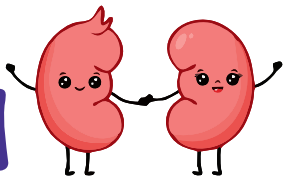
YOUNG KIDNEYS 2024



IPNA Teaching Course

Workbook

"All ABOUT HEMODIALYSIS"

July 20th 2024

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Workbook on Hemodialysis

Chapter 1: Kidney Replacement Therapy in Children

Acute kidney injury (AKI) commonly occurs in critically ill children. It affects nearly 30%-40% of patients admitted to the pediatric intensive care unit and is associated with high mortality rates of 40-50%. Approximately 5% of pediatric intensive care unit patients have AKI requiring Kidney replacement therapy (KRT).
The optimal treatment for children in End Stage Kidney Disease (ESKD) is Renal Transplantation. Awaiting renal transplantation, nearly 2/3rd of the children are on maintenance dialysis either blood based dialysis or peritoneal dialysis.

KRTs can be classified as intermittent, continuous or prolonged intermittent dialysis, based on the duration of treatment.
Continuous dialysis: In continuous modes of therapy, duration should be at least 24 hours
Intermittent dialysis: The duration of dialysis is 4-6 hours per day and performed 3-4 times a week
Prolonged intermittent kidney replacement therapy: It is a hybrid mode of KRT, which is given intermittently over a prolonged session (6 to 18 hours), with a low blood flow rate (3-5ml/kg/hour).

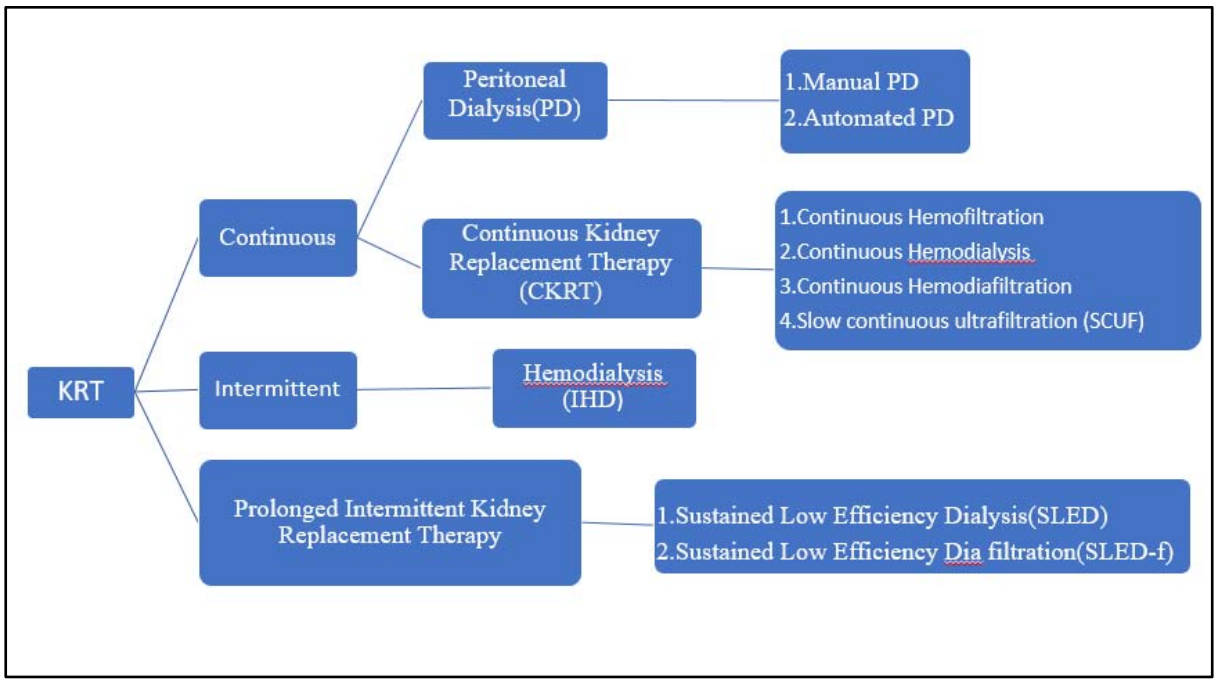


Figure 1: Types of KRT Modalities.

Choice of KRT modality:
The choice of modality of KRT depends on certain factors.

1. Patient's age and size
2. Patient's cardio vascular status
3. Availability of vascular access /condition of the peritoneal membrane and abdominal cavity
4. Available expertise.

Peritoneal dialysis (PD): PDis simpler and cost effective form of dialysis, which can be performed even in hemodynamically unstable children. It also offers gradual removal of toxin.
PD cannot be used for titrated fluid removal as indicated in pulmonary edema, or rapid removal of toxins.
Continuous Kidney Replacement Therapy (CKRT): If vascular access and use of anticoagulation are not a limitation, CKRT can be performed even in hemodynamically unstable patients which provides a gradual and sustained removal of toxins. The cost and technical expertise makes this modality difficult in many centers.

Hemodialysis (HD) will be the modality of choiceif rapid removal of toxins and fluid is desired.

Indications of Acute Dialysis:

1. Fluid overload (such as severe hypertension or pulmonary edema)
2. Uremic encephalopathy
3. Severe or persistent hyperkalemia
4. Severe metabolic acidosis (pH <7.15)
5. Oliguric AKI
6. Tumor lysis syndrome
7. Removal of toxins, either ingested or from inborn errors of metabolism.

Indications of Chronic Dialysis:

1. There is no consensus as to the specific level of GFR at which dialysis should be started.
2. Symptomatic uremia or metabolic disturbances such as hyperkalemia, hyperphosphatemia, mal-nutrition, or growth failure that cannot be managed conservatively are indications to initiate KRT.

Intermittent Hemodialysis (IHD):

- IHD is the most efficient method of KRT in terms of solute clearance and volume removal compared to PD or CKRT. It is highly effective in acute settings for the management of critical volume overload or intoxication and serves as an important method for maintenance dialysis. IHD is ideal method in management of drug intoxication, hyperammonemia, and tumor lysis syndrome.

- Another advantage of IHD is that it can accomplish isolated ultrafiltration, and the dialysis fluid solute concentration can be titrated to correct metabolic disturbances such as dysnatremias.

Chapter 2-Principles of Hemodialysis

Terminologies

Dialysis: A process by which the solute composition of a solution A (which is blood) is altered by exposing it to a solution B (Dialysate), through a semipermeable membrane.

Hemodialysis: A procedure in which the patient's blood passes against a semipermeable membrane (artificial kidney known as dialyser), with dialysis solution on another side.

Principles of Hemodialysis.

In Hemodialysis, solute and water transport happens through a semipermeable membrane which is a sheet perforated by pores. Solutes that can pass through the membrane pores are transported by two different mechanisms:

1. Diffusion.
2. Convection.

Water is removed by Ultrafiltration.

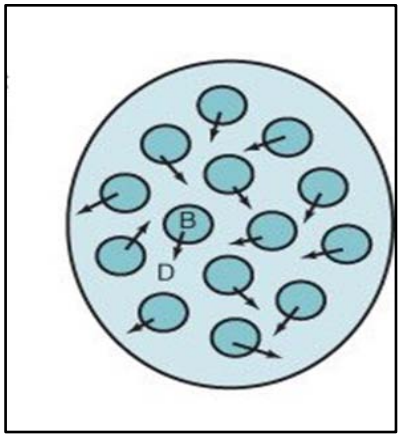


Figure 2: shows the pores of dialyser through which the blood passes (B-Blood, D-Dialysate)

1. **Diffusion:**Movement of solutes along the concentration gradient from the area of higher concentration to the area of lower concentration. The larger the molecular weight of a solute, the slower will be its rate of transport across a semipermeable membrane.

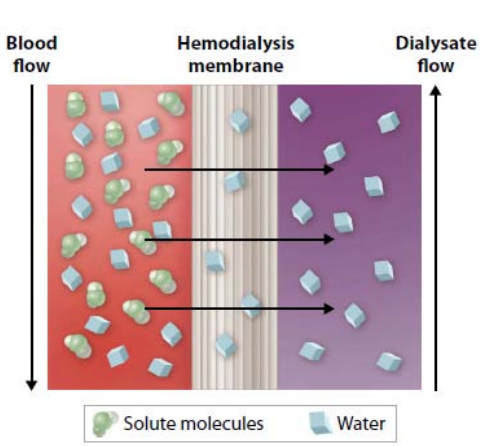


Figure 3: Principle of Diffusion

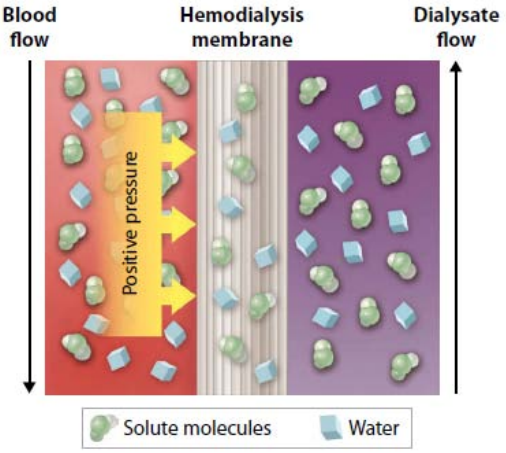


Figure 4: Principle of Convection

2. **Convection:** Convection (solute drag) is the passive movement of solute "dragged" by water moving down an osmotic or pressure gradient. It is independent of the concentration gradient but is dependent on the ultrafiltration rate and the sieving properties (coefficient) of the dialyser.

3. **Ultrafiltration:** Ultrafiltration is the process whereby water is driven either by osmotic force or hydrostatic force through a semi permeable membrane by generating transmembrane pressure

Diffusion depends on:

1) Molecular weight of solute:

- Molecular weight affects removal of solute. In figure 4, molecules in pink region represent small solutes, blue region represents middle molecules and green region represents large molecules.

  -Small molecules like urea and creatinine rapidly removed through hemodialysis

  -Large molecules (MW 11,800), cannot get through the pores of standard (low-flux) dialysis membranes .High flux Dialysers with large pore size can remove β2 microglobulin

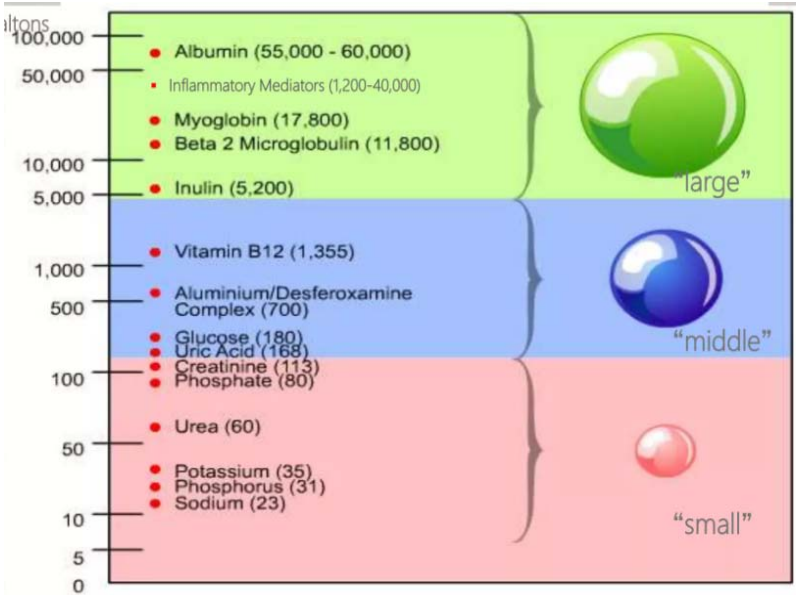


Figure 5: Molecular size of solutes

2) Surface area of dialyser: The ability of a dialyser to remove solutes is primarily a function of its membrane surface area. A high- efficiency dialyser is basically a big dialyser by virtue of its larger surface area has a high ability to remove solutes.

3) Effective pore size: The permeability to solutes depends on the size of pores in the dialyser membrane. The development of high-cut off hemodialysis membranes (with increased pore size of 8 to 10 nm) may allow clearance of larger toxins and molecules.

4) Blood flow rate: Solute clearance is dependent on the blood flow rate.The rate of clearance increases proportionately with increase in rate of blood flow.

5) Dialysate flow rate: Faster the dialysis solution flow rate, better is the efficiency of diffusion of urea from blood to dialysate although the effect is usually modest. The optimum dialysis solution flow rate is 1.5–2.0 times the blood flow rate. Above which the increase in efficiency is quite less.

Convection/ Ultrafiltration depends on:

1) Trans membrane pressure (TMP): The pressure difference between the dialyser and blood compartment is the driving force for ultrafiltration. As blood flows through the hemofilter, a transmembrane pressure gradient between the blood compartment and the ultrafiltrate compartment causes plasma water to be filtered across the membrane.

2) Ultrafiltration coefficient (KUF): Volume of fluid transferred across the membrane per hour when 1 mm Hg of TMP is applied is the ultrafiltration co efficient. Dialysers with high KUF, helps in achieving higher ultrafiltration.

Chapter 3: Understanding Hemodialysis Circuit

Hemodialysis (HD) apparatus can be broadly divided into a blood circuit and a dialysis solution circuit, which meet at the dialyser interface.

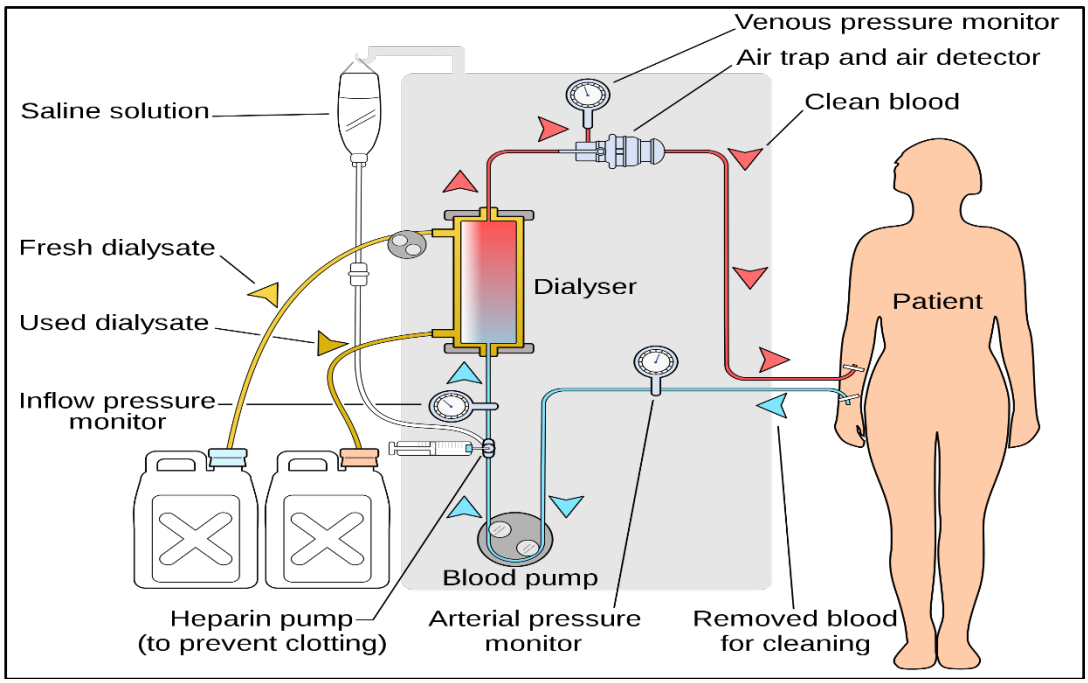


Figure 6: Hemodialysis circuit with blood circuit and the dialysis fluid circuit

1) Blood Circuit:

A) Inflow line (Arterial line): This connects the vascular access to the dialyser and it has 3 segments.

i. Pre pump Segment: connects patient's access to the blood pump. This segment has a sampling port, a saline infusion line, and a "prepump" pressure monitor (P1) in some lines. The blood pump is demanding blood at a fairly fast rate (200–600 mL/min) and because of the resistance to flow at the "arterial" opening of the vascular access, the pressure in this area is always is **negative** (below zero).

ii. Roller pump segment: Blood is moved through the dialyser by a roller pump.

iii. Post pump segment: This contains a port for heparin infusion and a pressure monitor (P2) in some lines. The pressure reading in this segment is always **positive.**

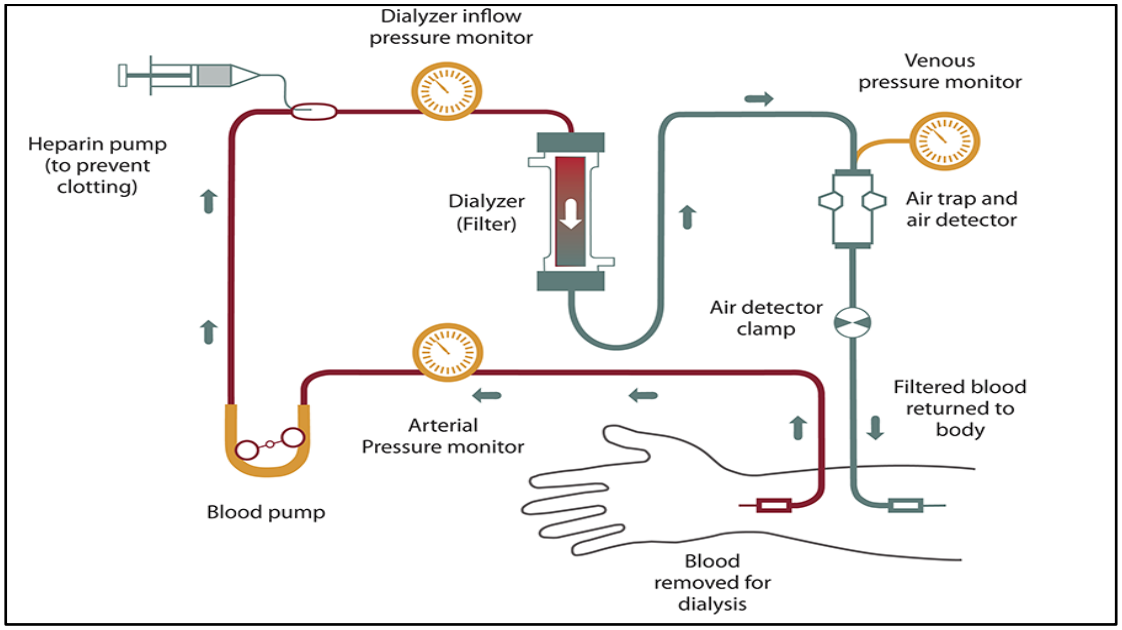


Figure 7: The blood circuit

B) Outflow line (Venous line): Outflow line runs from the dialyser back to the vascular access. It contains a venous "drip chamber" that allows for the collection and easy removal of any accumulated air from the line, a "venous" pressure monitor (P3) and an air detector.

The pressure at P2 can be combined with the reading at the venous pressure monitor P3, to estimate the average pressure in the blood compartment of the dialyser.

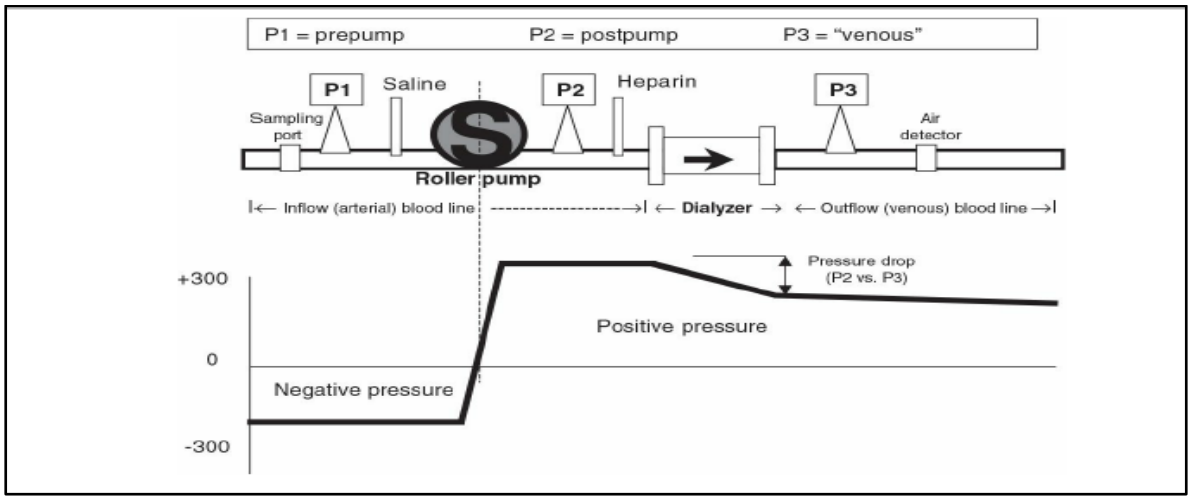


Figure 8: Pressure changes on the pre and post pump segment of the blood circuit

2) Dialysis Fluid Circuit.

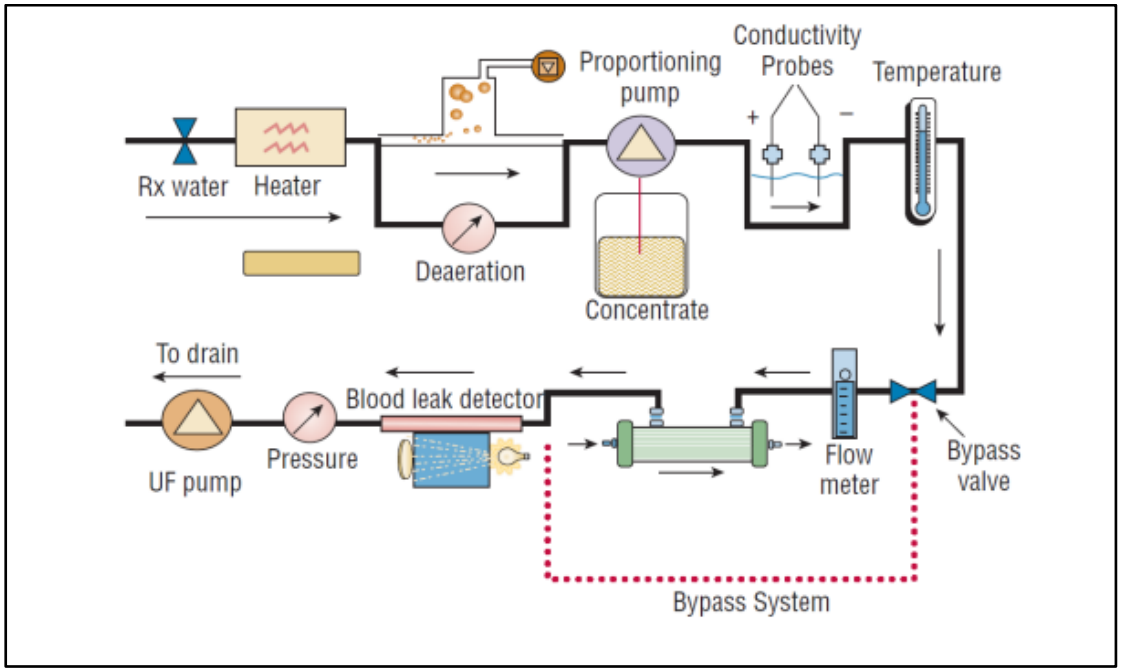


Figure 9: Dialysis fluid circuit

Dialysis solution is prepared from purified water and concentrates, the latter containing the electrolytes necessary to provide dialysis solution of the prescribed composition.

The dialysis fluid circuit contains
A) Water purification system
B) Proportionating system
C) Heating and Degassing
D) Monitors and alarms
E) Ultrafiltration control

A) Water purification system:

- Dialysis solution should contain < 100 colony-forming units (CFU)/mL of bacteria and < 0.25 endotoxin units (EU)/mL of endotoxin.
- Ultrapure water should contain a bacteria level below 0.1 CFU/mL and endotoxin level below 0.03 EU/mL,
- **Steps in Water purification:**
    i. Pre treatment
    ii. Primary Purification
        Reverse osmosis
        Deionization
    iii. Distribution of purified water

B) Proportionating system: Dialysis machines mix concentrated electrolyte solutions or powders with purified water to make a final dialysis solution that is delivered to the dialyser. Two types of proportioning systems exist, they are central delivery system and individual system

C) Heating and Degassing: Dialysis solution must be delivered at the temperature between **35–38°C** and hence to be heated up, to prevent vasoconstriction. Degassing is performed by exposing the heated water to a negative pressure.

D) Monitors and Alarms:

i. Conductivity: If the proportioning system malfunctions, an excessively dilute or concentrated dialysis solution can be produced. The normal conductivity range for dialysis solution is **12–16 mS/cm.** If the dialysis fluid conductivity is outside the range, it is bypassed to the drain via a bypass valve
ii. Temperature: If the temperature of the dialysis fluid sensed by the sensor is outside the range of **35–38°C**, the fluid is diverted to the drain.
iii. Blood leak detector: Blood leak detector is placed in the dialysate outflow line. If the detector senses blood, alarm is activated and the blood flow through the dialyser is stopped.

E) Ultrafiltration control: This is applied in newer dialysis machines. The most advanced method of UF control is a volumetric method. A separate line from the dialysate outflow line goes through a UF pump, which sets the UF rate. The pump is controlled by a central microprocessor, which tracks the desired UF and the total UF and adjusts the UF pump speed accordingly.

Chapter 4: Hemodialysis Apparatus and Alarms

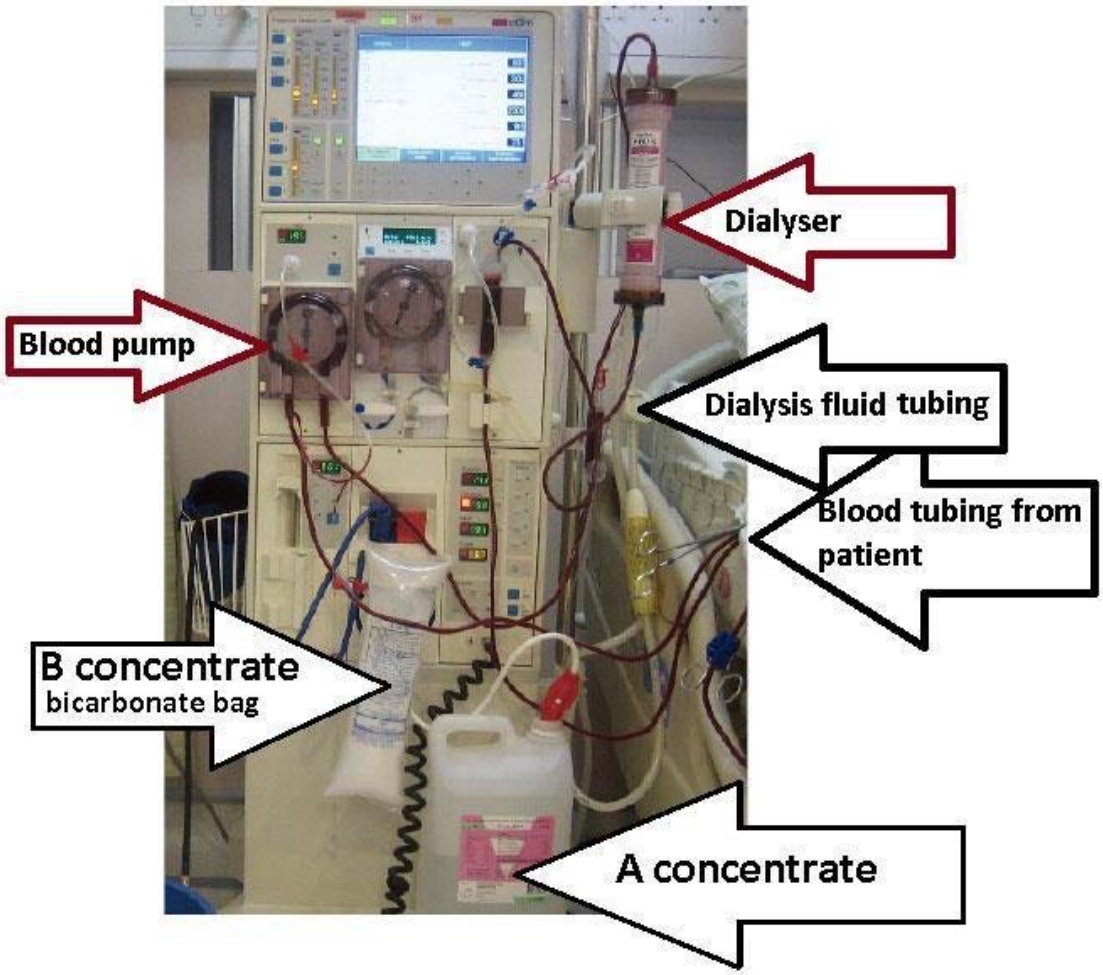


Figure 10: 4008 S HD apparatus

1) Machines:

Table 1: Commonly used machines and comparison of parameters

Parameter	Machine			
	Fresenius 4008 S	Fresenius 5008 S	Gambro AK seris	Diamax
Blood flow (ml/min)	5-500	5-500	20-500	15-600
Dialysate flow (ml/min)	300, 500, and 800	100-1000 increments of 100	300-700 increments of 100	300-700 increments of 100
Ultrafiltration	1 ml/h to a maximum of 9990 ml	1 ml/h to a maximum of 9990 ml	0-4000 ml/h	100-5000 ml/h

Maximum treatment time (hrs)	10	24	24	6
Sodium and ultrafiltration profiling	Custom	Custom	Custom	Flexible
Dialysate sodium/conductivity range (mEq/L)	128-148	128-148	130-150	10-17mS/cm
Dialysate temperature range(°C)	35-39	35-39	30-39	30-40
Dry powder concentrate use*	Yes (Bibag)	Yes (Bibag)	Yes (Bicart)	No
Online replacement fluid preparation	No	Yes	yes	No

2) Dialysate

Dialysis fluid is manufactured in concentrated form and machines proportion it with water before delivering it to the dialyser.
There are two concentrates

A) Acid concentrate: Contains acetic or citric acid, sodium, potassium, calcium, magnesium, chloride, and dextrose (optional). The low pH of the acid concentrate keeps the calcium and magnesium in solution, even in concentrated form.

