

من و دیالیز و پیوند

DIALYSIS AND TRANSPLANTATION & ME

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Learning Objectives

- ▶ Describe treatment options for renal replacement therapy to improve awareness and understanding.
- ▶ Use evidence-based strategies to manage patients with kidney failure in need of renal replacement therapy to improve outcomes.
- ▶ Manage patients receiving dialysis or living with a kidney transplant, from a primary care perspective.

Question 1

A patient with progressive CKD has opted for hemodialysis for renal replacement therapy. Which type of vascular access is associated with better outcomes in hemodialysis patients?

- A. Central venous cuffed catheter
- B. Arteriovenous graft
- C. Arteriovenous fistula
- D. Temporary central venous catheter

Question 2

Another patient with progressive CKD is considering a kidney transplant. Which one of the following statements is correct?

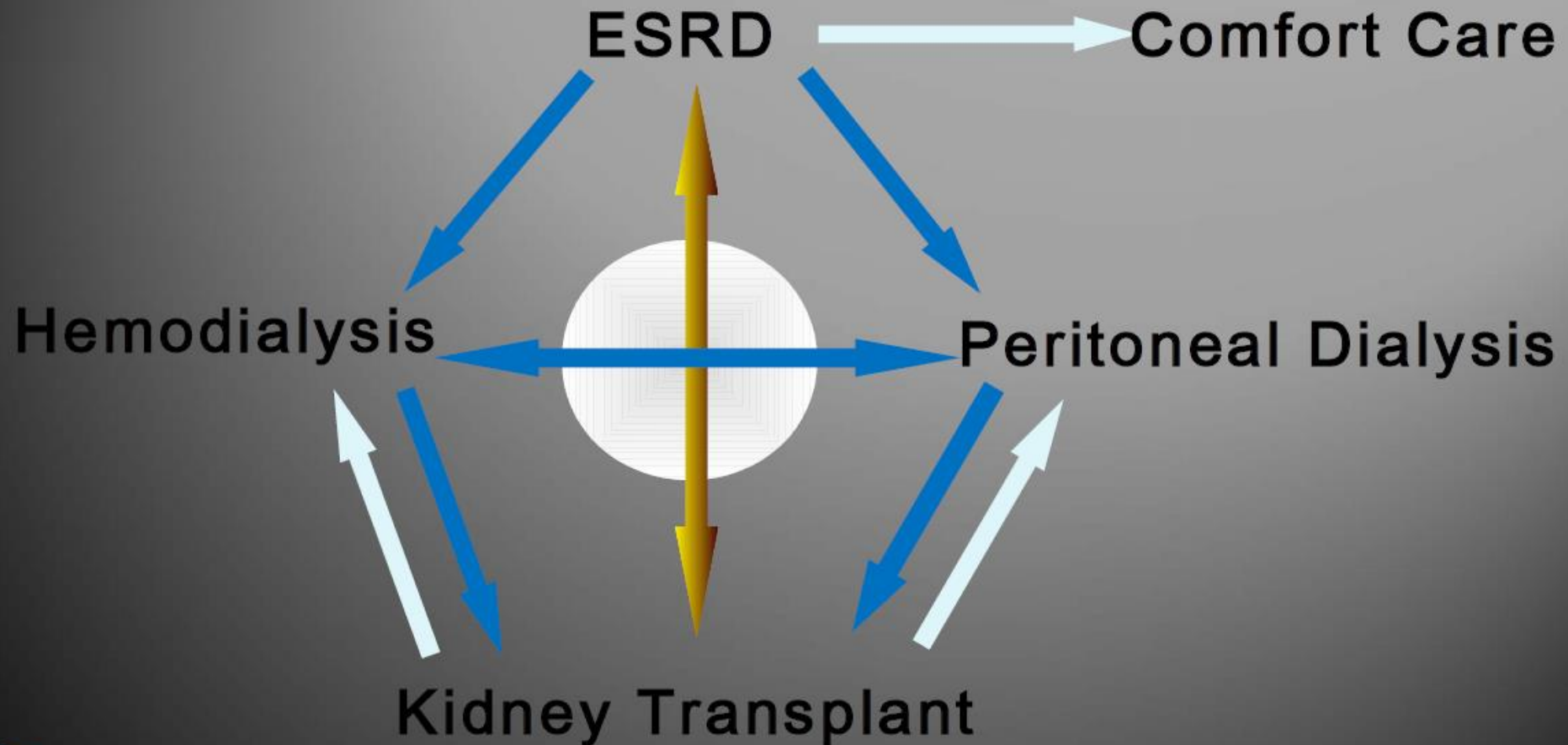
- A. CKD patients can be referred to a transplant center when their GFR is $< 20 \text{ mL/min/1.73m}^2$
- B. Pre-emptive and live kidney transplants are associated with better graft survival
- C. Most common cause of kidney transplant loss is death with a functional transplant
- D. All of the above

Renal Replacement Therapy Overview and Considerations for the PCP

Indications for Renal Replacement Therapy

- ▶ Hyperkalemia
- ▶ Metabolic acidosis
- ▶ Fluid overload (recurrent CHF admissions)
- ▶ Uremic pericarditis (rub)
- ▶ Other non specific uremic symptoms:
anorexia and nausea, impaired nutritional status, increased sleepiness, and decreased energy level, attentiveness, and cognitive tasking, ...

Treatment Options for Renal Replacement Therapy



Referral and Education for Patients with Progressive CKD

- ▶ Refer patients early, when eGFR < 30 ml/min/1.73 m²
- ▶ Education about types of renal replacement therapy:
 - Hemodialysis (vascular access +++)
 - Peritoneal Dialysis (QOL advantage +++)
 - Kidney Transplantation
 - ▢ Refer when eGFR < 20 ml/min/1.73 m²
 - ▢ Living kidney transplant (family, friends)
 - ▢ Build time on list before dialysis initiation
 - ▢ Even transplant before dialysis initiation (pre-emptive)
- ▶ No PICC lines for patients with eGFR < 45 mL/min/1.73m²

Advantages of Timely Referral in Patients with Progressive CKD

- ▶ Improves patient preparation for RRT
- ▶ Greater use of permanent vascular access
- ▶ Avoidance of emergent hemodialysis initiation
- ▶ Greater utilization of transplantation and self-care dialysis (i.e., peritoneal dialysis or home hemodialysis)
- ▶ Management of medications which may help to delay the need for RRT
- ▶ Gives the nephrologist adequate time to counsel patients through this challenging transition in their lives

Medical Health and Wellness: Components of Multidisciplinary Care in Progressive CKD

- ▶ Education and counseling about different RRT modalities, transplant options, and vascular access surgery
- ▶ Protocols for laboratory and clinic visits; with attention to CKD and CVD-associated comorbidities (e.g., high blood pressure)
- ▶ Ethical, psychological, and social care (e.g., social bereavement, depression, anxiety)
- ▶ Dietary counseling and education on other lifestyle modifications (e.g., exercise, smoking cessation)
- ▶ Vaccination program

Early Vaccination for Hepatitis B: Too Often Forgotten!

- ▶ Patients with ESRD have ↓ response to vaccination
(Secondary to general suppression of immune system)
- ▶ After Hepatitis B vaccination in ESRD patients:
 - 50 – 60 % develop antibodies, compared to > 90% in patients without renal failure
 - Have Lower titers
 - Have protective levels for shorter duration

Other Considerations for Vaccination in Patients with Progressive CKD

- ▶ Influenza vaccine annually, unless contraindicated.
- ▶ Polyvalent pneumococcal vaccine:
 - eGFR <30 ml/min/1.73m²
 - High risk of pneumococcal infection (e.g., nephrotic syndrome, diabetes, receiving immunosuppression), unless contraindicated.
 - Offer revaccination within 5 years.

