Tailoring the best peritoneal dialysis care in children in acute setting

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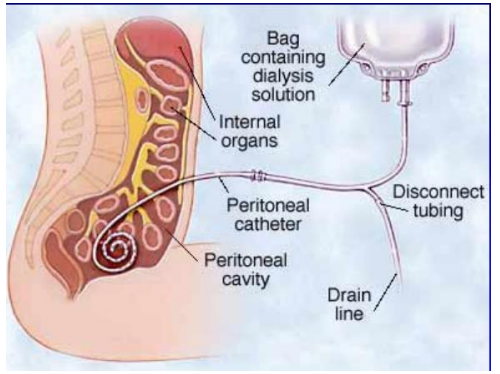
Objectives

- Introduction
- Principles of dialysis
- How to write basic prescription of Acute PD
- Case scenario I – Oliguirc AKI with need for extra fluid replacement
- Case scenario II – ALF with lactic acidosis, hyperammonemia & AKI
- Case scenario III – Acute pulmonary edema & Hyperkalemia
- Case scenario IV – Hypernatremic Dehydration with AKI

Introduction



Peritoneal dialysis:

- A common modality for solute & fluid removal in children with renal dysfunction.

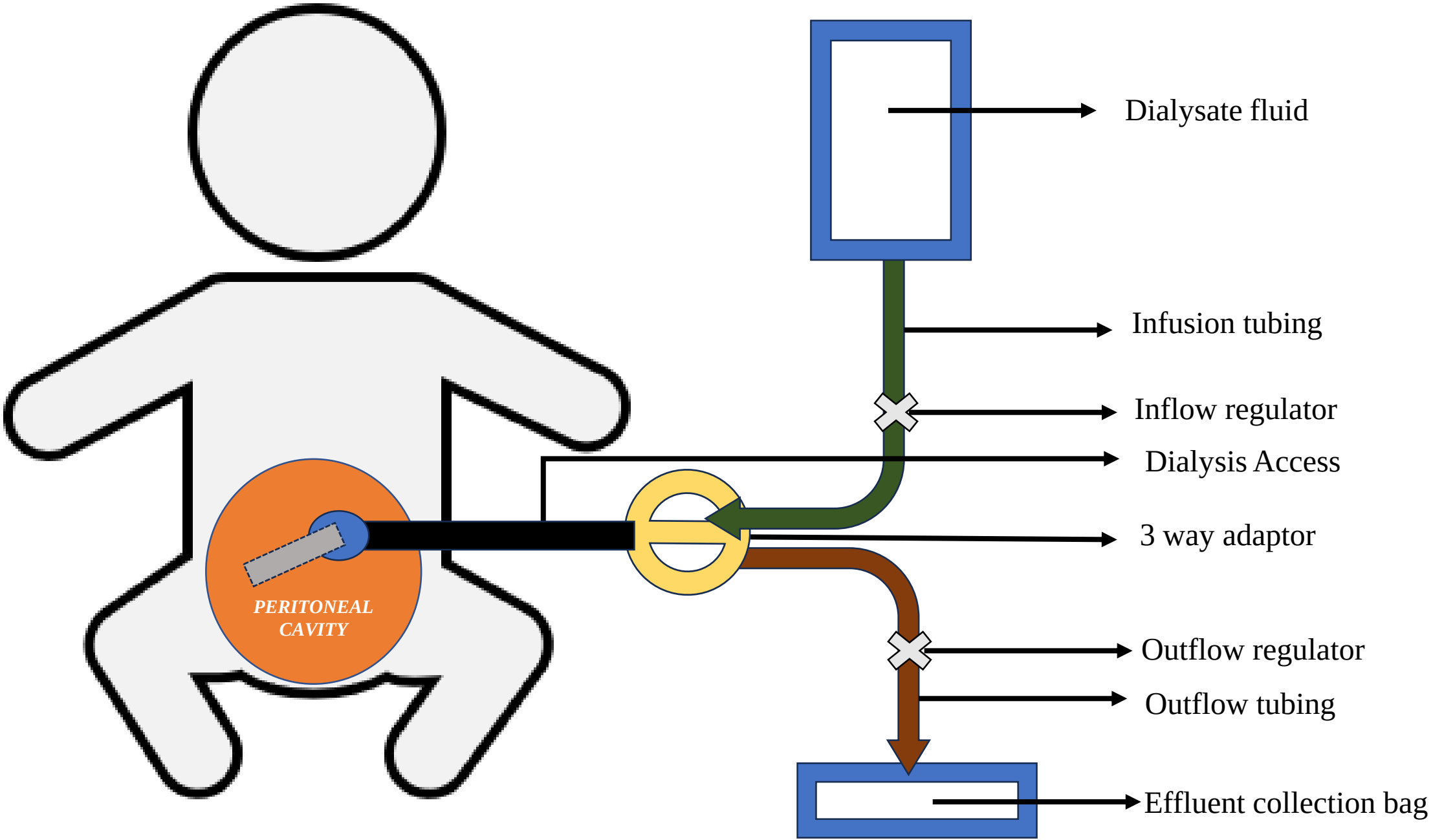
Functioning of PD is based on the transport of fluid & solute happens b/w the 2 compartments

- The blood in the peritoneal capillaries
- Dialysis solution in the peritoneal cavity.

The vascularized peritoneum serves as the semipermeable dialysis membrane separating the 2 compartments.

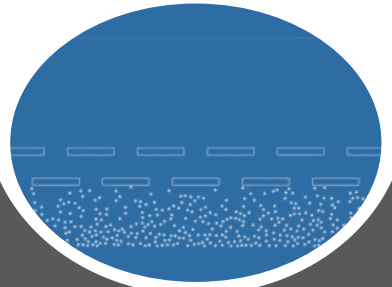
Solute removal in dialysis – ***clearance*** & Fluid removal - ***ultrafiltration***

Peritoneal Dialysis Functioning System



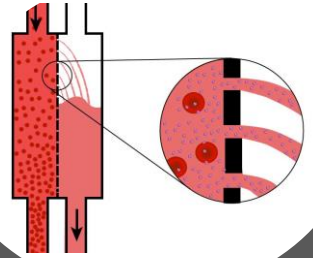
Principles of Peritoneal dialysis

Diffusion



Movement of solutes along the ***concentration gradient***, from area of high concentration (blood in peritoneal capillaries) to low concentration (PD fluid in peritoneal cavity.

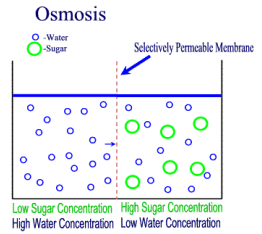
Convection



Movement of solute along with the water from blood to PD fluid

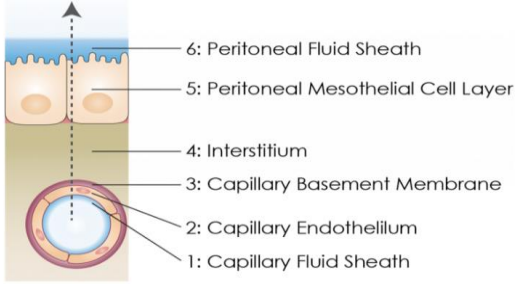
Solvent drag - Hydrostatic pressure forces molecules across the semipermeable membrane

Osmosis



Movement of water along the ***osmotic gradient,*** from low osmolality (blood in peritoneal capillaries) to high osmolality (PD fluid with high dextrose concentration)

Factors affecting Diffusion



Concentration gradient: Higher the concentration gradient of the solute, better will be the diffusion.

