Chronic Kidney Disease (CKD) in Children

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Outlines

Definition

Pathogenesis

Stages

Etiology

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Laboratory findings

Treatment

RRT

Definition

Kidney damage for ≥3 months

defined by structural or functional abnormalities of the kidney, with or without decreased GFR.

Or:

GFR < 60 ml/min/1,73 m2 for > 3 months .

Criteria for CKD (Present for >3 Months)

1. Markers of kidney damage *(one or more)*

- *Albuminuria (increase albumin excretion rate;*
- *Increase albumin-to-creatinine ratio*
- *Urine sediment abnormalities*
- *Electrolyte and other abnormalities due to tubular disorders*
- *Abnormalities detected by histology*
- *Structural abnormalities detected by imaging*
- *History of kidney transplantation*

2. Decreased glomerular filtration rate *(GFR)GFR <60 ml/min/1.73 m² (GFR categories G3a–G5).*

Prevalence

*- Globally, the prevalence of chronic kidney disease(CKD)stage II or lower in children is approximately **18.5-58.3** per million children*

*The frequency of chronic kidney disease **increases with age** and is much more common in adults than children.*

Among children, chronic kidney disease is more common in children older than 6 years than in those younger than 6 years.

Stages

*The Kidney Disease Outcomes Quality Initiative (KDOQI) recommended the following classification of chronic renal disease by stage (**2008-2009**) :*

Stage I *disease is defined by a normal glomerular filtration rate (GFR) (> 90 mL/min per 1.73 m ²) and persistent albuminuria*

Stage II *disease is characterized by a GFR of 60-89 mL/min per 1.73 m ² and persistent albuminuria*

Stage III *disease is characterized by a GFR of 30-59 mL/min per 1.73 m ²*

Stage IV *disease is characterized by a GFR of 15-29 mL/min per 1.73 m ²*

Stage V *disease is characterized by a GFR of less than 15 mL/min per 1.73 m ²or end-stage renal disease (ESRD)*

Categories - Stages

GFR Categories in CKD(ml/min/1.73 m²)

G1: ≥90 *Normal*

G2: 60–89 *Mildly decreased*

G3a: 45–59 *Mildly to moderately decreased*

G3b : 30–44 *Moderately to severely decreased*

G4: 15–29 *Severely decreased*

G5: <15 *Kidney failure*

Schwartz equation for e-GFR

$$CrCl\ (ml/min/1.73m2) = \frac{[length\ (cm) \times k]}{Scr}$$

k = 0.45 for infants 1 to 52 weeks old
k = 0.55 for children 1 to 13 years old
k = 0.55 for adolescent females 13-18 years old
k = 0.7 for adolescent males 13-18 years old

Pathogenesis

Hyperfiltration injury: possible final common pathway of glomerular destruction, independent of the underlying cause of renal injury

. When nephrons are lost, the remaining nephrons undergo an increase in glomerular blood flow

.This compensatory hyperfiltration temporarily preserves renal function, however it might cause damage to the surviving glomeruli by time

***Proteinuria*:** direct toxic effect on tubular cells, recruitment of monocyte and macrophages : enhancement of glomerular sclerosis and tubulointerstitial fibrosis.

***Hypertension*:** Arteriolar nephrosclerosis, increase hyperfiltration injury.

***Hperphosphatemia*:** Deposition of calcium phosphate in the renal tissue and vessels

***Hyperlipidemia*:** Glomerular dysfunction through oxidant-mediated injury

Causes of CKD in Children

Congenital abnormalities:

-Aplasia, Hypoplasia, Dysplasia

-Obstructive uropathy

- Reflux nephropathy

Herditary conditions:

- Polysystic kidney disease AR
- Hereditary nephritis
- Cystinosis
- Primary oxalosis
- Congenital NS

Glomerulonephritis

Multisystem diseases

- SLE
- HSP

-HUS

Miscellaneous

- Renal vascular disease

Renal tumors

Unknown causes

Clinical presentation

Depends on the severity of renal impairment and the *underlying disorder*

Pts in the early stage of CKD may be **asymptomatic** unless there are signs/symptoms from the underlying disease or systemic disease with renal involvement:

- Tubulointerstitial disorder.. reduce concentrating ability –Polyuria

- Lupus Neph. Or Wegener's..fever, rash, arthralgia, pulmonary symptoms

- Poor growth : as the CKD progress

- Signs & symptoms of uremia (severe renal impairment) : vomiting, loss of appetite, weakness, fatigue, anorexia, pericarditis, neurocognitive dysfunction

Modes of presentation of CKD

Antenatal ultrasound scanning
Urinary tract infection
Enuresis, Polyuria-polydipsia
FTT
Short stature
Pallor & Lethargy
Proteinuria
Hypertension
Congestive heart failure
Seizures
Bony abnormalities from renal osteodystrophy
Failure to recover from acute renal failure

Manifestations & mechanisms (pathophysiology) of CKD

Accumulation of waste products: decrease in GFR
Acidosis*: impaired bicarbonate reabsrption, decreased net acid excretion*
Na retention*: excessive renin production, oliguria*
Na wasting: *tubular damage*
Urinary concentrating defec*t: tubular damage*
Hyperkalemia*: decreased GFR, excessive intake, metabolic acidosis*
*R**enal osteodystrophy** : see next slide*
Growth retardation: *see next slide*
Bleeding tendency*: defective PLT function*
Anemia: *see next slide*
*I**nfection**: granulocyte defect, impaired cellular immune function, indwelling dialysis catheter*
Neuro-manifestations*: uremia, aluminum toxicity, hypertension*
Hypertension: *overload, rennin production*
Hyperlipidemia*: decreased plasma lipoprotein, lipase activity*
Pericarditis, cardiomyopathy: *uremia, overload, hypertension*
Glucose intolerance*: glucose tissue resistance*