TABLE 12.**Summary of routine vaccinations for kidney transplant candidates**

Routine Vaccines	Dosing Guidelines*	Comment
Inactive Vaccines		
Diphtheria, Pertussis, Polio, Tetanus, HiB	Generally given in childhood; Ensure these are up-to-date	
Pneumococcal Vaccination: PCV13, PPV23	One dose of PCV13 followed by one dose of PPV23 with a minimum of 8-week interval in between	One booster of PPV23 five years from previous PPV23
Influenza	One dose annually	
Hepatitis B	Three doses at 0, 1, 6 months	Check anti-HBs titer Monitor annually and give booster dose if titers decline <10 IU/ml
Hepatitis A	Two doses at 0, 2 months	Check titers; If not immune, give vaccination again (i.e., repeat if no response to first series)
Human Papillomavirus	Three doses in both males and females if not previously given (ages 9 to 45)	No boosters
Meningococcal quadrivalent conjugate (Serogroups A,C,Y,W-135)	Two doses given 8 weeks apart; Indicated for travel to endemic areas, prior or planned splenectomy or planned use of eculizumab	Repeat one dose every five years in patients at risk
Meningococcal B vaccine	One dose if planned use of eculizumab	

splenectomy or planned use of eculizumab

Meningococcal B vaccine	One dose if planned use of eculizumab	
Shingles (Herpes Zoster Subunit)	Two doses at 0, 2-6 months for those age \geq 50 years and VZV IgG positive	Unknown if benefit in less than 50 years of age No boosters
Live Vaccines		
Measles, Mumps, Rubella	Two doses given 4 weeks apart. Considered immune after two doses regardless of seroconversion.	Check serology and provide vaccination if negative
Varicella	Two doses given 4 weeks apart. Considered immune after two doses regardless of seroconversion.	Check serology and provide vaccination if negative
Shingles (Herpes Zoster Live)**	One dose in those age \geq 50 years and VZV IgG positive	Unknown if benefit in less than 50 years of age No boosters

*Duration and doses are suggestive only as they may be variable in different regions. Please check your local guidelines.

**The herpes zoster subunit inactivated vaccine is preferred over the herpes zoster live vaccine. If the herpes zoster live vaccine has already been administered, the transplant candidate can be reimmunized with the inactivated vaccine a minimum of one year after the live vaccine.

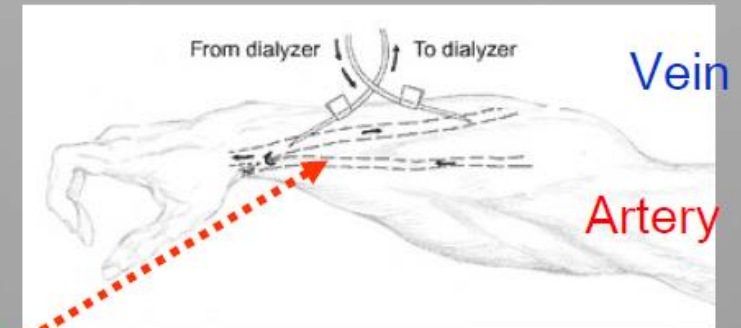
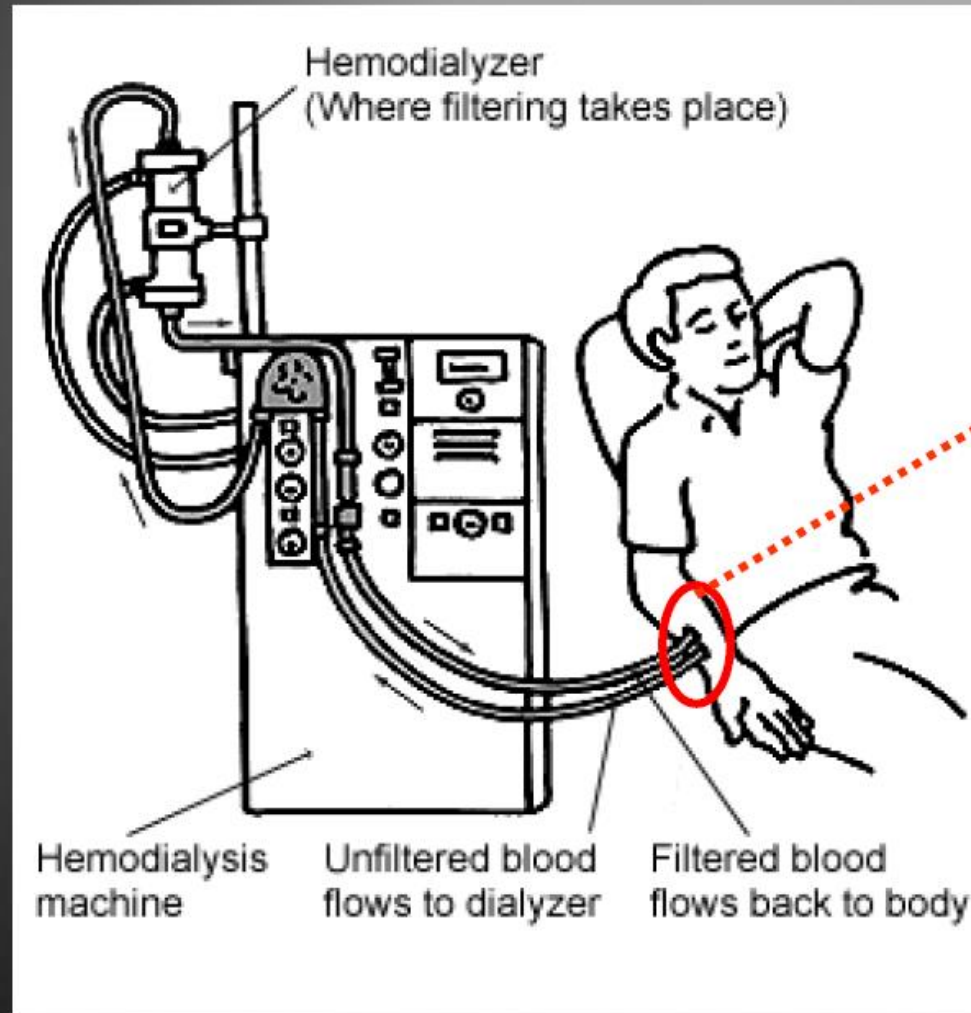
Anti-HBs, hepatitis B surface antibodies; HiB, hemophilus influenzae type b; IgG, immunoglobulin G; IU, international unit; PCV13, pneumococcal conjugate vaccine-13 valent; PPV23, pneumococcal polysaccharide vaccine-23 valent; VZV, varicella zoster virus.