B) Bicarbonate concentrate: Contains Sodium chloride and Sodium Bicarbonate
In 5008 S -Bibag is used as bicarbonate concentrate

Specially designed double proportioning systems mix the two concentrates sequentially with purified water to make the final dialysis solution.

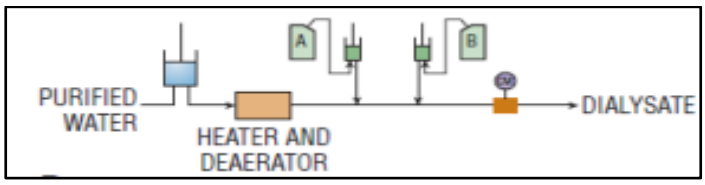


Figure 11: Proportionating system

The ratio of acid concentrate to base concentrate to water in the various proportioning systems available depends on the machine manufacturer.

Table 2: Composition of Standard Dialysate

Component	Concentration (mM)
Sodium	135-145
Potassium	2-3
Calcium	1.25-1.75 (2.5-3.5 mEq/L)
Magnesium	0.25-0.375 (0.5-0.75 mEq/L)
Chloride	98-124
Acetate	3-8
Citrate	0.8-1.0 (2.4-3.0 mEq/L)
Bicarbonate	25-35
Glucose	0-11
pCo2	40-110 mm Hg
pH	7.1-7.3

3) Dialyser.

The dialyser is where the blood and dialysis solution circuits interact and where the movement of molecules between dialysis solution and blood across a semipermeable membrane occurs.

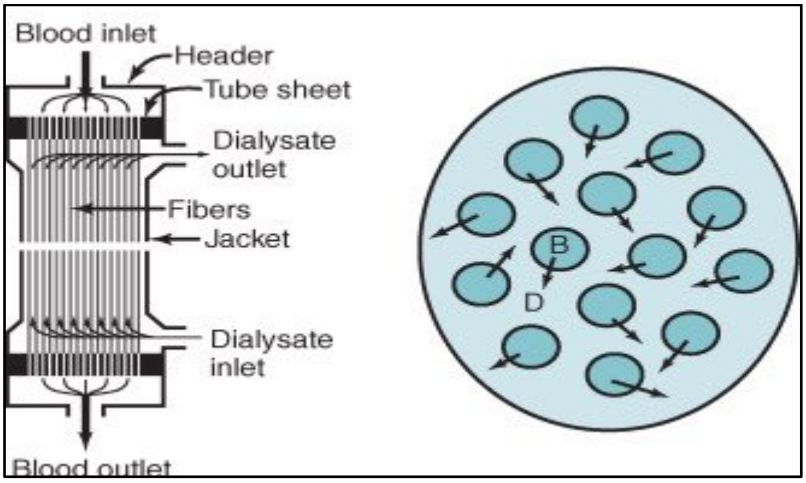


Figure 12 : Dialyser and cross sectional view of hollow fibers

A) Structure: Hollow fiber type

B) Membrane: Types

1. Cellulose membrane: Poor biocompatibility
2. Synthetic membrane: Biocompatible
    i. Polysulfone
    ii. Polyethersulfone
    iii. Polyacrylonitrile (PAN)
    iv. Polyamide
    v. Polymethylmethacrylate (PMMA)

C) Membrane Efficiency: It is the ability of a dialyser to remove solutes, which is measured as the product of membrane surface area and permeability of the membrane to the solute.

- **Mass transfer area coefficient (K0A):** The K0A is the maximum theoretical clearance of the dialyser in milliliters per minute for a given solute at infinite blood and dialysis solution flow rates.

    - **Low Efficiency Dialysers: K0A Urea < 500**
    - **Moderate Efficiency Dialysers: K0A Urea: 500-800**
    - **High Efficiency Dialysers: K0A Urea > 800**

  Higher the efficiency, higher clearance of small molecular solutes

D) Membrane Flux: High-flux membranes have large pores that are capable of allowing larger molecules. High-flux membranes also have high water permeability, with coefficient of UF (KUF) values > 20 mL/h per mm Hg.
Importance of knowing flux is aimed for better clearance.

UF coefficient (KUF): KUF is the volume of plasma water filtered in milliliters per hour for each mm Hg of TMP. Dialyser membranes can be classified into low-flux or high-flux in accordance with their KUF and large-molecule clearance.

- **KUF < 8 mL/h per mm Hg - low-flux**
- **KUF > 20 mL/h per mm Hg - high-flux**

High flux and low flux is also classified based on the removal of large solutes like Beta 2 microglobulin (B2M).

Higher the flux, higher the large molecular clearance and better ultrafiltration

Table 3: Low Flux Dialysers

Properties	FX 5	FX 8	F4 HPS	F5 HPS	F6 HPS	F7 HPS	F8 HPS	F10 HPS
Surface area(m2)	1	1.4	0.8	1	1.3	1.6	1.8	2.2
Ultrafiltration Co efficient KuF	8	12	8	10	13	16	18	21
Bundle Volume(ml)	54	74	51	63	78	96	113	132
Blood Flow Range (ml/min)	100-300	150-400	50-200	100-300	150-400	200-500	250-600	300-600
Membrane material	Helioxone	Helioxone	Poly sulfone	Poly sulfone	Poly sulfone	Poly sulfone	Poly sulfone	Poly sulfone

Table 4: High Flux Dialysers:

Properties	FX 40	FX 50	FX 60	FX 80	FX 100
Surface area(m^2)	0.6	1.0	1.4	1.4	2.2
Ultrafiltration Co efficient	20	33	46	59	73
Bundle Volume(ml)	32	53	74	95	116
Blood Flow Range(ml/min)	50-200	100-300	150-400	200-500	250-600
Membrane Material	Helioxone	Helioxone	Helioxone	Helioxone	Helioxone

4. Monitors in Hemodialysis Machine and Alarms

Figure 13: 4008S HD machine monitor.

Monitors on the Hemodialysis machine includes Blood circuit monitors and Dialysate circuit monitors.

A) Blood Circuit Monitors:

i. Inflow (Arterial)Pressure Alarm
ii. Outflow (Venous) Pressure Alarm
iii. Transmembrane Pressure Alarm
iv. Air detector

B) Dialysis Circuit Monitors:

i. Conductivity
ii. Temperature
iii. Haemoglobin

A) Blood Circuit monitors

i. **Inflow (Arterial)Pressure Alarm**:
- It is the pressure between the arterial access of the patient and the blood Pump (Pre blood pump segment)
- Normal values: − 80 to − 200 mm Hg
- High values : above − 250 mm Hg

Table 5: High arterial pressure alarms and management.

Causes of High Arterial Pressure Alarm	**Management**
Kinked Vascular Line	Inspect the line
Patient Position	Reposition
Clots	Aspirate both lumens/fibrinolytic agents
Mal positioned catheters	Rotate or pull out slightly
Hypovolemia	Manage with fluids
If still High Pressure	Reverse the lumens(Chances of recirculation)

ii. Outflow (Venous) Pressure Alarm:

- It is the pressure between the dialyser and the venous access of the patient
- Normal is 50-150 mmHg
- High pressure : > 200-250 mmHg
- High pressure is due to obstruction in return limb of circuit or catheter

Table 6: High Venous pressure alarms and management.

Causes of High Venous Pressure Alarm	**Management**
Kinked Vascular Line	Inspect the line
Patient Position	Reposition
Clots	Aspirate both lumens/fibrinolytic agents
Mal positioned catheters	Rotate or pull out slightly

iii. Transmembrane Pressure alarm:

- Transmembrane pressure is the hydrostatic pressure gradient across the dialyser, which is a positive pressure difference between blood and ultra-filtrate (or effluent pressure)
- Max allowable = 450 mm Hg
- Causes of high transmembrane pressure(TMP):
  - Protein deposition in filter which decreases membrane permeability
  - Excessive ultrafiltration relative to blood flow rate
  - Replacement fluid rate too high for the filter size

iv. Air detector :

- Most common sites of inadvertent air entry include the region around arterial needle/ leaky blood tubing connections or via the saline infusion set. Air embolism can be a fatal complication.
- Air detector will prevent entry of air into the venous access, by shutting off the blood pump.

B) Dialysis Circuit Monitors:

i. Conductivity:

- **Increased conductivity:**
  - Kink in the tubing routing purified water to the dialysis machine
  - Low water pressure
- **Decreased conductivity:**
  - Empty concentrate bottle

The normal conductivity range for dialysis solution is **12–16 mS/cm.** If the dialysis fluid conductivity is outside the range, it is bypassed to the drain via a bypass valve

ii. **Temperature:** If the temperature of the dialysis fluid sensed by the sensor is outside the range of **35-38°C**, the fluid is diverted to the drain.

iii. **Blood leak detector**: Blood leak detector is placed in the dialysate outflow line. If the detector senses blood, alarm is activated and the blood flow through the dialyser is stopped.

Chapter 5: Components of Prescription

Dialysis Prescription Chart:

Patient Name:	Age/Sex:	BSA:	Height:
OP/IP No:		Date:	

Pre Dialysis	Post Dialysis
Weight: BP: HR:	Weight: BP: HR:

1. Vascular access site :
2. Vascular catheter size :
3. Duration of Dialysis:
4. Dialyser size:
5. Circuit:
6. Priming:
7. Co- Current/ Counter current:
8. Blood Flow Rate:(QB):
9. Dialysate Flow Rate(QD):
10. Ultrafiltration Goal:
11. Anticoagulation: Heparin /Citrate/ Saline Flush
    Loading Dose:
    Maintenance Dose:
12. Dialysate:
13. Dialysate potassium:
14. Dialysate Sodium:
15. Pre Dialysis orders:
16. Post Dialysis orders:

1. Vascular access site:

A. Central Venous Access

B. AV Access (AV fistula/ AV Grafts)

A.Central Venous Access:Central Venous Access is most commonly used in urgent initiation of Hemodialysis.

Site of Central Venous Access: (In order of preference - KDOQI)

- Right internal jugular vein
- Femoral vein
- Left jugular vein
- Subclavian vein

Table 7: Pros and Cons of various vascular access site

	Internal Jugular Vein	**Femoral Vein**	**Subclavian**
Pros	• Direct angle to the heart thus high blood flow rate • Shorter catheter- less resistance to better flow • Less recirculation	• Easily Accessible • Easier to maintain hemostasis	• Shorter catheter, better flow • Less recirculation
Cons	• Difficult hemostasis • Less accessible with cervical trauma • Difficult in small infant due to catheter length	• Potential for kinking • More recirculation • Thrombosis • Flow issues if abdominal pressure is high	• Potential for kinking • Difficult hemostasis • Venous narrowing very common • Less accessible with cervical trauma

Preference of site of insertion is based on patient's indication for dialysis and aim to preserve vein in children in chronic kidney disease (CKD).

B. Arteriovenous Access:AV Access (AV fistula/ AV Grafts).

- Commonest form of vascular access used for maintenance hemodialysis.
- Arteriovenous access is either by AV fistulas or AV grafts.
- An AV fistula involves creating an anastomosis between an artery and a native vein, allowing the blood to flow directly from the artery to the vein.
- Fistulas are most commonly created in the wrist between the radial artery and the cephalic vein and other sites are anastomosis in the snuffbox, in the forearm area, or at the elbow or upper arm (distal to proximal sites are preferred).
- An AV graft is similar, except that the distance between the feeding artery and vein is bridged by a tube made of prosthetic material. The most commonly used bridging material is polytetrafluoroethylene (PTFE) polymer.

Rule of 6s is as follows

- 6 weeks for maturation of AV Fistula.
- Fistula should be able to support a blood flow of 600 ml/min.
- Fistula should be at a maximum of 6 mm from the surface.
- Fistula should have a diameter of greater than 6 mm.
- There should be a 6 cm straight segment.

KDOQI Recommendations:

- AV access (AVF or AVG) in preference to a CVC in most incident and prevalent HD patients.
- The choice of AV access (AVF or AVG) be based on the operator's/clinician's best clinical judgment.
- If sufficient time and patient circumstances are favourable for a mature, usable AVF, such a functioning AVF is preferred to an AVG.
- It is reasonable to use tunneled CVC in preference to non-tunneled CVC due to the lower infection risk with tunneled CVC.
- It is reasonable to use non-tunneled internal jugular CVC only for temporary purposes for a limited time period (< 2 weeks or per individual facility policy) to limit infection risk.

2. Vascular catheter Size:

- Catheter can be tunneled and non-tunneled catheters.
- The catheter size depends on patient weight.
- Largest diameter of CVC should be chosen to optimize blood flows and circuit survival.

Table 8: Selection of weight specific catheter size (adapted from Bunchman et al)

Patient Weight	Catheter Size	Site Of Insertion
Neonate	Double lumen,7 Fr	Femoral artery or Vein
3-6kgs	Double or Triple Lumen 7 Fr	Jugular, subclavian or femoral
6-30kgs	Double -Lumen 8 Fr	Jugular, subclavian or femoral
> 15kgs	Double -Lumen 9 Fr	Jugular, subclavian or femoral
> 30 kgs	Double-Lumen 10 Fr or triple lumen 12 Fr	Jugular, subclavian or femoral

- Preferred site of insertion is based on patient's indication for dialysis and aim to preserve veins in case of CKD.

3. Duration of Dialysis:

- **First Session:**
  - Duration of first session is preferably based on Kt/V calculation but for practical convenience **not to extend the session longer than 2 hours**
  - Urea reduction rate should be less than 30% (to prevent DDS)
  - Consider use of **Mannitol (0.25gm/kg/dose)** just prior to initiation if S. Osmolality > 300 mOsm or BUN > 100 mg/dl

- **Second Session:**
  - Re-evaluate the child
  - Can be increased to 3 hours provided Urea is < 100 mg/dl
  - **Subsequent session**: 3- 4 hours

- **Aim for Urea reduction ratio (URR)**
    - To have a clearance of 25-30% during 1st dialysis, duration will be approximately 1.5 -2 hours.
    - For 50% during 2nd session , duration should be 3 hours
    - For $\geq$ 70% reduction, subsequent sessions may be 3.5 to 4 hours.
    - Till 4 hours session of dialysis is achieved, better to have co current dialysis.
    - URR is based on duration of dialysis.
    - Short and long sessions will have its own pros and cons.

- **Short sessions:** For clearing small molecules like potassium
- **Longer sessions**: Removing cumulative large volumes of fluid without compromising hemodynamic stability
- **SLED**: In slow Low efficient dialysis ,the session can be from 6 to 12 hours

4. Dialyser Size: Selection of Dialyser is based on

A. Body Surface area (BSA)

B. Ultrafiltration Co efficient (KUF)

C. Mass Transfer area co efficient (K0A)

A. Body Surface area (BSA):

- The dialyser size can be equal to, but not more than BSA.
- Greater BSA ensures better clearance of water and solutes, but increases the risk of disequilibrium syndrome during initiation.
- Thus for the first session of dialysis, it is always better to use a dialyser about **75% of the BSA.**
-

B. Ultrafiltration Co efficient (KUF):

- Low flux dialysers: KUF < 8 mL/h per mm Hg.
- High Flux dialysers: KUF > 20 mL/h per mm Hg.
- More β2 microglobin clearance.
- The clearance of urea and low molecular weight solutes is similar in low and high flux Dialysers.

- High flux Dialysers increase the clearance rates of large solutes and should be considered in amyloidosis and others requiring large molecule clearance and those requiring rapid amounts of removal of large ultra-filtrate.

C. K0A-Mass Transfer area Coefficient:

- Low Efficiency Dialysers: K0A Urea <500
- Moderate Efficiency Dialysers: K0A Urea: 500-800
- High Efficiency Dialysers: K0A Urea >800
- Higher the efficiency of Dialysers, more the diffusive clearance, thus small molecules are removed.

5. Extracorporeal Circuit:

- A child can tolerate 8-10 % of total blood volume (TBV) in the extracorporeal circuit.
- Extracorporeal circuit involves blood in needles, dialyser and also the tubings (arterial and venous lines)

Table 9: Blood volume in children.

Age	**Total Blood Volume**
Neonates	100 ml/kg
Children	80 ml/kg
Adolescents	60 mL/kg

Table 10: Filter size and volume.

Filter Size	**Filter Volume (ml)**
F4 HPS	51
F5 HPS	63
F6 HPS	78
F8 HPS	113
F10 HPS	132
FX Paed	18
FX 40	32
FX 60	74
FX 80	95

Table 11: Circuit tubings and volume.

Tubing	**Volume (ml)**
Neonatal	56
Pediatric	117-126
Adult	161-172

6. Priming:

- Priming is a process in which **normal saline is rinsed and filled into the dialyser and bloodlines** to expel air and expand the membranes to achieve effective surface area and to remove traces of ETO.
- The priming volume of the dialyser and the tubing should not exceed calculated extracorporeal circuit volume.
- If the total blood volume of the circuit is greater than 10% of the estimated total blood volume (TBV), circuit should be primed with 5% albumin or blood is recommended, to prevent hypotension, based on the hemodynamic status of the child.

7. Co- current / Counter current:

When the blood flow and dialysate flow happens in the same direction it is called co current or concurrent. If it happens in the opposite direction it is called counter current

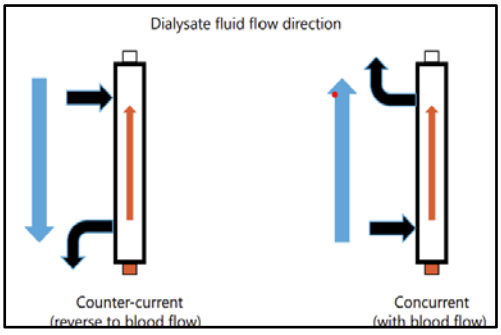


Figure 14 : Co current and counter current Flow

Co current Flow:

- Reduces the clearance of small molecules by about 20% during the HD.
- It is usually done in the first few dialysis sessions where rapid removal of urea is not aimed.

Counter current Flow:

- Provide maximum diffusive gradient as fresh dialysate fluid is continuously exposed to solute-laden blood(Blood and dialysate flow in opposite directions)
- Thus it is most commonly used in maintenance IHD.

8. Blood Flow Rate(QB):

- It is the rate at which the blood flows in the blood compartment of the dialyser.
- As the blood flow rate increases, the clearance also increases proportionately.
- It also depends on size of vascular access.

    - Initial sessions: Preferable to have low blood flow rate of 2-3ml/kg/min.
    - Regular sessions: 5-8 ml/kg/min.
- Minimum blood flow rate is 10ml/min (4008 S).
- Maximum blood flow rate is 600ml/min.
- As the blood flow rate is increased, hemodynamics has to be carefully monitored as they are at risk of hypotension.

9. Dialysate Flow Rate (QD):

- Dialysate flow rate should be at least 1.5 times > blood flow rate for efficient solute clearance.
- Above 1.5 times, the increase in efficiency is quite small.
- Usually 300 ml/min to 500 ml /min of dialysate flow rate is commonly used in Children.
- Dialysate flow rate is in fixed proportion in 4008 S machine(300ml/min, 500ml/min and 800 ml/min)
- In 5008 S machine, dialyser flow rate can be in increments of 100ml/min.

10. Ultrafiltration Goal:

Acute Dialysis:

- Fluid overload may be an indication of dialysis in acute settings. Large volume dialysis will not be tolerated by the child and can even result in electrolyte imbalance.
- Initial 1-2 hours isolated ultrafiltration alone can be done, without the dialysate.
- It is extremely important to avoid hypotension at all times, including during dialysis, particularly in the setting of AKI, which may worsen the renal perfusion.

Chronic Dialysis:

- “Dry weight” or optimum post dialysis weight is the post dialysis weight at which all or most excess body fluid has been removed, thus patient is as close to euvolemia without experiencing symptoms.
- If the dry weight is set too high, the patient will remain in a fluid-overloaded state.
- If the dry weight is set too low, the patient may suffer frequent hypotensive.

- In children, growth and changes in lean body mass and body habitus necessitate regular and frequent re-evaluation of the dry weight, at leastonce in 2 weeks.
- Volume status can be assessed by clinical examination(Heart rate, Blood pressure, respiratory rate), Ultrasound assessment of collapsibility index of IVC, Bio-impedance and on-line non-invasive blood volume monitoring (NIVM).
- NIVM provides information on intradialytic blood volume changes and vascular refilling rates.
- NIVM is used in newer machines like Fresenius 5008 S.
- **Ultrafiltration rate of 10 ml/kg/h is the safe starting point and not to exceed 0.2ml/kg/min or more than 5% of body weight per session**

11. The Dialysate:

Dialysis fluid is manufactured in concentrated form and machines proportion it with water before delivering it to the dialyser.
There are two concentrates

Part A: Acid Concentrate
Part B: Base concentrate

Table 12: Acid concentrate composition. **Table 13:** Base concentrate composition.

Contents	**mmol/L**
Sodium	82-103
Potassium	2
Calcium	1.5
Magnesium	0.375
Chlorides	86-108
Acetic acid	3.0-4.0
Dextrose monohydrate	10.4 (200 mg %)

Contents	**mmol/L**
Sodium	54
Bicarbonate	35
Chloride	19

Table 14: Composition of Dialysate.

Contents	**mmol/l**
Sodium	135-145
Potassium	0-4
Calcium	1.25 to 3
Magnesium	0.375 to 0.75
Chloride	99-124
Bicarbonate	30-40
Dextrose	200 mg/dl

Part A and part B are mixed in a proportion, along with the ultra-pure water.
Proportioning ratio is 1:34:1.83(Acid: Ultrapure water: Base)

In 5008 S machine, Part B is the Bi Bag, which contains sodium bicarbonate 650gms.

- The dialysate content may be adjusted to address specific therapeutic needs.

i. Sodium:

- Hyponatremic dialysis causes osmotic fluid shift from the extracellular to intracellular compartment, contributing to dialysis disequilibrium and intra-dialytic hypotension.
- Hypernatremic dialysis transfers sodium to the patient, causing interstitial edema, interdialytic thirst, increased inter-dialytic weight gain and worsening hypertension.
- A therapeutic advantage can be gained by manipulating the dialysate sodium concentration throughout dialysis, known **as sodium profiling.**
- Sodium profiling can be done in a step, linear, or exponential fashion.
- The higher dialysate sodium at the start allows a diffusive sodium influx to counter balance the rapid decline in plasma osmolarity due to clearance of urea and other small molecular weight solutes. Low dialysate sodium at the end aids diffusive clearance of the sodium load and minimizes hypertonicity.
- Sodium profiling prevents DDS, reduces intradialytic cramps and fatigue.
- **Dialysate sodium should not differ by more than 10 mEq/L from blood sodium to avoid disequilibrium**

ii. Potassium:

- The standard dialysate potassium is 2 mEq/L.
- If Patient Pre dialysis potassium is < 4 mEq/L, dialysate potassium of 3–3.5 mEq/L can be used.
- Pre dialysis potassium is > 7mEq/l, a zero-potassium dialysate can be used for a short period of time and then changing to a normal potassium dialysate.

Rule of 7: Patient's Potassium and Dialysate Bath potassium should equal approximately 7. Example: If patient's Potassium is 5.2, put them on "2K" bath (2 mEq/L potassium)

iii. Calcium:

- Dialysate calcium concentrations vary between 1.25 mmol/L to 1.75 mmol/L.
- KDOQI recommends to maintain a low normal range of plasma Calcium to avoid the risks of extra skeletal calcification.
- Use 1.25 mmol/L if child is on Vitamin D and calcium based phosphate binders.
- Hypocalcemia also depresses myocardial contractility and reduced vascular reactivity and hypotension.

iv. Magnesium:

- The concentration of magnesium in dialysate is 0.5–1 mmol/L.
- Low magnesium concentration (0.5mmol/L) can be used if child is on magnesium containing phosphate binders
- Low magnesium levels can result in cramping and arrhythmias and therefore higher magnesium baths may help to improve cardiovascular stability and intra-dialytic symptoms

v. Dialysate temperature:

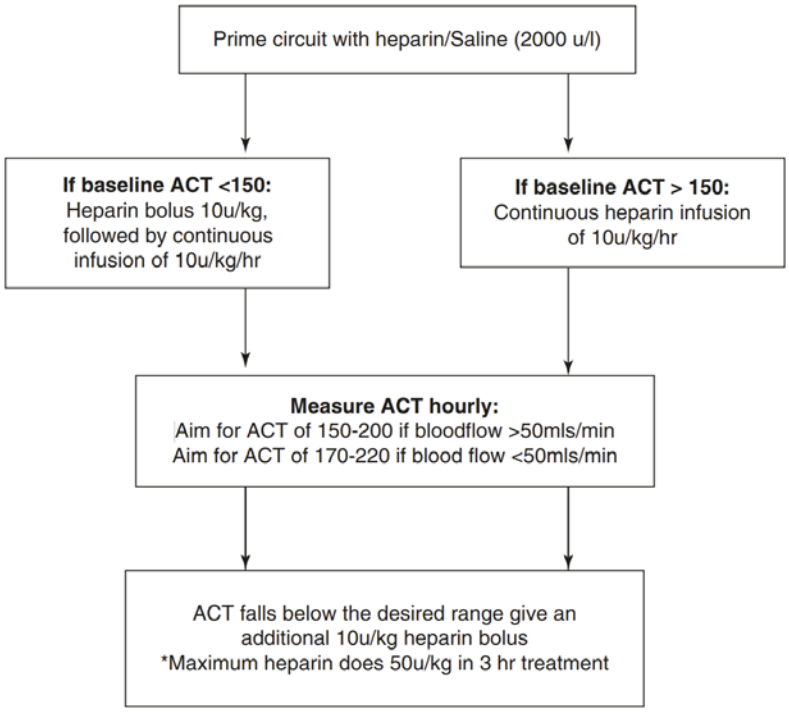
- This is usually set at 35°C–39°C (In 4008 S).
- Low Dialysate temperature will cause vasoconstriction.

12) Anticoagulation:

- Anticoagulation of the extracorporeal circuit is usual but not mandatory and should be determined by estimating the risk of bleeding against that of clotting the circuit which results in blood loss and reduced dialysis efficacy.
- Unfractionated heparin (UFH) remains the agent of choice.

- Unfractioned Heparin:
  - Binds with antithrombin and inhibits thrombin.
  - Inhibits fibrin formation and thrombin-induced platelet activation.
  - Increases vessel wall permeability.
- Standard regimens:
  - Bolus dose : 15-20 U/kg up to 40 U/kg of heparin.
  - Maintenance dose: 15–20 units/ kg/hr.
  - Stop the heparin infusion over the last 30 min of dialysis.
- Alternate regimens:
  - If there is risk of bleeding as with recent surgery, coagulopathy, thrombocytopenia, or planning a renal biopsy or any other procedure within 12 hours.
  - Tight heparin protocol can be used.
  - Alternative options like regional anticoagulation with citrate, use of prostacyclin infusion, high flow rate HD, calcium free dialysate with calcium infusion back to the patient in a closely monitored setting can be tried.
  - Regular intermittent saline flushes (100 mL in < 20 kg, 150 mL in > 20 kg) every 30 mins and make sure to remove the flushes given.
  - High blood flow rate is maintained.

- Tight Heparin Protocol:



Adapted from Schaefer (Pediatric Kidney Disease).

Chapter 6. HD/ SLED

KRT is one of the major therapeutic interventions in both acute and chronic kidney disease. Broadly it is in 2 forms one being blood based dialysis and peritoneal dialysis.

Further 3 different methods are available in blood based dialysis.
1 Intermittent Haemodialysis (IHD).
2) Sustained low efficiency dialysis (SLED).
3) Continuous kidney replacement therapy (CKRT).

Depending on the diagnosis, age at diagnosis, its severity, availability of dialytic mode, cost and technical staff, specific dialysis modality is chosen and offered. Each method has its own advantages and disadvantages.

Table 15. Advantages and disadvantages of IHD.