Gradient will be highest in the peritoneal blood at the start of the PD dwell, where maximum exchange of solutes occurs, which then diminishes gradually.

Effective peritoneal surface area: Maximal the dwell volume, better will be the diffusion.

Dwell volume of 30ml/kg or 1100 ml/m^2, brings more dialysate in contact with peritoneum, thus increasing the effective peritoneal surface area for dialysis

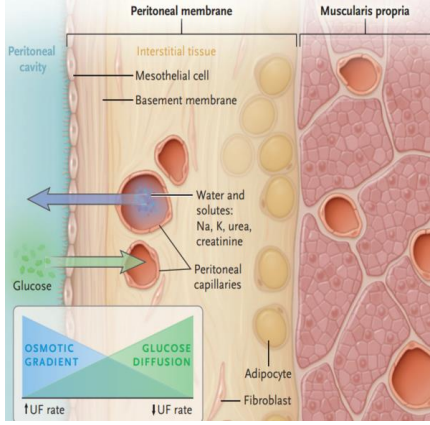
Molecular weight of the solute:

Substances with low molecular weight diffuses rapidly as compared to substances with higher molecular weight

Peritoneal blood flow: better peritoneal blood flow, better will be the diffusion.

Vasoactive agents and even peritonitis recruits more peritoneal capillaries and enhances diffusive clearance.

Factors affecting Osmosis



Concentration gradient of the osmotic agent: Higher the concentration gradient, better will be UF.

Higher the concentration of the osmotic agent (glucose) in the dialysate, more gradient is established and thus more ultrafiltration occurs. Frequent exchanges maximize the concentration gradient.

Effective peritoneal surface area: Maximal the dwell volume, better will be the ultrafiltration.

Dwell volume of 30ml/kg or 1100 ml/m^2, brings more dialysate in contact with peritoneum, thus increasing the effective peritoneal surface area for dialysis

Peritoneal blood flow: better peritoneal blood flow, better will be the diffusion.

Better peritoneal blood flow increases the hydrostatic pressure gradient b/w the compartments, enabling better ultrafiltration & convection.

Components of basic acute PD prescription

Indication for dialysis	Renal /Non renal indications
Dialysis Access:	Soft PD catheters / Rigid PD catheters / Improvised catheters
Dialysate fluid:	Lactate buffered electrolyte balanced fluid with variable dextrose concentration
Dwell volume:	Initial fill volume - 10-20 ml/kg; Maximum fill volume – 30-40 ml/kg or 1100 ml/m^2
Cycle Time: exchange time is usually 1 hour / cycle	• Fill Time:10 minutes • Dwell Time: 30 minutes • Drain time: 20 minutes • Dwell time 1-4 hours in continuous PD using flexible catheter
Target Ultrafiltrate/cycle:	Determined by the hemodynamic status & CFO – target UF/day < 5% of body wt.
Additives:	Potassium 3-4 mmol/L if serum potassium less than 4mEq/L Heparin 500-1000 U/L
Monitoring:	Fluid balance q 4- 6 hours, Serum electrolytes q 6 – 12 hours, Blood sugar q 6 -12 hours, Blood urea and serum creatinine q 24 hours

Goal oriented approach

What is the removal needed?

- Solute only
- Fluid only
- Both solute & Fluids

What kind of solute?

- Small molecules
- Middle molecules
- Large molecules

What is the fluid plan?

- Target intake & negative balance /day

What is the rapidity of removal needed?

- Rapid removal of solute
- Rapid removal of Fluid

What are all the other comorbidities which will influence your PD prescription?

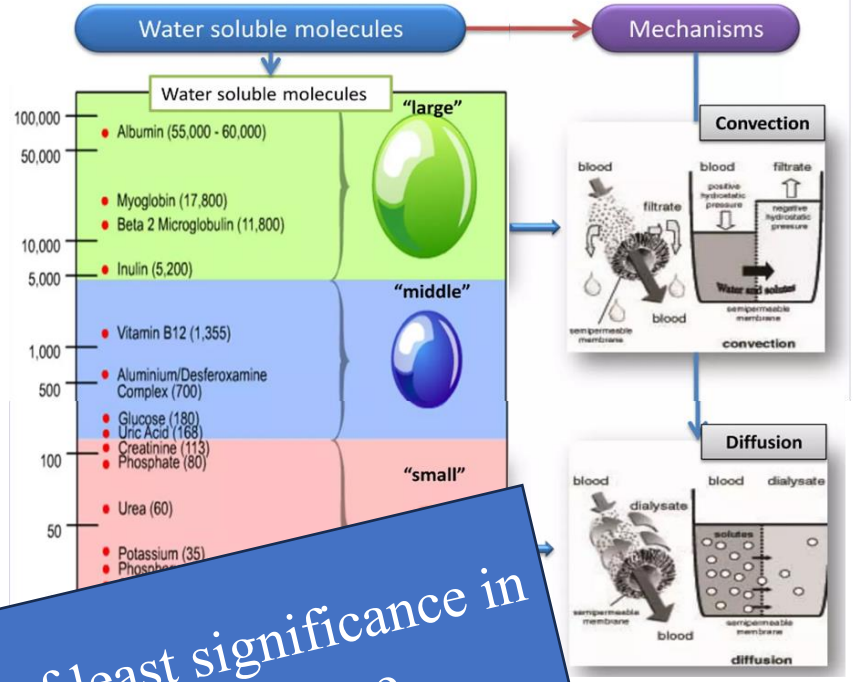
- Coagulopathy
- Hemodynamic instability
- Respiratory status
- Pre existing electrolyte disturbances
- Systemic illness

What kind of removal needed?

- Depends upon the underlying indication for starting dialysis.

Kind of removal required	**Common clinical indications**	**Strategy required**
Both solute clearance & ultrafiltration	Oligo-anuric AKI with • Severe fluid overload • Treatment-recalcitrant dyselectrolytemia & acidosis • Symptomatic uremia	• Regular dialysis with targeted fluid removal
Only ultrafiltration	Need to give extra fluids / blood products especially in the setting of Third space losing conditions	Regular dialysis with targeted fluid removal with ***frequent replacement of solutes***
Only solute clearance	• Intoxication (salicylates, ethylene glycol, methanol, isopropanol, metformin, valproic acid, lithium) • Severe hyperammonemia > 400 • Hypercatabolic states	Dialysis plan depending upon the nature of solute with ***fluid replacement to target nil Ultrafiltration***

What kind of solute to be removed?



Solute removal depends on:

- **The size of the solute:**
  - Smaller the solute, rapid is the diffusion
- **Dosage of dialysis:**
  - More frequent the cycles, bett
- **Nature of the**

membrane surface area , better

ection & large molecule clearance

In general, the middle molecule & large molecule clearance is of least significance in acute PD setting as they require long dwell cycles for effective clearance

Peritoneal dialysis in common settings like life threatening hyperkalemia, hyperammonemia requires ***short duration, more frequent cycles for better clearance.***

What is the fluid plan?