High Blood Pressure

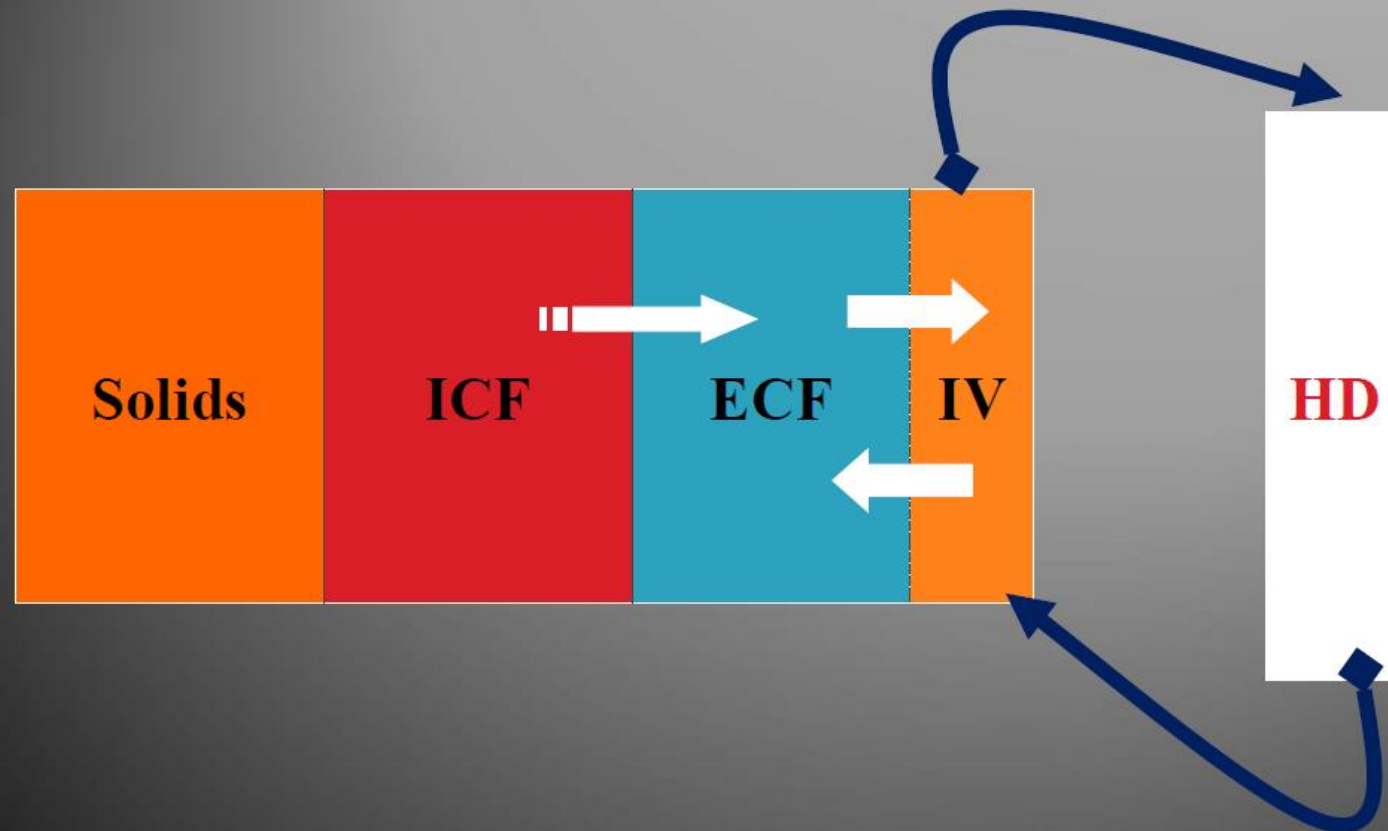
- ▶ Common in both dialysis and transplant populations
- ▶ Target blood pressure:
 - Dialysis:
 - ▢ Predialysis: <140/90 mm Hg
 - ▢ Postdialysis: <130/80 mm Hg
 - Transplantation: 130/80 mm Hg
- ▶ Managing high blood pressure in dialysis requires attention to fluid status and antihypertensive medications, while minimizing intradialytic fluid accumulation
- ▶ Can be impacted by certain immunosuppressants in kidney transplantation recipients. Monitor for adverse effects and drug–drug interactions

Hemodialysis (HD)

Principle of Hemodialysis



Urea Mass Transfer During Hemodialysis



Harmon W, Jabs K: Hemodialysis (chap 77) in Pediatric Nephrology, 4th ed
Barratt, Avner, Harmon (ed) Lippincott, 1999

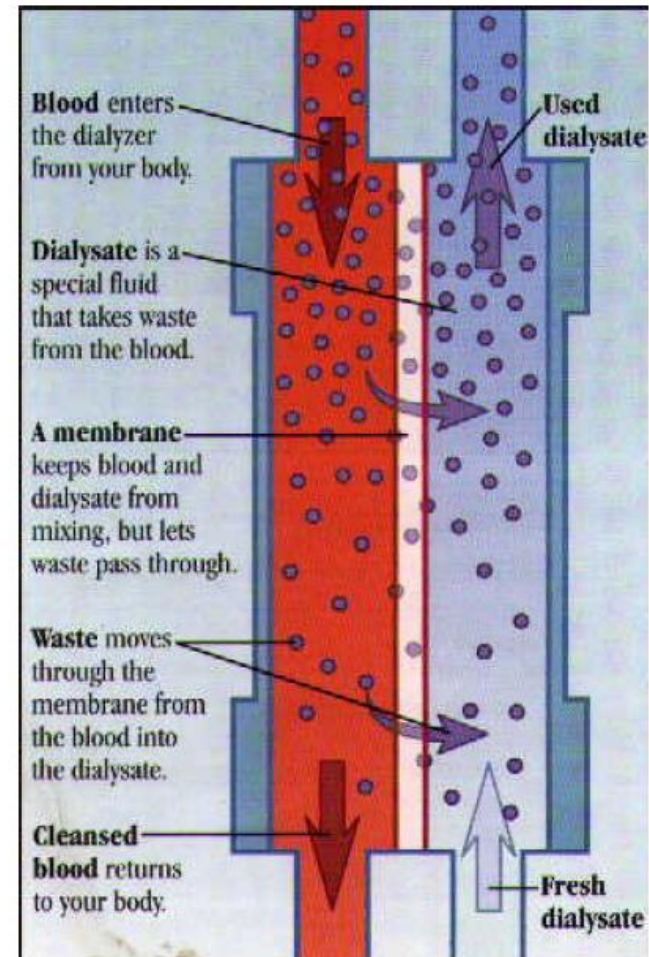
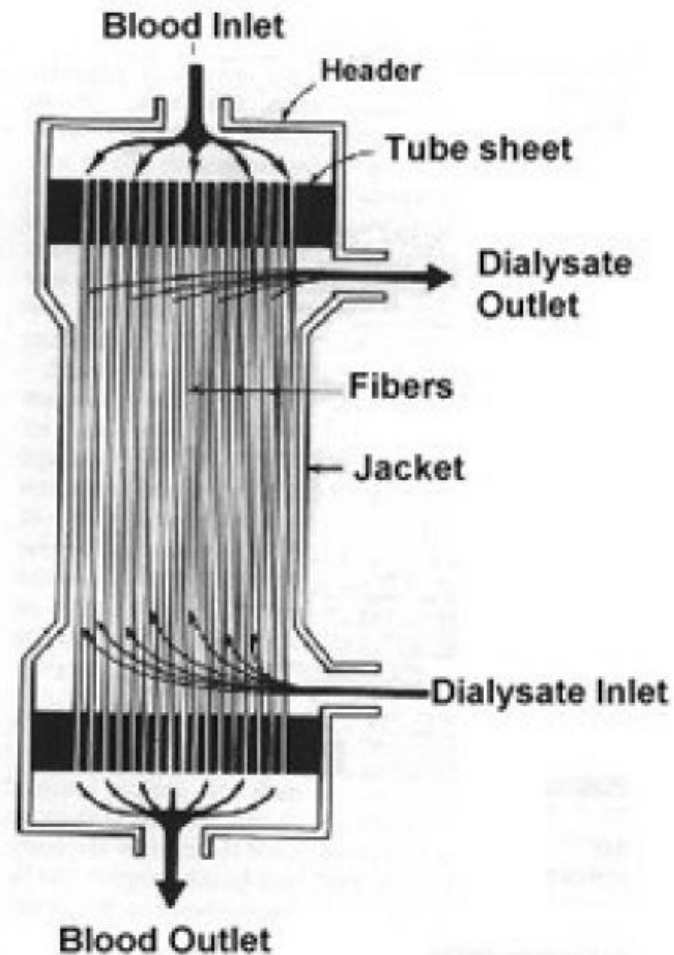
Dialyzer