Pathogenic Factors of the Anemia of CKD

Decreased erythropoiesis

- *Reduced availability of erythropoietin*
- *Inhibitor(s) of erythropoiesis**
- *Bone marrow fibrosis**

Shortened red blood cell survival*

- *Hemolysis due to extracorpuscular factor(s)*

Excessive blood losses

Deficiency states

- *Iron deficiency* ● *Folic acid deficiency*

**These factors seem to be exacerbated by hyperparathyroidism*

Mineral and Bone disorder

CKD leads to abnormal vitamin D, Ca, Phosphate, FGF23 and PTH metabolism.

. Decreased 25(OH)

. Decreased Ca intake

. Increased Fibroblast Growth Factor 23

. Increased Plasma phosphate

. Decreased 1a hydroxlation of 25(OH)D to the active form 1,25(OH)2D

. Decreased Ca absorption

. Increased PTH

Clinical manifestations

- Growth retardation
- Bone pain
- Myopathy
- Skeletal deformities
- Rickets signs in infants

Growth retardation in CKD ..Possible factors

Inadequate energy intake

Inappropriate protein intake

Disturbances in water and electrolytes balance

Renal osteodystrophy

Infections

Anemia

Corticosteroid therapy

Clinical evaluation

Hx of renal diseases or HTN
Growth Hx: poor linear growth
Polyuria, polydepsia, enuresis
Elevated BP
Recurrent uti's
Antenatal diagnosed renal malformation
Unexplained anemia
Orthopedic or urological abnormalities
Seizures
Fluids and electrolytes disorders

Physical evaluation

Growth parameters

BP measurement

Assessment of pallor

Exam of extremities: Deformities (MBD), edema

Signs of hypervolemia: edema, rales, hepatic enlargement, cardiac gallop

Cardiac auscultation: friction rub, diminished heart sounds

Laboratory test

- *CBC*
- *Biochemistry:*
    - *Electrolytes*
    - *KFT*
    - *Protein & albumin*
    - *Blood Ph & bicarbonate*
    - *PTH*
- *Left hand & wrist x-ray*
- *CXR*
- *ECHO*

Specific investigations - CKD

- *Renal tract USS*
- *MCUG*
- *Radio-isotope scans: DMSA, MAG3, DTPA*
- *IVU*
- *C3, C4, ANA, ANCA, Anti-GBM antibodies*
- *Renal biopsy*
- *White cell cystine level*
- *Oxalate excretion*

Management of CKD

<u>Overall aims:</u>

- *Slowing progression of kidney dysfunction*
- *Prevention of biochemical and hematological derangements*
- *Maintaining normal growth and development*
- *Replacing absent or reduced kidney function*

Management……

-Fluids and electrolytes balance

- Anemia

- Hypertension

- Growth

- CKD mineral and bone disease

- Nutrition

- Immunizations

- Preparation for RRT

Slowing progression……

1. *Optimum control of HTN*
2. *Control of proteinuria*
3. *Serum phosphorus within normal range*
4. *Serum ca-p within normal range*
5. *Prompt treatment of infections & dehydration*
6. *Correction of anemia*
7. *Minimization of regular use of NSAIDS*
8. *Control of hyperlipidemia*

Fluids & electrolytes management

Sodium: *as glomerular disease progress, stage4-5, salt restriction may become necessary, as well as in case of hypertension with edema and heart failure*

- Heavy electrolytes losers are those with tubulopathies, cystinosis : supplements

- Infants on PD lose excessive Na and need supplements

- Remember … Salt depletion contributes to poor growth

Potassium*:*

restriction of oral intake,

medications, kayaxalate

Acidosis: *Sodium bicarbonate is used to maintain the bicarbonate level above 22meq/l*

Anemia: *erythropoiesis stimulating agents are effective in improving the anemia of CKD:*

- *Erythropoietin , Darbepoitin*
- *Aim for Hb 10-12gr/dl*
- *Iron: iv or oral is required*

Hypertension

- Hypertensive children due to fluid overload should follow restricted salt diet (2-3gr/day), and may be benefit from diuretic therapy

- Thiazide diuretic may be used in mild renal insufficiency, and loop diuretic as GFR falls significantly.

- ACE inhibitors are a good antihypertensive drug in proteinuric renal disease

- Ca channel blockers and B blockers may also be used

Renal osteodystrophy (mineral bone diseases)

Goal is to prevent bone deformity and to normalize growth velocity using both dietary and pharmacologic intervention

- Low phosphorous diet and low phosphorous formula in infants

- Phosphate binders: enhance fecal excretion;

- calcium carbonate

- non-calcium based binders

- Vitamin D supplementation

Growth

Growth retardation occurs in up to 50% of children with moderate –severe CKD (GFR< 50ml/min)

Dietary supplements orally or enterally

Gastrostomy ! Feeding

Salt supplementation

Correct acidosis, hyperparathyroidism

Give recombinant growth hormone (rhGH)

Nutrition

Ensuring adequate nutrition is one of the most important aspects of care of the child with CKD (Pediatric renal dietician involvement is crucial)

- Energy

- Protein

- Vitamins and minerals

(see guidelines for energy intake & protein requirements in patients with CKD)

Vaccination

- *Children with CKD should receive and complete all routine childhood vaccines*

Exception: hold live vaccine if the patient is on steroids or other immunosuppressant… (GN!)