- The most difficult & unpredictable component to be decide….

With pre existing CFO:

- In a oligoanuric child, Target UF: Total Fluid intake per day + 10% of CFO volume
- In non-oliguric child, Target UF: (Total Fluid intake per day + 10% CFO volume) – (U/O)

Without pre existing CFO:

- In a oligoanuric child, Target UF: Total Fluid intake per day
- In non-oliguric child, Target UF: Total Fluid intake per day – urine output

The ultrafiltrate volume plan should be reassessed frequently and adjusted accordingly (ideally q4th hrly)

What is the rapidity of removal needed?

Rapid removal of solute:

- Shorter dwell time will maintain the concentration gradient & prevent the back-leakage of solutes into the blood.
- Frequent cycles enhances the total clearance of the solute.

Rapid removal of Fluid:

- High dextrose containing dialysates.
- Shorter dwell time
- Large dwell volume

2.5 % dextrose containing dialysate can be prepared by adding 25% Dextrose 35 ml to 965 ml of regular 1.7% PD fluid

Patient Comorbidity status

- **Coagulopathy**
  - # Soft catheter better than rigid catheters, FFP transfusion prior to catheter insertion.
  - # Intraperitoneal heparin isnot contraindicated
- **Systemic illness**
  - # Acute Liver failure / Severe Lactic acidosis: Bicarbonate based dialysate
- **Pre existing dyselectrolytemia**
  - # In the setting of Hypo/hypernatremia, where dialysate Na concentration to be adjusted so that the serum-dialysate Na gradient to be ~10-12 mEq/l
- **Respiratory status**
  - # Small volume dwells to reduce intra abdominal pressure
- **Hemodynamic instability**
  - # Nil UF for first few hours and then to be adjusted according to tolerance

Case Scenarios

Case scenario 1

- 22 months old girl baby presented with multiple episodes of diarrhea for a day. On examination
  - She was in hypotensive shock
- Received fluid boluses (30 ml/kg), intubated and started on ionotropic support
- Anuric for 2hours
- Length 85cm, wt 10 kg
- BUN -158 mg/dL, Creatinine-3.1mg/dL,
- Na^+-133 mEq/L, K^+- 3.2 mEq/L, $HCO3^-$ 4 mEq/L
- CBC – TC 28000; DC: 82%;L28%
- Prolonged INR (2.5)

Multi organ dysfunction syndrome

AKI – multifactorial cause

- Sepsis
- Dehydration

PD prescription Plan

Indication for dialysis	Oligoanuric AKI with need for extra fluid replacement & solute removal
Dialysis Access:	Soft PD catheter or Rigid PD catheter inserted under FFP cover
Dialysate fluid:	1.7% dextrose containing lactate based dialysate
Dwell volume:	200 ml /dwell
Cycle Time: exchange time : 1 hour / cycle	• Fill Time:10 minutes • Dwell Time: 30 minutes • Drain time: 20 minutes
Target Ultrafiltrate/cycle:	Estimated TFI: 1700 ml ; Target UF 40 ml/cycle
Additives:	Potassium 4 mmol/L Heparin 500 U/L
Monitoring:	Fluid balance q 4- 6 hours, Serum electrolytes q 6 – 12 hours, Blood sugar q 6 -12 hours, Blood urea and serum creatinine q 24 hours

Case 2

- 4 months old boy (wt 4.5 kg) presented with fever, vomiting and jaundice for 1 week, for which treated with native medications. He also had an episode of seizures.
- On examination
  - He had acidotic breathing, shock – fluid refractory
  - Urine output: 0.7 ml/kg/hr
- BUN -58 mg/dL, Creatinine-1.1mg/dL,
- Ammonia: 520 mcg/dl; AST/ALT: 1350/2450; Sr.bilirubin T/D : 3.2/1.3
- Na^+-143 mEq/L, K^+- 3.2 mEq/L, pH: 7.2, $HCO3^-$ 4 mEq/L, lactate 10
- CBC – TC 28000; DC: 82%;L28%, Plt: 35,000, Hb: 7.5
- Prolonged INR (3.5)

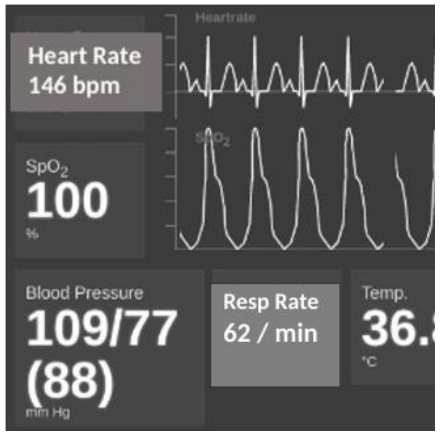
Fulminant hepatic failure with hyperammonemia / hepatic encephalopathy / Shock / AKI

PD prescription Plan

Indication for dialysis	Hyperammonemia with encephalopathy / AKI- oliguric – requiring both solute & fluid removal
Target Solute clearance	Ammonia – small molecule, rapid clearance for encephalopathy,
Ultrafiltration	No volume overload, Slow removal, zero balance required
Target Ultrafiltrate/cycle:	TFI: 500 ml (70% maintanence + blood products), UF: negative by 425 ml/24 hours (TFI-U/O)
Cycle Time: exchange time : 30 mins / cycle	• Fill Time:5 minutes • Dwell Time: 20 minutes • Drain time: 5 minutes, for the first 6 hours and repeat Ammonia
Dialysate– bicarb based (Na140 meq/l, HCO_3 -30 meq/l, & Dextrose 1.5%)	**prepare solution A: 440 ml of 5 % dextrose + 60 ml of $NaHCO_3$** **prepare solution B: 500 ml of normal saline** **Final dialysate: solution A 250 ml + solution B 500 ml**
Additives:	Potassium 4 mEq/L & Heparin 500 U/L
Monitoring:	Fluid balance q 4- 6 hours, Serum electrolytes q 6 – 12 hours, Blood sugar q 6 -12 hours, Blood urea and serum creatinine q 24 hours

Case 3

- A 11 months old boy weighing 7.5 kg, presented with the c/o bloody stools, vomiting, low grade fever followed by oliguria. He was diagnosed to have Hemolytic Uremic syndrome with severe AKI. He was managed with FFP transfusions initially and also received 2 units PRBC transfusion for severe anemia.
- On day 3 of admission, the status of the child is as follows:
  - Current weight: 8.5kg, pulmonary edema +.
  - U/O: 0.4 ml/kg/hr; CFB since admission: 1350 ml / 300 ml (FO: 14%)
- TLC / Hb / Plt: 13,000 / 5.7 / 21,000; PS: 4.8% schistocytes; LDH: 1350
- Urea / Creatinine: 122 / 2.5; Na / K / Cl: 142 / 7.2 / 108
- After Inj.Calcium gluconate / Glucose insulin infusion /K binder → K:6.8



aHUS/ AKI with volume overload /refractory Hyperkalemia

PD prescription Plan

Indication for dialysis	Oliguric AKI, Acute volume overload, Refractory hyperkalemia
Target Solute clearance	Potassium – small molecule, rapid clearance for life threatening ECG changes
Ultrafiltration	Rapid fluid removal for pulmonary edema
Target Ultrafiltrate/cycle:	TFI: 300 ml (AKI regime maintanence + blood products), UF: negative by 375 ml/24 hours (TFI + 5 % BW)
Cycle Time: exchange time : 30 mins / cycle	• Fill Time:5 minutes • Dwell Time: 20 minutes • Drain time: 5 minutes, for the first 6 hours and repeat Potassium
Dialysate– high dextrose containing	**Initially 2.5% dextrose containing fluid *(25% Dextrose 35 ml to 965 ml of regular 1.7% PD fluid)* for 1-2 hours followed by 1.7% dextorse containing fluid**
Additives:	**No Inj.KCl for 4 hours → Repeat K^+ & decide on adding KCl &** Heparin 500 U/L
Monitoring:	Fluid balance q hrly, Serum K^+ after 2 hrs and then q 6th hourly, Blood sugar q 6 -12 hours, Blood urea and serum creatinine q 24 hours