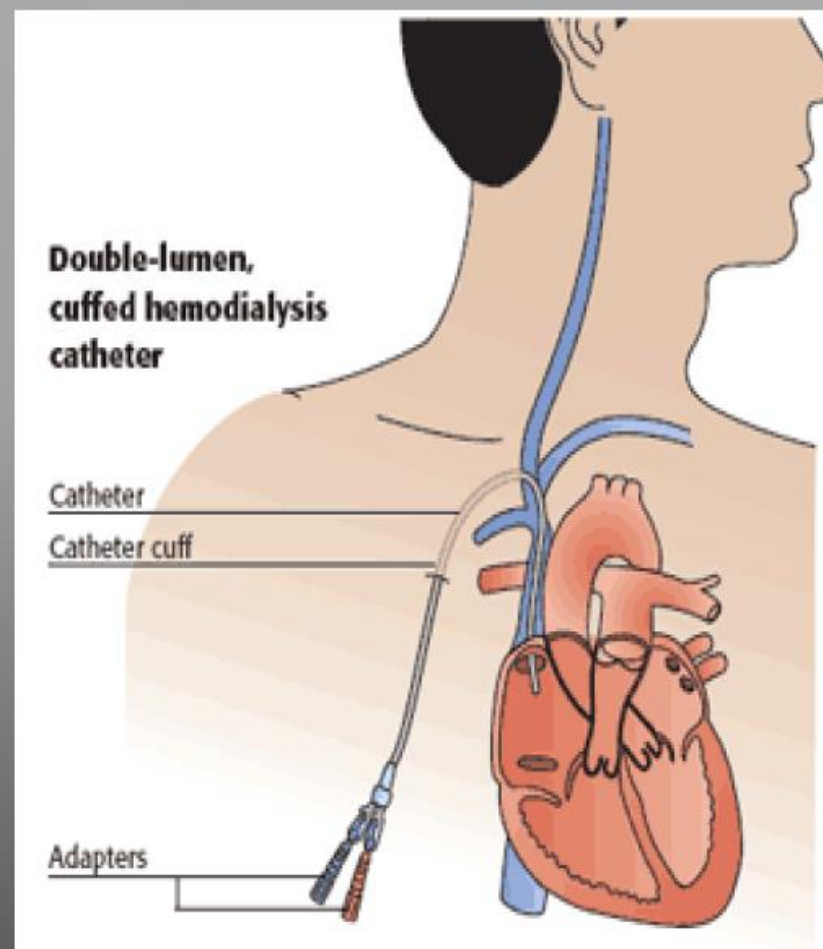
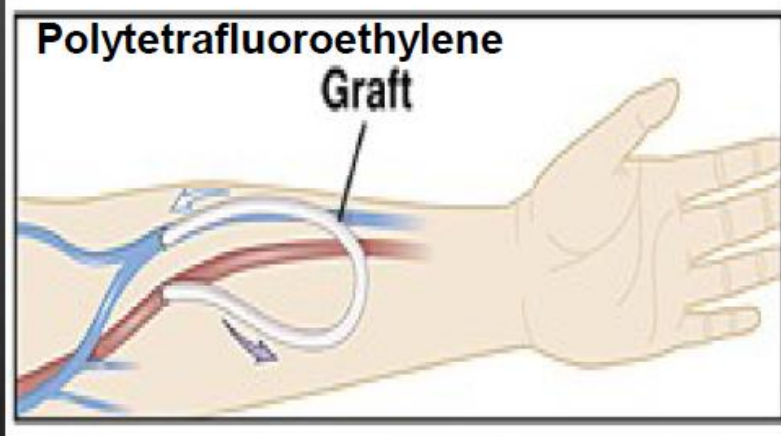
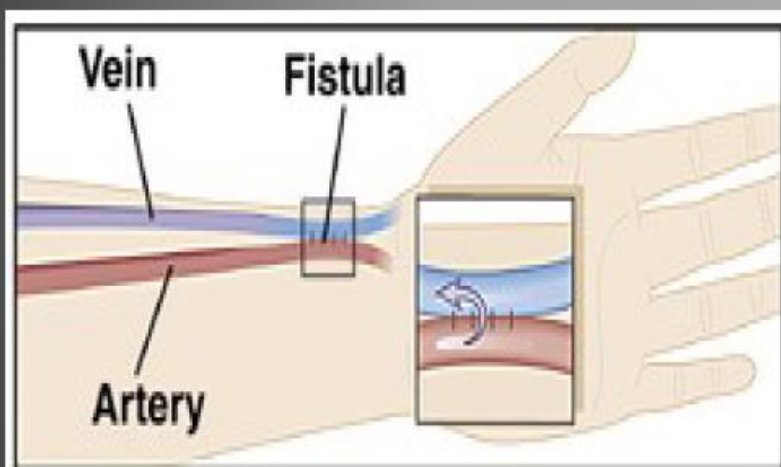
LST120 PAS Hollow Fiber Hemodialyzer



Hemodialysis Filter (Dialyzer)



Hemodialysis Vascular Access



Which Vascular Access and When Should It Be Placed?

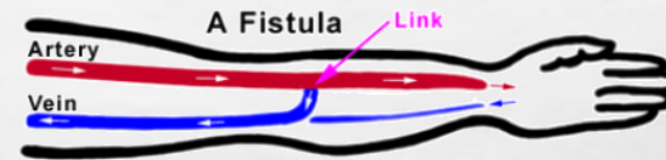
Dialysis Access

- ▶ Provides location for easy access to patient's blood for dialysis
- ▶ Bane of dialysis physician's existence
- ▶ Higher flows and cannulation can lead to stenosis or thrombosis
- ▶ Maintenance of dialysis access patency is critical, at times life-saving
 - Patency is assessed while patient is on HD by multiple parameters
- ▶ Early detection of stenosis can lead to intervention before thrombosis occurs

Dialysis Access

▶ AV Fistula

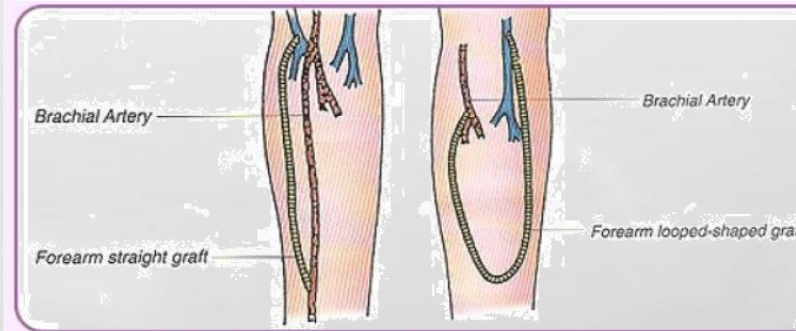
- Vein cross-cut, attached end-to-side to artery
- High-pressure flow dilates and thickens vein
- Best alternative:
 - ▢ Lowest infectious risk
 - ▢ Longest lasting with least thromboses
- Drawbacks
 - ▢ Takes 2-4 months to mature
 - ▢ Only about 50% ever mature
- Goal for all dialysis patients



Dialysis Access

▶ AV Graft

- Tube made of biocompatible material (gortex) attached end-to-side to artery and vein
- Often required in patients with vascular disease, occluded distal veins
- Advantages
 - ▢ Ready to use when swelling resolves (~2 weeks)
 - ▢ Able to use in most patients
- Disadvantages
 - ▢ High stenosis/thrombosis
 - ▢ Moderate infectious risk