Administer live virus vaccines before kidney transplant

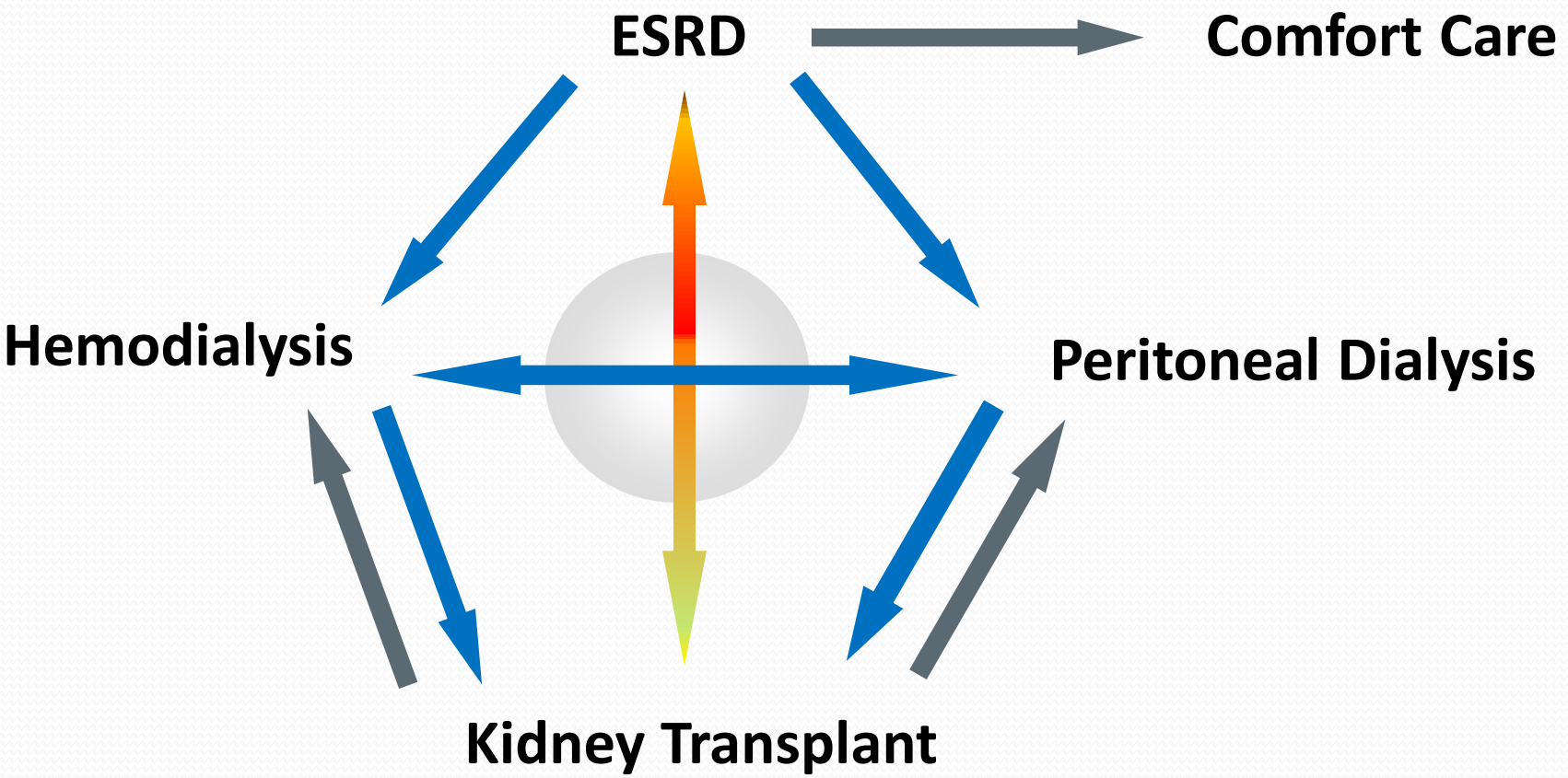
All CKD children should receive a yearly influenza vaccine