Case 4

- A 2.5 months old male child, previously healthy, with birth wt: 2.7 kg, no antenatal / perinatal / postnatal complications presented with
  - c/o loose stools for 4 days
  - c/o fever for 2 days
  - c/o no urine output & irritable cry for past 10 hrs.
- 1 week before, the documented weight was 4 kg and admission weight : 3.5 kg.
- O/E: signs of severe dehydration +.
- Investigations: Na/K/Cl: 187/5.7/137; Urea/Creat: 189/2.1; pH:7.02, Lactate: 5.6, HCO3- 10.6
- After 6 hours of rehydration fluid therapy, Na/K/Cl: 186/5.3/134, Urine output: 0.2 ml/kg/hr

Hypernatremic dehydration with oligoanuric AKI

PD prescription Plan

Indication for dialysis	Oligoanuric AKI with Need for large volume replacement, Refractory hypernatremia.
Target Solute clearance	Sodium – small molecule, slow clearance to prevent cerebral edema
Ultrafiltration	Needed for space creation to give replacement fluids
Target Ultrafiltrate/cycle:	TFI: 23.2 ml/hr for next 72 hrs (total water deficit + maintanence for 3 days) UF: negative by 550 ml/24 hours (TFI)
Cycle Time: exchange time : 60 mins / cycle	• Fill Time: 5 minutes • Dwell Time: 40 minutes • Drain time: 15 minutes, for the first 6 hours and repeat Sodium
Dialysate– high Na^+ containing	**Increase the [Na] content in PD fluid so that [Na] gradient will be 5-10 mEq/l** ***Amount of [Na] to be added [mEq] = V*(desired [Na] - initial [Na]),*** ***V: volume of PD bag***
Additives:	**No Inj.KCl for 4 hours → Repeat K^+ & decide on adding KCl &** Heparin 500 U/L
Monitoring:	Fluid balance q hrly, Serum Na^+ after 2 hrs and then q 6th hourly, Blood sugar q 6 - 12 hours, Blood urea and serum creatinine q 24 hours

Key messages

- Peritoneal dialysis is a effective modality of RRT in resource limited setting.
- Goal oriented approach will be helpful in enhancing the efficacy of peritoneal dialysis.
- Solute removal can be improved by increasing the dosage of dialysis (short duration, frequent exchanges).
- Fluid removal can be improved by increasing the osmotic content of the dialysate and by increasing the dwell volume.

Thank You

Bed wetting in a Teenager- an approach

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OUTLINE

- Introduction
- Physiology
- Etiology- types
- Pathophysiology
- Other Voiding disorders
- Management
- Approach

INTRODUCTION

- Voiding disorders are common in children

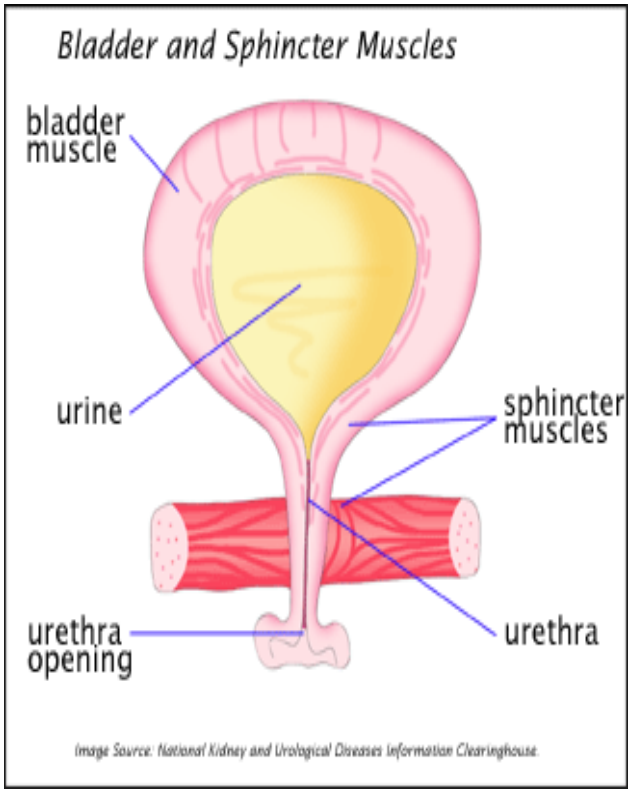
- It is important to identify conditions which are
  - -non pathological
  - -self limiting
  - -unassociated with functional or anatomical abnormalities

- These generally need
  - - reassurance
  - - training in bladder control voiding patterns
  - - limited need for drug therapy