Dialysis Access

- ▶ Catheter (IJ most common)
 - Tunnelled under skin to reduce communication from skin flora with blood
 - Advantages
 - ▢ Ready for use immediately
 - Disadvantages
 - ▢ High infectious risk
 - ▢ High thrombosis risk
 - ▢ A/W increased mortality
 - ▢ Can be a sign of poor pre-dialysis care or extensive vascular disease



Vascular Access Guidelines

- ▶ **Arm veins suitable for placement of vascular access should be preserved, regardless of arm dominance.** Arm veins, particularly the cephalic veins of the non-dominant arm should not be used.
 - **Avoid PICC lines**
- ▶ **Dorsum of the hand** could be used for IV.
- ▶ A Medic Alert bracelet should be worn to inform hospital staff to avoid IV cannulation of essential veins.
- ▶ **Subclavian vein catheterization should be avoided** for temporary access in all patients with CKD (→ stenosis → preclude use of ipsilateral arm for vascular access)

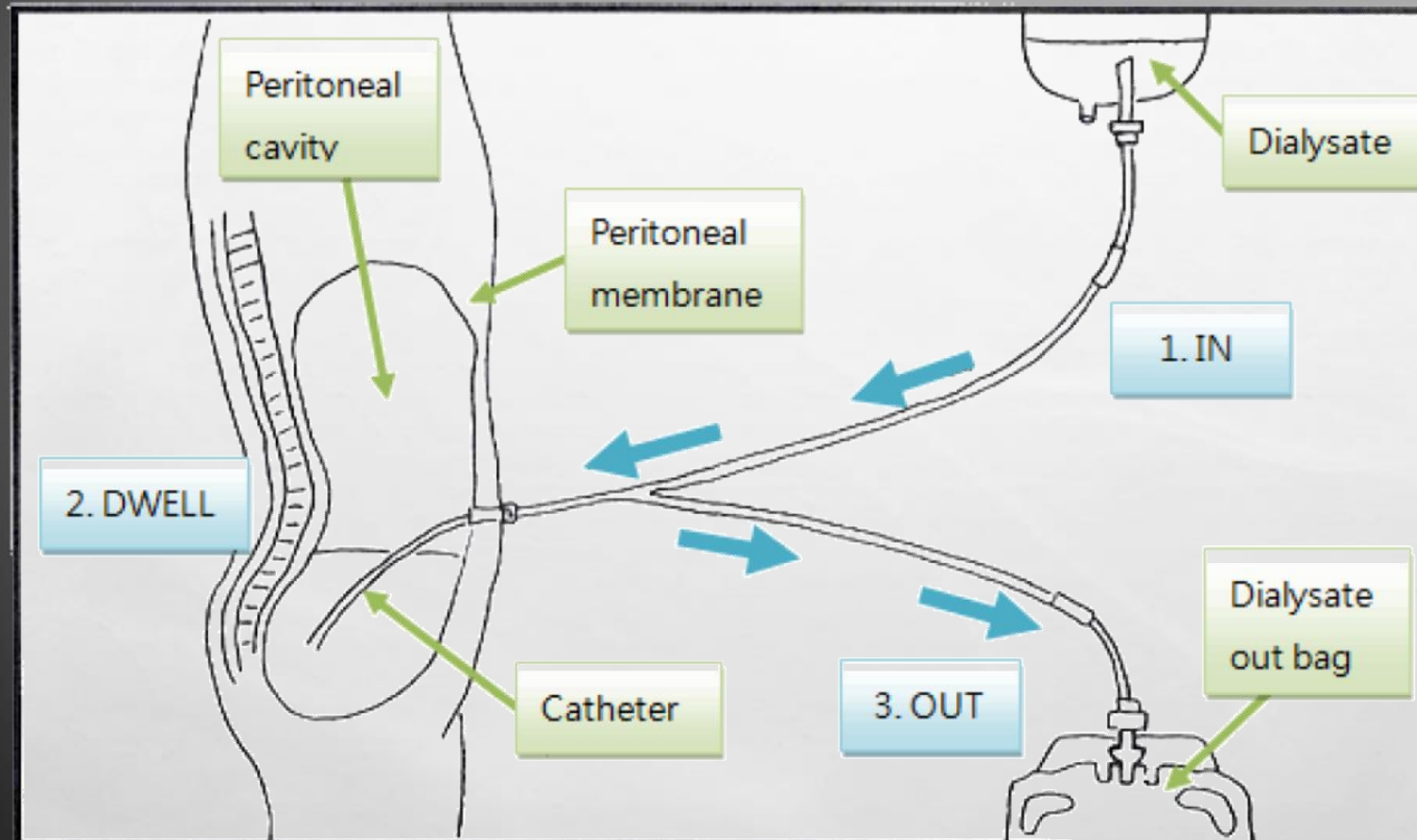
SAVE the Non-Dominant ARM for Vascular Access

- ▶ When GFR < 30 mL/min
 - No BP measurement
 - No IV
 - No Blood Draws
- ▶ Place vascular access within a year of hemodialysis anticipation ...

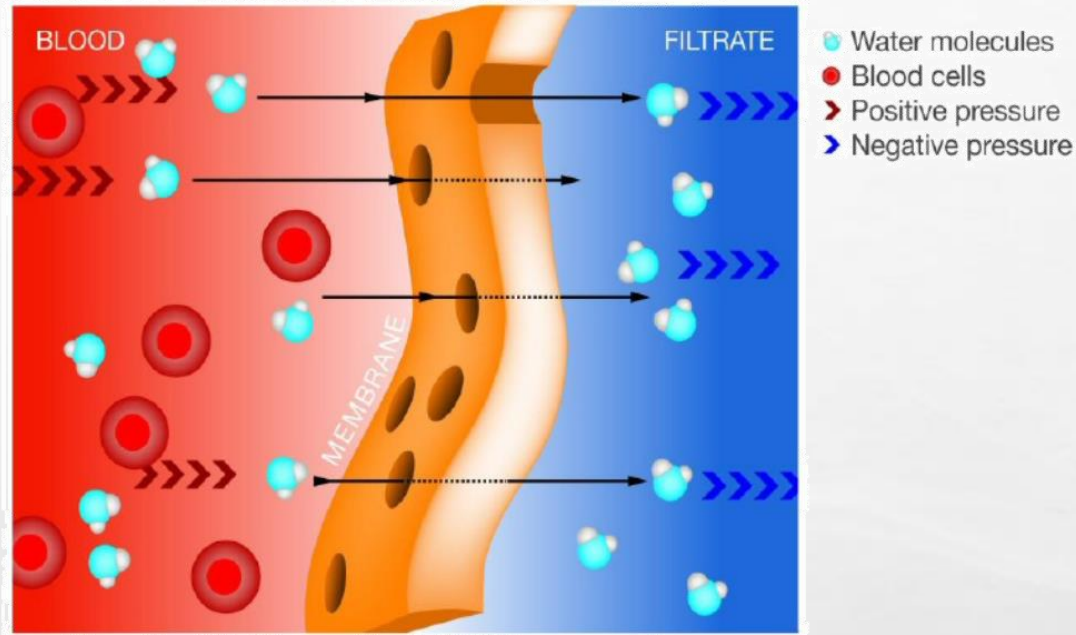
On Non-Dominant Arm

Peritoneal Dialysis (PD)