ESRF & RRT

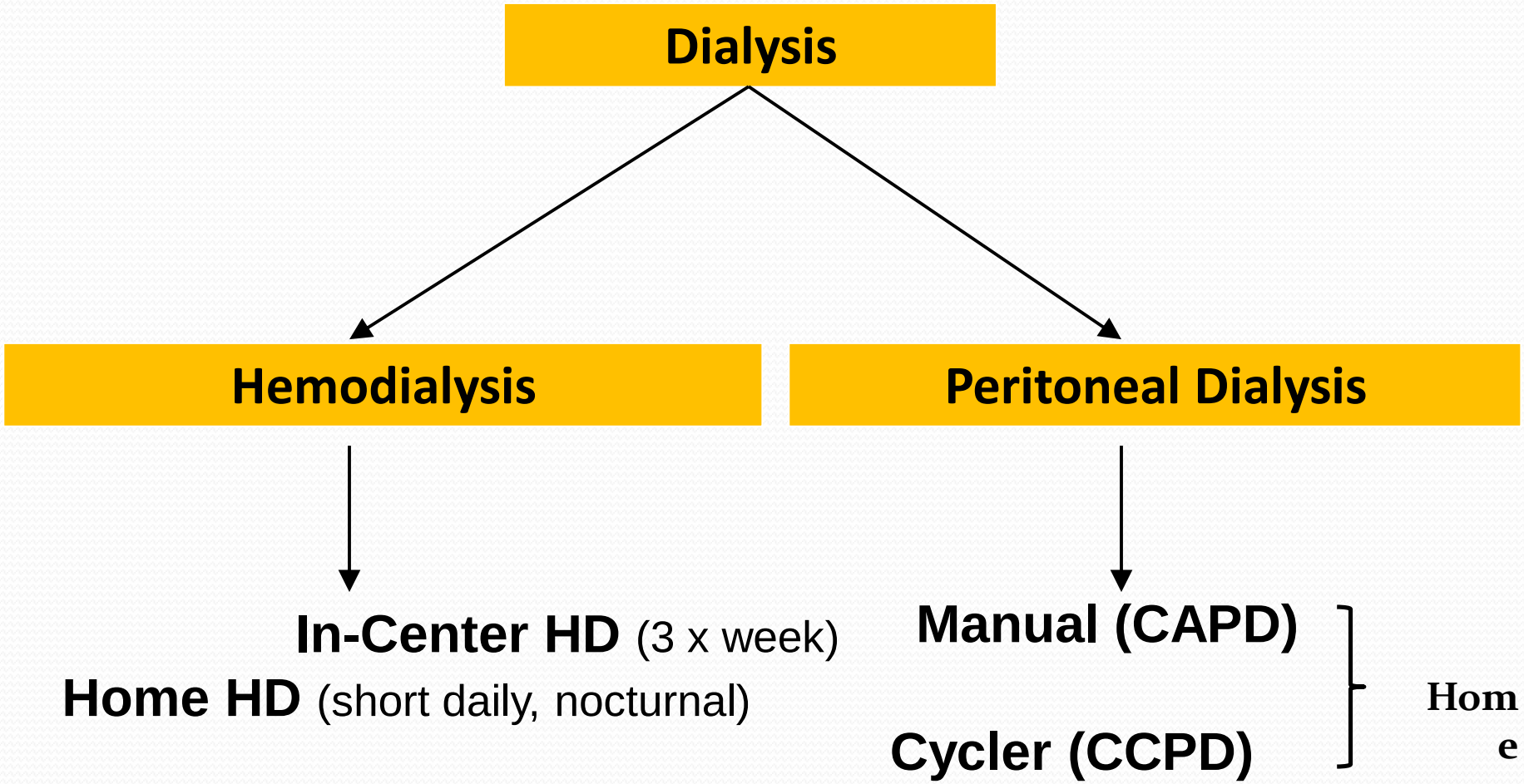
***ESRD** represents the state in which a patient's renal dysfunction has progressed to the point at which homeostasis and survival can no longer be sustained with native kidney function and maximal medical management.*

*At this point **Renal Replacement therapy** **RRT**(Dialysis or Transplantation) becomes necessary.*

Treatment Options for Renal Replacement Therapy



Dialysis Options



Dialysis

PERITONEAL DIALYSIS VERSUS HEMODIALYSIS

- The choice of dialysis modality is most often based on ***patient*** *and* ***family preference***, ***center philosophy***, *and* ***availability of the desired modality***

- Chronic peritoneal dialysis (CPD) is the most common dialysis treatment modality used to treat pediatric patients with end-stage renal disease (ESRD), particularly in children ***less than five years of age***

Peritoneal dialysis

Principles:

*Solute moves down the concentration gradient across the peritoneal membrane by **diffusion** and water by osmosis (ultrafiltration, UF)*

*Ultrafiltration causes movement of solutes by **convection***

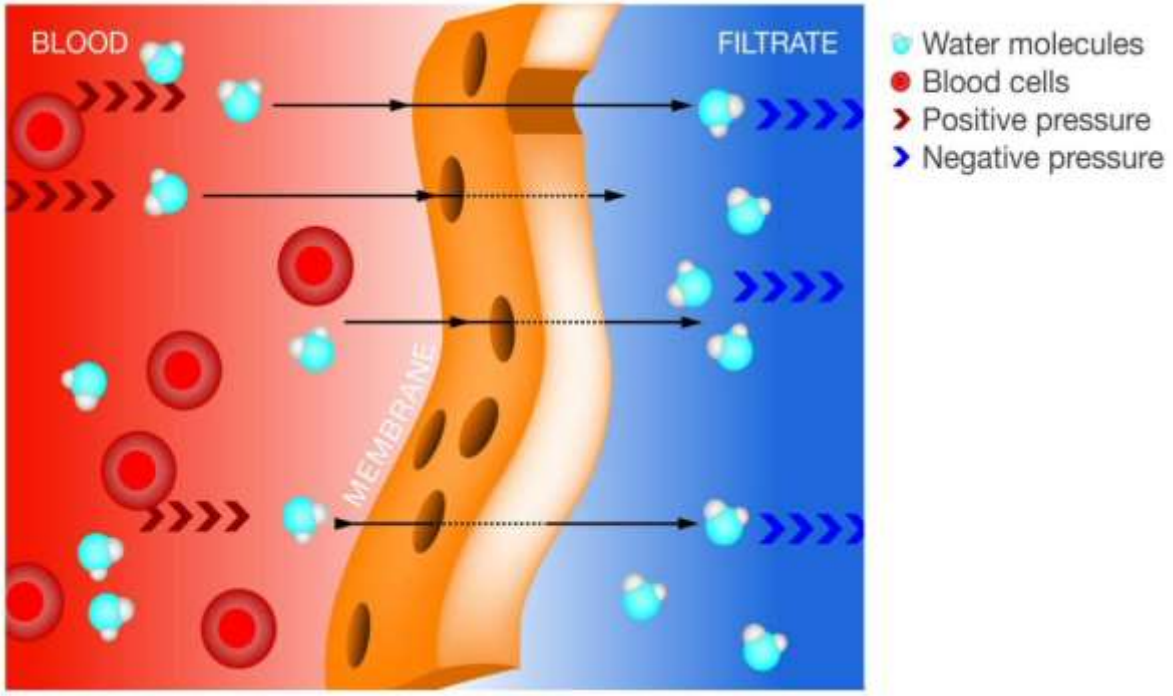
The efficiency of PD is affected by:

- The peritoneal membrane

- The peritoneal microcirculation

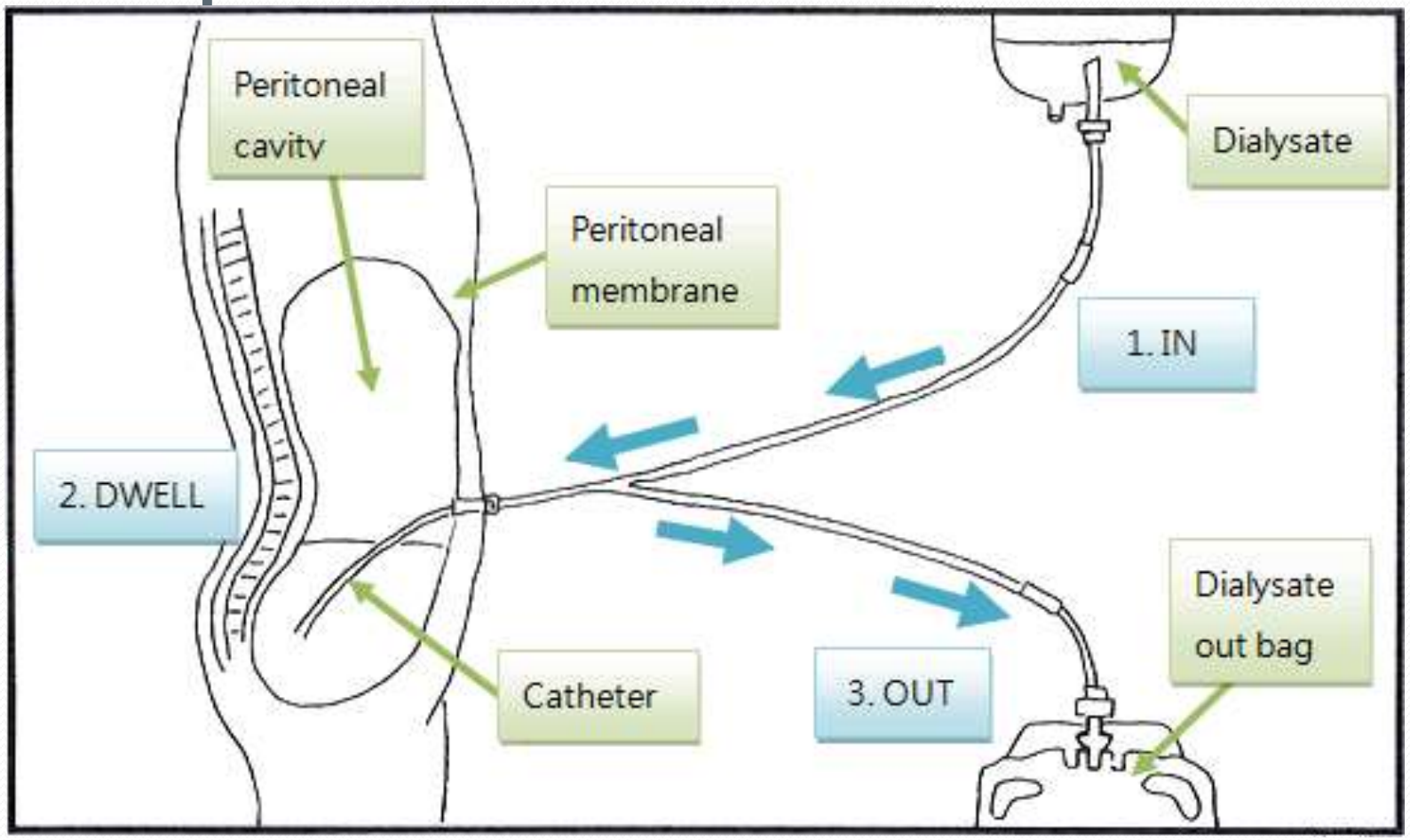
- The dialysis compartment(type and volume of solution)