Advantages	**Disadvantages**
Simplicity in procedure and has short duration (maximum of 4 hrs)	More prone to dialysis disequilibrium syndrome (DDS)
Cost Effective	Can't be used in hemodynamically unstable patients
Faster and better solute and solvent removal (Hyperkalemia, fluid overload causing pulmonary edema)	Can't be used in traumatic brain injury and intracranial hemorrhage as it causes more cerebral edema.
Flexible anticoagulation	High chance of rebounce phenomenon
Modifiable dialysate concentration.	
Best utility is in Hemodynamically stable patients with hyperkalemia, severe metabolic acidosis or poisoning with toxin/ drugs that is easily dialyzable (Salicylates, Barbiturates)	

Table 16. Advantages and disadvantages of SLED

Advantages	**Disadvantages**
Simplicity in procedure with flexibility in duration	Needs ultra-pure water for dialysate
Can be used in hemodynamically unstable patients	Chances of Hypothermia / hypophosphatemia
Being slow dialysis method with a longer duration it has minimal chances of dialysis disequilibrium syndrome and clearance rebounces.	unknown effects on pharmacokinetics of drugs
Lesser anticoagulation due to shorter duration there by limiting bleeding risk	Requires ultrapure water
Modifiable dialysate concentration	Clinical unfamiliarity
Cost effective	
Can incorporate diafiltration (SLED-f)	
Best utility is in Hemodynamically unstable patients. Another advantage is it can be coupled with other extra corporeal support systems	

Table 17. Comparing SLED/IHD.

	IHD	**SLED**
Machine	4008S (Fresenius)	4008S / 5008S (Fresenius)
Complexity	++	++/+++
Vascular Access	According to age/weight	
Blood Flow rate (Qb)	Rapid, controlled 5 - 10 ml/kg/min	Slow, controlled 3-5ml/kg/min
Dialysate Flow rate (Qd)	4008s set values 300/500/800 ml/min. 5008 S rate can be individualized	
Qb/Qd ratio	1:2 to 1:3	1:1 to 1:2
Anticoagulation	Heparin/saline flushes	Heparin/saline flushes/citrate
Water for dialysate	Pure	Ultra-pure
Dialysate	Solution A/B	Bibag and solution for acid
Clearance principle	Diffusion	Mainly diffusion, convection added in SLED-f
Filters	Low flux/High flux	SLED: High flux SLED-f: High flux/hemofilters
Solute Clearance	+	++ (due to higher duration time)
UF	Rapid, controlled	Slow, controlled
Duration	4 hrs	6-12hrs
Utility hemodynamically unstable patients	No	Yes
DDS	++	+/-

Chapter 7: Adequacy in Hemodialysis.

Adequacy of hemodialysis refers to how well the urea and other toxins are removed from patients' blood. This has a very important bearing on the wellbeing and survival of the patient. Dialysis can be considered adequate if it provides,

- Relief from uremic symptoms.
- Controls acidosis, fluid, electrolytes and Blood pressure.
- Correction of anemia.
- Feeling of physical and physiological wellbeing.

There are multiple indicators of hemodialysis adequacy

1. Urea Reduction Ratio: URR.
2. Kt/V: Single pool Kt/V: sp Kt/V.
   Equlibrated (Double pool) Kt/V: eq Kt/V.
   Weekly standard Kt/V: std Kt/V.
3. Ultrafiltration.
4. Normalised protein catabolic rate (nPCR).

URR and Kt/V are the most commonly utilised parameters.

1. Urea reduction ratio: It is calculated by
[(Predialysis urea – Post dialysis urea) / Predialysis urea] x 100

It is very simple to calculate, and is a good predictor of mortality.
URR is expressed in percentage.

2. The sp Kt/V index is defined as the amount of serum that is cleared from urea via the distribution volume in a single session of dialysis. K represents dialyser clearance, t: duration. V: Volume of distribution. The measurement is done at the end of dialysis session.

$$sp\ Kt/V = -\ln(1-URR)$$

Single pool method doesn't take into account the rebounce of urea that happens after the end of dialysis session over estimating the true urea mass removed. To account for this and to determine exact values the blood sample is drawn 30 to 60 min after the dialysis session ended as most of the rebouncing happens by then. This is termed as eq Kt/V.
Generally eq Kt/V is 0.2 units less than sp Kt/V but can be as high as 0.6 units.
It is calculated by using formula

$$eq\ Kt/V = sp\ Kt/V \times t / (t + 30.7)$$

std Kt/V is a measure of total clearance per week, and as such, accounts for the number of treatments during the week. Calculation of duration of dialysis is discussed in the following chapter 13 as a case-based discussion.

3. Optimising fluid status.
Dry weight is defined as post HD weight of the patient as close to euvolemia without experiencing symptoms indicative of over hydration or under hydration at or after the end of HD. Methods to estimate dry weight include,

- Clinical assessment: Weight, edema, Blood pressure.

- Laboratory assessment: Haematocrit, Albumin, Serum sodium.
- Ultrasound guided measurement of IVC.
- Bioelectrical impedance.
- Intradialytic non-invasive blood volume monitors.
- Biomarkers such as ANP, BNP.

Targets for adequate dialysis: NKF-KDOQI 2006 guidelines for a thrice weekly HD recommends a minimum value of spKt/V > 1.2 or URR ≥ 65% for maintenance hemodialysis, but recommends a target 1.4 for sp Kt/V and 70% for URR. In terms of std Kt/V minimally adequate dose is 2.0 and target dose is 2.2 per week.

Causes of inadequate dialysis.
- Improper dialysis prescription.
- Inadequate blood flow.
- Improper blood collection.
- Reduced time of dialysis.
- Filter clots and leaks.
- Recirculation.

Improving adequacy of dialysis
- Improve Kt/V :
  1. Optimise blood flow by ensuring adequate size of catheter, needle size, treat catheter thrombosis, and decrease recirculation.
  2. Use of dialyser with appropriate surface area and higher flux.
- Optimise UF by increasing frequency and or duration of dialysis and excess intradialytic weight gain.
- Avoid missing dialysis or short durations of dialysis sessions.

Table 18: .Laboratory and Clinical indices of adequate HD.

Indices	**Recommendation**
Pre dialysis Bicarbonate	20-26 mEq/L
Pre dialysis Potassium	3.5-6.5 mEq/L
Pre dialysis Phosphate	Up to 50th centile for age appropriate range
Serum Calcium (adjusted to albumin)	Appropriate for age appropriate normal range
Parathyroid hormone	Less than twice the upper limit of normal
Hemoglobin	Greater than lower limit of normal range
Ferritin	100-800 mcg/L
Dry weight	2-4 weekly depending on the age of child
Pubertal Maturity	Every quarterly in more than 10 yr old
Blood pressure	Age appropriate normal range
URR	More than 65%, Target 70%
Sp Kt/V	Greater than 1.2, Target 1.4

Chapter 8: Complications of Hemodialysis

Common complications of hemodialysis are:

1. Intradialytic Hypotension.
2. Dialysis Disequilibrium Syndrome.
3. Dialyser Reactions.
4. Hemolysis.
5. Air embolism.
6. Arrhythmias.
7. Others: Headache, Chest and Back pain, Muscle Cramps, Nausea, Vomiting, Itching.

1) **Intradialytic Hypotension (IDH):** There are various definitions for IDH, including a nadir (lowest) systolic BP less than 90 mm Hg or a fall in systolic BP of 20 or 30 mm Hg than starting blood pressure.

Table 19: Cut off systolic Blood pressure (mm Hg) for hypotension.

Age	Systolic BP (mm of Hg)
0-28 days	< 60
1-12 months	< 70
1-10 years	< 70 + (age in years x 2 yrs)
More than 10 years	< 90

Causes of Intradialytic Hypotension

Volume-related:

- Excessive weight gain (high ultrafiltration rate)
- Shorter weekly dialysis time (high ultrafiltration rate)
- Too low target ("dry") weight

Inadequate vasoconstriction:

- High dialysis solution temperature
- Autonomic neuropathy
- Antihypertensive medications
- Eating during treatment
- Anemia

Cardiac factors:

- Diastolic dysfunction

Prevention of Intradialytic Hypotension-

- Use a dialysis solution temperature of 35.5°C.
- Review dietary sodium intake and any other reasons for excess fluid intake.
- Consider raising the patient's target weight.
- In refractory cases, consider a trial of higher (140–145 mM) dialysis sodium.
- Give daily dose of antihypertensive medications after dialysis (not before or during dialysis)
- Avoid food consumption immediately preceding or during dialysis
- Consider diuretics if residual renal function is good.

Management-

- Trendelenburg position
- Decrease the blood flow rate
- Bolus of 0.9% Normal saline (100 ml or more as necessary)

- UFR should be reduced to as near zero as possible → can be resumed once vital signs have stabilized.
- As alternative to saline, Glucose, Mannitol and albumin solutions can be used to treat hypotensive episodes.

2) Dialysis Disequilibrium Syndrome (DDS):
DDS is a set of systemic and neurologic symptoms associated with characteristic electroencephalographic findings that can occur either during or following dialysis.
It is due to resultant cerebral edema due to rapid removal of solute (Urea).

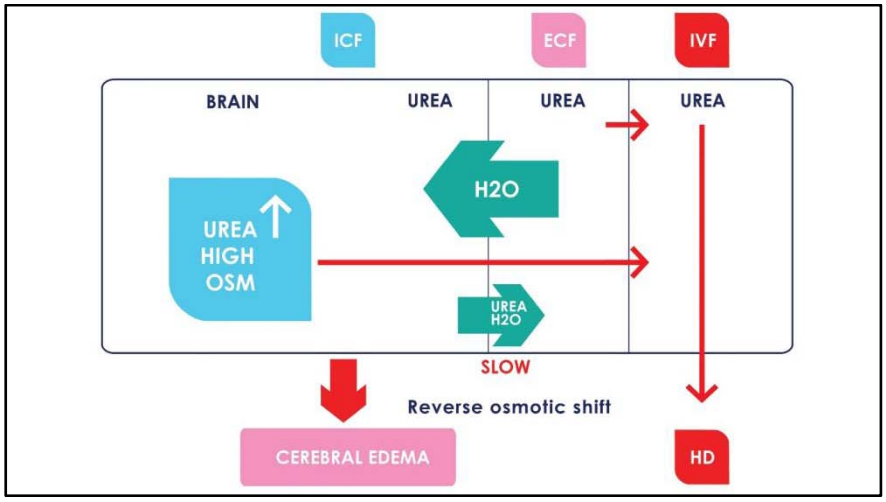


Figure 15: Mechanism of DDS.

Table 20: Symptoms and Management of DDS.

	Mild Disequilibrium	**Severe Equilibrium**
Symptoms	Nausea, Vomiting, muscle cramps, restlessness, headache.	Seizures, Coma.
Management	Symptomatic. Blood flow rate should be reduced. Hypertonic Saline or glucose solution can be given for muscle cramps. Terminate dialysis earlier than planned	Stop the dialysis Supportive, ABC. IV Mannitol . Antiepileptics. If coma is due to disequilibrium, then patient should improve within 24 hours.

Prevention of DDS:
- A urea reduction ratio of <40% should be targeted.
- Use smaller dialyser (not exceeding BSA of the child).
- Decreasing the blood flow rate and dialysate flow rate.
- First session of hemodialysis not exceeding 1-2 hours.
- Using IV mannitol (20%) during first session of hemodialysis.

2) Dialyser Reactions:

Type A (Anaphylactic) Reaction:

- Cause: Ethylene Oxide (used for sterilisation), Filters containing AN69 membrane, contaminated dialysis solution (bacteria and endotoxin), heparin.
- Symptoms: Dyspnea, Cough, Sneezing, Rhinorrhea, Urticaria, Itching, diarrhea, abdominal cramps.
- Management: Stop Dialysis, Discard dialyser and tubings, without returning the contained blood. Cardiorespiratory Support, IV antihistamine, epinephrine, steroids.
- Prevention: Proper rinsing of dialyser, pre-dialysis administration of antihistamines.

Type B Reaction:

- Cause: Unknown but Complement activation has been suggested to be a culprit.
- Symptoms: Chest pain and back pain.
- Management: Supportive including nasal oxygen. Dialysis can be continued as symptoms are likely to abate after the first hour.
- Prevention: Trying a different dialyser membrane.

3) Hemolysis

- Etiology:
    - Obstruction/ Narrowing of blood lines- Due to kinks, narrow blood lines or obstruction to blood flow cause large pulling force and sheer stress on RBCs which result in hemolysis.
    - Abnormalities in dialysis solution (Overheated, hypertonic, contamination with chloramine, copper, fluoride, nitrates)
- Manifestations: Back pain, chest tightness, shortness of breath, port-wine appearance of blood in blood lines, a pink discoloration of plasma in centrifuged blood sample.
- Investigations may show sudden drop in hemoglobin, marked fall in hematocrit, hyperkalemia.
- If massive hemolysis is not detected early, then hyperkalemia can result in muscle weakness, ECG abnormalities and ultimately cardiac arrest.
- Management: Blood pump should be stopped immediately, blood lines should be clamped and blood should not be reinfused (due to high K content).
- Treat resultant hyperkalemia.

5) Air Embolism:

- Air enters bloodstream through dialysis circuit or through vascular access.
- Causes include poor connection between arterial needle and circuit, defects in tubing in arterial portion of circuit, inadequate priming of dialyser, improper medication administration, uncapped dialysis catheter, dialysis catheter placement/ removal
- Manifestations: depends on the position of the patient
- Seated (infused air tend to migrate into cerebral venous system)- loss of consciousness, convulsions and even death
- Recumbent (infused air tend to enter heart, generate foam in right ventricle and enter into the lungs)- Dyspnea, cough, chest tightness and arrhythmia
- On auscultation, one can get peculiar Churning sound
- Management: Clamp the venous blood line and Stop the blood pump

- Immediately place in recumbent position on the left side of the chest and head tilted downwards.
- Cardiorespiratory support.
- Aspiration of air from the atrium or ventricle with a percutaneously inserted needle or cardiac catheterization may be needed

6) **Arrhythmias:** Frequent exposure to arrhythmic triggers, including rapid changes in serum potassium, changes in serum calcium, and metabolic alkalosis, occurring in the setting of coronary artery disease and structural heart disease bradycardia, asystole, atrial fibrillation, ventricular tachycardia/fibrillation
Management: CPR
Prevention: avoid low potassium and low calcium dialysate, avoid metabolic alkalosis, limit UFR, lower dialysate temperature, consider frequent HD; consider pacemaker/ICD if indicated

7) Others :

A) Muscle Cramps:

- Etiology: Hypotension, Hypovolemia, High UF rate, hypocalcemia, hypomagnesemia, use of low sodium dialysis solution → muscle hypoperfusion → impairment of muscle relaxation → muscle cramps.
- Management: If hypotensive, management with 0.9% Saline might be beneficial.
- Prevention: Stretching Exercises, Biotin (1mg/day), Carnitine, , Oxazepam (5-10 mg given 2 hours prior to dialysis), Vitamin E.

B) Nausea and Vomiting:

- Etiology: Hypotension, Dialysis Disequilibrium syndrome, Type A and B dialyser reaction, Contaminated or incorrectly formulated dialysis solution (high sodium or calcium)
- Management: Treat hypotension, Antiemetic's as needed
- Prevention- Predialysis dose of Antiemetic

C) Chest and Back Pain: Mild chest pain or discomfort (often associated with some back pain) occurs in 1%–4% of dialysis treatments. The cause is unknown. There is no specific management or prevention strategy, though switching to a different variety of dialyser membrane may be of benefit.

D) Itching- Itching may be due to hypersensitivity to dialyser or components of blood circuit. Viral hepatitis or scabies should also be looked for. General moisturising and skin lubrication using Emollients and symptomatic treatment with use of antihistamines may be beneficial. If related to abnormal values of calcium, phosphorus and parathormone (PTH), these should be corrected.

Chapter 9: Monitoring of patients on Hemodialysis

9a) Monitoring patient on Chronic HD

Name: **Age:** **Sex:** **Hospital ID:**
Diagnosis: **Date:**

Table 21: Monitoring on Chronic HD patients

Evaluation	Frequency
Adverse events	Throughout dialysis session
Vitals	Every Half an hour during dialysis
Physical Evaluation	Every Session
Access site	Every session
RBS, Electrolytes	Every session
Blood counts	Once every week
Liver function tests	Once every week
PT/APTT	If any bleeding occurs
Urea, Creatinine	Once every week
Nutritional evaluation and consultation	Once every week
Calcium, Phosphorus, uric acid	Quarterly
, Iron studies, Parathormone	Quarterly
URR, Kt/V	First 4 dialysis and then Quarterly
nPCR	Quarterly
Echo, ECG	Half yearly
HIV, HBsAg, HCV	Half yearly
Viral PCR	If transaminases are elevated

.

9b) Monitoring patient on Acute HD

Name: **Age:** **Sex:** **Hospital ID:**
Diagnosis: **Date:**

Table 22: Monitoring on Acute HD patients.

Evaluation	Frequency
Adverse events	Throughout dialysis session
Vitals	Every Half an hour during dialysis
Access site	Every session
RBS	Every 1 hr during HD session
Electrolytes	Before and after session depending on the indication of HD
Liver function tests	Once a day depending on indication of HD
PT/APTT	Before starting HD,and if any bleeding occurs
Urea, Creatinine	Once after every session
Evaluation for fluid over load	Twice daily
Calcium, Phosphorus.	Twice daily (for transfused and citrate anticoagulation
URR, Kt/V	Every session
Echo, ECG	At initiation of 1st session of HD
HIV, HBsAg, HCV	At initiation of 1st session of HD
Viral PCR	If viral markers are positive

Chapter 10: Special Filters and its Uses

1. **Polymyxin B- fibre column(Specific Hemadsorption):**

In cases of gram negative of sepsis or suspected sepsis the disease severity, survival depends on activity of the endotoxin. Endotoxin (lipopolysaccharide) and its fragments are pathogen associated molecular patterns which activate monocytes, leucocytes, endothelial cells, complement and coagulation pathway. These activated cell sare responsible for sepsis and need to be removed from circulation. Polymyxin B neutralises the endotoxin. This filter is marketed as TORAY.

2. Cytosorb (Nonspecific hemadsorption):

Cytosorb is a non-specific synthetic resin hemadsorption device made of synthetic resin Compared to conventional hemofilters surface area (1.2-2.5 m2) cytosorb has a very wide surface area of 45000 m^2, effectively adsorbing most cytokines between 5 to 60 kb.This device can be run stand alone or in series with CKRT. It can also be used during ECMO (Extra corporeal membrane oxygenation or cardiopulmonary bypass.

3. Seraph -100 (Pathogen adsorbent):

This cartridge specifically targets of removal of pathogens from circulation. It mimics action of heparin sulphate on cell surface by using ultra high molecular weight polyethylene beads coated with heparin. This is believed to immobilise the pathogens, toxins and anti-thrombin III in the blood circulation. This device can be run stand alone or in series with CKRT.

4. OXiRiS. (Multifunctional Hemofilter):

This hemofilter can be used for both hemoadsorption and plasma adsorption It removes endotoxins, fluid, uremic toxins all simultaneously using a tri-layered structure. The base layer is made of AN69 with negatively charged methallyl sulphonate molecule incorporated in it which adsorbs cytokines with additional function of solute removal by convection. The middle layer is made of positively charged polyethyleneimine (PEI) that improves biocompatibility and adsorbs endotoxins. The superficial, third layer is heparin coated that confers the filter local anti-thrombogenic property.

5. Jaffron Filter:

This novel cartridge like oxiris can be used both in hemo and plasma-adsorption. Made of styrene divinyl benzene copolymer resin in neutron-macroporus structure is available in different pore sizes for different molecular weight substrates.

Table 23: Special filters: Jaffron Filters.

Model with pore size distribution	Mol Wt removed	Use
HA 130	500 D- 40 KD	Chronic conditions
HA 230	200 D- 10 KD	Acute intoxication
HA 300/380	500 D- 60 KD	Acute inflammatory conditions

Acute Intoxications: drug over doses, pesticide and industrial poisoning.
Acute Inflammatory Conditions: Sepsis, Pancreatitis, cytokine release syndromes, trauma, burns

6. Charcoal and anion filters

a) **Molecular Adsorbent Recirculation System (MARS):** High albumin requirement in Single Pass Albumin Dialysis (SPAD) has a very high albumin requirement which led to development MARS in which the utilised albumin is recycled. The first step is purifying the spent albumin using high flux filter to remove water soluble toxins. This partially filtered albumin passes through two sequential adsorbent columns made of activated charcoal and anion exchange resin. The end product is processed albumin that can be reused as fresh dialysate to purify patients' blood.

b) Fractioned Plasma Separation and Adsorption (**FPSA):** In this method the albumin rich plasma fraction is filtered first and then passed through neutral resin and ion exchanger resin. This is then reconstituted as blood and undergoes conventional dialysis with a high flux polysulphone dialyser.

Table 24: Comparison of special filters

Filter	**Type**	**Removal**	**SA ($m^{2)}$**	**Mol wt Cut off kDa**
Oxiris	**AN69 ST**	**Endotoxin+ cytokine + renal replacement**	**1.0**	**~20**
Toramyxin	**Polymixin B column on PMMA**	**Endotoxin adsorption**	**2.1**	**~20**
Cytosorb	**Polymer beads**	**Cytokine removal**	**-**	**10-70**
HA Jaffron	**Polycarbonate**	**Cytokine+Infl Mediator + Complement**	**According to model**	**10-60**

Chapter 11: Dialysis in Special situations

Hemodialysis in poisonings:

- Majority of poisonings need supportive care alone.
- Extracorporeal treatments required in 0.1%.
- Useful for agents that cause metabolic & electrolyte derangements, AKI.
- Common toxins removed by dialysis are methanol, ethylene glycol, diethylene glycol, propylene glycol, salicylates, metformin, lithium.

Criteria for HD in poisonings:

- Progressive deterioration despite supportive therapy.
- Midbrain depression causing hypoventilation, hypothermia, hypotension.
- Impairment of drug excretion due to kidney, cardiac or hepatic insufficiency.
- Intoxication with substances causing metabolic acidosis/delayed effects-methanol, ethylene glycol & paraquet poisonings.
- Extractable drug/poison that can be removed at a rate exceeding endogenous clearance.

Determinants of clearance:

- Molecular Weight.
- Protein binding.
- Endogenous clearance.
- Volume of distribution.

Dialyser choice:

- Molecular Weight of the substance 500 Da-Low flux dialysers.
- Molecular Weight up to 5000 Da-medium, high flux dilaysers.
- > 50,000 Da-high flux dialysers, hemoperfusion.
- > 1000,000 Da-Plasma exchange.
- Most poisons have Mol Weight 100-1000 Da hence amenable to HD using low flux to high flux dialysers.
- > 80% protein bound poisons not removed by HD.
- Removal from blood compartment alone hence less effective for highly lipophilic & protein bound substances.

- Poisons with multi compartment kinetics may cause rebound; hence would need multiple & prolonged sessions.

Table 25: Volume of distribution of drugs

Small volume of distribution	Large volume of distribution
Alcohols	Opioids
Lithium	Tricyclic antidepressants
Phenobarbitone	Digoxin
Phenytoin	Camphor
Salicylates	Phenothiazines
Valproic acid	Glutethimide

Table 26: Indications of HD in drug overdose / intoxication

Toxic Alcohols
• Ethylene glycol or methanol concentration > 50 mg/dL without ADH inhibitor (fomepizole or ethanol) • Ethylene glycol concentration > 200-300 mg/dL with ADH inhibitor and normal kidney function • Methanol concentration > 70 mg/dL with ADH inhibitor and normal kidney function • Isopropanol concentration > 400-500 mg/dL • Any toxic alcohol: severe acidemia (pH < 7.2) or AKI
Salicylate
• Concentration > 7.2 mmol/L (100 mg/dL) • Concentration > 6.5 mmol/L (90 mg/dL) with AKI or CKD • Concentration > 6.5 mmol/L (90 mg/dL) after IV fluids, sodium bicarbonate, and potassium • Concentration > 5.8 mmol/L (80 mg/dL) after IV fluids, sodium bicarbonate, and potassium and with AKI or CKD • Altered mental status • Respiratory distress or new hypoxemia requiring supplemental oxygen • pH ≤ 7.2
Metformin
• Lactate > 10 mmol/L • pH < 7.2 • Shock • Failure of standard supportive measures (IV fluids, sodium bicarbonate) • Decreased level of consciousness
Lithium
• Concentration > 5.0 mEq/L • Concentration > 4.0 mEq/L with AKI or CKD • Decreased level of consciousness, seizures, or life- threatening dysrhythmias at any lithium concentration • Estimated time to reach lithium concentration < 1 mEq/L exceeds 36 hours
Acetaminophen
• Concentration > 1,000 mg/L (6,620 µmol/L) • Concentration > 700 mg/L (4,630 µmol/L) with altered mental status, metabolic acidosis, or elevated lactate

- **Early use of HD in salicylate poisoning in presence of indications improves outcomes.**

- **Use of antidotes combined with HD improve outcomes with methanol & ethylene glycol poisonings.**

Table 27: Role of HD in acute liver Failure

Causes of Pediatric ALF
Infections-Hepatitis A, B, C, EBV, CMV, herpesviruses, adenoviruses leptospirosis, malaria **Metabolic-** Wilson's, tyrosinemia, galactosemia, hemochromatosis **Drug induced-**acetaminophen, salicylates, Isoniazid, sodium valproate Autoimmune hepatitis Idiopathic-30% idiopathic

Etiology of AKI in ALF:

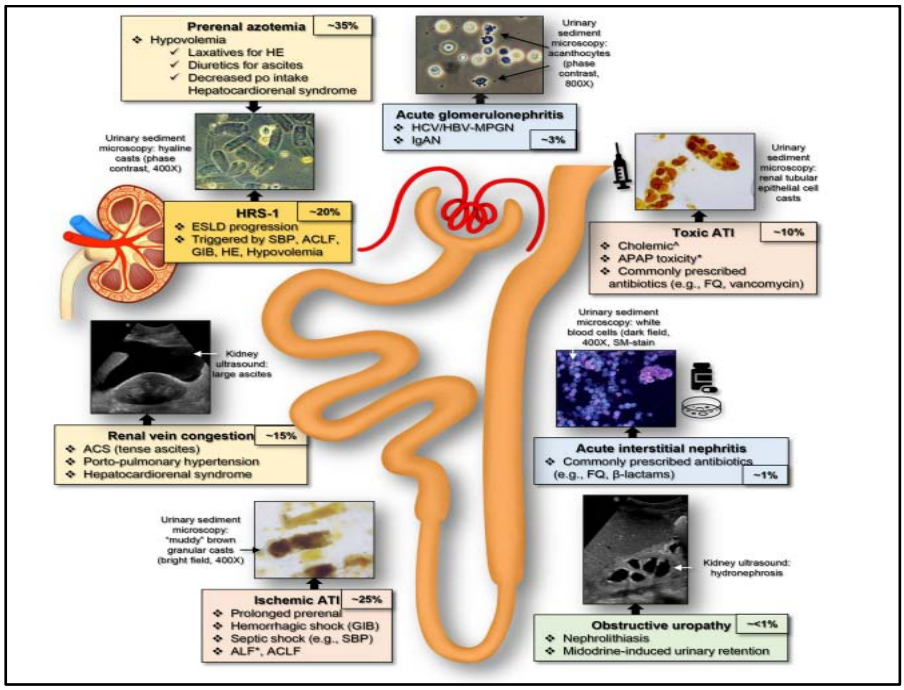


Figure 16: Etiology of AKI in acute liver Failure.

AKI in Acute Liver Failure:

- Leptospirosis related ALF & AKI.
- Malarial AKI/ALF.
- **Patients with ALF have 48% chances of AKI.**
- **Sepsis on a background of ALF also contributory to AKI.**
- CRRT is more suitable than IHD in patients with ALF.
- SLED may be a better alternative than IHD.
- While CRRT removes small water soluble molecules high protein bound substances can't be removed effectively.
- Need for albumin assisted dialysis or plasma filtration/absorption.

Challenges in ALF

- Line placement-bleeding due to coagulopathy/femoral preferred/need for FFP
- NAC is dialysable hence dose need to be increased with HD
- Use of anticoagulants for HD a concern/saline dialysis may be preferable
- With significant transfusion, risk of hypocalcaemia increases hence would require monitoring & replacement
- Higher risk of cerebral edema, intracranial hypertension & bleeds -need careful monitoring

Modalities for ALF

- **MARS**-molecular adsorbents recirculation system
- **Single pass albumin dialysis**-using HD or CVVHDF machine using a high flux hemodiafilter against albumin gradient; albumin in dialysate
- Ammonia clearance similar between MARS/SPAD/CVVHD
- Clearance of bilirubin much better with MARS while bile acids had similar removal

Hemodialysis in the treatment of patients with severe electrolyte disorders:

Hyperkalemia

- A dialysate prescription of 4mEq/L for patients with predialysis serum K <4 mEq/L especially in malnourished children.
- **In most other situations dialysate prescription of 2 mEq/L.** Intradialytic K removal mostly in first 2 hrs by diffusion & convection; after that rebound rise from intracellular release .
- On a background of severe hyperkalemia >8mEq/L minimum K of upto 1mEq/L can be used but with intensive monitoring & K checks every 30 min

Hyponatremia

- Hyponatremia occurs in **6-29% of Kidney failure patients** on maintenance HD
- **Dialysate Na prescription** vary between **136-145 mEq/L** based on predialysis Na levels & hemodynamic status. A dialysate conc of 2-3 mEq/L below serum Na levels decreases post dialysis Na & osmolality; negatively effects UF. Acute hyponatremia-Na conc 136-145 mEq/L in dialysate
- Chronic hyponatremia-130mEq/L; daily short dialysis recommended; flow rates can be decreased to slow the Na transfer rates; **2-3 hrs dialysis sessions**
- If symptomatic during dialysis-3% saline bolus. Tolvaptan not effective-not recommended
- **Dialysate Na Values >138mEq/L** associated with increased thirst during HD & intradialytic Wt gain. **Values <136 mEq/L** associated with cramps, hypotension

Chapter 12: Plasmapheresis

Therapeutic plasma exchange (TPE) is a process where in plasma is removed from a patient's blood for therapeutic purposes and replaced by donor's plasma, colloid or crystalloid depending upon the indication of plasmapheresis.