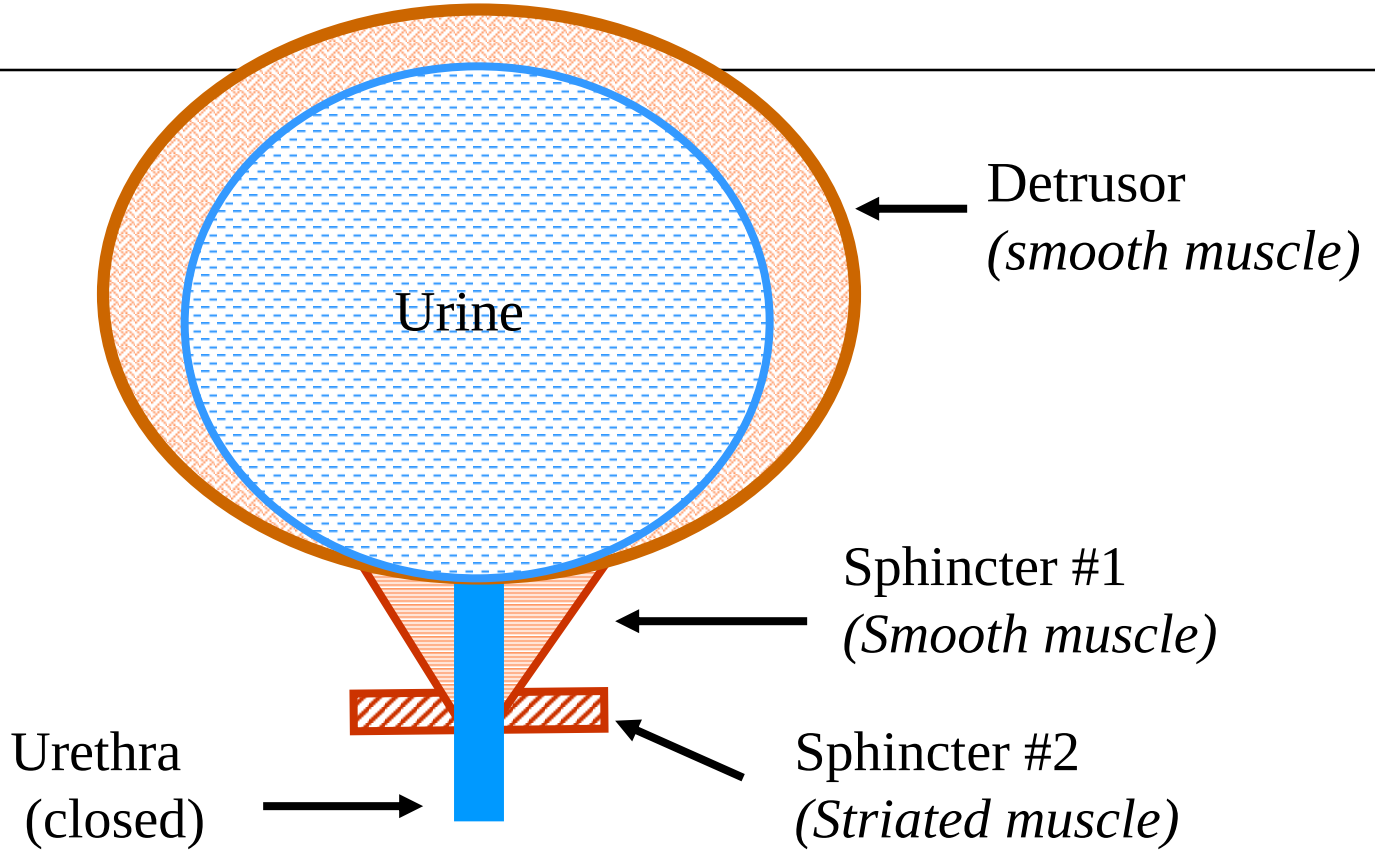
PHYSIOLOGY

- Lower urinary tract has 2 primary functions related to transport of urine
  - adequate storage
  - efficient emptying

