}	0.5 – 1 mEq/L	Net movement from blood into dialysate
Glucose	0 – 200mg/dL	Prevent hypoglycemia

Example of Pre- and Post-Hemodialysis Lab Values

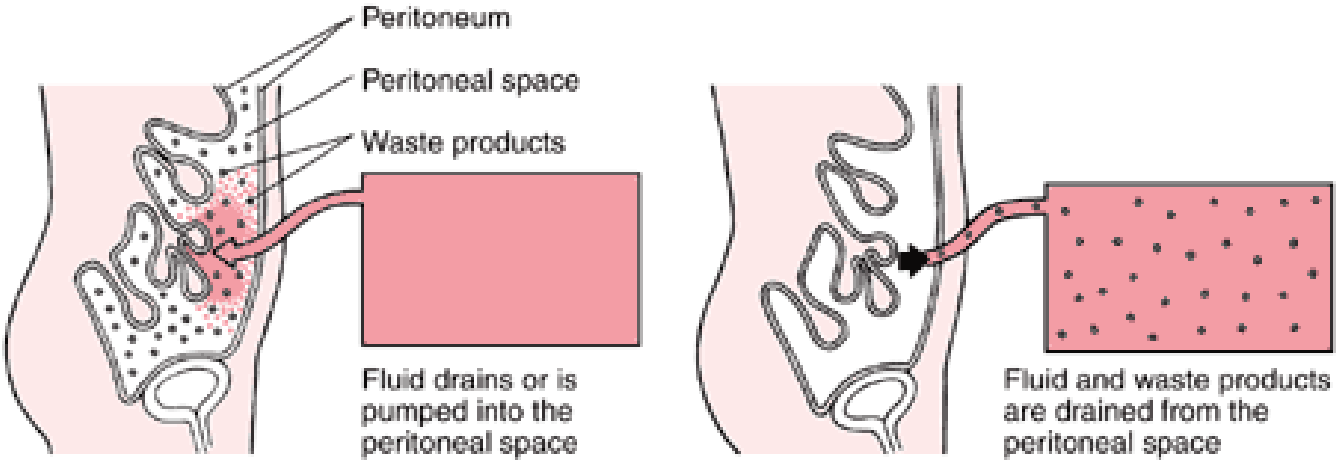
- Na^+ 140 mEq/L (same pre and post)
- K^- 6.5 mEq/L (4.5 mEq/L post)
- $HCO3^-$ 16 mEq/L (22 mEq/L post)
- pH 7.30 (7.4 post)
- BUN 100 mg/dL (40 mg/dL post)
- Serum Creatinine 6 mg/dL (5.4 mg/dL post)

More than one type of Dialysis

- Hemodialysis
- Peritoneal Dialysis



Hemodialysis



Peritoneal Dialysis

Removal of solutes during Peritoneal Dialysis

- **Diffusion** is the principle mechanism by which peritoneal dialysis removes waste products and selected electrolytes (urea, creatinine, potassium, magnesium, etc.)
- The **concentration gradient** between the dialysis solution and the capillary blood drives diffusion.
- **Maximum diffusion** occurs when fresh dialysis fluid is first instilled in the peritoneal cavity but diffusion efficiency decreases over time.
- **Frequent exchanges** of dialysate solution (usually 4 -5 times per day) maintains diffusion efficiency.