Two technologies are available for the removal of plasma and its pathogenic substance(s): **Centrifugation** and **Membrane filtration**. Membrane filtration TPE can only separate plasma, whereas centrifugation TPE can fractionate any of the blood components (e.g., erythrocytes, platelets, plasma).

Table 28: Comparison of Therapeutic Plasma Exchange and HD.

Characteristic	Centrifugation	Membrane Filtration	Hemodialysis
Mechanism	Centrifugal force	Convection	Diffusion and/or convection
Blood flow, mL/min	10-150	150-200	Continuous: 100-300; intermittent: 200->400
Blood volume in circuit, mL	180	125	160-280
Plasma extraction, %	80	30	NA
Molecular weight cutoff, Da	>15,000	>15,000	<15,000
Vd, L/kg	Low (<0.3)	Low (<0.3)	Moderate (≤1.5-2)
Protein binding, %	>80	>80	<80
Anticoagulation	Citrate	Heparin	Heparin
Sterilization	γ-Irradiation; ethylene oxide	γ-Irradiation; ethylene	Ethylene oxide; steam;oxide electron beam; y-irradiation
Abbreviations: NA, not applicable: Vd, volume of distribution.			

Therapeutic Plasma Exchange

1. **Renal Indications**
   a) **Rapidly Progressive Glomerulonephritis (RPGN)**
      - Pauci immune GN
      - Antiglomerular basement membrane GN
      - IgA Nephropathy
      - Henoch- Schonlein purpura nephritis
      - Cryoglobulinemia

   b) **Renal Transplant recipient**
      - Pre transplant desensitization in ABO incompatible transplant
      - Acute ABMR
      - Post-transplant recurrence of Focal Segmental Glomerulosclerosis(FSGS)

   c) **Others**
      - TTP
      - Thrombotic microangiopathy(TMA)-complement mediated (aHUS)

2. Non renal indications

- Acute and chronic inflammatory demyelinating polyradiculoneuropathy
- Demyelinating polyneuropathy with IgG, IgA.
- Gullian-Barre syndrome
- Refsums Disease
- Wilsons disease
- Myasthenia gravis,
- N-Methyl-d-aspartate(NMDA) receptor antibody encephalitis
- Sickle cell anaemia-Acute stroke

Filters

Table 29: Baxter Plasma Exchange Filters.

Type	TPE 1000	TPE 2000
Surface area (m2)	0.15	0.35
Min Qb (ml/min)	50	100
Max Qb (ml/min)	180	250
Filter vol (ml)	23	41

TPE 1000 min Qb is 50ml/min and max 180 ml/min, TPE 2000 min Qb is 100 and maximum 400 ml/min.

Table 30: Fresenius Plasma Exchange Filters.

Type	P Su 1S	P Su 2S
Surface area (m2)	0.3	0.6
Min Qb (ml/min)	40	80
Max Qb(ml/min)	150	250
Filter Volume ml	36	70
Max filtrate flow	20% of effective blood flow rate.	

- Optimal blood flow for plasma exchange is 100-150 ml/min. If lower flows are achieved than anticoagulation must be increased accordingly
- The plasma volume (PV) to be replaced is determined by calculating the total body volume (TBV) and the total plasma volume (TPV) of the patient.

The goal is to exchange 1-1.5L of plasma which is estimated by the formula:

PV (in litres) = (TBV) *(1-Hct/100).

Table 31: Weight based Total Blood Volume.

Age and body weight	Total Blood Volume
Infant or <2kg	80 ml/kg
Child or < 20-50 kg	70 ml/kg
Adult or >50 kg	60 ml/kg

- In children as the TBV is variable based on body weight and age, the dose of replacement fluid may also be calculated as 40-60ml/kg/session.
- The extracorporeal blood circuit volume should not exceed 8-10% of the TBV, calculated at 80 ml/kg. If the volume exceeds then priming the circuit with blood is needed. This is usually in the case of children < 20 kg.

Anticoagulation: Initial Dose Heparin given at 30- 50 u/kg as loading dose with a maximum of 1000 units and maintenance at 15-20u/kg maximum of 500 u/hr**.**The above dosage guidelines may need to be exceeded in patients with a low haematocrit or when the plasma filtration rate is high. target a prothrombin time/partial thromboplastin time (PT/PTT) more than 1.5 times of the normal.

Replacement Fluids:

Table 32: Replacement Fluids in Plasma Exchange.

Albumin	5% Albumin
FFP	Indications: Coagulopathy, thrombocytopenia, hypofibrinogenemia, HUS/TTP

Solution	**Advantages**	**Disadvantages**
Albumin	No risk of Hepatitis	Expensive
	Stored at room temp	No coagulation factors
	Rare allergic reactions	No immunoglobulins
	No concern of Blood group	
	Depletes Inflammatory mediators	
FFP	Coagulation factors	Risk of viral transmission
	Immunoglobulin	Allergic reactions
	Complement factors	Needs thawing
	Beneficial factors	Needs ABO compatibility
		Citrate load

IvIg may be given as there will be deletion of Ig and complements with plasmapheresis

Table 33: Relationship between plasma exchange volumes to removal

PV Equivalents	**Substance removal (%)**	**Post exchange Level (%)**
0.5	35	65
1.0	55	45
15	65	35
2.0	70	30

Rate of Exchange Filtration rate should commence slowly- 0.2 ml/kg/min grading up maximum of 0.5ml/kg/min when using FFP.When using 5% albumin, a faster rate of iso-volemic exchange can be undertaken (Eg 3 litre exchange over 2 hours).The limitation to rate of exchange when using FFP is due to the presence of 17% acid citrate dextrose (ACD), which is only around 5% in albumin replacement

Complications and Management in Plasmapheresis

Table 34: Complications and Management of Plasmapheresis

Complications	**Management**
Related to Vascular Access	
-Hematoma	Compression, PRBC transfusion if big /on-going blood loss
-Pneumothorax	ICD placement
-Local or systemic infection	IV antibiotics, changing the vascular access if required
Related to the Procedure	
-Hypotension from externalization of blood in the extracorporeal circuit	Prime with PRBC/ albumin
-Hypotension due to decreased intravascular oncotic pressure	Use 5% albumin as Replacement fluid alone or in combination with other replacement fluids as per clinical condition. NS bolus can be given.
-Bleeding from reduction in plasma levels of coagulation factors	Use FFP as replacement fluid; give a gap of at least 24-36hrs until next session of TPE.
-Thrombocytopenia	Platelet transfusion; decrease heparin dose
Related to Anticoagulation	
-Bleeding, especially with heparin	Platelet/FFP transfusion; decrease heparin dose
-Hypocalcemic symptoms (with citrate)	IV calcium infusion; decrease citrate dose/blood flow; decrease use of blood products if feasible as they contain citrate which further precipitates with ionized calcium worsening hypocalcemia.
- Metabolic alkalosis from citrate	Avoid in patients with renal failure as citrate generates bicarbonate, the excretion of which is limited in renal failure
Related to Replacement Fluids	
-Hypotension (use of hypo-oncotic saline)	Use 5% albumin as replacement fluid
- Anaphylaxis (FFP)	Use pre medications to prevent- IV hydrocortisone/prednisolone, anti-histamines. In fatal anaphylaxis stop apheresis, stabilize with steroids.

Table 35: Plasmapheresis monitoring sheet.

Name:	Age:	Gender:	Hospital ID
Indication:			Initiated on:
Concerns:			
Vascular access			Plasma filter:
Prescription:			
Frequency			Duration
Plasma infusion calculation:			

Date / Time	**PR**	**RR**	**BP**	**CRT**	**Intake**		**Output**		**Effluent Color**	**Complication/ Remarks**
					Fluids	**FFP + Albumin**	**Urine**	**Effluent**		

Case Based Discussion

Station 1-Know Your HD apparatus

Case 1:
11-year-old girl a child with ESRD on maintenance HD through right femoral Access, Initiated on HD session from PICU
10 min into initiation of HD call given in view of high arterial pressure alarms
How would you approach and manage?

Case-2:
11-year-old girl undergoing HD in ITU, 4-hour session planned from right femoral catheter
At end of 3rd hour of HD call given in view of high venous pressure alarms
How will you approach and manage?

Station -2-HD/SLED Prescription

Case -1:
A 7 year old boy is admitted in Pediatric ICU with complaints of oliguria for 2 days associated with respiratory distress. He had H/O bee sting all over the body 7 days back ,when he was returning home from school. His urine output is 40 ml last 12 hours after admission.
His weight is 25 kg , Ht: 140 cm , BSA:0.9 m2 , BP : 100/60 (95^{th} centile) .
S.Creatinine : 8 mg/dl , blood urea : 400mg/dl , urine RE (pus cell 4-6 HPF , RBC nil , protein: 2+) Electrolyte Na : 130mmol/L, K : 6 mmol/L ,Coagulation profile is normal.

1) Does this child requires RRT?
2) What is the indication for RRT?
3) Write Hemodialysis prescription for this child for his first session

Case-2:6 years old male child with Chronic Kidney disease, secondary to Bilateral Grade 5 VUR, with multiple episodes of UTI in the past, who is on maintenance dialysis for past 1 year, has come now for his dialysis session
His Current weight is 15.5kgs and his dry weight is 14kgs, Height 98cms, BSA: 0.6m^2, BP-110/70 mmHg.
He has minimal edema and genu valgus deformity in both lower limbs, He has AV fistula in the left forearm
His urine output is around 400 ml/ day. His labs are as follows

Hb	9.1gms
TC	9240
Platelets	330,320
S.urea/creatinine	95/3.9
Na/K/Cl	140/5/111
Hco3	21
Ca+/Po4	9.5/4.6
SAP	1100
PTH	786
Urine albumin	2+

1) What is Intermittent Haemodialysis?
2) How to target Fluid removal in a child on IHD?
3) Write dialysis Prescription.

Case 3: A 3 year old girl, admitted with Dengue Hemorrhagic shock. Her admission weight in 15kg & BSA: 0.6m^2. In ER, he presented with shock (BP: 70/50 mm of Hg) for which he received 40 ml/kg of NS bolus and then 20 ml/kg of colloids and then fluids tapered. Child is having fluid leakage with worsening of ascites & pulmonary edema. Echo s/o myocarditis with EF: 45%. In view of cardiogenic shock with respiratory distress, fluids tapered to 3 ml/kg/hr and started on Inj. Adrenaline infusion and started on mechanical ventilation.

Child is currently on ventilator support, BP-80/44 mmHg (one inotrope), Labs shows, Hb-15, HCT-54.5, plt-35,000, S.urea-54, creatinine-0.8, Na/K/Cl-128/5.9/96, pH- 7.1,

Lactate: 4, HCO3-13.2, SGOT/SGPT-264/211, S.Ferritin-3423

He continued to have fluid leakage with worsening distress (increasing pressure requirements), Urine output- 100 ml over 24 hours. Call given for initiating RRT in this child.

1. What is the indication of RRT in this child?
2. Write the SLED prescription for this patient

After 24 hours of RRT, child continued on mechanical ventilation, BP-96/68mmHg off inotropes, Urine out increased to 0.8ml/kg/hour(CFO-6%).

Labs: pH/ Lactate/ HCO3: 7.32/ 1.4/19.5. S.urea-35, creatinine-0.7,Na/K/Cl-138/3.8/100

1. Do the child needs RRT now?
2. What changes needed in the prescription?
3. Write the new prescription for this child.

Case 4:A 12 year old male child wt. 60 kg, ht 148 cm with B cell ALL (poor prognostic markers) on high dose methotrexate had features of methotrexate toxicity . Methotrexate levels at 24hrs >10 umol/L, with decreased urine output, AKI (S. Cr increase to 3 mg/dl from baseline 0.6 mg/dl and urea 120 mg/dl from 30 mg/dl). He also had pancytopenia. Hb 6 g/dl, TLC 2000, PLT- 20000. He was started on leucovorin, hydration therapy with alakalinisation with lasix despite which methotrexate levels dint decrease, urine pH 6 and he had oliguria.

1. What is the next line of management?

2. If dialysis - Vascular access:Dialysis mode:Why do you choose this?

3. Write a dialysis prescription for this child.

Case 5:A 15 yr old girl presented to ER with a 2-day history of altered mental status and decreased oral intake. She was treated with fluids and started on antibiotics and was referred to our hospital for further management. It was later revealed that she was taking lithium for her depressive psychosis. Since her symptoms were not adequately controlled the dose has been increased in the last week. On examination, Vitals were stable but she was disoriented, restless and had involuntary tremors with hyper- reflexia. Investigations done showed high serum lithium levels, parathormone, thyroid hormones, urine specific gravity, urinary electrolytes, urea, and creatinine. A diagnosis of lithium-induced acute kidney injury along

with nephrogenic diabetes insipidus (NDI), low anion gap, metabolic acidosis, leukocytosis, hyperparathyroidism and hypothyroidism was made. Plan was made to start her on IHD. Write HD prescription for her.

Case 6: A 6 yr-old normally developing male child after vacation presented with complaints of fever for 2 days with loss of appetite and weakness. The local paediatrician treated him symptomatically. Two days later fever did not subside and developed vomiting. She noticed yellowish coloration eyes and was brought to OPD. On examination, vitals were stable but he had icterus, was very lethargic, confused.. His initial laboratory tests showed a bicarbonate level of 18 mEq/L, urea of 60 mg/dl, creatinine of 3 mg/dl, anion gap of 32, INR of 3.1, lactic acid of 13.3mmol/L, creatine kinase of 11731 IU/L, AST of 1111 U/L, ALT of 869 U/L, and total bilirubin of 4.1 and Hep A positive. An abdominal ultrasound showed no liver abnormalities. He was initially given intravenous fluids for AKI, NAC was also started but his ure, and creatinine progressively got worse and peaked at 80 mg/dl, 5 mg/dl. His liver function tests also progressively worsened. Plan was made to start him on IHD. Write a prescription for him.

Station 3: Trouble shooting -case based discussion

Case 1: 7 yr old male child was referred to a tertiary care center with history of self-settled fever and diarrhea that lasted for 2 days. 2 weeks later he developed edema. Oliguria that progressed to anuria and mild breathlessness. On examination he had severe pallor, anasarca, BP of 140/100 mm Hg. Lab investigations showed Hb of 5.5 g/dl, PLT of 70,000/mm3, Urea of 180 mg/dl, creat 3.8 mg/dl. Potasssium 6 mEq/L. He was started on HD with F4HPS and pediatric tubing. Three hrs later he complained of headache and 10 min later he had altered sensorium and seizures.

1. What do you think is the diagnosis?
2. What are the possibilities of the neurological status?
3. How to manage the case?
4. How can you prevent this?

Case 2: 12 yr old child got admitted in PICU with severe dengue shock, AKI and electrolyte imbalances. She was ventilated and started on multiple inotropes. Her AKI started to worsen and she developed signs of fluid over load. Decision was made to start her on Heparin free SLED with Qb of 100 ml/min and Qd of 300 ml/min and UF of 1800 ml. After starting 30 min later there was an alarm showing excess negative arterial pressure which was immediately sorted out. One hrs later her TMP showed a value of 30 mm of Hg and at 2 hrs it increased to 60 mm of Hg and by 3.5hrs increased to 150 mm of Hg

1) What can the reasons of the first alarm within 30 min of starting SLED?
2) What can be the causes of raising TMP and how to manage it?

Case 3: 16 yr old boy has been on regular thrice a week HD for the last 1 year. Apart from CKD he had hypertension, hyperthyroidism and ECHO had shown left ventricular hypertrophy. He was receiving all maintenance drugs for CKD and with that he also was taking Lisonopril and Metoprolol. The single pool Kt/V on this prescription was 1.49. His average interdialytic weight gain was 3 kg per treatment, and his dry weight was 52 kg. Two hrs after starting the session he felt uncomfortable had fatigue like feeling. The technician noticed he had tachycardia and BP had dropped to 90/60 mm of Hg. He doesn't have history of previous similar episodes.

1. What do you think happened?
2. What is immediate steps to correct?
3. Long term what can be done to prevent this?

Station 5: Plasmapheresis

Pt A, 6year /girl
Indication for PLEX: Atypical HUS (Anti CFH positive)
Access: Right IJV HD catheter
Weight 20kg, height 130cm
Oliguric u/o 0.3ml/kg/hr, Stage 2 hypertension
Labs: HB – 8, HCT 24, PLT 54000, Urea 220, S.Creatinine 3.5, K 4.2, HCo3 19

1) Calculate the Estimated plasma volume?
2) What is the choice of replacement fluid?
3) What is his PLEX prescription?
4) Duration and frequency of plasmapheresis?

Plasma Exchange (PLEX) Prescription Reference Sheet

Patient weight	Catheter size	Catheter length
Temporary catheter		
3 – 6 kg	Double or triple lumen 7 Fr	10 cm
6 – 15 kg	Double lumen 8 Fr	11 – 12 cm
15 – 30 kg	Double lumen 10 Fr	10 Fr - 12cm
>30 kg	Double lumen 10 F or 11.5 Fr	10 Fr - 12cm / 11.5 Fr - 13cm
Permanent (tunneled) catheter		
Pediatric	24 cm, 28 cm	

Filter Type	BSA (m^2)	Priming volume (ml)	Blood flow range) (ml/min
P 1 <25kg	0.3	36	40 – 150
P 2 >25kg	0.6	70	80 - 250

Estimation of plasma volume	Plasma volume = [0.065 × weight (kg)] × (1 – Hematocrit). (Rule of thumb: 35 – 40 ml/kg)
Pre Medication	Pre PLEX : Inj Avil , Inj Hydrocortisone, Inj Paracetamol Inj Calcium Gluconate (Pre, mid, post PLEX)
Volume of tubings	Pediatric 110ml, Adult 150 ml
Extracorporeal volume	<10% of blood volume
	Initial Dose Patient Weight / Units of Heparin /Kg / Total initial dose 5-15 / 30-50 / 150-750 15-25 / 30-50 / 450-1000 25-35 / 30-50 / 750-1000 35-55 / 30-50 / 1000 >55 / 30 / 1000 **Maintance Dose** – 15 to 20 units/kg/hour The above dosage guidelines may need to be exceeded in patients with low hematocrit or when the plasma filtration rate is high.
Blood flow rate	3- 8 ml/kg/min, generally 5ml/kg/min Optimal blood flow for plasma exchange is 100-150 ml/min. If lower flows are achieved, then anticoagulation must be increased accordingly
Rate of exchange	Filtration rate should commence slowly- 0.2 ml/kg/min grading up to no more than 0.5ml/kg/min when using FFP. When using 5% albumin, a faster rate of isovolemic exchange can be undertaken (eg 3 litre exchange over 2 hours). The limitation to rate of exchange when using FFP is due to the presence of 17% ACD, which is only around 4% in albumin replacement.

Example to calculate duration of dialysis:

- 14 years old adolescent girl presented with tetanic spasm of all 4 limbs on & off for past 3 months. She was admitted for evaluation with no significant past history
- Her weight was 44kgs, Height 130 cms (<3rd centile) , BSA: 1.25
- She had mild pallor, no edema , BP-150/100mmHg and noticed to have reduced urine output since admission(0.8ml/kg/hour). Her labs are as follows

Hb	10gms
TC	8700
Platelets	2,25,320
S.urea/creatinine	112/2.3
Na/K/Cl	138/4.9/100
Hco3	16
Ca+/Po4	8.9/5
SAP	356
Urine albumin	1+
Urine RBC	Nil

USG abdomen:
Right Kidney-5.6 cms
Left Kidney-5.2 cms
Loss of CMD

Calculate the duration for her 1st dialysis session

- Kt/V =-ln C1/C0

K –K0A (Urea), specific to that blood flow rate
t -time (min),
V- Total body water (ml)
• C1 = post dialysis urea levels, C0 = pre dialysis urea levels

Dialyser	**Surface area(m2)**	**K0A (urea)**	**QB 50 ml/min**	**QB 100 ml/min**	**QB 150ml/min**	**QB 200ml/min**	**QB 300ml/min**
F3	0.4	250	49	89	114	130	149
F4	0.7	369	50	96	130	154	184
F5	1.0	402	50	97	133	159	192
F6	1.3	458	50	98	137	166	203
F7	1.6	522	50	99	141	173	215

Calculation of total body water (V) using Mellits · Cheek Formula

- Boys (Ht <132.7cm) V(ml) = (-1.927 + 0.465*Wt + 0.045* Ht) x 11.100
- Boys (Ht >132.7cm) V(ml) (-21.993 + 0.406*Wt + 0.209* Ht) x 1000
- Girls (Ht <110.8cm) V(ml) = (0.076 + 0.507*Wt + 0.013* Ht) x 1000
- Girls (Ht >110.8cm) V(ml) = (-10.313 + 0.252*Wt + 0.154* Ht) x 1000

Urea Clearance(%)	C1/C0	In (C1/C0)
90	0.1	-2.302
80	0.2	-1.609
70	0.3	-1.204
60	0.4	-0.916
50	0.5	-0.693
40	0.6	-0.511
30	0.7	-0.357
20	0.8	-0.223
10	0.9	-0-105

In this child, who is 14 years, who is weighing 44kgs, height-130 cm, BSA-1.25 who is planned for her 1st dialysis session.

Planned for 30% urea reduction and F5 dialyser, BFR-100ml/min
So applying in the formula

Kt/V =-In C1/C0

K: K0A (Urea), specific to that blood flow rate
t: time (min),V: Total body water (ml)

C1 = post dialysis urea levels, C0 = pre dialysis urea levels

K – for F5 dialyser at 100 ml/min BFR is 97
V (ml) = (-10.313 + 0.252*Wt + 0.154* Ht) x 1000
= (-10.313+ 11.088 +20.02) ×1000
=20,795
C1/C0= 0.7
-In C1/C0=-0.357

$$t = \frac{-\ln C1/C0 \times V}{K}$$

$$= \frac{-(-0.357 \times 20{,}795)}{97}$$

= 76 min (1 hour 15 min)

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Notes

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Fellowship Courses Offered:

- International Pediatric Nephrology Association (IPNA) Fellowship Program
- Indian Society of Pediatric Nephrology (ISPN)
- Dr. MGR University Post Doctoral Fellowship in Pediatric Nephrology

A child with proteinuria: How do I approach?

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Young Kidneys 2024 CME, Chennai, 21 July, 2024

Outline

- Physiology
- Types of proteinuria
- Detection methods
- Approach to evaluation
- Case discussion

Schematic representation of Renal handling of protein in health and in disease

LMW: B2 microglubin, A1 microglobulin, RBP.

Intermediate MW: Albumin

HMW: IgG, IgM

Urinary protein loss =

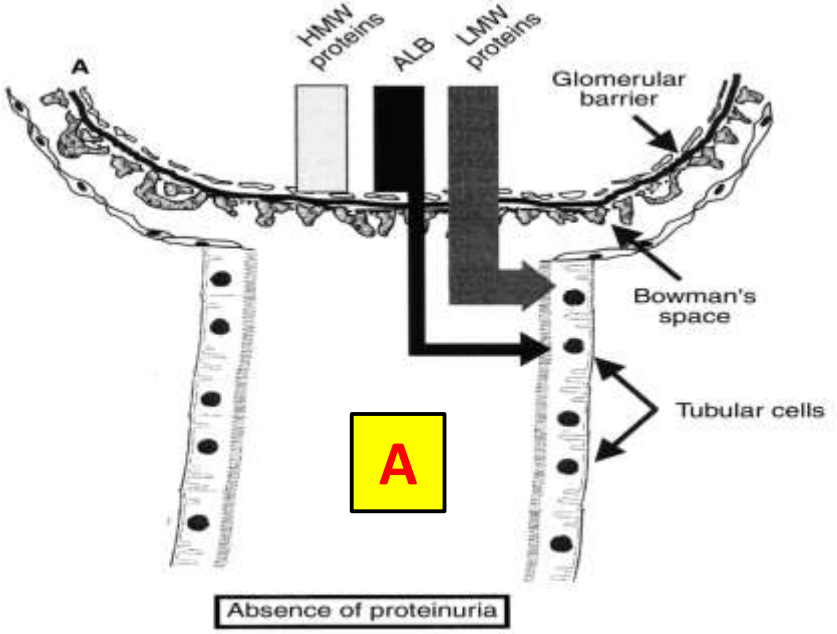
Filtered – Reabsorbed + secreted protein

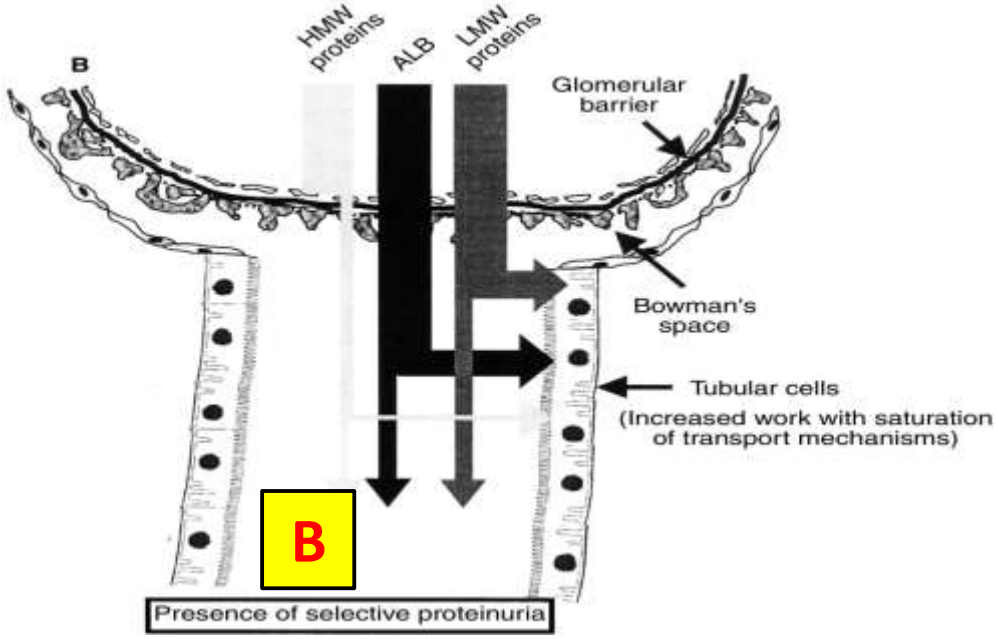
(A) In physiologic conditions,

all LMW proteins and a fraction of albumin

cross the glomerular barrier and are completely reabsorbed by the tubular cells.

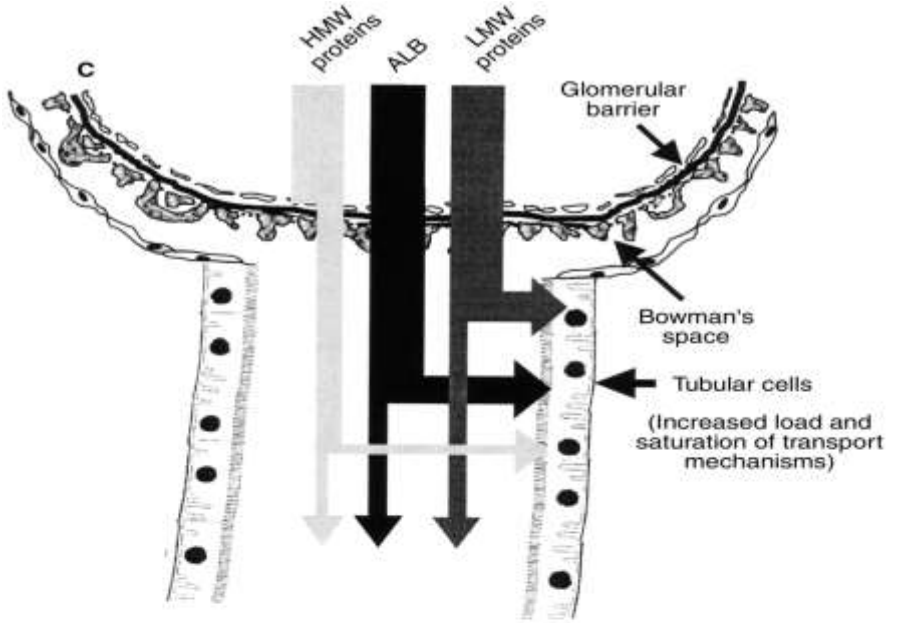
(*B*) The alteration of the permeability of the glomerular barrier is moderate, involving mainly a loss of restriction to passage of negatively charged proteins (especially albumin); **[selective proteinuria].**



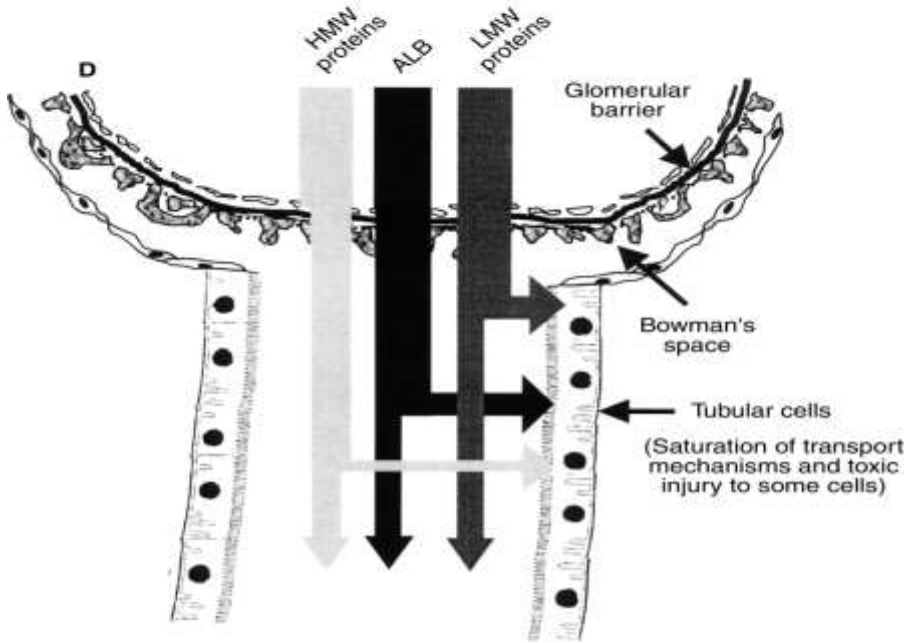


(C) A more severe damage

progressively increases size permeability of the glomerular barrier, and, due to the saturation of the reabsorptive mechanisms of tubular cells, a greater percentage of HMW proteins is excreted in the urines **(nonselective proteinuria).**



***(D) Permeability of the glomerular* barrier is further increased,** and the massive and protracted reabsorptive load of the tubular cells **induces toxic lesions of these cells** and reduces their reabsorptive capacity; excretion with the urines of all three classes of proteins and, in particular, of LMW and HMW proteins, is increased, and represents a valid marker of the severity of the glomerular and tubular damage.