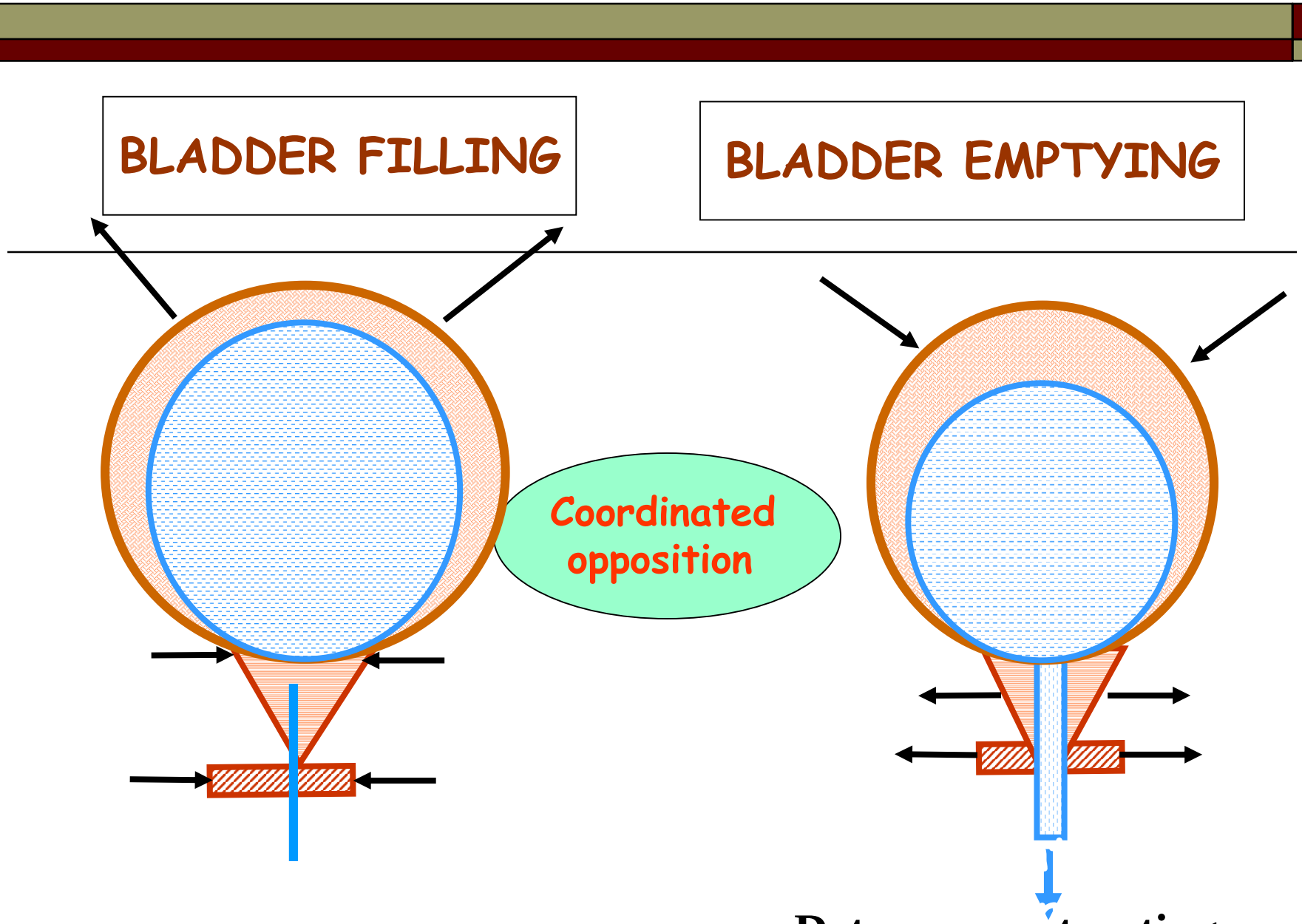
- Both work in coordinated manner



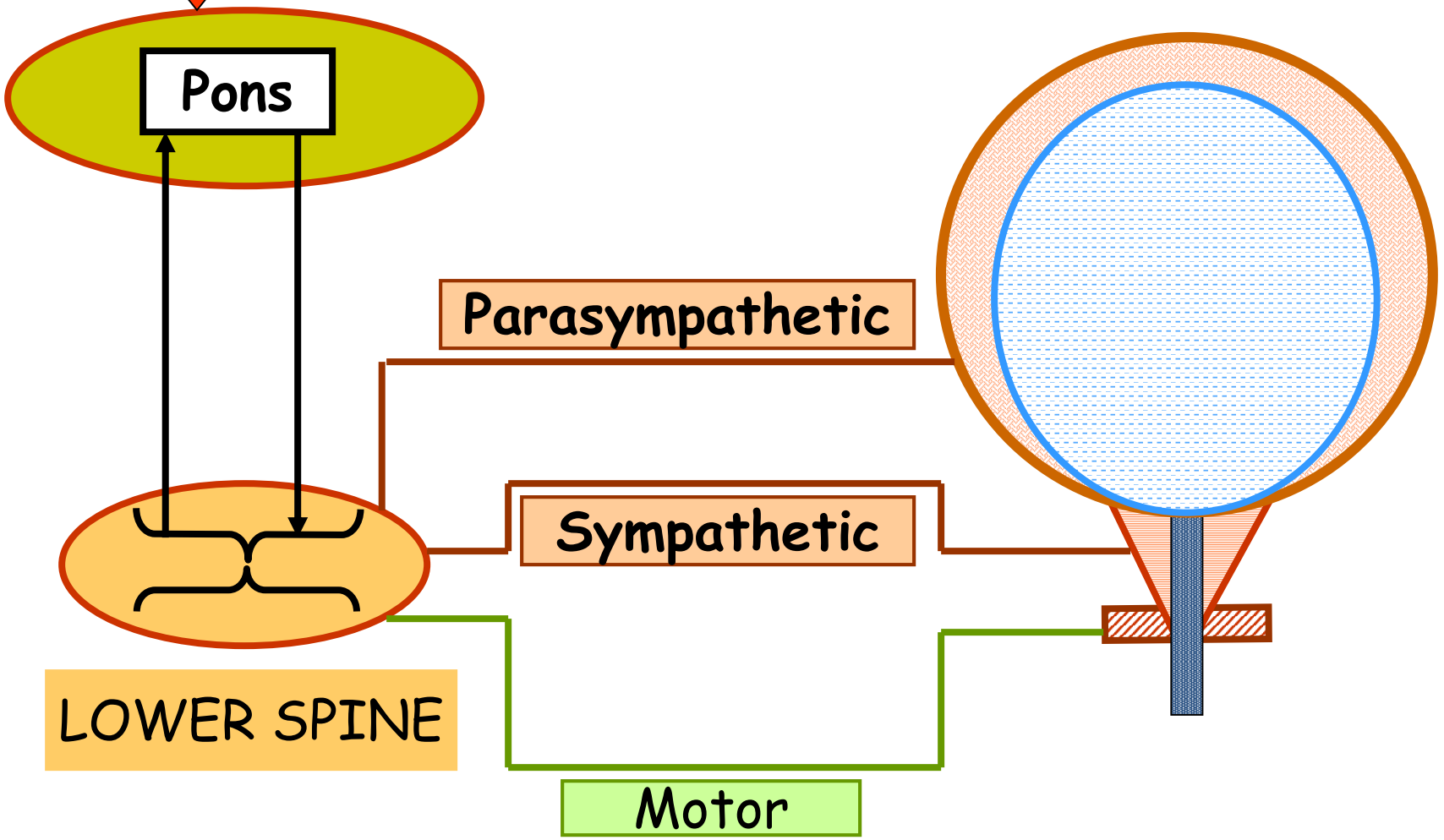
THE HUMAN URINARY BLADDER



Control of micturition is both automatic and voluntary…

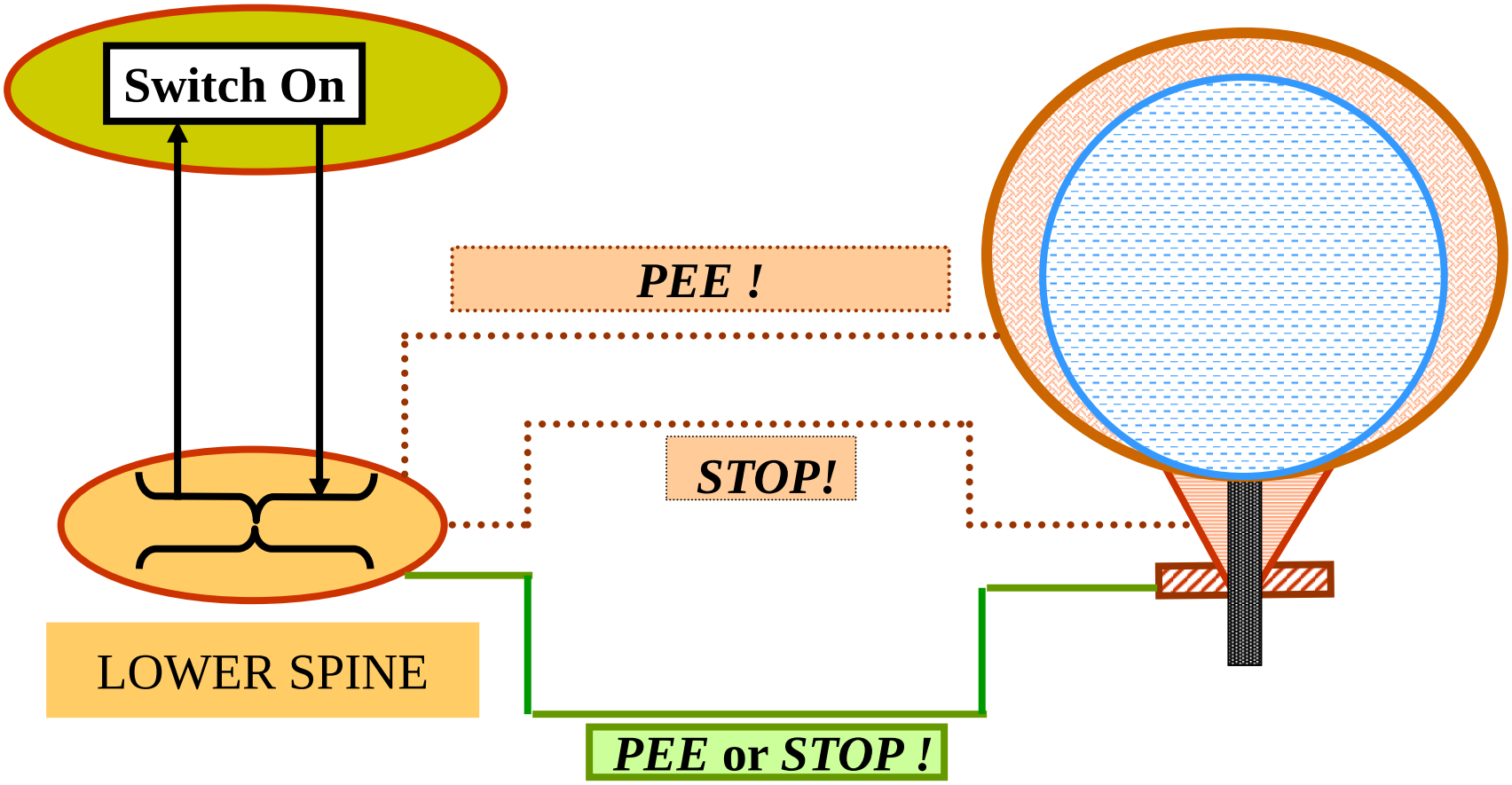

BLADDER FILLING
BLADDER EMPTYING
Coordinated opposition
Detrusor relaxed
Sphincters contracted
Detrusor contracting
Sphincters relaxed