Principle of PD Treatment

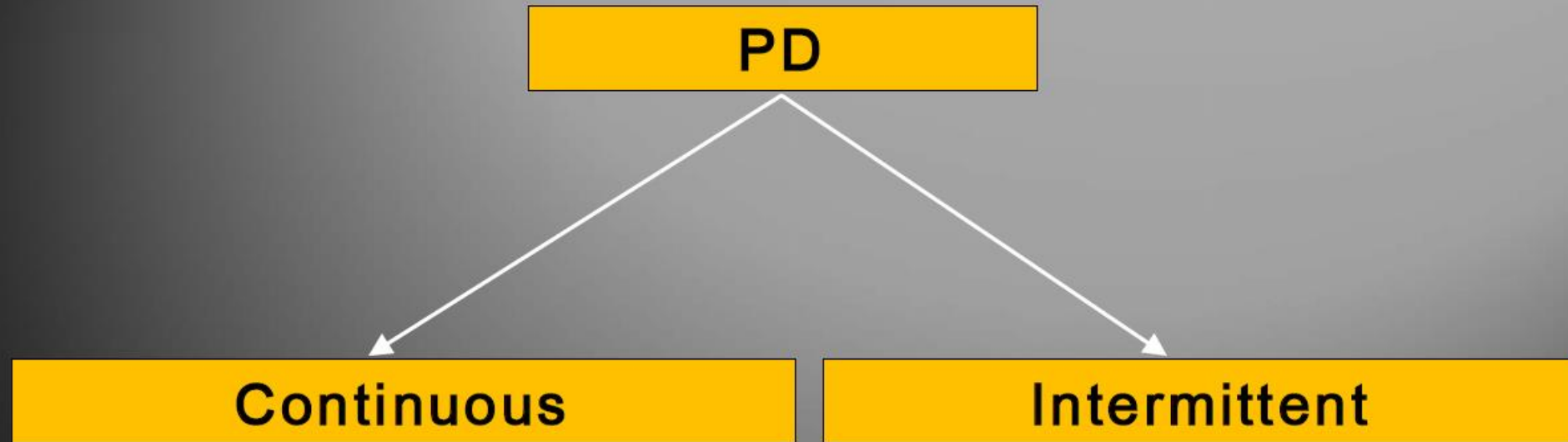


PD Treatment



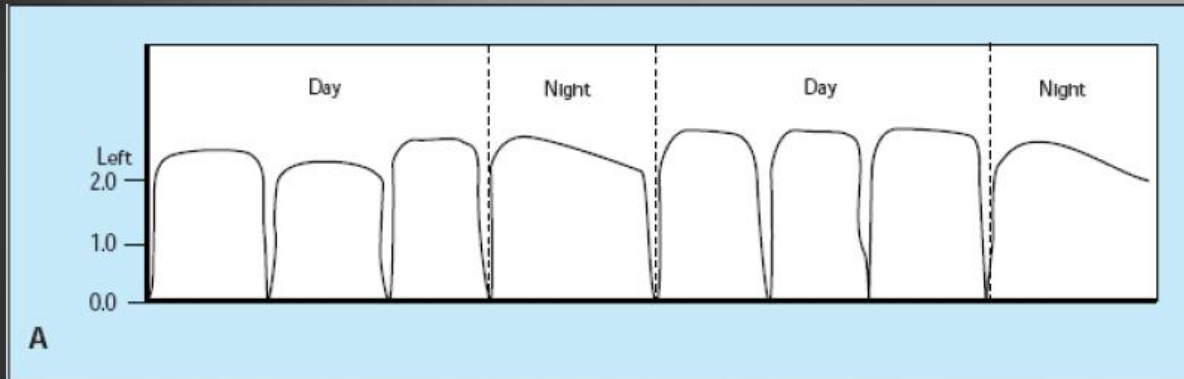
- Abdominal cavity is lined by a vascular peritoneal membrane which acts as a semi-permeable membrane
- Diffusion of solutes (urea, creatinine, ...) from blood into the dialysate contained in the abdominal cavity
- Removal of excess water (ultrafiltration) due to osmotic gradient generated by glucose in dialysate

Peritoneal Dialysis (PD)

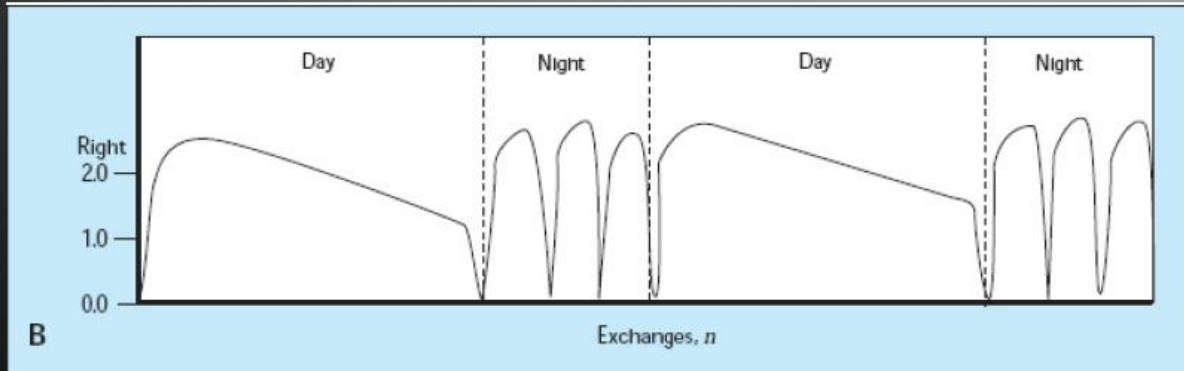


Continuous PD Regimens

Multiple sequential exchanges are performed during the day and night so that dialysis occurs 24 hours a day, 7 days a week



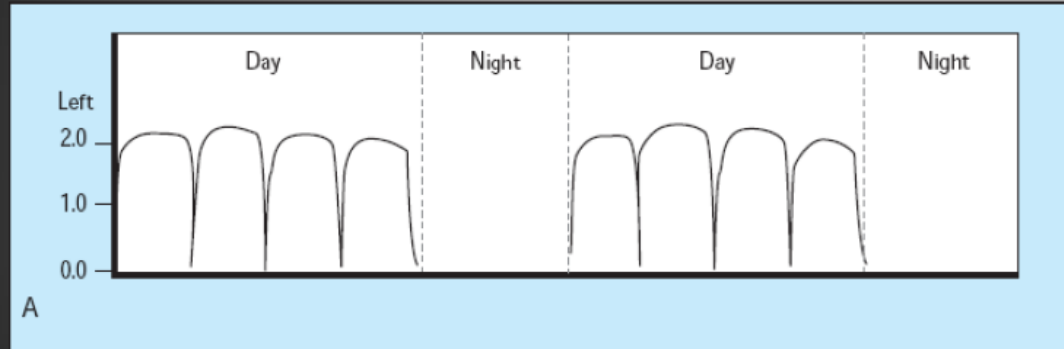
CAPD: Continuous Ambulatory PD



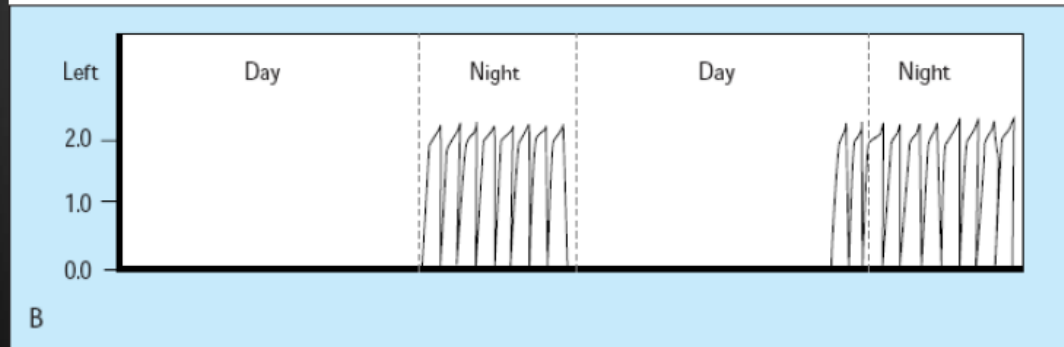
CCPD: Continuous Cyclic PD

Intermittent PD Regimens

PD is performed every day but only during certain hours



DAPD: Daytime Ambulatory PD. Multiple manual exchanges during waking hours



NPD: Nightly PD. Performed while patient asleep using an automated cycler machine. Sometimes, 1 or 2 day-time manual exchanges are added to enhance solute clearances