Types of Proteinuria

1] Glomerular: **Detected by Uristix**

- **Selective,** due to loss of charge selective barrier, albumin loss

  eg MCD

- **Non selective** [more severe glomerular damage with loss of charge and size barrier resulting in loss of albumin, + HMW protein]

  eg, FSGS, GN, HSP, SLE, vasculitis, HUS

2] Non-glomerular: **NOT detected by Uristix**

- Tubular
- Overflow
- Secretory: TH protein in neonates, UTI's, analgesic nephropathy

Tubular proteinuria

- Proteins < 60,000 Daltons are freely filtered across GBM and reabsorbed almost completely by PCT
- Hence, damage to PCT – tubular proteinuria
- Etiology: Fanconi syndrome, Dent disease, Ischemia (ATN), ATIN, Drugs (Analgesics, Chemotherapy drugs, Amninoglycosides), Toxins, etc
- usually, < 1 gram/1.73m^2
- Can be differentiated from glomerular proteinuria by **urine protein electrophoresis** (the LMW proteins migrate in the α and β regions)
- β2-microglobulin (12,000 Daltons), α1-macroglobulin (26,000 Da), and RBP (21,000 Da) are markers of tubular proteinuria

NOT DETECTED BY URISTIX

Overflow proteinuria

- Increased filtered load of LMW proteins
- Filtered load >>> reabsorptive capacity of PCT
- Rare in children
- Adults: Multiple myeloma, AML (Lysozyme)
- Other causes: Myoglobinuria, hemoglobinuria

NOT DETECTED BY URISTIX BUT BY 24 HOUR COLLECTION

Methods to detect proteinuria

- **Qualitative:**

  - Standard Uristix → Specific for albumin. LMW proteinuria will be missed
  - Sulfosalicyclic acid → Detects all types of proteins
  - Urine protein electrophoresis – Multiple myeloma, LMW proteins

- **Quantitative:**

  - 24 hour urine protein estimation [Gold standard]
  - Random urine protein creatinine ratio → Co-relates closely with 24 hour collection report

Urine disptick

- **Tetrabromophenol + Albumin** = change in color (light yellow to darker shades of green)

- Specific for albumin [DOES NOT DETECT TUBULAR PROTEINS]

- **Grading:** 1+, 15-30 mg/dl
  2+, 30-100 mg/dl
  3+, 100-300 mg/dl
  4+, 300-1000 mg/dl

- **Limitations:** Not sensitive: Positive 1+ (15-30 mg/dl) - albumin is > 300 mg per 24 hours
  Always interpret result in context of urine specific gravity
  False positive: Radio-contrast, pyuria (UTI), bacteriuria, hematuria, alkaline pH, prolonged immersion in urine, concentrated urine

Urine dipstick

- Insensitive in detecting early albuminuria and LMW proteinuria
- Result should be interpreted in context of urine specific gravity
- Both tests are subject to the caveat that a ***concentration*** of protein is being tested.
- *The more dilute the urine, the lower will be the concentration of protein for any absolute rate of excretion.*

Urine Dipstick Readings

False Positive:

- Dehydration / high specific gravity / recent exercise
- UTI
- Hematuria
- Alkaline urine pH of more than 8
- Use of radio-contrast agents

False Negative:

- Very dilute urine
- Positively charged proteins (light chains)

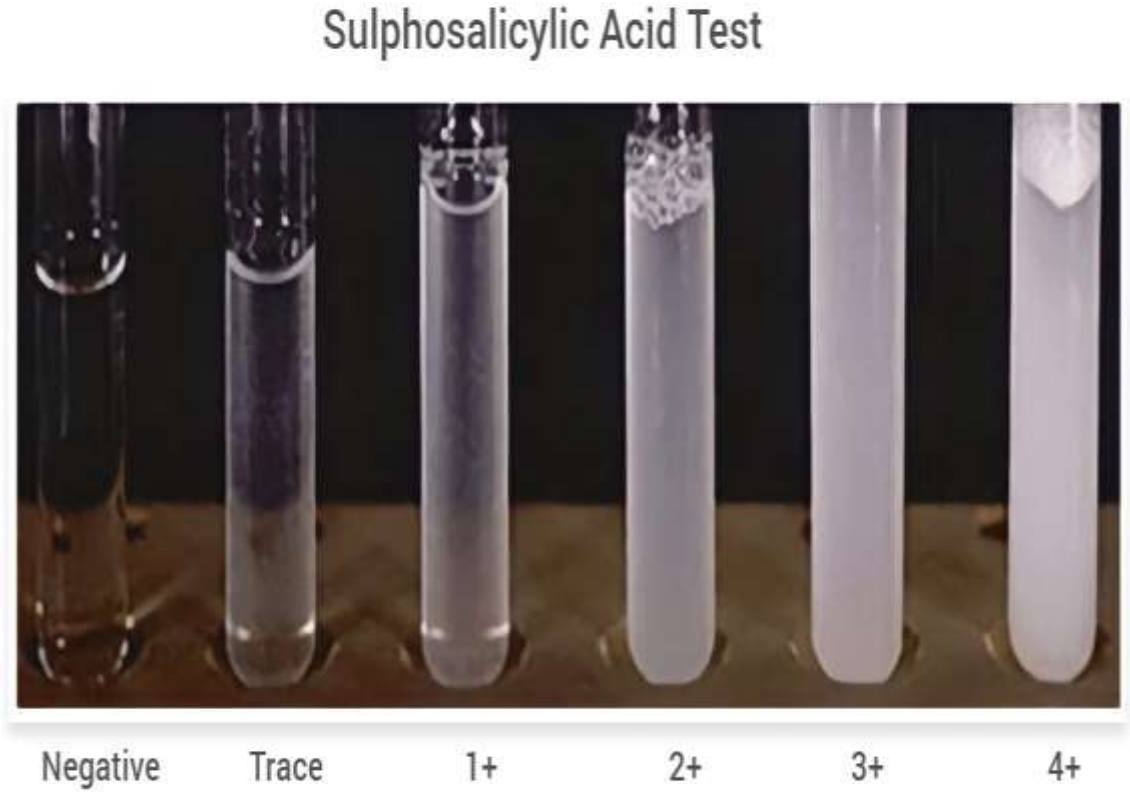
Sulfosalicylic acid test

- Simple, low cost test - detects all types of protein (albumin, LMW, Hgb, Myoglobin)

- Equal parts of urine & 3% SSA are mixed
  - turbidity
  - subjectively graded

- Normal urine – test is negative

- False positive:
  - Radio-contrast agent
  - Drugs (penicillin, Sulfa)
  - High urine urates



Random urine protein creatinine ratio

- Random or first morning sample
- Both are reported in mg/dl
- Reference < 0.2, children > 2 years

  < 0.5, 6 months – 2 years

  < 0.8, infants < 6 months

Reduced reabsorption due to tubular immaturity, and lower urinary creatinine

24-hour urine protein

- Gold standard
- For standardization, relate to body surface area
- **Normal reference** < 4 mg/m^2/hour = 96 (100) mg/m^2/24 hours OR < 4 mg/kg/day
- **Proteinuria** 4-40 mg/m^2/hour – 100-1000 mg/m^2/24 hours OR 4-40 mg/kg/day
- **Nephrotic proteinuria** > 40 mg/m^2/hour = > 1000 mg/m^2/24 hours OR > 40 mg/kg/day
- **Ensure adequacy of 24 hour collection by measuring urinary creatinine value**

  10-15 mg/kg/day in children

  15-18 mg/kg/day in women

  20-25 mg/kg/day in men

Proteinuria

- Abnormal level of protein in urine

- **What is normal?**
  - Adults, < 150 mg per day
  - Children, < 4 mg/kg/day or < 100 mg/m^2/ day

- **Urine protein composition in health:**
  - Tamn-Horsfall protein, 60%
  - *Albumin, 5-10% (of 150 mg = 30 mg in an adult)*
  - LMW protein (alpha, Beta, macroglobulin), 20%
  - Immunoglobulin, < 5%
  - Light chains, < 5%

Most filtered protein is reabsorbed by proximal tubular cells and broken down in to amino acids

Micro-albuminuria (Albuminuria)

- **Albuminuria (mg/d)**

  - **Normal**: Less than 30

  - **Micro**albuminuria: 30-300 [Not detected by usual Urine dipstick test]

    MISNORMER, Now called as Moderately increased albuminuria

  - **Macro**albuminuria: More than 300

    Severely increased albuminuria

Detected by specific dipstick
OR
Urine albumin/creatinine ratio

Detected by dipstick

Categories of proteinuria

TRANSIENT

Most Common

Fever
Exercise
Dehydration
Viral infection

Resolves quickly

ORTHOSTATIC

Common in teenagers, 2%

Proteinuria usually below 1000 mg per day

Upright > supine

Benign

PERSISTENT

Indicates kidney disease

Needs further evaluation

Blood, urine tests and kidney biopsy

Approach to Isolated proteinuria (Asymptomatic)

- Detected by Urine dipstick
- Understand the limitations ie false positive and false negative results
- If doubt exists, repeat Urinalysis with fresh sample and analyse immediately
- If factors are ruled out, evaluate further
- **3 possibilities:** Transient
  Orthostatic
  Persistent

False positive:
- Dehydration / high specific gravity / recent exercise
- UTI
- Hematuria
- Alkaline urine pH of more than 8
- Use of radio-contrast agents

False negative:
- Very dilute urine
- Light chains

Asymptomatic isolated proteinuria

ie No hematuria, Normal BP, Normal RFT

TRANSIENT

- Fever
- Infection
- Dehydration
- Exercise
- UTI

Repeat CUE

ORTHOSTATIC

- Always, sub-nephrotic / < 1000 mg/day
- Teenagers
- RBC's +/-
- Check 1st morning and evening sample

PERSISTENT

- U protein > 2+ or Urine PCR > 0.2 on 3 weekly urine analysis
- Possibility of glomerular or tubular pathology
- Needs evaluation

Persistent asymptomatic proteinuria

U protein > 2+ or U PCR > 0.2 on at least 3 occasions

Isolated

- **Glomerular:**
  - FSGS
  - Glomerulonephritis
  - Hypo-dysplasia
  - Orthostatic
- **Tubular:**
  - Renal Fanconi syndrome
  - Dent disease
  - Inherited (ARPKD, ADTKD)

Proteinuria + hematuria

- **Glomerular:**
  - Alport syndrome
  - Glomerulonephritis (SLE, C3G, IgAN)
  - FSGS
  - Vasculitis
  - Orthostatic
- **Tubular:**
  - Dent disease
  - Inherited (ADTKD)

Symptomatic proteinuria

- **What symptoms?**
  - Facial / leg swelling; gross hematuria
  - Headache (high BP)
  - Fever, skin rash, joint pains

- **Possibilities?**
  - Glomerulonephritis (IRGN, SLE, C3G, IgAN, Vasculitis, FSGS, MGN, rarely ATIN)

- **Family h/o kidney disease / high BP?**
  - FSGS
  - Alport syndrome
  - ADPKD / ARPKD / ADTKD

Symptomatic proteinuria: Evaluation

HISTORY

- Gross hematuria
- Facial puffiness
- Skin rash / joint pains / fever
- Hearing / Eye problems
- Intake of meds (NSAID's / chemotherapy / Chelating agents)
- Family h/o hematuria, high BP, CKD, hearing / eye prolems

PHYSICAL EXAM

- Growth parameters
- BP
- Edema
- Pallor / Icterus
- Skin rash / Purpuric rash
- Arthritis

INVESTIGATIONS

- Urinalysis (glucose / RBC / WBC)
- Random / 24-hour Urine protein
- Urine Calcium / creatinine
- Blood urea / creatinine
- Blood electrolytes / serum albumin / cholesterol
- USG abdomen
- Serum C3, ANA, ANCA, etc
- KIDNEY BIOPSY

Case 1

- 5 year boy with transient eye swelling x 2 days one week ago
- No gross hematuria
- BP is normal, and there is no edema
- CUE: 1005 / trace albumin / no RBCs/ 2-3 WBC's
- Diagnosis: Allergies / Physiological / Nephrotic syndrome
- What next?

Reassure family and review SOS

√

Obtain spot Urine PCR & blood tests

Case 2

- 14 year, boy with incidental detection of protein in urine
- ROS is negative, well grown, BP 110/70 mm Hg, no edema
- CUE: 1020 / 3+ protein / 5-10 RBC's / 2-3 WBCs
- Spot Urine PCR: 0.8 and 24 hour urine protein 900 mg
- What next?
  - Repeat CUE: 1020 / 2+ albumin / 3-5 RBC's
  - Serum biochemistry, normal
  - USG abdomen, normal KUB

Reassure family and review SOS

Serum albumin, cholesterol, Serological tests

Split Urine collection for protein

Case 2 contd …

- **Split urine collection:**

  - Day collection: 650 mg protein / 1150 ml

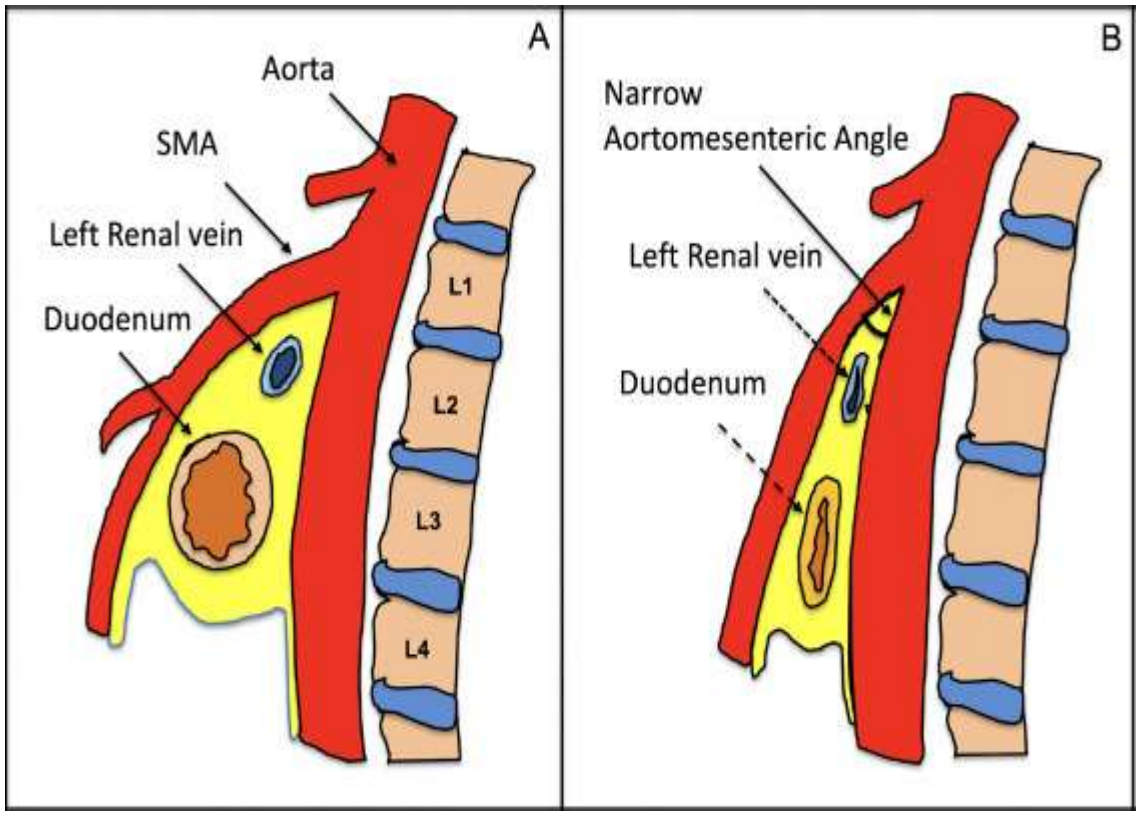
  - Night collection: 100 mg/400 ml

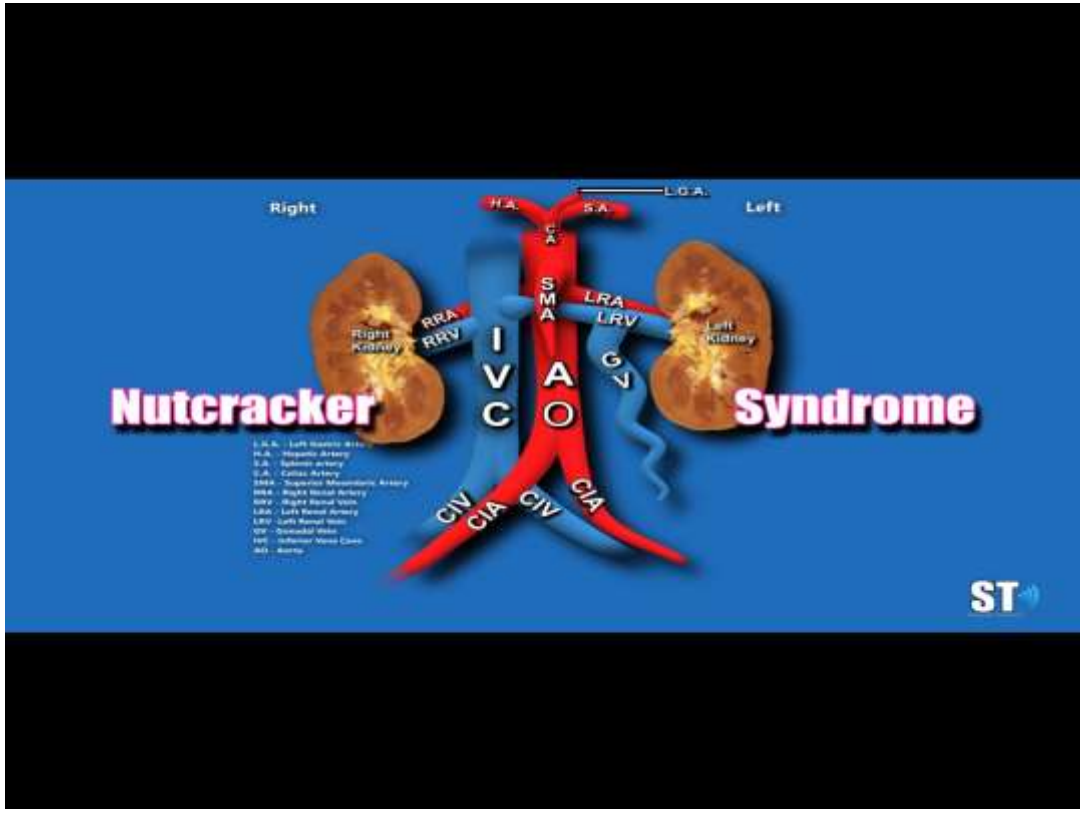
  - Night / Day protein ratio = 100 / 650 ~ 15%

    [< 25% is suggestive of orthostatic proteinuria]

- Or Random Urine PCR of first morning (represents night) and evening sample (day sample)

Orthostatic proteinuria





Teenagers, Sub-nephrotic proteinuria, Minimal protein loss in night sample, +/- microscopic hematuria, spontaneous resolution

Case 3

- 10 years boy, intermittent foamy urine x 1 month
- Well grown, BP 100//60 mm Hg, No pallor, No edema, No rash
- CUE: 1010 / 2+ protein / 10-15 RBC's / 5-7 WBC's
- Spot Urine PCR 1.0
- 24 hour U protein is 800 mg
- RFT & USG normal, Serum albumin 3.2 grams/dl, serum cholesterol 195 mg/dl,
- What next?

CUE: 1010 / 2+ protein / No RBCs

Spot U PCR 1.1

Clue: Proteinuria and low serum albumin

C3 N/ ANA neg / **pANCA positive**

KIDNEY BIOPSY
CGN due to vasculitis

Summary

- Proteinuria can be qualitatively detected by Uristix, SSA method, and quantified using random or 24 hour urine sample
- Uristix detects only albumin (tubular proteins not detected and hence, 24 hour collection necessary when tubular proteinuria is suspected)
- Always analyze Uristix result in context of specific gravity and beware of false positives
- Transient proteinuria due to fever, dehydration, exercise is most common
- Orthostatic proteinuria should be considered in teenagers when proteinuria is less than 1000 mg / day, no significant hematuria, and normal RFT
- Proteinuria > 1000 mg / Spot U PCR > 2.0 with hematuria, symptoms, or abnormal RFT needs detailed evaluation including kidney biopsy

THANK YOU

Approach to Hematuria

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YOUNG KIDNEYS 2024

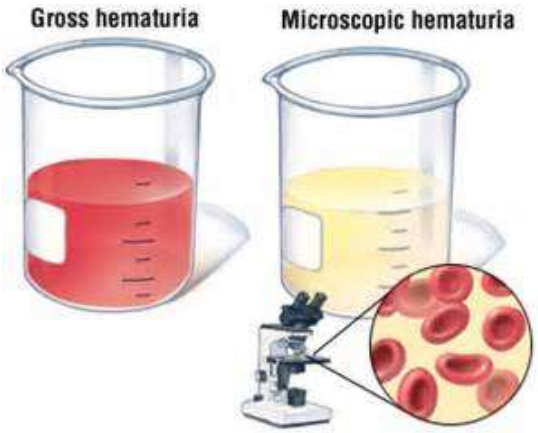
Scope of Presentation

- Recognize and confirm hematuria
- Site of origin (glomerular, non-glomerular [tubules, interstitium & urinary tract]or non-renal)
- Cause of hematuria
- Recognize significant disease for referral

- Red colored urine is alarming for the patient and of concern for the physician

- Is the history of a red colored urine sufficient to conclude the possibility of hematuria?

- What is the inference derived from the urine color?



- **Gross (Macroscopic) hematuria**
  - ✓Blood seen with the naked eye

- **Microscopic hematuria**
  - ✓Detected by dipstick & confirmed by microscopy
  - ✓Initial determination based on examination from a freshly voided, clean-catch urine
  - ✓No consensus to define microscopic hematuria

Agents that may color urine

- ***Red or pink urine***
  - Red cells, free hemoglobin, myoglobin,
  - Urates
  - Drugs: chloroquine, phenazopyridine
  - Beets, red dyes in food
  - Porphyrins

- ***Dark yellow or orange***
  - Normal concentrated urine
  - Rifampicin, pyridium

- ***Dark brown or black***
  - Bile pigments
  - Methemoglobinemia
  - Homogentisic acid

When is hematuria suspected, how is it confirmed?

- Suspected on history of brown/red urine or positive dipstick test. But all red urine is not hematuria !
- Defined by presence of an increased number of red blood cells (RBCs) in urine
- **Confirmation of hematuria requires** - Urine Microscopy (gold standard)
- Urine microscopy showing:
  - >5 RBCs/HPF of centrifuged urine
  - >5/µl in uncentrifuged urine
  - strips can detect 5 to 10 intact RBCs/microL, which roughly corresponds to a finding on microscopic examination of 2-5 RBCs/HPF from the sediment of a centrifuged 10 to 15 mL urine sample.

- **Urine dipstick – Adjunctive role** for mass screening (easy, cheap)

  - utilizes H_2O_2 to catalyse rxn btw Hb/Myoglobin & chromogen
  - corresponds to 2-5 RBCs/HPF
  - more sensitive for free Hb than RBCs
  - Often false +ve (e.g., hypochlorite, alkaline urine)
  - Occasionally false -ve

How do you differentiate hematuria from hemoglobinuria and myoglobinuria?

Hemoglobinuria, Myoglobinuria and Hematuria

- Positive dipstick & presence of RBCs in urine microscopy
  - Hematuria

- Positive dipstick & absence of RBCs in urine microscopy
  - Hemoglobinuria or Myoglobinuria

- Negative dipstick & absence of RBCs in urine microscopy
  - False or Pseudo-hematuria (drugs, dyes, etc)

Hematuria vs. Hemoglobinuria

Hematuria

- ✓ Urine: red/brown
- Dipstick blood test +
- Supernatant of centrifuged urine: Clear
- Microscopy: **RBCs present**

Hemoglobinuria

- ✓ Urine: red/brown
- Dipstick blood test +
- Supernatant of centrifuged urine: red/pink
- Microscopy: **no RBCs**

What is the etiology of hematuria in children?

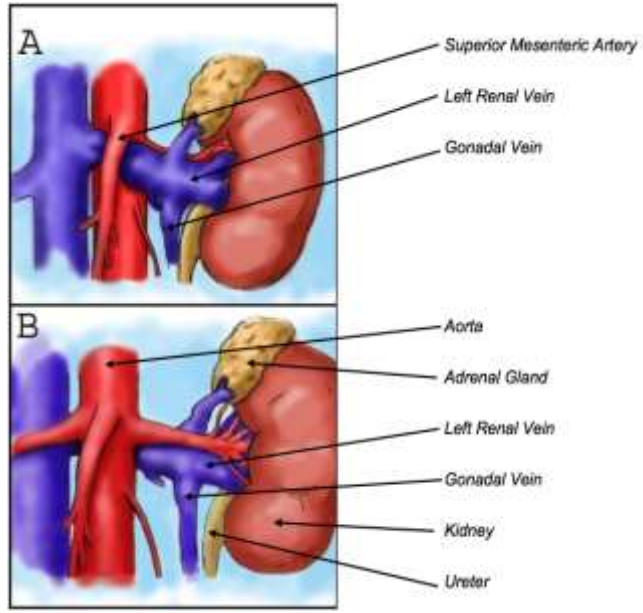
Causes of hematuria in children

Glomerular		Nonglomerular
Familial benign hematuria (thin basement membrane disease)	Glomerulonephritis (GN)	Urinary tract infection
Nonfamilial benign hematuria	Primary GN	Hypercalciuria
	Postinfectious acute GN	Renal calculi
	Membranoproliferative GN	Trauma
	Membranous nephropathy	Exercise
	Rapidly progressive GN	Chemical cystitis such as cyclophosphamide
	IgA nephropathy	Coagulopathy
	Secondary GN	Vascular malformations
	Systemic lupus erythematosus	Nutcracker syndrome
	Henoch-Schönlein purpura	Malignancy
	Polyarteritis nodosa	Renal: nephroblastoma
	Wegener granulomatosis	Bladder: rhabdomyosarcoma
	Hemolytic uremic syndrome	Menarche
	Hereditary nephritis (Alport syndrome)	Factitious
	Renal vein thrombosis	
	Interstitial nephritis	
	Cystic renal disease	

Comprehensive Pediatric Nephrology

Transient *versus* Persistent hematuria: causes

- **Persistent microscopic hematuria**
  - Glomerulopathies (e.g. IgAN, Alport, TBMD, PIGN), hypercalciuria, *nutcracker syndrome*, nephrolithiasis/ nephrocalcinosis



- **Transient hematuria**
  - UTI, trauma, fever, exercise, contamination from external genitalia, etc

What are the historical clues to the underlying etiology of hematuria?

Glomerular versus non-glomerular

- The identification of the glomeruli as the source of blood is important both prognostically and to optimize the subsequent diagnostic evaluation.