BLADDER INNERVATION

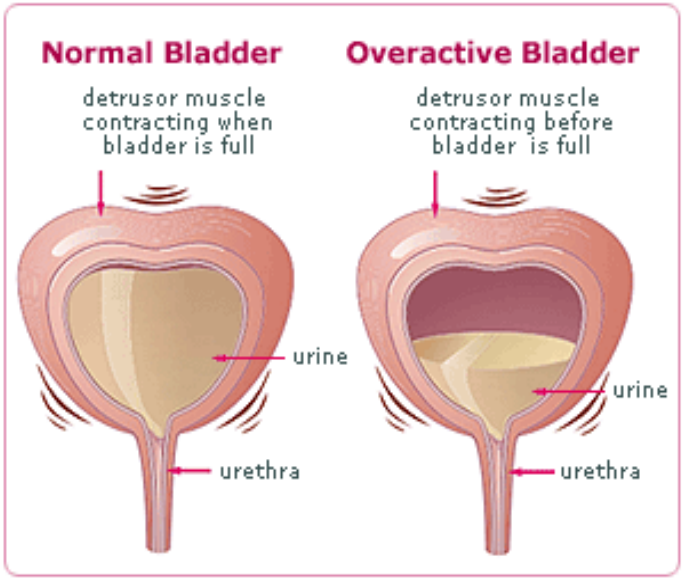


BLADDER INNERVATION

Pontine Micturition Center Switch



LUT -Lower Urinary Tract dysfunction



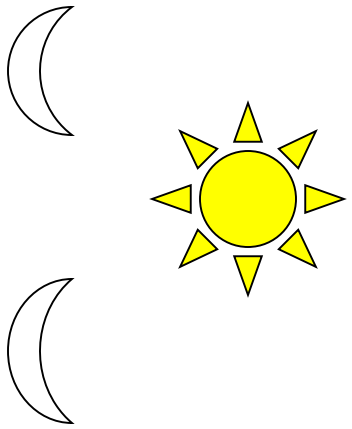
- **Storage problems :**
  - symptoms of frequency
  - urgency
  - incontinence
  - pain
- **Emptying:**
  - difficulty in initiating voiding flow
  - diminished emptying
  - urine retention

Occurs due to neuromuscular functional anomalies and structural organic changes

Neural Control

- Bladder and bowel control follows a sequential pattern

- *A child first achieves*
  - Night-time bowel continence
  - Day-time bowel control
  - Day-time bladder control
  - Night- time bladder control



Case 1

A 13-year-old child is brought by her distressed mother with complaints of wetting her bed every night

There seems to be no respite despite her parents being reassured that she will gradually outgrow this problem

The Enuretic child

Persistence of sleep wetting > twice a month past the age of 5 years

Primary

Never been dry

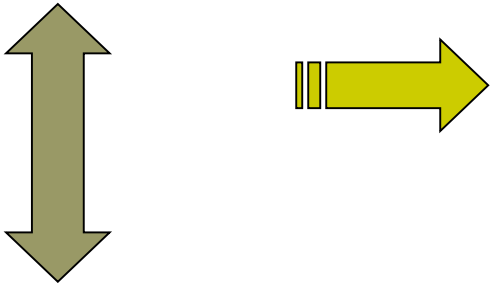
Secondary

Onset after a dry period of 6 months

Prevalence of Enuresis

Primary Enuresis

5-year old – 15-20%*



15% sleep wetters attain control/year

Teenagers 3% Adults 0.5-1%

Secondary Enuresis

Constitute 20-25% of all enuretics

Diurnal enuresis seen in 15-20% of all sleep wetters

*Bower WF et al Br J Urol 1996

The Enuretic child

The involuntary voiding of urine beyond the age of anticipated control is defined as enuresis

Nocturnal enuresis ~ night time or sleep wetting

Diurnal enuresis ~ daytime or awake wetting

Monosymptomatic and Non monosymptomatic

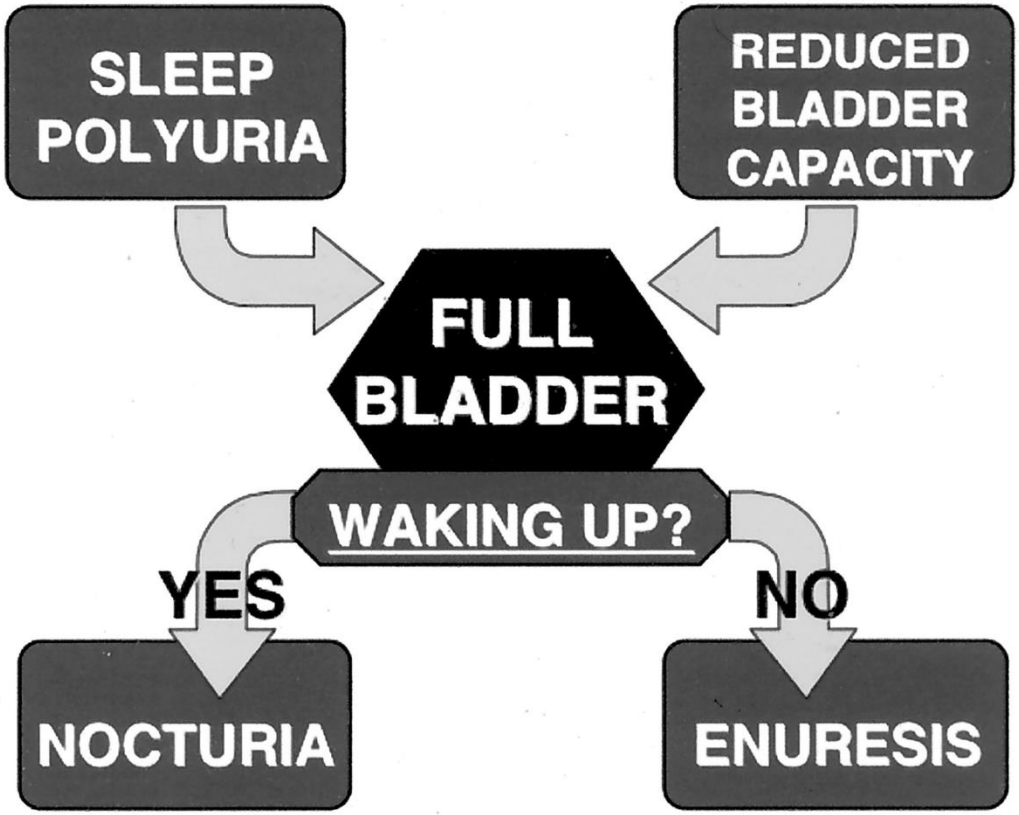
Etiology

- Excessive nocturnal urine production
  - inadequate ADH secretion
- Poor sleep arousal
  - suppression of arousal centre
- Reduced bladder capacity*
- Nocturnal detruser over activity **