**Is Timing of Dialysis Initiation
Important in ESRD Patients?
(Controversial)**

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A Randomized, Controlled Trial of Early versus Late Initiation of Dialysis

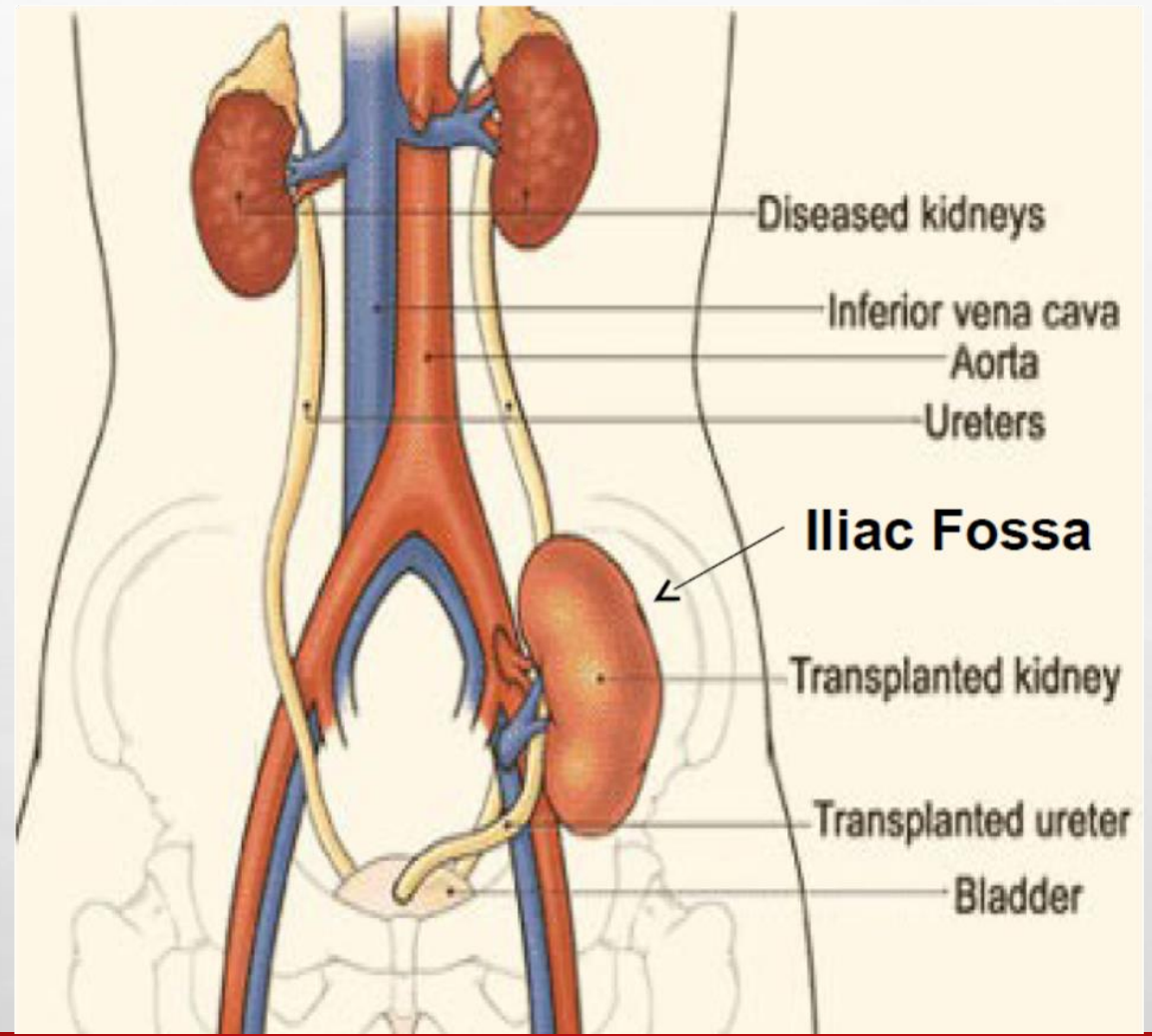
Bruce A. Cooper, M.B., B.S., Ph.D., Pauline Branley, B.Med., Ph.D., Liliana Bulfone, B.Pharm., M.B.A.,
John F. Collins, M.B., Ch.B., Jonathan C. Craig, M.B., Ch.B., Ph.D., Margaret B. Fraenkel, B.M., B.S., Ph.D.,
Anthony Harris, M.A., M.Sc., David W. Johnson, M.B., B.S., Ph.D., Joan Kesselhut,
Jing Jing Li, B.Pharm., B.Com., Grant Luxton, M.B., B.S., Andrew Pilmore, B.Sc., David J. Tiller, M.B., B.S.,
David C. Harris, M.B., B.S., M.D., and Carol A. Pollock, M.B., B.S., Ph.D., for the IDEAL Study*

Implications

- Total of 75.9% of the patients in the late-start group started dialysis when eGFR was $> 7.0 \text{ mL/min/1.73m}^2$, owing to the development of symptoms!
- In this study, planned early initiation of dialysis in patients with stage V CKD was not associated with an improvement in survival or clinical outcomes (QOL)
- → OK to delay initiation of dialysis (eGFR $< 7-10 \text{ mL/min/1.73m}^2$)
- → Dialysis initiation should be based upon clinical factors (symptoms) rather than eGFR alone