- Differentiation can be done using a combination of

  - **History and Physical examination**
  - **Urinalysis**
  - **Other laboratory tests**

HISTORY

Glomerular causes

- ✓ Oliguria
- ✓ Recent respiratory, skin or gastrointestinal infection
- ✓ Deafness
- Medication (NSAID,native)
- ✓ Family history of hearing loss or renal failure
- ✓ Rash
- ✓ Joint pain/ Swelling
- ✓ Hemoptysis

Non- Glomerular causes

- ✓ Dysuria **or** Polyuria
- ✓ Renal colic / Abdominal pain
- ✓ Fever
- ✓ Medication exposure
- ✓ Trauma history
- ✓ Family history of sickle cell disease, hemophilia, Von Willibrand disease
- ✓ Strenuous excercise

Physical examination

GLOMERULAR CAUSES

- ✓ Hypertension
- ✓ Edema
- ✓ Rash
- ✓ Arthritis
- ✓ Pallor

NON - GLOMERULAR CAUSES

- ✓ Normotension
- ✓ Costovertebral angle tenderness
- ✓ Suprapubic pain
- ✓ Signs of Trauma

How do you differentiate glomerular from non-glomerular hematuria?

Differentiate glomerular from non-glomerular on urinalysis

Look for

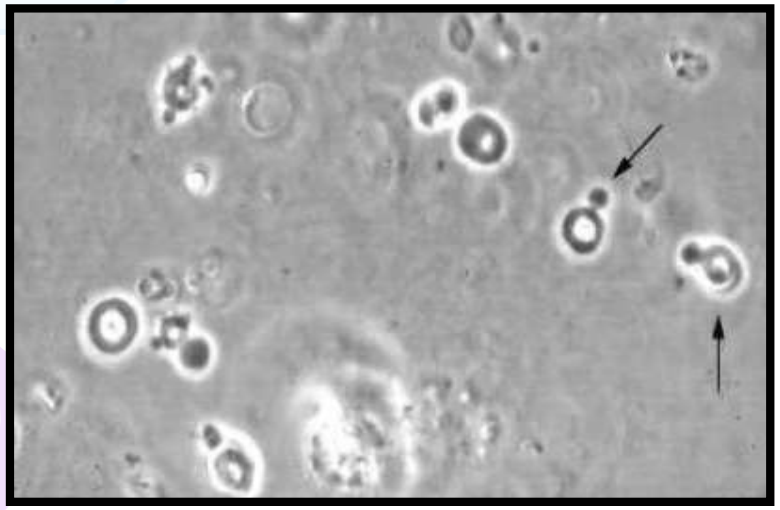
Shape of RBCs (normal or dysmorphic)

- ✓ Presence of RBC casts (glomerular)
- ✓ Presence of proteins (glomerular if >2+)
- ✓ Presence of white blood cells (Infection, glomerulonephritis)
- ✓ Presence of crystals (RSD)

Urinalysis

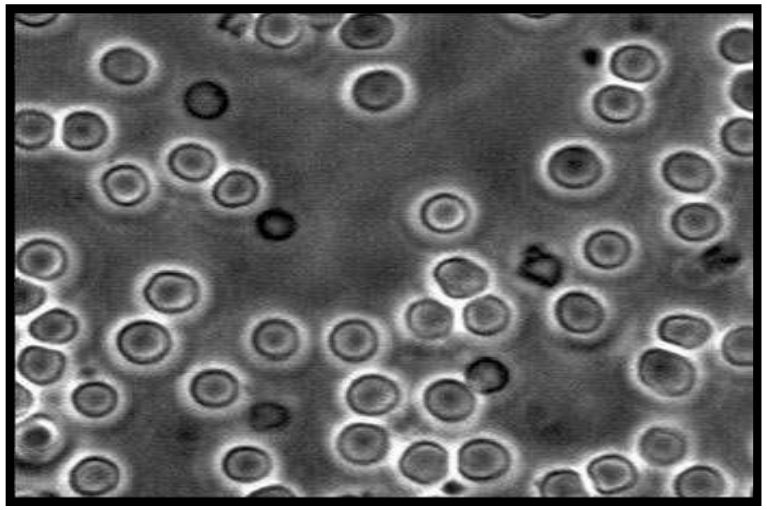
GLOMERULAR

- ✓ Brown, Tea or "Cola-colored" urine
- ✓ Clots absent
- ✓ Proteinuria >2+
- ✓ Red blood cell casts may be present
- ✓ > 20 % dysmorphic RBC s

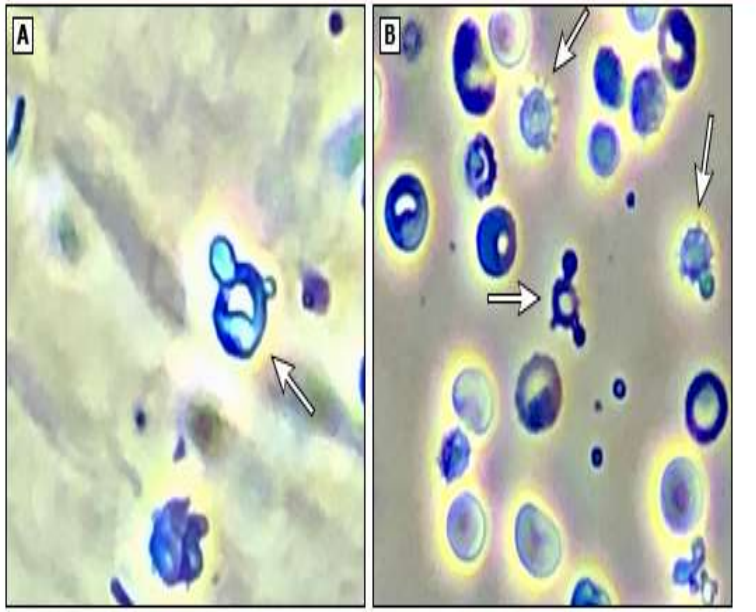


NON-GLOMERULAR

- ✓ Bright red or pink urine
- ✓ Clots may be present
- ✓ Proteinuria +/-
- ✓ No red cell casts; <15% dysmorphic RBC
- ✓ Crystals ±; Nitrates/Leukocyte esterase ±



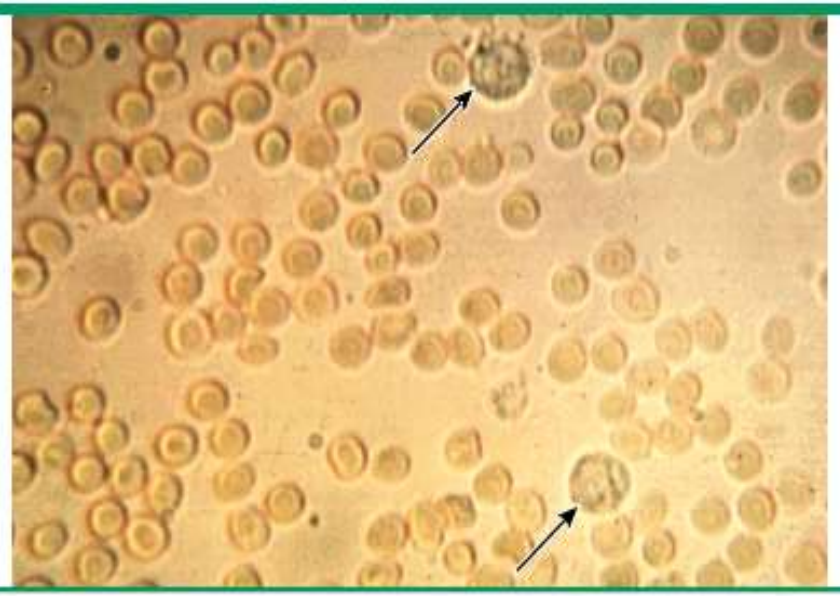
Phase-contrast micrograph showing dysmorphic RBCs in urine sediment



Glomerular

Phase-contrast microscopy - dysmorphic red blood cells (RBCs) and acanthocytes

Phase-contrast micrograph showing monomorphic red cells in urine sediment



Non-Glomerular

Urine sediment viewed by phase-contrast microscopy
The red cells have a uniform size and shape.
Hypercalciuria can be associated with dysmorphic RBCs, but not red cell casts

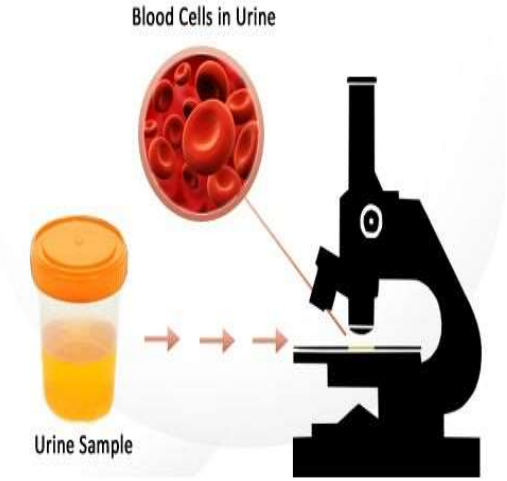
Laboratory testing

GLOMERULAR CAUSES

- Elevated BUN / Creatinine
- Anemia
- ASO
- Abnormal complement levels (C3, C4)

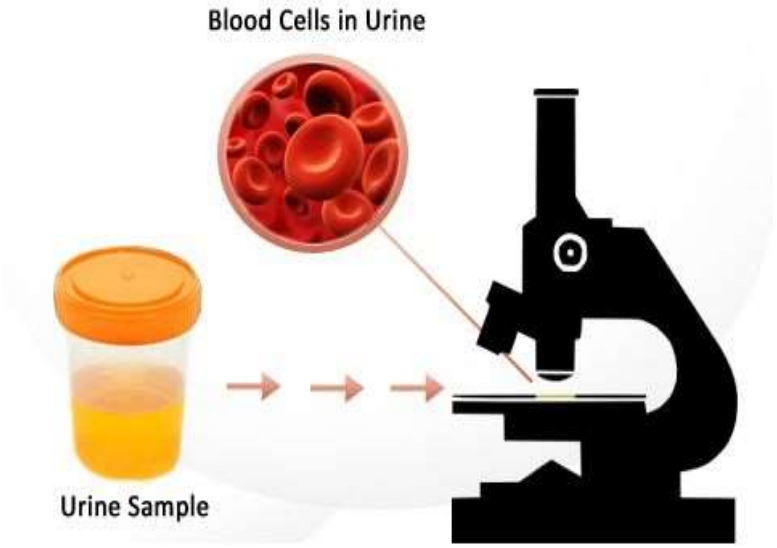
NON -GLOMERULAR CAUSES

- Normal BUN / Creatinine



YOUNG KIDNEYS 2024

How do you evaluate a child with non-glomerular hematuria?



Approach to Non glomerular Hematuria

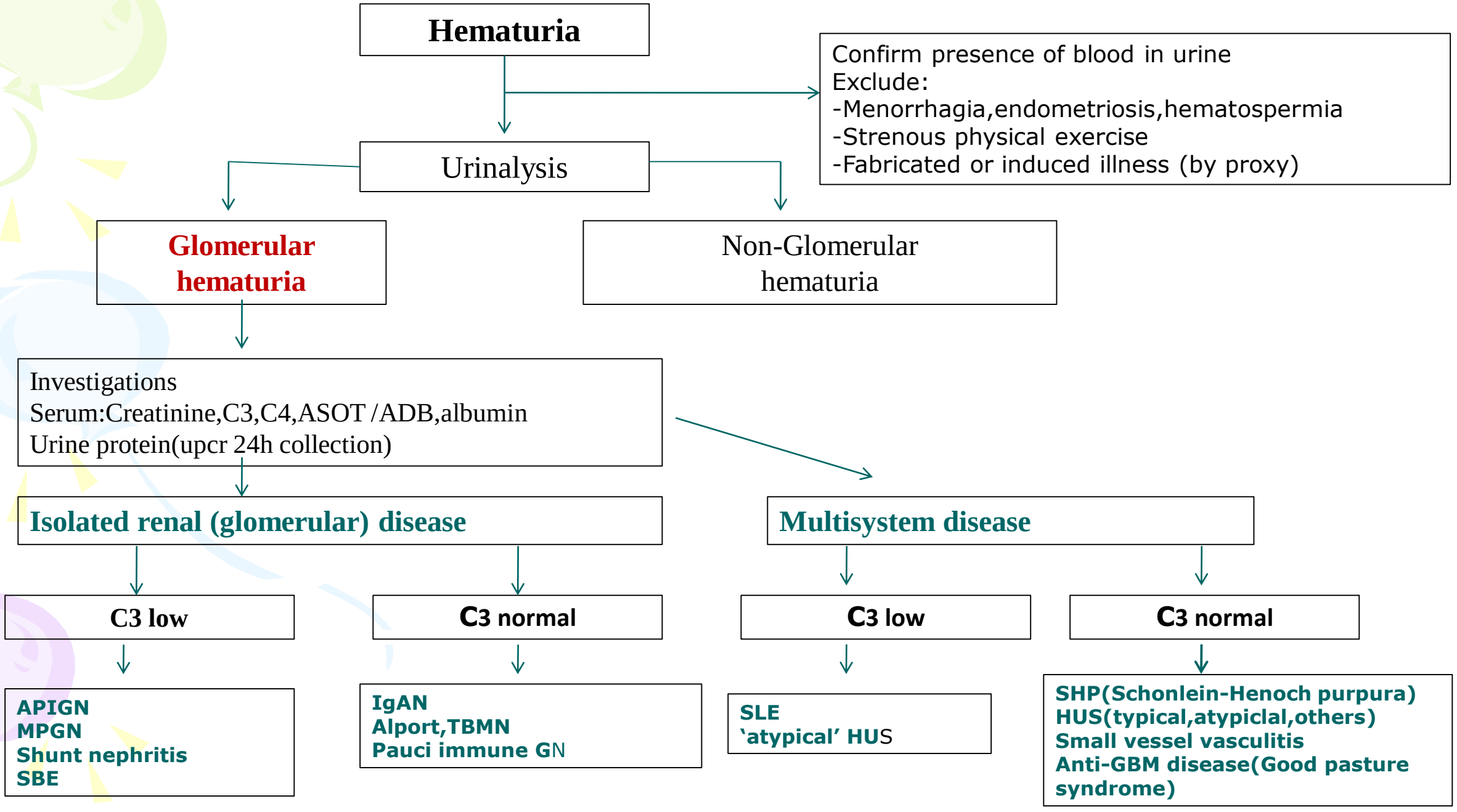
Basic Investigation:
Urinalysis, culture, Ca/Cr
Sr Create, CBC, USG

Symptoms	Dysuria	Renal colics	Painless isolated hematuria	Renal mass	Petechiae, echymosis	Cutaneous vascular signs, exercise exacerbation
Suspected Diagnosis	**UTI**	**Urolithiasis**	**Hypercalciuria**		**Hematologic**	**Vascular**
Additional Investigation	MCUG, DMSA	CT, 24 hr urine Ca, oxalate, uric acid, Se Ca, P, ALP, ABG		USG, CT/MRI	Coags, CBC	CT Angio
Diagnoses	UTI	Metabolic disorders/idiopathic hypercalciuria/tubulopathy		Wilms tumor, ADPKD, Renal venous/arterial thrombosis	Hemophilia, vWD, ITP	HHT, Renal AVM, Nut cracker syndrome

How would you evaluate Glomerular hematuria?

Common causes - Glomerular hematuria

Primary Glomerulonephritis	Secondary Glomerulonephritis	Familial
Post infective GN	Lupus nephritis	Alport syndrome
IgA nephropathy	Henoch-Schonlein purpura	Thin basement membrane
MPGN	Hemolytic-uremic syndrome	
FSGS		


Hematuria
Confirm presence of blood in urine
Exclude:
-Menorrhagia,endometriosis,hematospermia
-Strenous physical exercise
-Fabricated or induced illness (by proxy)
Urinalysis
Glomerular hematuria
Non-Glomerular hematuria
Investigations
Serum:Creatinine,C3,C4,ASOT /ADB,albumin
Urine protein(upcr 24h collection)
Isolated renal (glomerular) disease
Multisystem disease
C3 low
C3 normal
C3 low
C3 normal
APIGN
MPGN
Shunt nephritis
SBE
IgAN
Alport,TBMN
Pauci immune GN
SLE
'atypical' HUS
SHP(Schonlein-Henoch purpura)
HUS(typical,atypiclal,others)
Small vessel vasculitis
Anti-GBM disease(Good pasture syndrome)

Is a detailed evaluation of a child with persistent asymptomatic microscopic hematuria required?

Persistent asymptomatic microhematuria

Persistent asymptomatic hematuria-≥ 2/3 urine R/E +ve over 2 wks (exclude heavy exercise)

No assoc. symptoms & signs (edema/HT)

No associated proteinuria

Tests needed –Urine culture, Urine Ca/Cr, USG, Urine RE of relatives, Hb electrophoresis

May represent-resolving AGN, Thin basement membrane, IgA nephropathy, Hypercalciuria.

Rationale –Detect serious illness but avoid unnecessary labs at presentation however close FU

(Familial hematuric syndromes carry risk of CKD)

Reasonable approach

FU -3mthly-clinically (HT, edema) urine RE, Up/Uc ratio. Annually - Serum Cr

If course changes –further evaluation

Biopsy: Isolated microhematuria persist for >1-2 years

Asymptomatic microhematuria with proteinuria >6 months

Categories of microhematuria

- Asymptomatic, Isolated microhematuria
  - Require a follow-up examination and stepwise evaluation with detailed family history (Alport syndrome, benign familial microscopic hematuria)

- Asymptomatic microhematuria with proteinuria
  - Require rapid evaluation for glomerular and early referral to a nephrologist.

- Microhematuria with clinical symptoms
  - Require emergency evaluation for glomerular and non-glomerular; early referral to a nephrologist

Take home message

- Hematuria should always be confirmed by microscopy
- It is useful to differentiate between glomerular and Non-glomerular hematuria
- Hematuria with proteinuria >2+ (>100 mg/dL) indicates a sig. glomerular renal disease
- Significant anemia can never be accounted for by hematuria alone
- Oliguria, hypertension, renal failure and recurrent macroscopic hematuria are red flags

YOUNG KIDNEYS 2024

Thank You

YOUNG KIDNEYS 2024

Pediatric Glomerular disease and Renal Transplantation

Dr Manisha Sahay
Professor and Head
Nephrology
Osmania Medical college and General hospital
Hyderabad

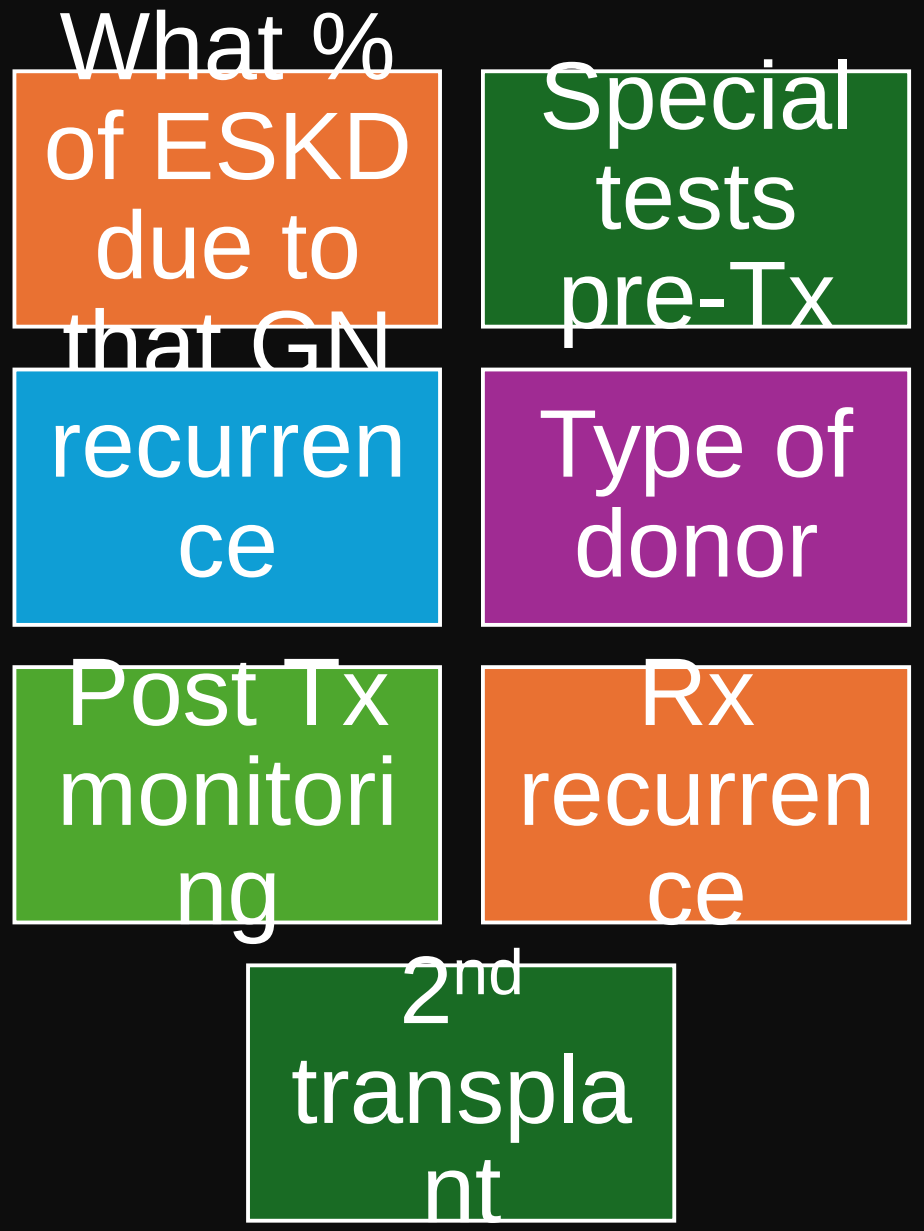
Disclaimer..

- Did MD ped then Nephrology
- Practice in tertiary care nephrology unit
- 40% admissions are pediatric

- 3000 dialysis per month, 100 CAPD patients
- 500 kidney transplants- personally involved
- Multiorgan transplant

17 pediatric transplants

What we need to know about Pediatric GN regd Tx?



Pediatric transplant

Usually 10 kg body weight

Parents or deceased donors

High immunological risk

Volume management in transplant

Vascular size incompatibility

Bladder issues in CAKUT

GN related issues

Tac+MMF+CS

CKD Etiology	Percentage (range)	ESRD Etiology	Percentage (range)
CAKUT*	48%–59%	CAKUT	34%–43%
GN†	5%–14%	GN	15%–29%
HN‡	10%–19%	HN	12%–22%
HUS¶	2%–6%	HUS	2%–6%
Cystic	5%–9%	Cystic	6%–12%
Ischemic	2%–4%	Ischemic	2%

Rare causes include congenital NS, metabolic diseases, cystinosis. Miscellaneous causes depend on how such entities are classified.

*CAKUT: Congenital anomalies of the kidney and urinary tract

†GN: Glomerulonephritis, ‡HN: Hereditary nephropathy, ¶HUS: Hemolytic uremic syndrome

From Harambat, *et al*. CKD data are from NAPRTCS, the Italian Registry and the Belgian Registry. ESRD data are from ANZDATA, ESPN/ERA-EDTA, UK Renal Registry and the Japanese Registry.

2016

Pediatric GN

Primary GN	Vascular disease	Secondary GN	Genetic
• FSGS • C3GN • DDD • MPGN • MN • IgA	• Vasculitis • HUS	• Lupus • DN • Amyloid	• CNS • Alport's syndrome • Fabry's

Glomerular Diagnosis $n = 129$ (22%)	% (n)	Nonglomerular Diagnosis $n = 457$ (78%)	% (n)
Focal and segmental glomerulosclerosis	33% (42)	Obstructive uropathy	26% (118)
Hemolytic uremic syndrome	22% (28)	Aplastic/hypoplastic/dysplastic kidneys	23% (105)
Systemic immunologic disease	9% (12)	Reflux nephropathy	19% (87)
Familial nephritis	7% (9)	Autosomal recessive polycystic kidney disease	4% (19)
IgA nephropathy	5% (7)	Renal infarct	4% (18)
Chronic glomerulonephritis	5% (7)	Syndrome of agenesis of abdominal musculature	2% (11)
Membranoproliferative glomerulonephritis type I	3% (4)	Pyelo/interstitial nephritis	2% (9)
Idiopathic crescentic glomerulonephritis	2% (3)	Cystinosis	2% (9)
Membranous nephropathy	2% (3)	Oxalosis	2% (7)
Henoch Schonlein purpura	2% (3)	Medullary cystic disease	1% (6)
Congenital nephrotic syndrome	2% (2)	Wilm's tumor	1% (4)
Membranoproliferative glomerulonephritis type II	2% (2)	Autosomal dominant polycystic kidney disease	<1% (2)

CKiD cohort n=586

Pediatric GN and Transplant- broad principles

Risk factors for recurrence

- IS related
  - Young age of recipient
  - No induction
  - Steroid free IS
  - Less HLA match
  - Non compliance
  - Genetics

Markers
Genetic tests , Antibody testing
Complement profile
Decide about donor type

MMF if on AZA

Eculizumab

Post transplant monitoring
Urine protein, cr, Biopsy

FSGS

FSGS

3rd leading cause of CKD in children

11.7% ESKD patients who undergo KTX d/t FSGS

NAPRTCS 2014

Genetic, Primary (CF)
Secondary (Inf, drugs, Ca)

20 -50% after 1st KTX
Upto 100% - subsequent Tx, graft loss 50%

Vinal et al, Ped transplant, 2010

Factors- Post transplant **recurrence** FSGS

Risk of recurrence

- **Lower BMI**
- **Primary FSGS vs genetic or secondary**
- **White race**
- **Nephrectomy**
- Young age
- NS
- Rapid progression to ESKD

Not related to recurrence

- FSGS histologic variants (collapsing, tip lesion, cellular, perihilar lesion, NOS)
  - *Canaud et al, NDT, 2010*
- no relation with degree of podocyte foot process effacement

TANGO cohort, Uffing et al, CJASN, 2020

Pre transplant -any tests?

Idiopathic/ Primary FSGS recurs

due to a circulating permeability factor (CPF)

No accurate biomarker to predict recurrence

Baum et al. Ped transplantation. 2004

FSGS		
Serum suPAR (37)	↑ Pre-transplant predicts post-transplant recurrence	Yes
Urine suPAR (38)	↑ Post-transplant predicts recurrence	Yes
Anti-CD40 autoAb (39)	↑ Pre-transplant predicts post-transplant recurrence	Yes
Urine apolipoprotein A-1b (40, 41)	↑ In relapses	No data
A1AT (42)	Differentiate from other causes	No data
CLC-1 (43)	↑ Recurrent disease	No data
Anti-AT1R Ab *Ant I Nephrin Ab, TNF alpha*	↑ Pre-transplant predicts post-transplant recurrence	Yes

Any tests-Should we do genetic testing pre

>50 genes associated with FSGS.

Monogenic/familial FSGS -low recurrence, except Fin major mutation, rarely Podocin and TRPC6

- *Jungraithmayr et al, JASN, 2011*

APOLI in patient low risk , donor APOL1 high risk of recurrence

- *Genovese, Science, 2010*

Comprehensive and low-cost genetic testing panels for FSGS

***Genetic testing should be considered an important tool for the risk stratification of FSGS recurrence*.**

- *Uffing et al, CJASN, 2021*

Dilemma: Should Patients with Primary FSGS Undergo Native Nephrectomies before Transplant?

Native nephrectomies Earlier-Yes

- Native nephrectomies have been performed due to refractory hypoalbuminemia and requirement for IV albumin
  - *Frasier, J Ped uro, 2013*

Native nephrectomies Presently-No

- Higher risk of FSGS recurrence
- Abandoned by most centers
  - *Uffing, CJASN, 2020*

Preventing FSGS recurrence

Preemptive Tx can be offered

Both LD and DD can be done - 1st transplant

LD should be tested for the mutation (1A)

No role for pretransplant PE- (2C)

Ongoing trials –pre-emptive use sparse data

- Rituximab (2C),Bleselumab, ACTH

What Is the Best Rx for r-FSGS after Kidney Tx?

Monitor proteinuria- DOTX, daily for 1 week, twice weekly in week 2, weekly for 4 weeks, monthly for the first year, and every 3 [illegible] after (1B) if yes early Kidney Bx including EM

PE & IA

- **Plasmapheresis (1A)**
  - removes circulating factor
  - daily PLEX for 3 days and then 3 times a week for 2 weeks.