PD Treatment

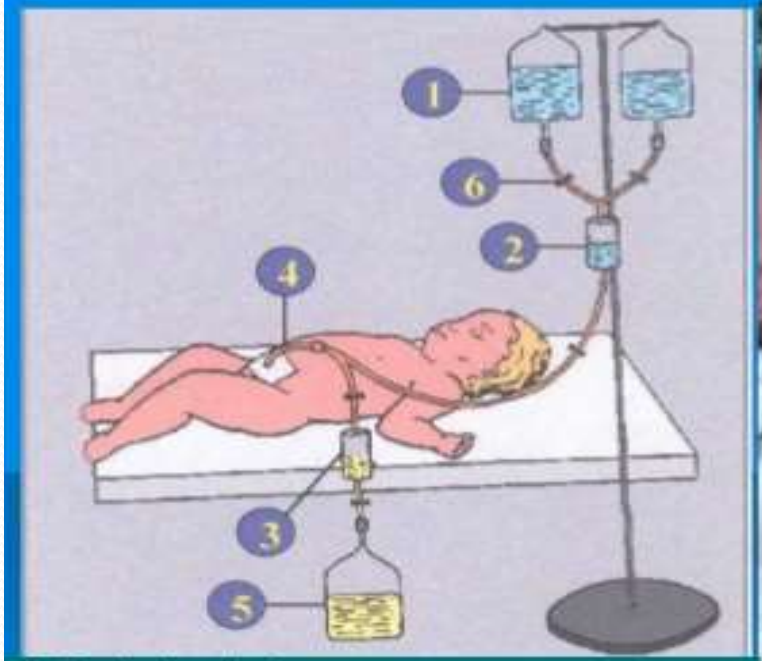


- Abdominal cavity is lined by a vascular peritoneal membrane which acts as a semi-permeable membrane
- Diffusion of solutes (urea, creatinine, …) from blood into the dialysate contained in the abdominal cavity
- Removal of excess water (ultrafiltration) due to osmotic gradient generated by glucose in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

Principle of PD Treatment



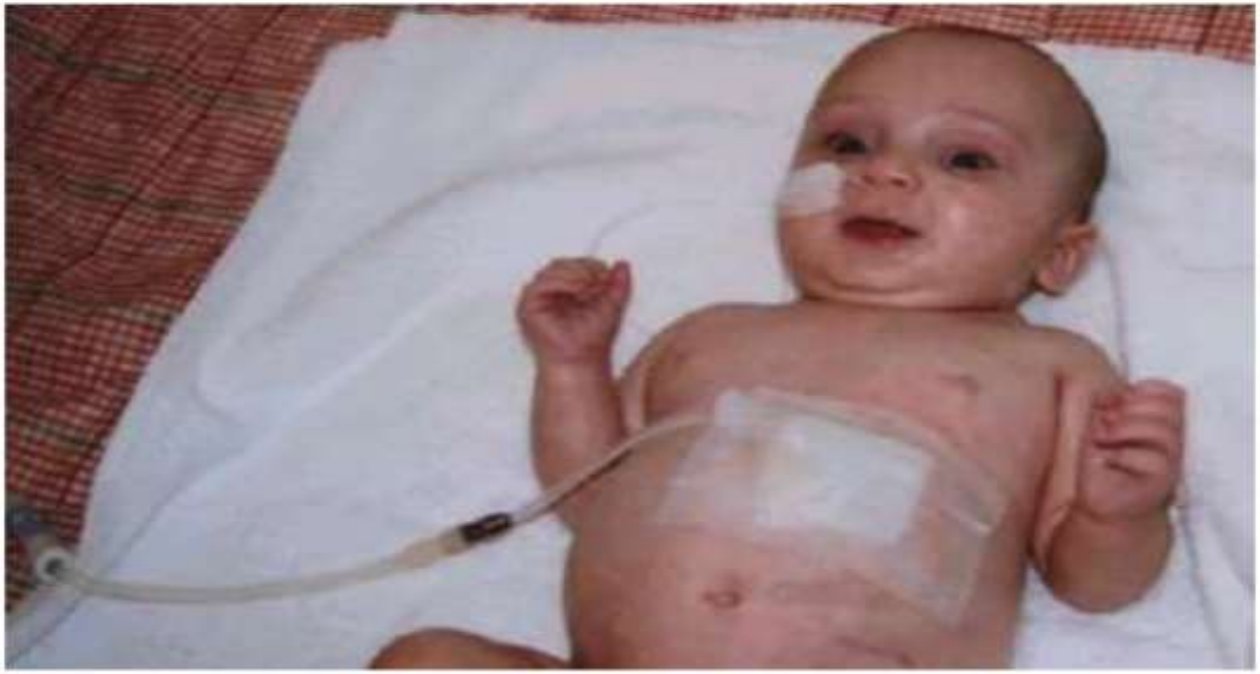
Peritoneal dialysis



1. Dialysis solution
2,3. Containers
measuring cylinders
4. Peritoneal catheter
5. Container for the drained solution
6. Clip

Begins from 10 ml/kg
Exposition 0,5 – 1 hour

Tenckhoff Catheters



PD

Advantages

- *Ability to perform PD at home*
Technically easier than hemo.
Freedom to attend school and activities
Less restrictive diet
Less expensive than hemodialysis !!

Disadvantages

Catheter malfunction
Catheter related infections
Reduced appetite
Negative body image

Hemodialysis

(The machine, dialysate and Water)