Kidney Transplantation

Principle of Kidney Transplantation



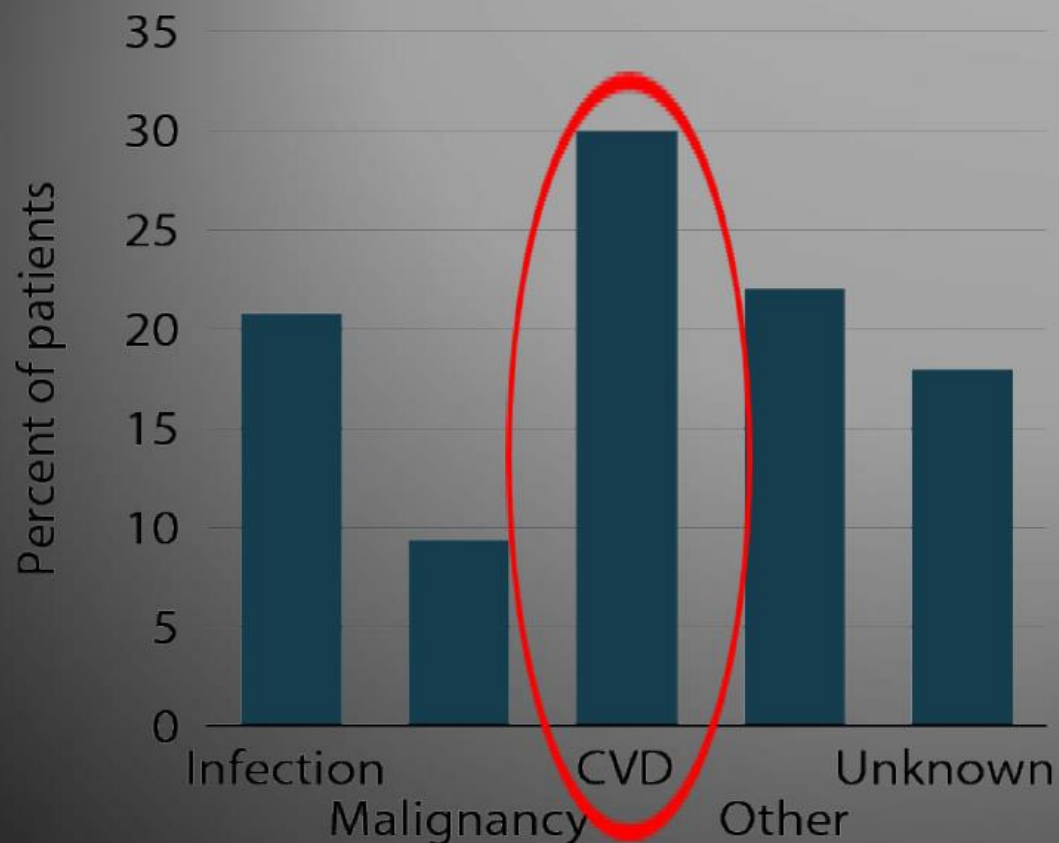
Eligibility

- ▶ Able to be evaluated once GFR <20 mL/min
- ▶ Need just one listing less than 20 mL/min to remain active
- ▶ With GFR 15-19 mL/min- can be transplanted if live donor or if six antigen match
- ▶ If GFR <15 mL/min- open to all offers
- ▶ Why starting early- if certain blood types with long wait time, no potential live donors

Absolute contraindications

- ▶ Active malignancy
- ▶ Advanced lung disease
 - Chronic O2 needs
 - FEV 1 < 1
- ▶ Ongoing infections
- ▶ Life expectancy less than 2 years
- ▶ Active substance abuse
- ▶ Ischemic Cardiac disease
 - Not amenable to revascularization
- ▶ Severe peripheral vascular disease
- ▶ Liver cirrhosis/primary oxalosis- unless combined liver/kidney
- ▶ Poorly controlled psychiatric illness
- ▶ Minimal rehabilitative potential
- ▶ Morbid obesity – BMI > 40

Causes of Death in Kidney Transplant Patients with Functioning Graft 2006–2010



First-time, kidney-only transplant recipients, age 18 & older, 2006–2010, who died with functioning graft.

Post-transplant Malignancy

- ▶ Risk is 4X to 100X compared rates of malignancy in the general population (especially skin cancer)
- ▶ No comprehensive reporting system
- ▶ Available data suggesting 2- to 3-fold under-reporting
- ▶ The precise rate is UNKNOWN
- ▶ Accounts for 10% of deaths in kidney recipients with functioning graft
- ▶ → SCREENING is KEY!
 - Threshold for screening should be low.

TABLE 13.**Recommendations for cancer screening in the general population and potential transplant candidates**

Cancer	General population	Potential transplant candidates
Breast	<ul style="list-style-type: none"> • Women ages 40 to 49 should have the choice to start annual breast cancer screening if they wish to do so • Biennial mammography is recommended for women age 50 and above • Screening should continue as long as woman is in good health and is expected to live 10 more years or longer³⁶² 	<ul style="list-style-type: none"> • As per general population³⁶³
Colorectal	<ul style="list-style-type: none"> • Biennial fecal immunochemical testing (FIT) is recommended for all people age 50 years and above. Those with positive FIT should have full examination of the colon, preferably by colonoscopy • Flexible sigmoidoscopy (every 5 or 10 years) may also be considered for people age 50 years and above • Screening can be stopped for people who are older than 75 years or with life expectancy less than 10 years 	<ul style="list-style-type: none"> • As per general population^{364,365}
Liver	<ul style="list-style-type: none"> • Annual liver ultrasound and alpha-fetoprotein screening for those with known cirrhosis 	<ul style="list-style-type: none"> • As per general population (see Rec 11.1.4)
Cervical	<ul style="list-style-type: none"> • Papanicolaou (Pap) test is recommended for women starting at the age of 21 and screening should be done every 3 years. Alternately, screening using HPV testing should be done every 5 years up to age 65 years. Women older than 65 should talk to their doctors about whether or not they need to have regular cervical screening. The decision to stop is often based on a woman's history of having normal or negative Pap test results • Women who had a previous total hysterectomy (removal of the uterus, including the cervix) do not require routine Pap screen 	<ul style="list-style-type: none"> • As per general population³⁶⁶

Lung

- uterus, including the cervix) do not require routine Pap screen
- Routine screening for lung cancer using chest radiography and low-dose computed tomography (LDCT) *is not recommended* for average risk individuals
- However, there is some evidence to suggest annual screening for people at high risk of lung cancer using LDCT. Individuals at high risk are adults aged 55 to 80 years who have a smoking history of at least 30 pack-years and currently smoke or have quit within the past 15 years³⁶⁷

Prostate

- Men between the ages of 55 to 69 can undergo periodic screening for prostate cancer using prostate specific antigen if they wish to do so after understanding risks and benefits
- Clinicians should not screen men who do not express a preference for screening and screening should stop at the age of 70

Kidney

- Routine screening for renal cell cancer is not recommended for average risk individuals

Bladder

- Routine screening for bladder cancer is not recommended for average risk individuals

- LDCT of the chest may be recommended for individuals who are at high risk of lung cancer, including a prolonged heavy smoking history (see Rec 11.1.1.2)

- As per general population³⁶⁸

- Ultrasonographic screening of the native kidneys may be recommended for individuals who have a family history of renal cancer, a personal history of acquired cystic disease, analgesic nephropathy, long-term smoking and/or prolonged waiting time on dialysis³⁶⁹ (see Rec 11.1.2)
- Urine cytology and cystoscopies may be recommended for individuals who had been previously exposed to chemotherapeutic agents such as cyclophosphamide, regular users of compound analgesics and for heavy smokers (≥ 30 pack-year history) (see Rec 11.1.3)

Key Concepts

- ▶ Kidney transplantation is the most cost-effective modality of renal replacement
- ▶ Transplanted patients have a longer life and better quality of life
- ▶ Early transplantation (before [pre-emptive] or within 1 year of dialysis initiation) yields the best results
- ▶ Living donor kidney outcomes are superior to deceased donor kidney outcomes
- ▶ Early transplantation is more likely to occur in patients that are referred early to nephrologists
- ▶ Refer for transplant evaluation when $\text{eGFR} \leq 20$ mL/min/1.73m²

Key Concepts

- ▶ The most common cause of transplant loss is death with a functional transplant due to
 - Heart disease
 - Infections
 - Malignancies
- ▶ Immunosuppressants are essential to prevent immunological loss of the transplant, but side effects can also lead to potential loss of transplant

What About No Renal Replacement Therapy Option?

Starting Dialysis in the Elderly...Or Not?

- ▶ Among patients > 75 yrs with stage 5 CKD who chose NOT to start dialysis:
 - Overall, more likely to die over next 1-2 years
 - But if they had ischemic heart disease or other significant comorbidity → NO DIFFERENCE in survival
- ▶ Active disease management and supportive care may be appropriate without starting dialysis in the ill elderly
- ▶ **Must have end-of-life discussions!**

The Future ...

- ▶ Regenerative Medicine ...
- ▶ Stem Cell Therapy ...
- ▶ Wearable Artificial Kidney