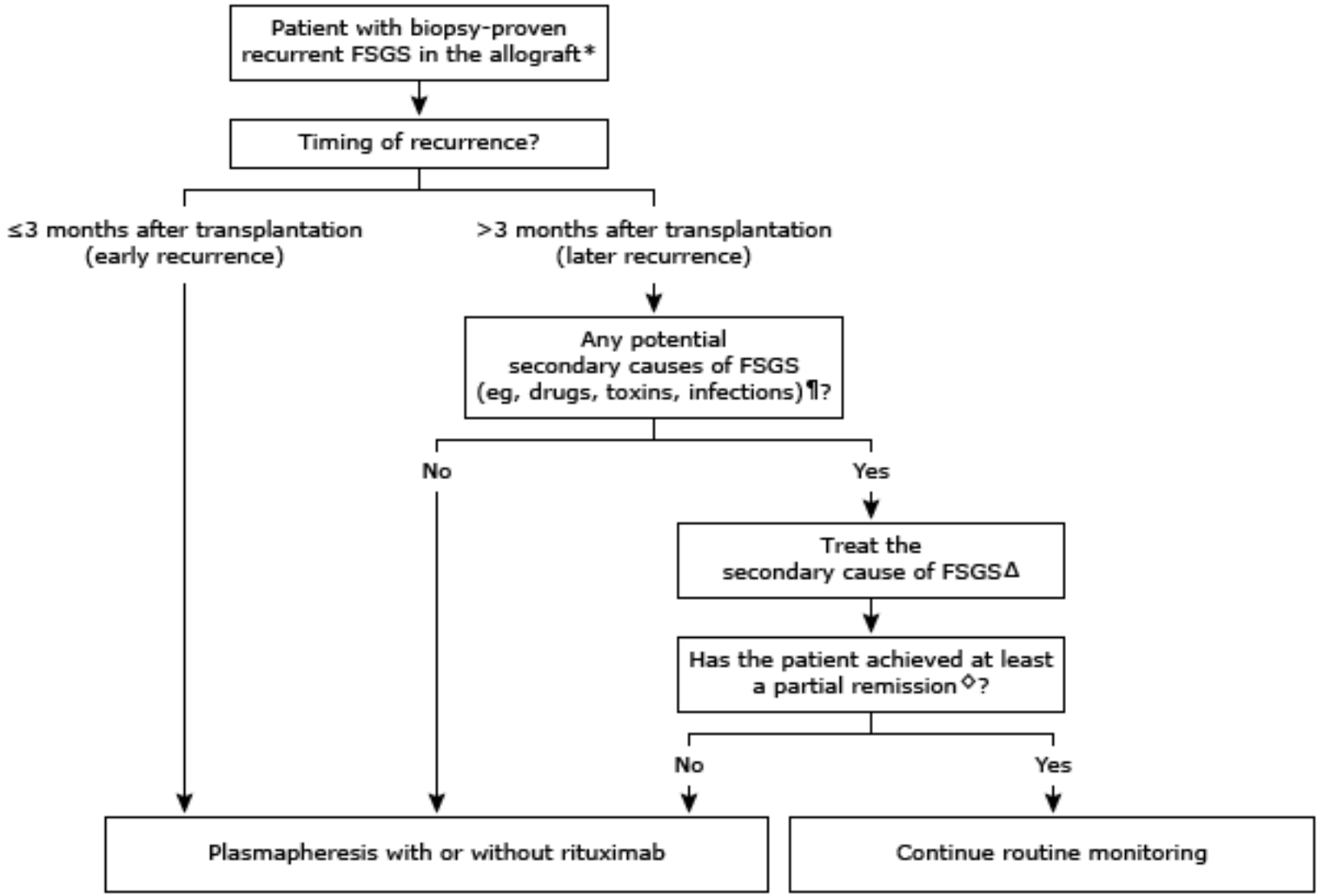
CNI

- High dose CNI –CSA and steroids (1C)

Rituximab (1E)

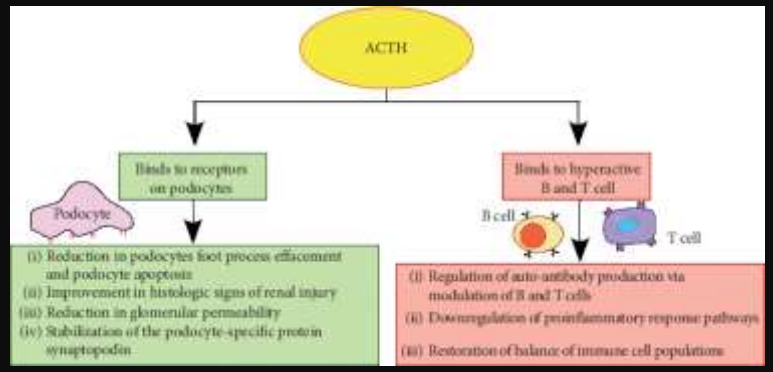
- Remission rates vary widely likely
  - 375mg/m2 weekly x 4doses
  - Stop PLEX for 48 hrs

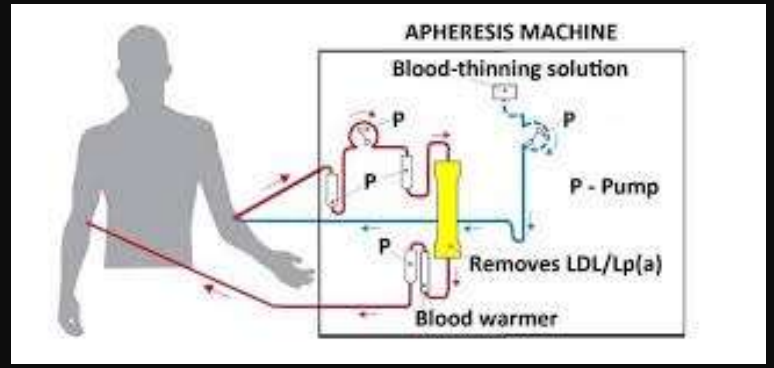
Rupesh Raina et al Consensus guidelines KI


Patient with biopsy-proven recurrent FSGS in the allograft*
Timing of recurrence?
≤3 months after transplantation (early recurrence)
>3 months after transplantation (later recurrence)
Any potential secondary causes of FSGS (eg, drugs, toxins, infections)¶?
No
Yes
Treat the secondary cause of FSGSΔ
Has the patient achieved at least a partial remission◇?
No
Yes
Plasmapheresis with or without rituximab
Continue routine monitoring

Refractory cases

- Cyclophosphamide
- LDL apheresis
- Abatacept-
  - soluble fusion protein which inhibits CD 80
- ACTH gel
  - Acthar gel will be **80 units/1.73 m^2 per dose twice a week** .
- Adalimumab
  - anti TNF. 160mg, 80 mg then 40 mg ever 2 wks
  - bimonthly infliximab at a dose of 3 mg/kg along with high-dose corticosteroids (60 mg/1.73 m2 per day)
- Mesenchymal stem cell





Dilemma: Should Patients with Previous Graft Loss Due to FSGS Recurrence Be Considered for Another Kidney Transplant?

Risk of recurrence 80% in 2nd, almost 100% recurrence in 3rd allograft

Many patients with FSGS young, & precluding them from Tx unethical

1 previous graft loss due to rFSGS did not have 2nd recurrence

Partial or complete remission after recurrence in a subsequent Tx- TANGO cohort

2 previous Tx losses due to r-FSGS, with graft loss soon after Tx with no response to Rx

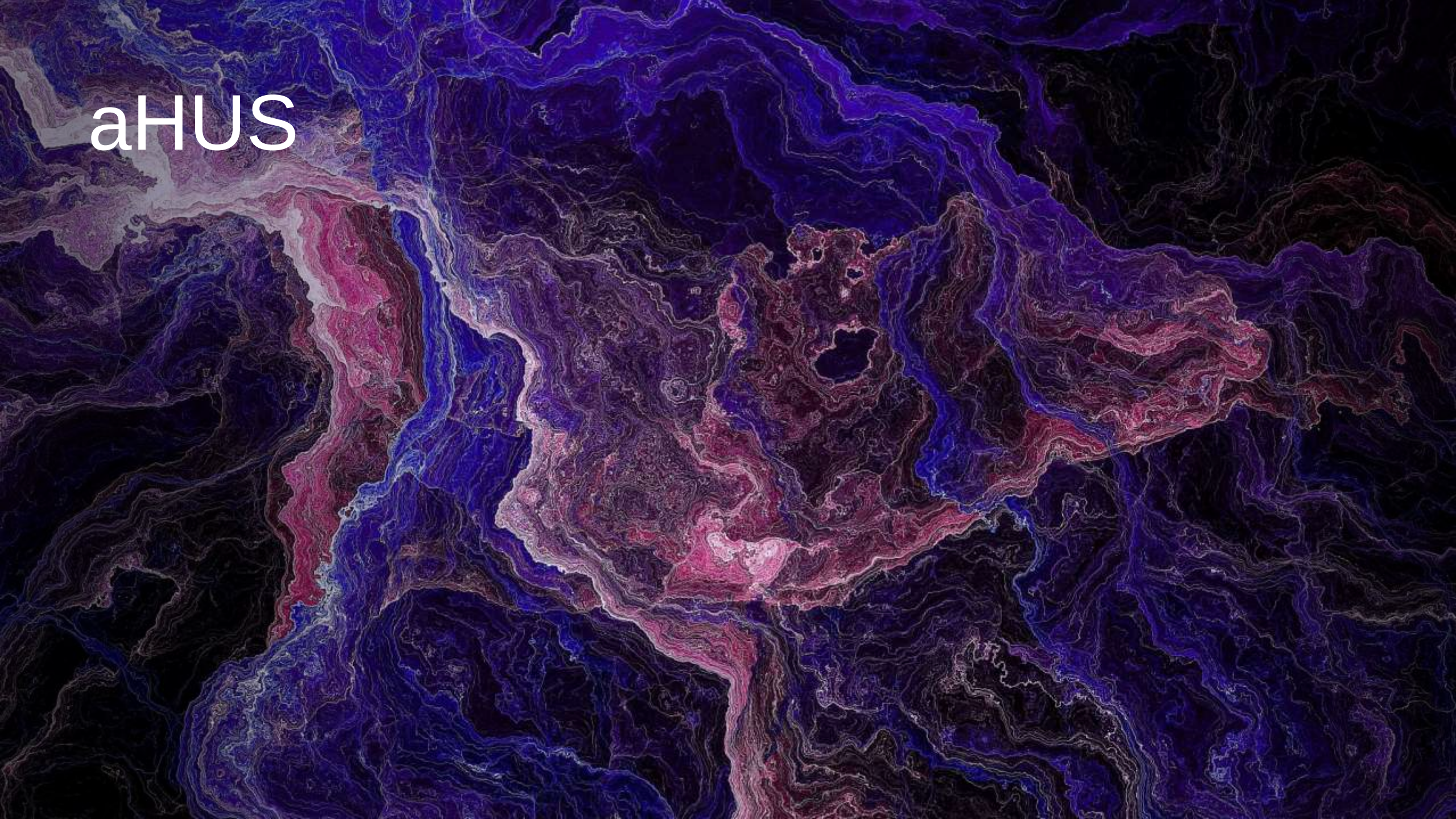
Decisions on an individual level

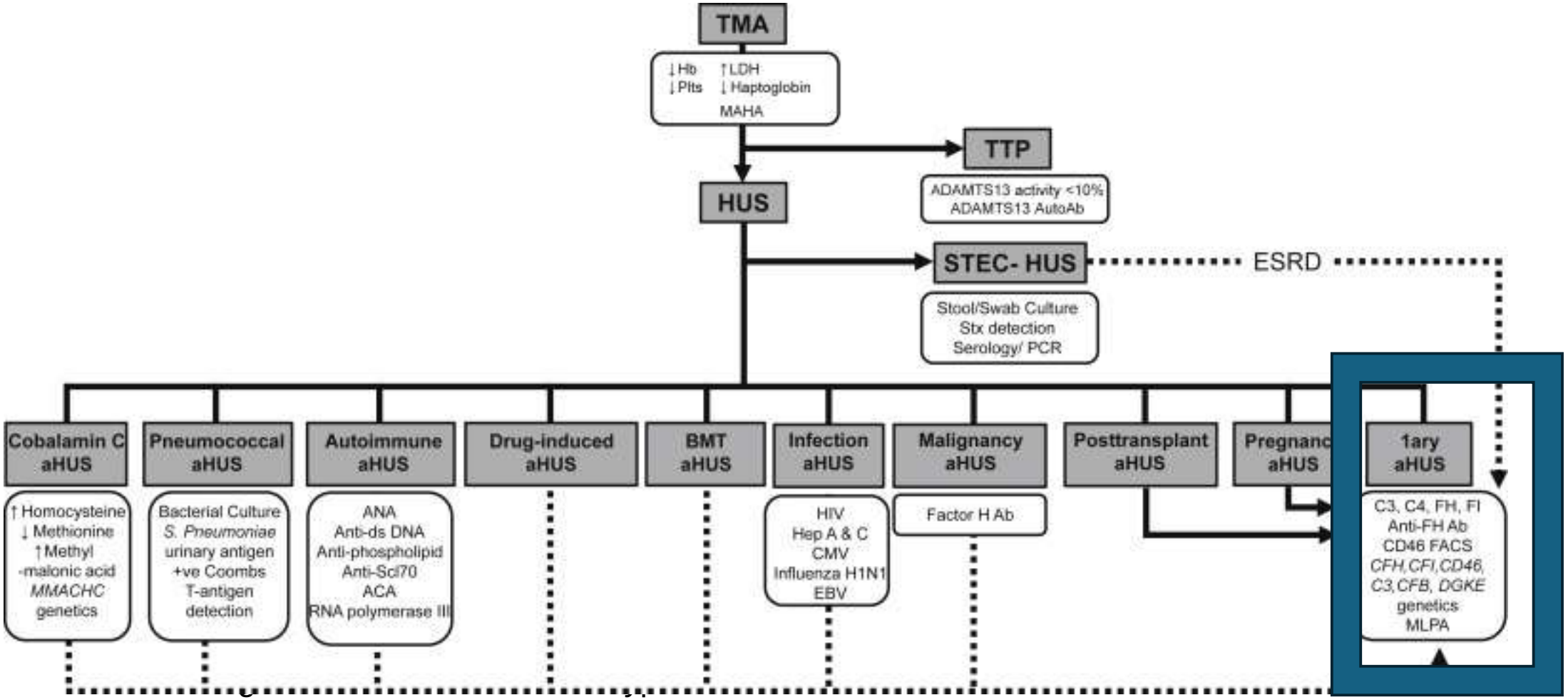
Kidney International
Volume 105, Issue 3, March 2024, Pages 450-463

Meeting Report

Post-transplant recurrence of focal segmental glomerular sclerosis: consensus statements

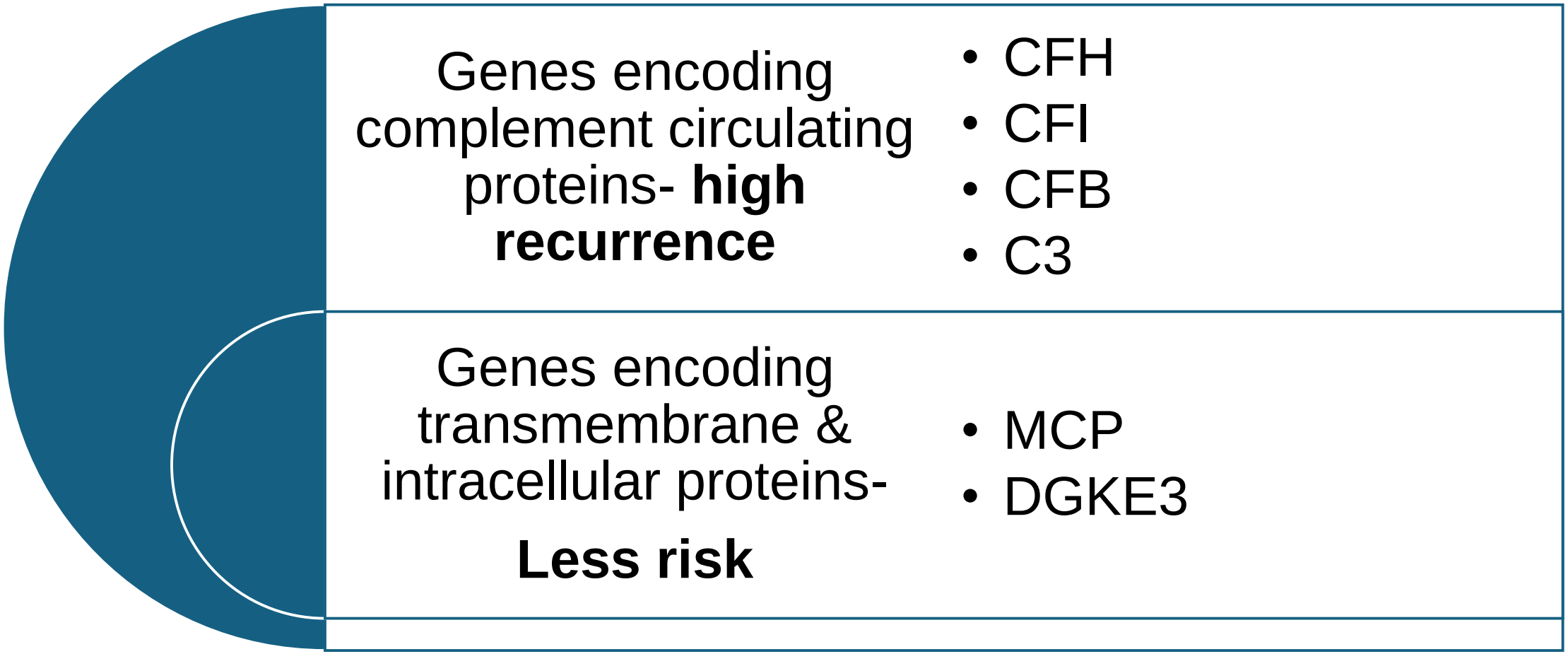
Rupesh Raina [1 2 31], Swathi Jothi [1 31], Dieter Haffner [3], Michael Somers [4], Guido Filler [5 6 7], Prabhav Vasistha [1], Ronith Chakraborty [1 2], Ron Shapiro [8], Parmjeet S. Randhawa [9], Rulan Parekh [10], Christopher Licht [11], Timothy Bunchman [12], Sidharth Sethi [13], Guneive Mangat [1], Joshua Zaritsky [14], Franz Schaefer [15], Bradley Warady [16], Sharon Bartosh [17], Mignon McCulloch [18], Khalid Alhasan [19 20]...
Jai Radhakrishnan [30]


aHUS



Atypical HUS

Pre transplant risk assessment check for Complement mediated HUS



Genotyping for the risk haplotypes *CFH-H3* and *MCP*

Only NGS method is not sufficient, MLPA method should be done so as not to miss CNVs

Pre transplant testing

Test for FH autoantibodies

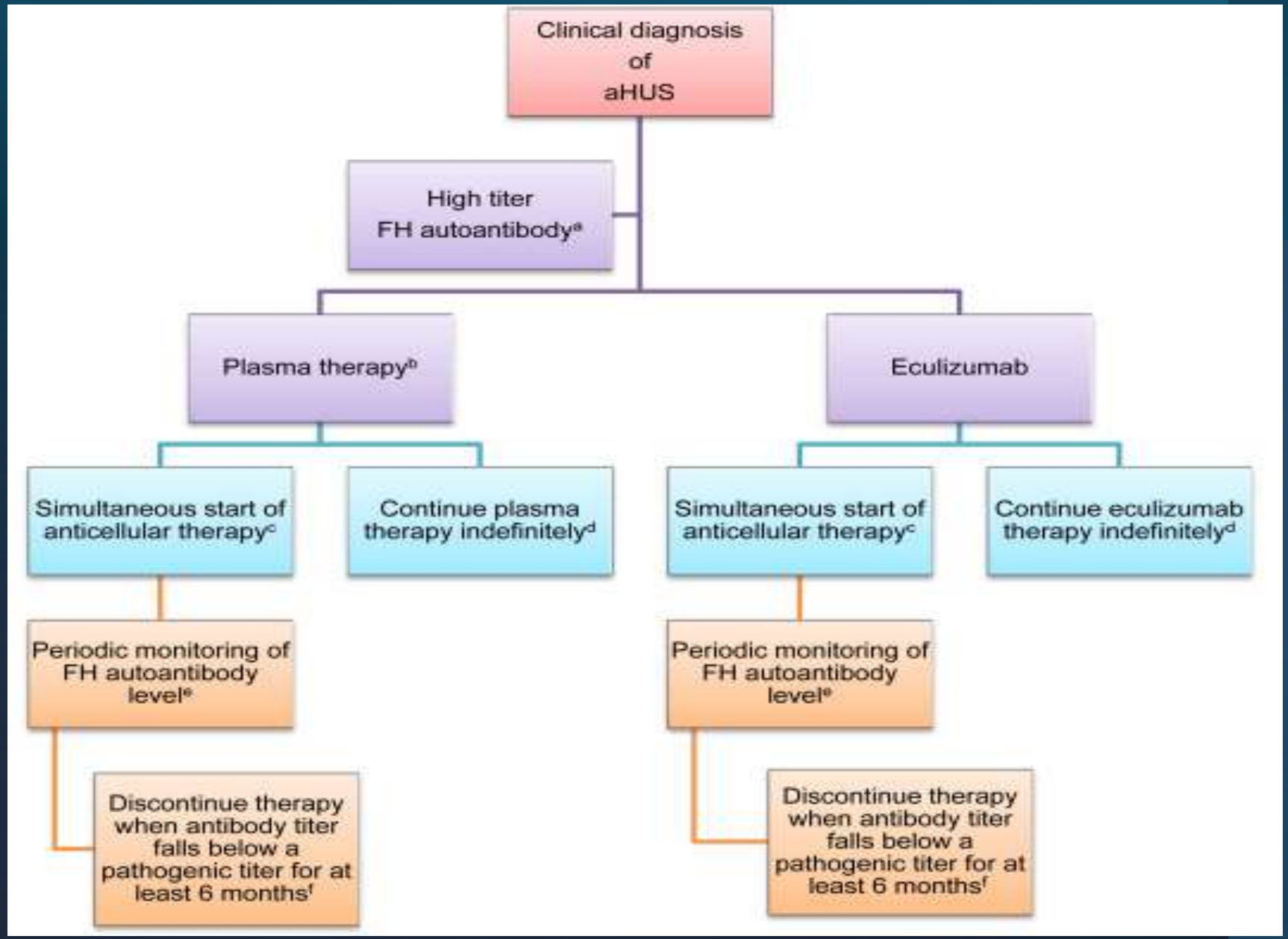
associated with homozygosity for del*CFHR3-CFHR1*

Positive results should be confirmed in a 2nd sample at least 4 weeks after the initial sample.

should be performed at diagnosis and, if positive, at days 7, 14, and 28, monthly, and at 1 year

Pre transplant treatment

Risk Category	Criteria	Recommendation
High risk (50%–100%)	Previous early recurrence of aHUS Pathogenic mutation in aHUS gene Gain-of-function mutation	Prophylactic eculizumab recommended


Clinical diagnosis of aHUS
High titer FH autoantibody[a]
Plasma therapy[b]
Eculizumab
Simultaneous start of anticellular therapy[c]
Continue plasma therapy indefinitely[d]
Simultaneous start of anticellular therapy[c]
Continue eculizumab therapy indefinitely[d]
Periodic monitoring of FH autoantibody level[e]
Periodic monitoring of FH autoantibody level[e]
Discontinue therapy when antibody titer falls below a pathogenic titer for at least 6 months[f]
Discontinue therapy when antibody titer falls below a pathogenic titer for at least 6 months[f]

Pretransplant testing

Transplantation from living-related kidney donors should only be considered if causative genetic (or acquired) factors are clearly identified in the recipient

related donor is free of these factors & N complent levels

presence in the donor of *CFH* or *MCP* aHUS risk haplotypes is not a contraindication to donation.

KTx in aHUS- Rx recurrence

- Strict early BP control
- Statin therapy
- RAASi

- PLEX

- Eculizumab

- Eculizumab weekly IV infusion 300-900mg IV , 2 weekly
- Very costly
- Meningococcal vaccination
- may be discontinued after remission
- relapse –resume anti-C5 therapy.

- No Eculizumab prophylaxis.
  - living donors to limit ischemia-reperfusion injury
  - Basiliximab, prednisone, high-dose MMF, Tac 30% dose for 1 month *Duineveld et al AJKD2017*

KDIGO Controversies Conference KI. 2017


MPGN

MPGN-

- **IC**
- **C3 glomerulopathy**
  - **DDD/C3GN**

Pre transplant testing

Secondary causes for IC-MPGN

Biopsy including EM to differentiate C3 GN or DDD

Genetic testing-CFH, CD46, CFI, C3, CFB, THBD, CFHR1, CFHR5, DGKE

Serology- C3 nephritic factors, FH autoantibodies, sMAC levels

Type of donor

if a genetic abnormality is found, the donor should be tested to exclude that genetic abnormality.

If the donor is found to carry the same genetic abnormality as the recipient, may not constitute an absolute contraindication to donation

each case should be evaluated on an individual basis as per family history and specific genetic abnormality.

Theoretical risks that donation may trigger disease onset must be discussed

Rx
Continue CNI+MMF+CS

IC-MPGN- Rule out secondary cause

- Urine Pr <3.5 g/d, N eGFR-RAASi
- U Pr - 1.5–3.5 g/d, abnormal KFT, active urine sediment CS 1 mg/kg x16 wks then taper
- RPRF, NS, crescentic GN- pulse IV MP, CYC, MMF

C3 GN/DDD in KT

- Rituximab?
- Eculizumab ?
- C defects-
- Plasma infusion
- PLEX?

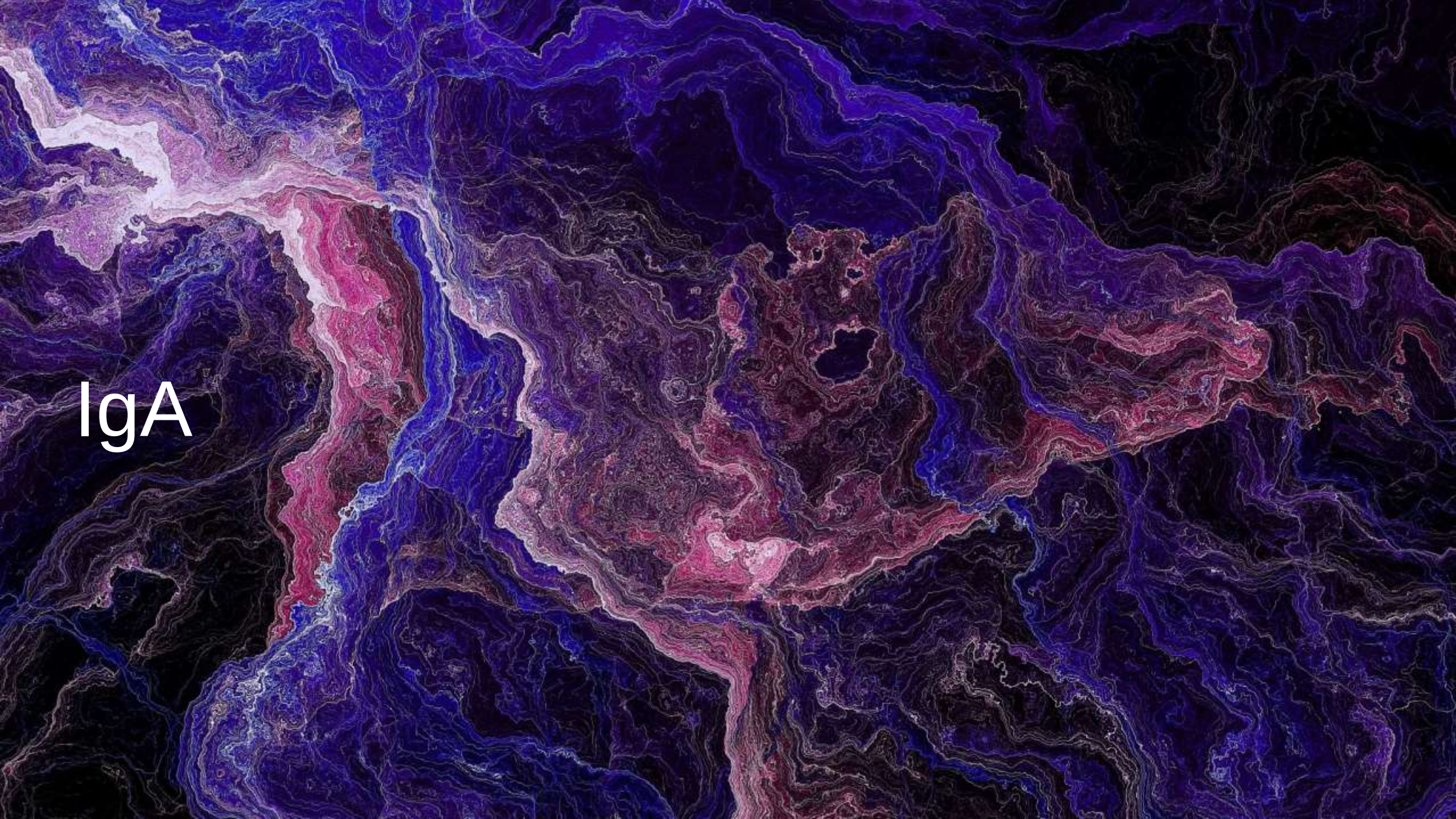
C3 GN

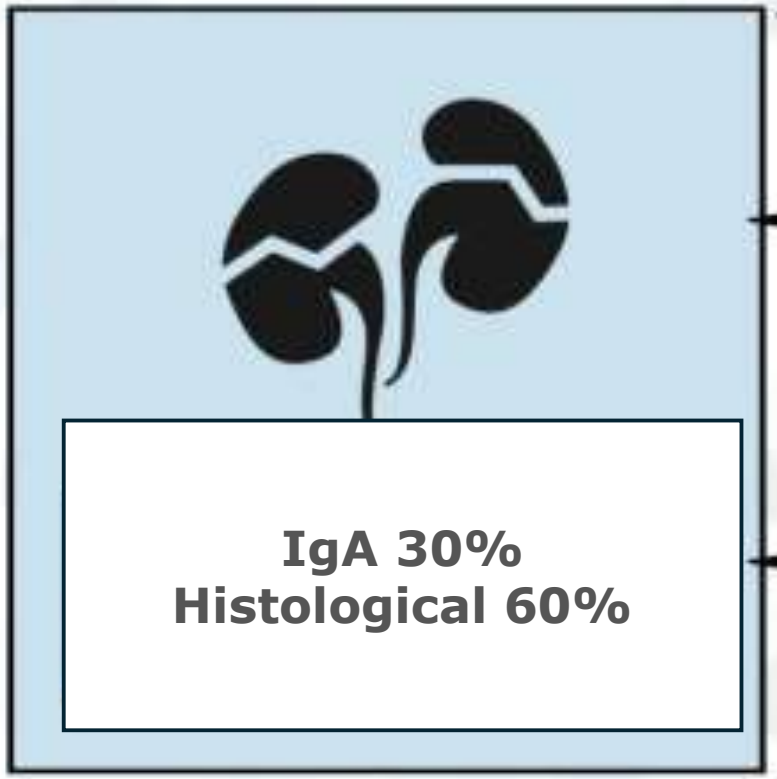
Outcomes

- Graft loss
  - No Rx-40%.
  - Eculizumab-33%
  - PLEX-42%
  - Ritux-81% for rituximab.