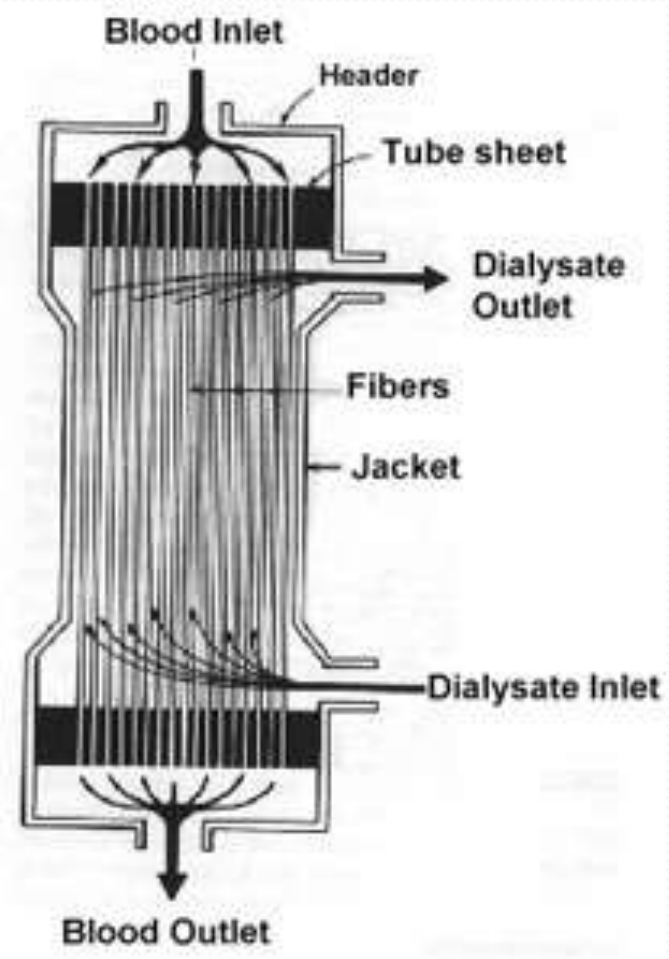
Principles:

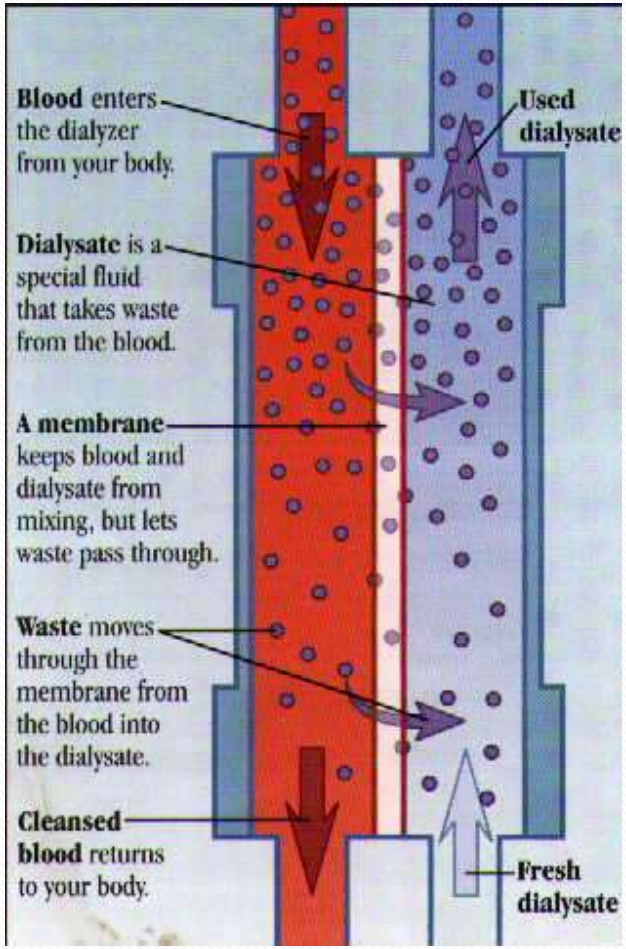
A semi-permeable membrane allows the passage of water and small molecular weight molecules