Removal of fluids during Peritoneal Dialysis

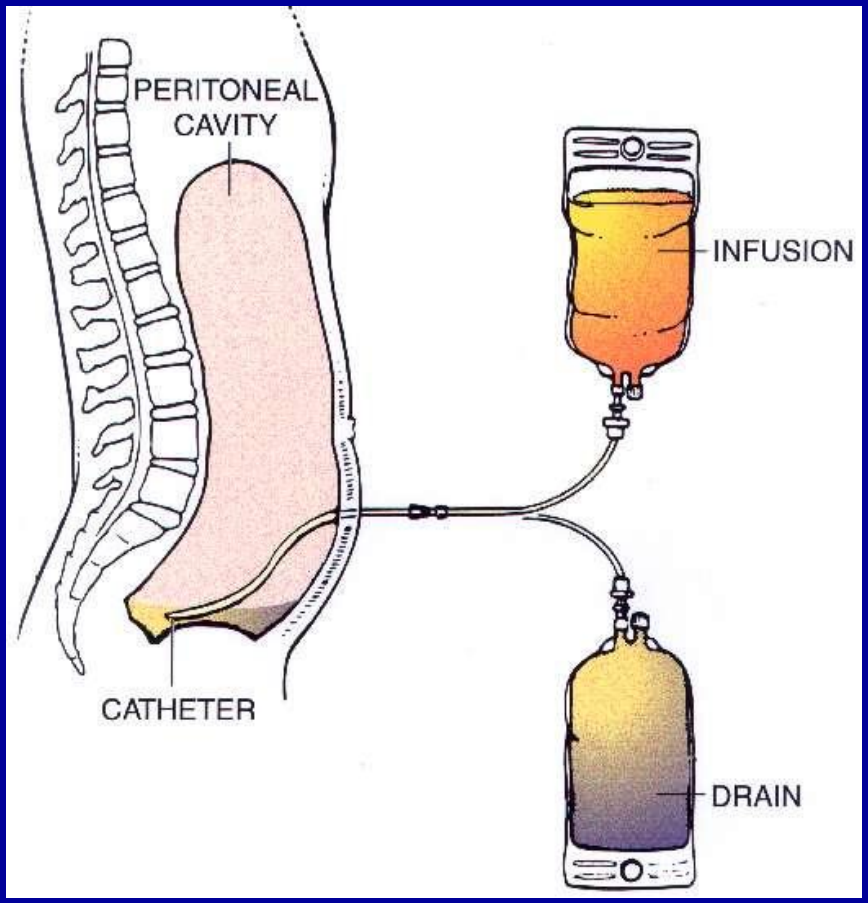
- **Ultrafiltration** is the mechanism by which the bulk movement of water from the capillary blood moves across the peritoneal membrane into the PD dialysis solution in the peritoneal cavity.
- **The osmotic pressure of the high glucose concentration** in the PD dialysate solution draws water from the capillary blood supply into the dialysate solution (osmotic ultrafiltration). This differs from HD in which the hydrostatic pressure gradient is the driving force for ultrafltration during hemodialysis.

Typical Peritoneal Dialysis Solution

Dextrose	2.5%	Drives Osmotic Ultrafiltration (2.5% = 2500mg/dL in PD fluid vs 100 mg/dL in plasma). Can add insulin to each PD bag if patient has persistent hyperglycemia.
Sodium	132 mEq/L	No net diffusion of sodium
Sodium Lactate	40mEq/L	Buffer (cannot use bicarbonate in bag – will precipitate as calcium carbonate)
Magnesium	0.5 mEq/L	Net diffusion of Mg^{++} from blood into PD solution
Calcium	3.5 mEq/L	Net diffusion of Ca^{++} into blood (not all PD dialysate bags have high Ca^{++})
Chloride	96 mEq/L	No net diffusion of chloride
pH	5.5	Low pH prevents carmelization of glucose during sterilization-may cause discomfort for the patient when new PD fluid instilled

Peritoneal Dialysis

- CAPD vs cycler



Treatment of peritonitis during CAPD

- **Antibiotics** can be added to the PD dialysate solution to treat peritonitis (at home by patient or in hospital by RN)
- The concentration of the antibiotic in the PD fluid is similar to the concentration that could be achieved in the blood during IV antibiotic therapy.
- Patients can initiate antibiotic treatment at home under the direction of the PD nurse .
- Example: adding cefazolin to each PD bag to obtain a concentration of 125 mg/L to treat gram positive cocci (Staphylococcus).