80% of C3G treated patients with elevated sMAC (alternate C3 pathway activation) respond to eculizumab

Gonzalez Suarez, et al Review. Medical sciences , 2020


IgA



IgA 30%
Histological 60%

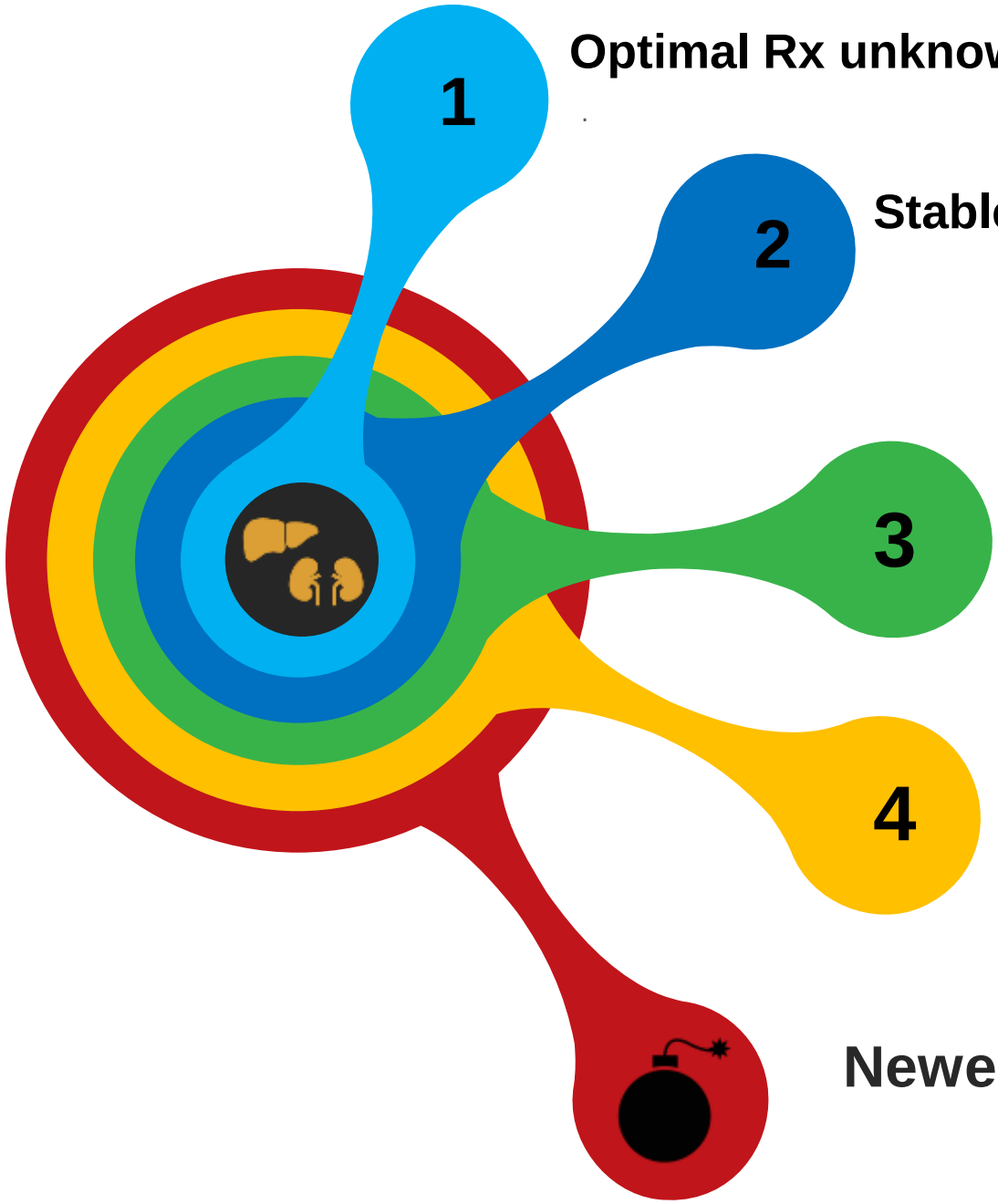
Increases with Tx vintage

Graft survival not affected in short term,
long term poor survival if IgA-r

Risk- RPRF, young, crescents, no ATG,
Steroid withdrawl – no effect (TANGO)

Gal def IgA Ab, Anti Glycan Ab,
CD89 – biomarkers
Donor- live or deceased

R-IgA Rx options



Optimal Rx unknown

Stable- RAASi, steroids

Rapid progression- CYC, Ritux

Role of Tonsillectomy ?

Newer drugs for IgA- no studies

MN

- Rare in children
- 30% progress to ESKD
- Recurrence may occur
- Risk factor for recurrence
  - Serum PLA2R Ab using IIF & ELISA
    - If high titer >45 RU/ml high risk
    - 1/3 with negative pretransplant PLA2R Ab – rMN
  - Donor SNP in between *HLA-DRB1* & *HLA-DQA1,* & 3 SNPs in *PLA2R1,* associated with post-Tx MN
- Rx of recurrence- RAASi, BP, IS- NS, RPRF eg CS, CNI, Rituximab, Bortezomib
- PLEX??

Congenital NS

- Check for cause- Genetics, Infection, TORCH
- Albumin, anticoagulation, infection prophylaxis, vaccination, Growth and Thyroid, specific Rx for infections
- ESKD- dialysis and transplant
- Recurrent nephrotic syndrome 25%
- Pre Transplant
  - Check genetics
    - Finnish children with NPHS1 with Fin-major/Fin-major genotype, Podocin
  - Anti NEP antibodies for congenital Membranous nephropathy
  - Biopsy if genetic testing negative
- Pre Tx
  - Role of nephrectomy U/L or B/L (WT1 mutation).
- Rx
  - cyclophosphamide instead of MMF or AZA for 3 months
  - , antinephrin antibody titres check, PLEX for 3 months
  - Re-Tx also possible

Lupus nephritis- Pearls for transplant

30% ESKD

Tx can be done NIH 1975

dsDNA need not be - for 6 months

IS is similar to other transplants

APLA positive and APLA syndrome

- Monitor APLA prior to Tx
- Only Ab present- Aspirin
- APLsyndrome- Anticoagulation

Rx recurrence- only histological – No Rx, graft dysfunction or proteinuria Rx

- Same IS intensified
- Change from AZA to MMF
- Give CYC instead of MMF or AZA
- Rituximab can be added to Triple IS- 21g 2 doses 15 days apart or 375mg/m2 for 4 wkly doses

Graft loss 3% @ 10 yrs

IMPORTANT POINTS

Pediatric GN important cause of ESKD

Recurrence may be seen more frequently in some

- FSGS, DDD,C3GN, aHUS

Assess Risk factors

Serology and genetics

Donor type

Pre transplant treatment

Post Tx- monitoring , upr, cr, antibodies , early biopsy including EM

Rx-

- RAASi, Triple IS, Statins
- MP, Ritux, Eculizumab (aHUS), CYC (IC MPGN), PLEX (FSGS, aHUS)


Thank You

Hypertension: Evaluation and Management

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Chennai, July 21, 2024

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School of Medicine

Primary Versus Secondary Hypertension

	Primary (Essential)	Secondary
Prevalence	More common	Uncommon
Patient Age	Older children	Younger children (Age < 6 years)
Risk factors	Obesity, family history, unhealthy diet, physical inactivity	Known condition associated with HTN in some cases
Severity of hypertension	Generally mild increase in BP or stage 1 HTN	More severe
Systolic versus Diastolic BP	Mostly systolic, particularly daytime	Systolic as well as diastolic

Diagnosis of Primary Versus Secondary HTN

Primary hypertension is a diagnosis of exclusion

- Good medical history for risk factors or an underlying disease.
- Thorough physical examination- femoral pulsus, birth marks, fundus examination etc.
- Appropriate investigations

Laboratory Evaluation

All Patients

1. Urinalysis
2. Blood chemistry
3. CBC
4. Renal ultrasound examination
5. Echocardiogram

Obese patients (BMI >95th percentile)

1. A1c
2. ALT/AST
3. Fasting lipid profile

Laboratory Evaluation

Additional investigations in selected patients

1. Renin/Aldosterone
2. Urinary catecholamine
3. TSH
4. Serum cortisol
5. Drug screen
6. Sleep study
7. Renal angiography- gold standard for RAS

17-year-old Male with Recent Onset Hypertension

Previously healthy, asymptomatic, competitive swimmer with BP 150-160/ 75-90 mm Hg and normal examination.

Blood Tests

- Blood chemistry: Sodium 143 mEq/L, Potassium 4.1 mEq/L, Chloride 102 mEq/L, **CO2 32.6 mEq/L,** Creatinine 0.9 mg/dL, (Ca, Mg, Po4, uric acid LFT all normal)
- CBC: Normal

Urinalysis: Normal

RBUS and Doppler flow: Normal

Echocardiogram: Normal

Started on antihypertensive medication

17-year-old Male with Recent Onset Hypertension

Additional Workup

- Blood tests
  - Serum renin: 12.3
  - Serum aldosterone: 43

Renal Imaging

- DMSA renal scan: Normal
- Renal angiography: Normal except for two renal arteries (anterior/posterior) both kidneys

Renal Vein Renin Levels

Right renal vein	6.1
Left renal vein	8.4
IVC above RV	9.5
IVC below RV	4.5

17-year-old Male with Recent Onset Hypertension

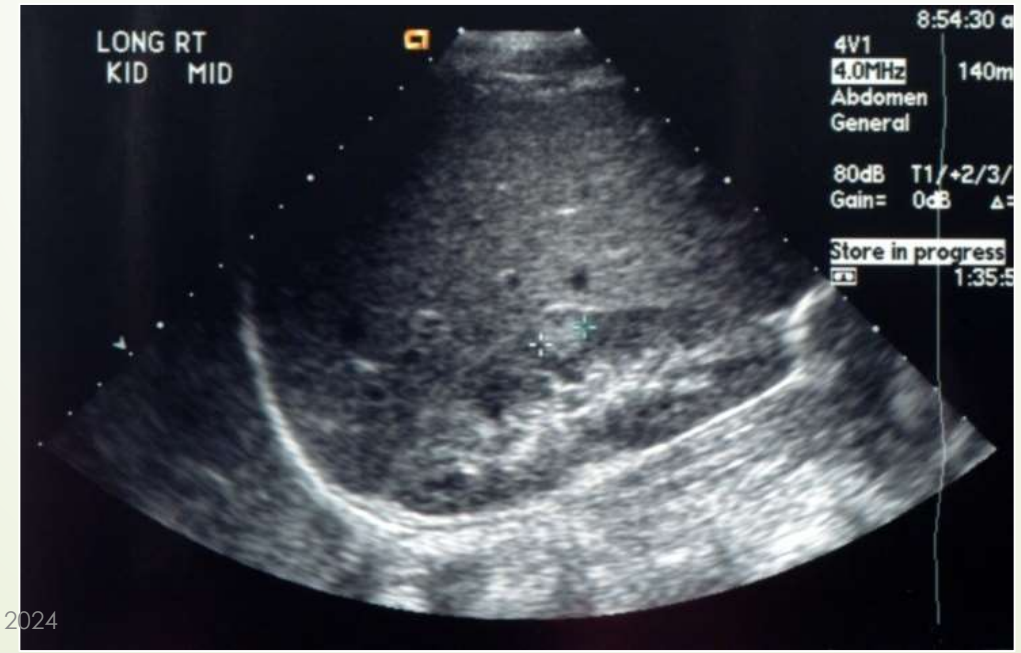
Follow-up Three Months Later

- Repeat Blood chemistry: Sodium 139 mEq/L, Potassium 3.9 mEq/L, Chloride 99 mEq/L, **CO2 31 mEq/L**, Creatinine 0.9 mg/dL, (Ca, Mg, Po4, uric acid LFT all normal)

- Urine chloride: **149 mEq/L**

17-year-old Male with Recent Onset Hypertension

Repeat renal ultrasound Examination
1.0 cm solid appearing mass in the lateral aspect of the right mid kidney



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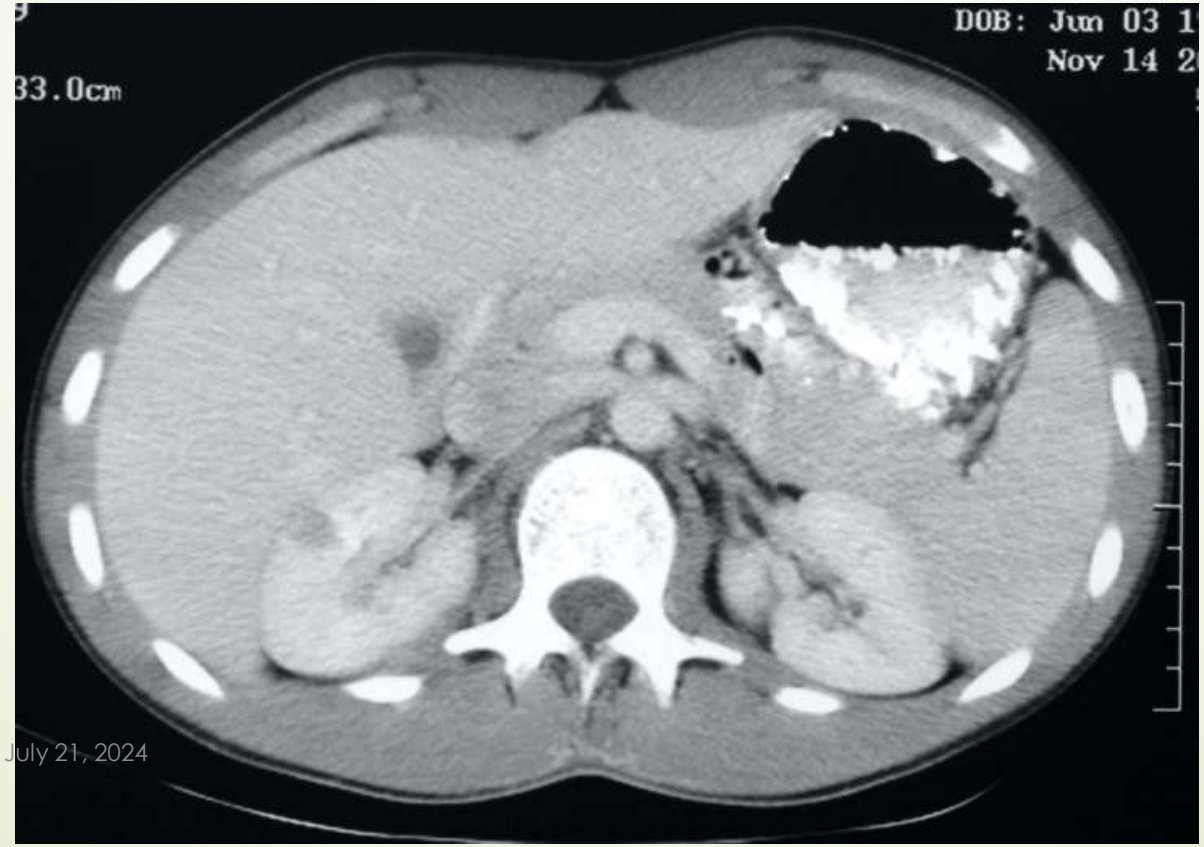
17-year-old Male with Recent Onset Hypertension

CT Scan of Kidneys

1.2 cm hypodense mass in mid lateral portion of Right Kidney



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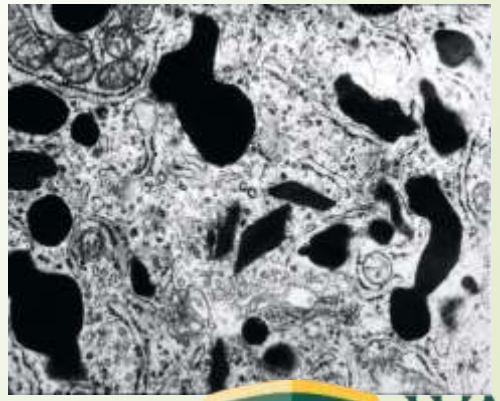
17-year-old Male with Recent Onset Hypertension

Tumor was resected

<u>Electron micrograph</u>

- Round and rhomboidal secretory granules- typical of renin- producing juxtaglomerular cells



10-year-old Female With Recurrent Headache and HTN

Valentini et al Pediatr Nephrol. 2005; 20:1192-1194

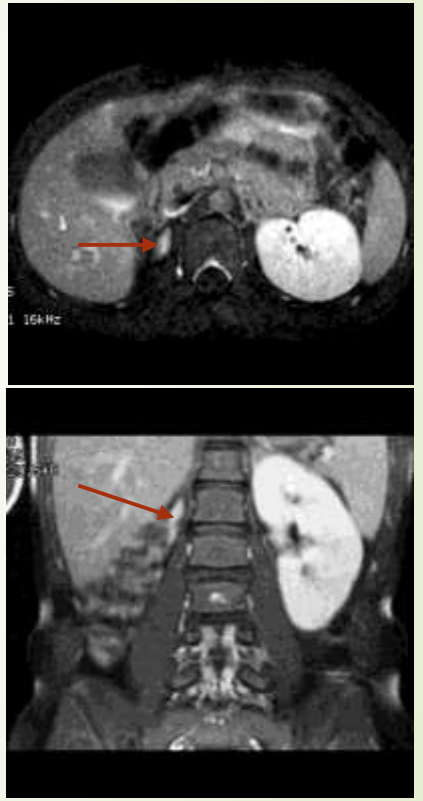
- Urinalysis: Normal
- Blood chemistry: Normal
- CBC: Normal
- Renal US: Absent R kidney
- DMA renal scan: Normal L and absent R kidney

10-year-old Female With Recurrent Headache

MR Angiography (MRA)

No renal artery stenosis in the left kidney

A very small kidney on the right side, the removal of which resolved HTN

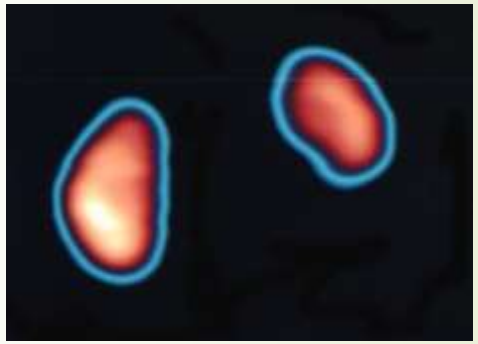


2-Month-old Baby with HTN

Mustafa AE et al Pediatric Radiology 2005; Dec 3: 1-4

INVESTIGATIONS

- Blood tests
  - Urinalysis: Normal
  - Blood chemistry: Normal
  - CBC: Normal
  - Renin: Normal
  - Aldosterone: **>120 (N=1-31)**

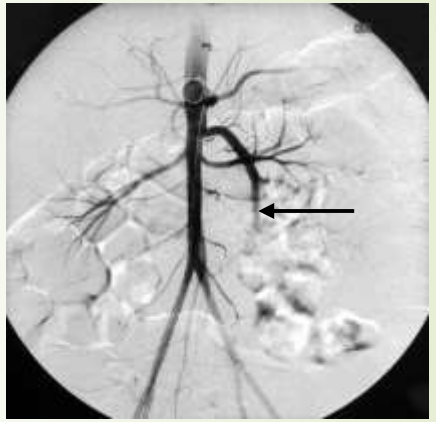


- Echocardiogram: **Moderate LVH**
- Renal US and Doppler: **Small left kidney, normal flow**
- DMSA renal scan: **Small left kidney; differential uptake 63% RK and 37% LK**

2-Month-old Baby with HTN

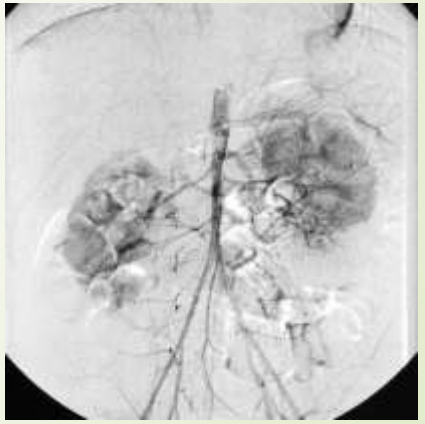
Renal Arteriogram

Severe stenosis of the branch to the lower pole arising from the mid-portion of the left main renal artery



Renal vein renin

No significant difference on the two sides.



Procedure

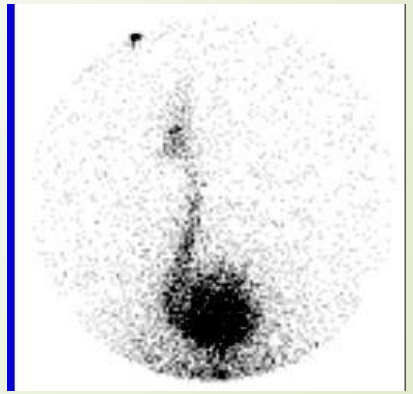
Left partial nephrectomy resolved HTN

15-year-old Female with Recently Diagnosed Hypertension

History of UTIs in childhood

Investigations

- Blood chemistry: Normal
- CBC: Normal
- Urinalysis: Normal
- Renal ultrasound: **Slightly smaller LK**
- DMSA renal scan: **Bilateral renal scarring, L > R**
- VCUG: **Left intrarenal VUR**



15-year-old Female with Recently Diagnosed Hypertension

Diagnosis

Reflux nephropathy

Management

Ureteral reimplantation

BP controlled with ACEI

DMSA Renal Scan for evaluation of hypertension in children

Maheen et al. Pediatr Nephrol (2008) 23:435–438)

- Renal scars found in 21% (33/159) of otherwise healthy children who were evaluated for newly diagnosed hypertension.
- 22 patients had unilateral and 11 had bilateral scarring.

Five-Year-Old Male with Hypertension

Congenital hydrocephalus due to aqueductal stenosis s/p VP shunt after birth. Also had vein of Galen malformation with recurrent venous aneurysm requiring embolization at age 4 years.

1. Developmental delay
2. Seizure disorder
3. Hyponatremia, which has been attributed to cerebral salt wasting (Being treated with sodium chloride)
4. Increased BP

Five-Year-Old Male with Hypertension

	March 2021
Blood pressure	116/78
Daily sodium chloride supplements	Nacl (4 mEq/mL,18 mL BID) (8.4 Gm/Nacl/3.25 Gm Na/day).
Polyuria and polydipsia	Drinking more than ten 10 oz bottles/day with frequent urine output (8 weight diapers/day) and a soaked diaper overnight.
Sleep disorder	• Clonidine 0.5 mg/daily • Melatonin and Benadryl before going to bed.
Seizures	Gabapentin, and Keppra.
Blood chemistry	Na 139, K 3.2, Cl 108, CO2 24.

Nacl supplements gradually decreased and eventually discontinued in May 2021

Five-Year-Old Male with Hypertension

	March 2021	September 2021 to July 2023
Blood pressure	116/78	87/62
Daily sodium chloride supplements	Nacl (4 mEq/mL,18 mL BID) = 8.4 Gm/Nacl and 3.25 Gm Na/day).	None
Polyuria and polydipsia	Drinking more than ten 10 oz bottles/day with frequent urine output (8 weight diapers/day) and a soaked diaper overnight.	Normal fluid intake/ dry nighttime
Sleep disorder	• Clonidine 0.5 mg/daily • Melatonin and Benadryl before going to bed.	Discontinued
Seizures	Gabapentin and Keppra.	No seizures for at least a couple of years, continues on Keppra
Blood chemistry	Na 139, K 3.2, Cl 108, CO2 24.	Na 136, K 4.3, Cl 104, CO2 25

Treatment of Hypertension

Elevated BP	Dietary advice, exercise, weight control, obesity/sleep apnea management. No medication unless CKD, DM, LVH, or heart failure
Stage 1 HTN	+ Initiate medication if failed non-pharmacologic management or LVH is present.
Stage 2 HTN	+ Initiate medication

Medications

Antihypertensive drug	Advantage
Thiazide diuretics	Cheap
	Enhances effectiveness of other agents
Vasodilators	Cheap
	Effective in severe HTN (Minoxidil>Hydralazine)
Alpha-blockers	No decrease in cardiac output
	Improves insulin sensitivity
	No alteration in blood lipids
	No sedation
Beta-blockers	Reduce manifestations of anxiety
	Reduce the risk of recurrence of cardiac disease
Calcium antagonists	No CNS side effects
	Coronary vasodilation
ACE inhibitors/ARB	No CNS side effects
	Renoprotective / Antiproteinuric
Centrally acting agents	No alteration in blood lipids
	No fluid retention
	Transdermal Therapeutics system (Catapress TTS)

Which Medication to Use?

- A simple regimen increases compliance (single medication, number of pills, frequency of intake).
- Family familiarity with the medication is helpful
- Add second medication (preferably thiazide) if BP is not well controlled with the maximum dose of the current medication.
- It is more important to know which medication **NOT** use in a particular patient.

Commonest Antihypertensive Drugs in children in the U.S.

Calcium Antagonists
&
ACE inhibitors

(Thiazide diuretic)

Treatment Objective

Normalize the blood pressure

Hypertensive Urgency

↓

A severe elevation in BP without severe symptoms or evidence of acute target organ damage

Outpatient management

Hypertensive Emergency

↓

A severe symptomatic elevation in BP with evidence of acute target organ damage

(Brain, kidneys, eyes, and heart)

Inpatient management preferably with IV medication

Summary

- Primary hypertension is a diagnosis of exclusion.
- The probability of secondary hypertension increases in younger patients and those with CAKUT.
- A thorough history and physical examination are essential for diagnosis.
- Most patients with hypertension require only a basic workup. Subtle changes in serum K+ and/or CO2 should not be ignored.
- Plasma renin, aldosterone, catecholamine, and renal vein renin levels should be interpreted with caution.
- Counseling for lifestyle changes benefits everyone.
- A simpler medication regimen aids in patient and family compliance.
- The treatment objective should be to normalize blood pressure.

Thanks

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Chennai, July 21, 2024

WAYNE STATE
School of Medicine

11-year-old Male with Severe HTN

Known History of Multiple Polyposis

Blood Tests

- Blood chemistry: Sodium 140 mEq/L, Potassium **K 2.5 mEq/L**, Chloride 98 mEq/L, **CO2 33 mEq/L**, Creatinine 0.7mg/dL,
- CBC: Normal
- Urinalysis: Normal
- RBUS and Doppler flow: Normal
- Echocardiogram: Normal

11-year-old Male with Severe HTN

Known History of Multiple Polyposis

Blood Tests

- Blood chemistry: Sodium 140 mEq/L, Potassium **K 2.5 mEq/L**, Chloride 98 mEq/L, **CO2 33 mEq/L**, Creatinine 0.7mg/dL,
- CBC: Normal
- Urinalysis: Normal
- RBUS and Doppler flow: Normal
- Echocardiogram: Normal

Urine chloride: 64 mEq/L

11-year-old Male Severe HTN

Known History of Multiple Polyposis

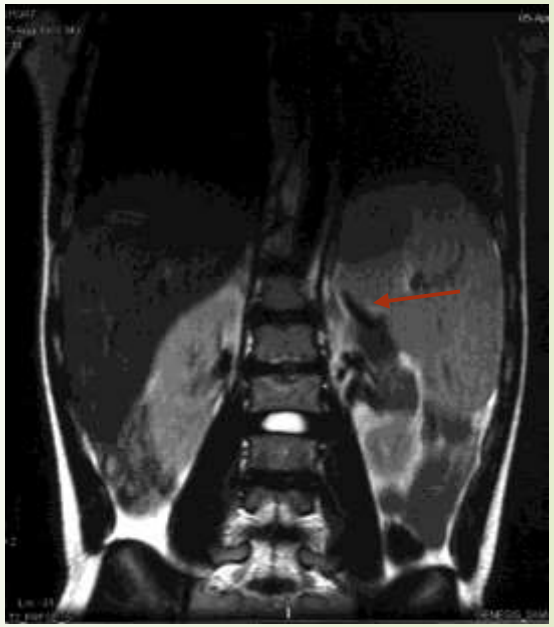
Further Investigations:

- Blood:

  Serum renin: Low normal

  Serum Aldosterone: **High**

- MRI Abdomen: Hypointense oval mass in the left adrenal gland (9 x 5 x 8 mm)



- Biopsy: Adrenal adenoma (Aldosterone secreting adenoma)