Solute transfer occurs by diffusion and convection

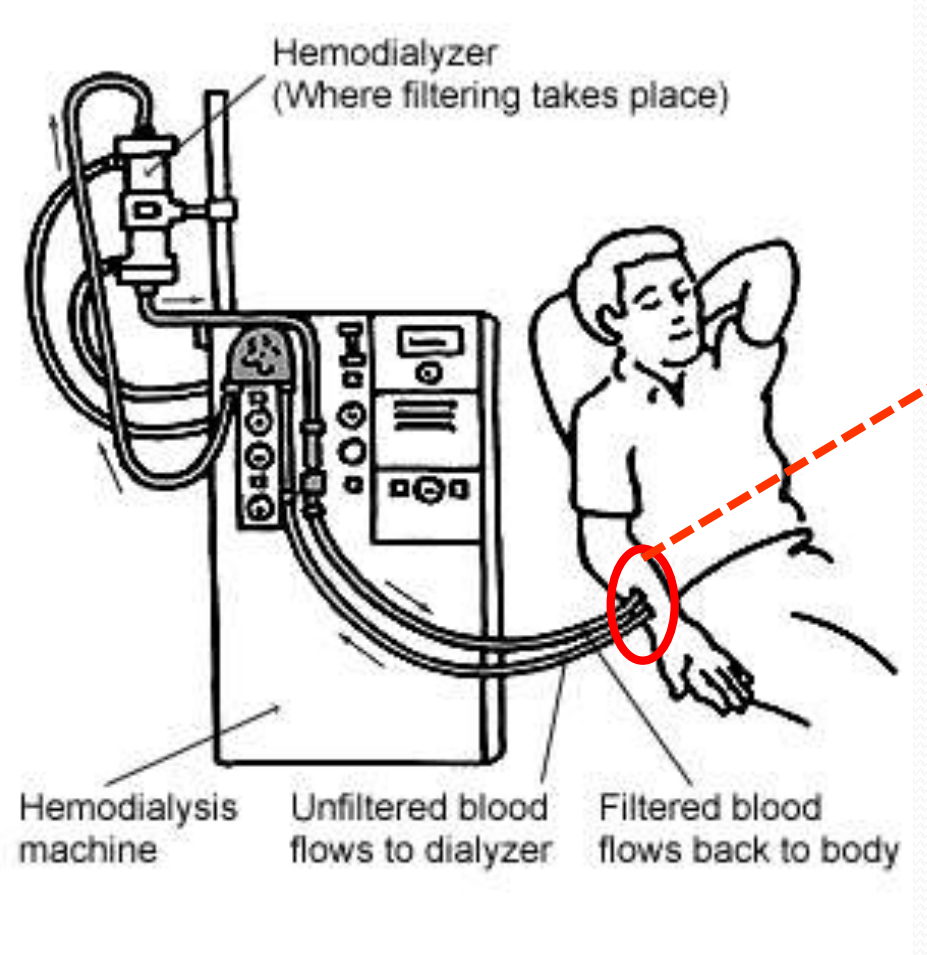
Water is removed by ultrafiltration

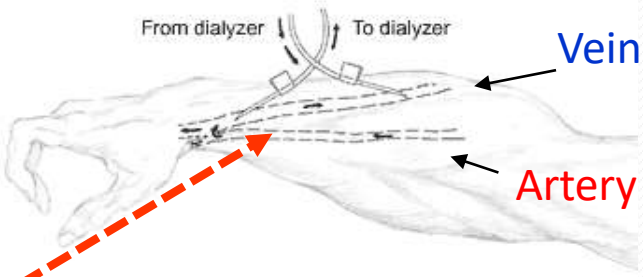
Hemodialysis Filter (Dialyzer)





Principle of Hemodialysis

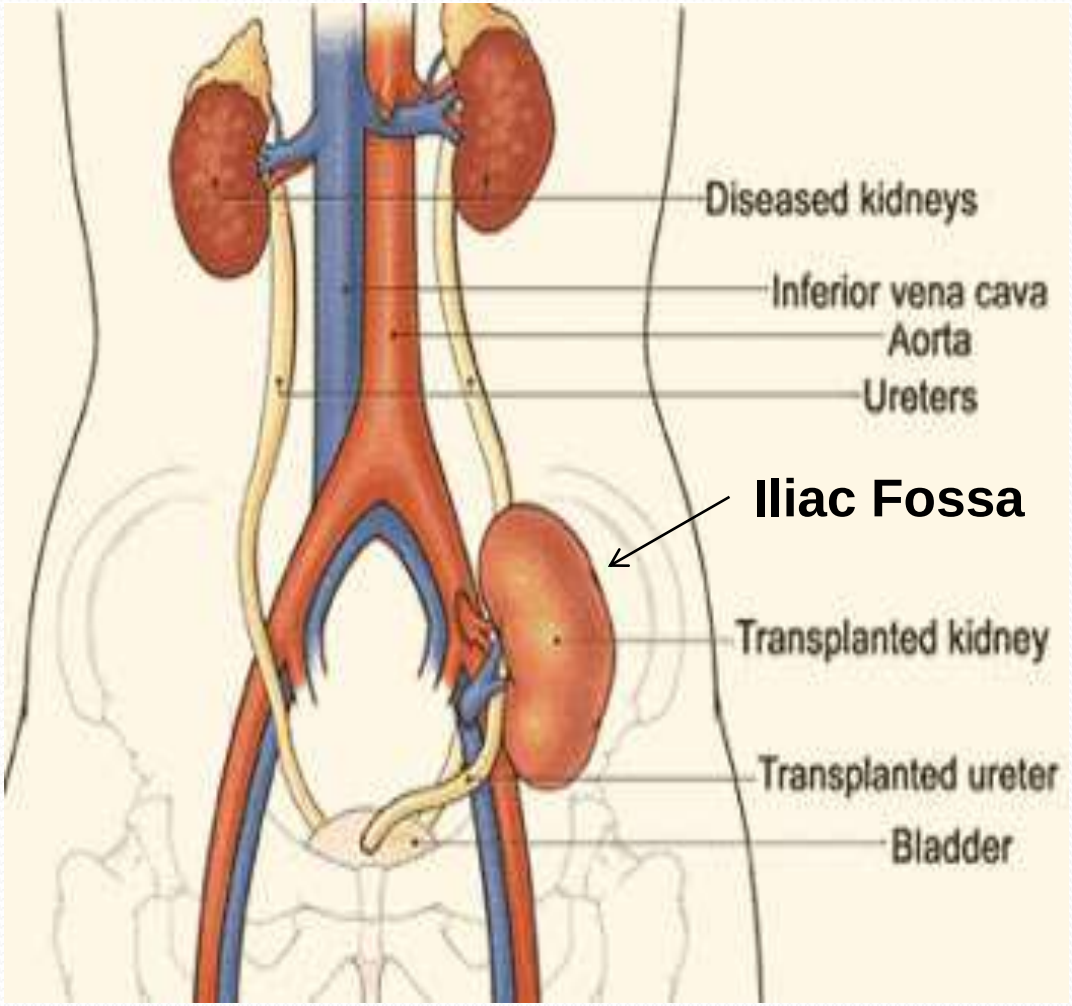




Kidney transplantation

The general principle is that transplantation should be the ultimate aim for the majority of children with CKD stage 5.

Kidney Transplantation



Kidney Transplantation

- 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.

Thank you

Questions ..... ??