Continuous Renal Replacement Therapies (CRRT)

- Since CRRT is continuous, there is less fluctuation of volume status, solute concentration and acid-base balance overall.
- The major advantage of CRRT is the *slower rate* of solute or fluid removal per unit of time. Important for hemodynamically unstable patients in an ICU setting.
- CRRT better tolerated than intermittent HD since most complications related to intermittent HD are due to *rapid loss* of fluid and solutes

CRRT

- Continuous Renal Replacement Therapy
  - Slow Continuous Ultrafiltration: SCUF
    - **Provides only ultrafiltration using conventional dialysis machines**
  - Continuous Hemofiltration
    - **CVVH**: continuous venovenous hemofiltration
    - CAVH: continuous arteriovenous hemofiltration
  - Continuous hemodiafiltration
    - combines continuous hemofiltration (convection) with continuous hemodialysis (diffusion)

Hemofiltration

- Hemofiltration (CVVH) – used when primary goal is fluid removal in patients with need to remove some small solutes.
- Removes fluids and solutes by convection only – the efficiency of solute removal is low.
- Requires the removal of 10-15L of ultrafiltrate per day to remove sufficient solutes. Must replace excess fluid loss by giving a balanced electrolyte solution as "replacement fluid"
- No dialysis solution involved in process (no diffusion).

CVVH vs. iHD

	CVVH	Intermittent HD
Blood Flow rate	**100-150 ml/min**	**250-450 ml/min**
Solute removal	**Convection**	**Diffusion**
Pharmacy orders	**Large amount of fluid replacement bags supplied by pharmacy**	**NA**
Technical complexity	**Technically less difficult but higher workload (24 hours/day)**	**Technically more demanding but lower workload (2-8 hours/day)**
Cost	**3 to 5 x more expensive than iHD**	**Relatively inexpensive**

Drug Dosing with Renal Replacement Therapy

- Clinical Pearls
  - Recommendations for drug dosing must be based on type of renal replacement therapy used (HD, PD, CRRT)
  - Drugs removed by hi-flux HD may not be removed by conventional filter HD
  - Peritoneal dialysis can remove drugs not removed by conventional and high flux HD
  - Distinguish between patients on renal replacement therapy vs. renal insufficiency without renal replacement.
  - Only knowing serum creatinine (or calculated CrCl) is **NOT** sufficient information. Hemodialysis clears creatinine – using a calculated CrCL for dosing is incorrect for HD patients – must use HD specific dosing recommendations.

Drug Dosing with Renal Replacement Therapy

- Clinical Pearls
  - Calculation of Creatinine Clearance is not appropriate for HD patients.
  - HD clears creatinine temporarily, so calculated Creatinine Clearance only reflects one point in time and may be misleading if calculated shortly after a HD session.
  - Vancomycin example
    - **Calculated CrCl after HD session = 30ml/min; if pharmacist not aware patient is on HD, would dose as 10mg/kg every 24 hours**
    - **Appropriate dosing for HD is 10-15mg/kg after each HD session (3 x per week if chronic HD) or after each HD session if on "as needed" HD for AKI**

Transition from CRRT to iHD

- Critically ill patients with acute renal failure may require CRRT in the ICU setting.
- If dialysis is still required when transferred from an ICU to an intermediate or general care unit, multiple consecutive daily dialysis sessions may be required before transitioning to a three times per week chronic dialysis schedule.

Transition from CRRT to iHD

- Dosing for daily or "as needed" dialysis requires that the pharmacist know the HD schedule (the date and time for each HD session)
- Considerations for dosing in this situation:
  - Residual urine output
  - Volume of ultrafiltrate removed
  - Length of HD session
  - Type of dialyzer filter: high flux versus conventional
  - Pharmacist clinical expertise and knowledge of drug clearance with hemodialysis
  - No easy answers – follow drug levels if possible

References

- Stefan, John and Eckardt Kai-Uwe *Renal replacement strategies in the ICU Chest* 2007:231(4) 1379-1388
- DeGaurdis(editor) Handbook of Dialysis 5th Edition
- Himmelfarb J and Ikizier TA *Hemodialysis* NEJM 2010 Nov ; 363: 1833-1845

- Please contact me via e-mail if you have any questions on the material

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