*Young CK et al New Eng J of Med2008

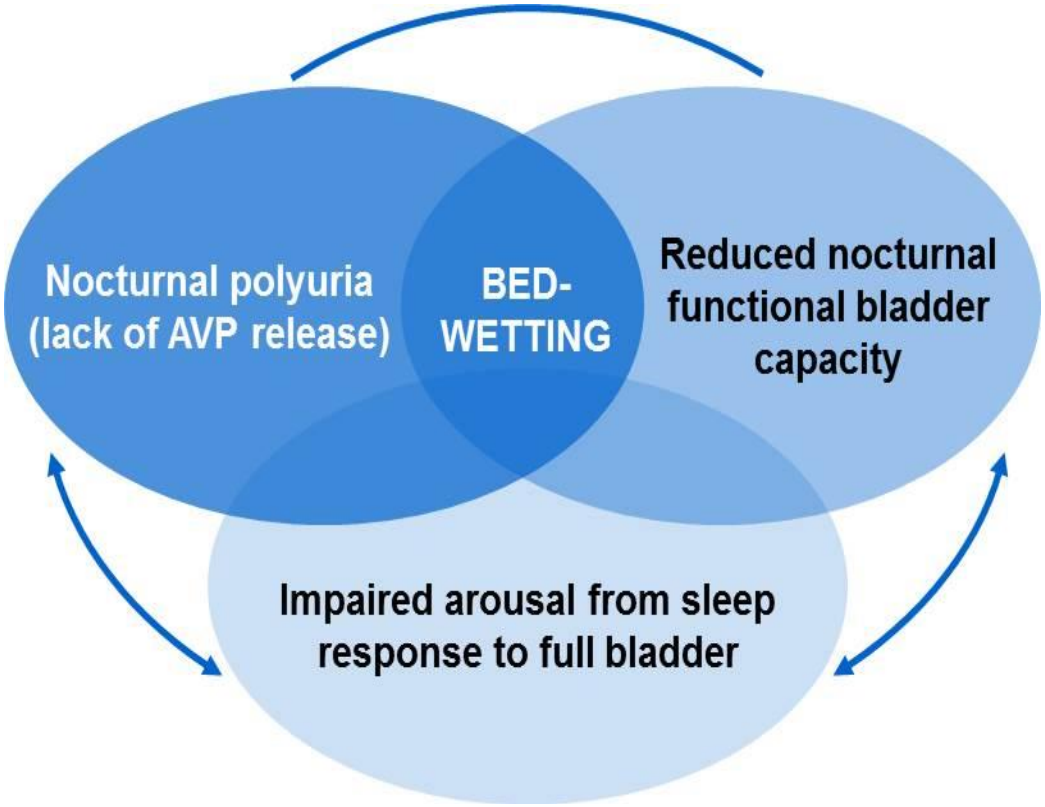
**Caldwell PHY et al BJU Int 2005

Pathophysiology



The Bladder becomes full at night either due to Nocturnal polyuria or due to reduced Bladder capacity

Pathophysiology



- Abnormal circadian release of ADH
- Smaller Bladder capacity and bladder instability at night
- Sleep related obstructive sleep apnoea

EPIDEMIOLOGY

Sleep wetting –more common in boys

Daytime frequency & wetting – more common in girls

Lower socioeconomic states

Larger families

Role of genetic factors

Risk for Enuresis

Both parents 77%

One parent 44%

Neither parents 15%

Localised to Chromosome 12, 13 and 22

(locus heterogenicity)*

ENUR1 gene

*Nocturnal Enuresis: an International interventional based management strategy. Journal of Urology 2004

Behavioral problems

- Rate of clinically relevant behavioral disorder: 12% (ICD 10 criteria)14.3% (DSM- IV)
- Behavioral disorder **can be a consequence** of the bedwetting problem
- Behavioral disorder **can precede and induce a relapse** in those genetically predisposed (secondary enuresis)
- Wetting and behavioral **disorder can be due to a** common neurobiological dysfunction as in ADHD, Autistic spectrum)
- Both being common disorder-no causal relationship may be present- and both **may co exist by chance**!

SOCIAL WITHDRAWAL AND LOW SELF ESTEEM CAN BE DISTRESSING

THE ENURETIC CHILD

In general, enuresis that is …

- is purely **nocturnal** represents a maturational delay

- is mostly **diurnal**, with ± nocturnal component represents abnormal maturation

- has **no diurnal or nocturnal preference** is probably of organic origin

(UTI, Obstructive uropathy)

Identifying the pathogenesis is not always straightforward ….

Table 1: Questions to be asked while taking history

Factor	Variables
When did bedwetting start	Days or weeks
Previously been dry at night without assistance for 6 months	Yes or no
Bedwetting pattern	Nights/week, times/night, time of bedwetting, awakening after bedwetting
	Whether volume of urine is large
Daytime symptoms and toileting pattern	Frequency, urgency, wetting
	Passing urine <4 times a day, poor urinary stream, pain while passing urine, abdominal straining
	Whether symptoms occur in specific situations
	Avoiding toilets when at school and other settings
	Going to the toilet more/less frequently than peers
Fluid intake during the day	Volume of fluid intake
Comorbidities	Constipation and/or soiling; consistency of stool
	Developmental, attention, or learning difficulties
	Behavioral, emotional, or family problems
	Diabetes mellitus

Table 2: Differential diagnosis of nocturnal enuresis

Condition	Differentiating signs/symptoms	Differentiating tests
Congenital abnormality of urinary tract	Urinary tract infections, continuous incontinence or dampness, hydronephrosis	Ultrasound of kidney and bladder; voiding cystourethrogram
Constipation	Fecal incontinence, hard stools, rectal bleeding	Bladder X-ray or ultrasound
Diabetes mellitus	Glycosuria, polyuria; possible weight loss and polydipsia	Urinalysis, fasting serum glucose, glycated hemoglobin
Detrusor overactivity/areflexia	Daytime urinary frequency, urgency; possible daytime incontinence	Urodynamics, bladder ultrasound
Emotional disturbance	Depression and/or defiant activity	Clinical diagnosis
Neurological disorder (spina bifida, epilepsy)	Daytime voiding dysfunction; spina bifida: sacral deformity Epilepsy: at least two unprovoked seizures and may be associated with incontinence	Electroencephalogram, radiograph, computed tomography, or magnetic resonance imaging scan
Urinary tract infection	Fever, dysuria, abdominal pain	Urinalysis and urine culture
Pediatric vesicoureteral reflux	Voiding symptoms, abdominal pain	Renal ultrasound
Chronic kidney disease	Increased urination especially at night, decreased urination, hematuria, puffy face or hands or feet	Renal ultrasound, urine tests, renal function test
Posterior urethral valve	Urethral obstruction, incontinence	Renal ultrasound
Neurogenic bladder	Spontaneous bladder contractions, incontinence	Uroflowmetry Filling cystometrogram

Journal of Pediatric Urology (2020) 16, 10—19

Review Article

Management and treatment of nocturnal enuresis—an updated standardization document from the International Children's Continence Society

Tryggve Nevéus [a,*], Eliane Fonseca [b], Israel Franco [c], Akihiro Kawauchi [d], Larisa Kovacevic [e], Anka Nieuwhof-Leppink [f], Ann Raes [g], Serdar Tekgül [h], Stephen S. Yang [i], Søren Rittig [j]

Table 1 Warning signs in the initial assessment of the child with enuresis.

Warning sign	Action
Weight loss, growth retardation and/or nausea	Check creatinine and urine glucose. Physical examination.
Excessive thirst with a need to drink at night	Check urine glucose. Complete a fluid intake list. Consider creatinine and morning urine osmolality. Physical examination.
Voiding difficulties—weak stream, need to strain to void	Check uroflow and residual urine. Physical examination.
Secondary nocturnal enuresis with recent debut	Check urine glucose. Physical examination.
Heavy snoring or sleep apneas	Contact otorhinolaryngologist. Physical examination.

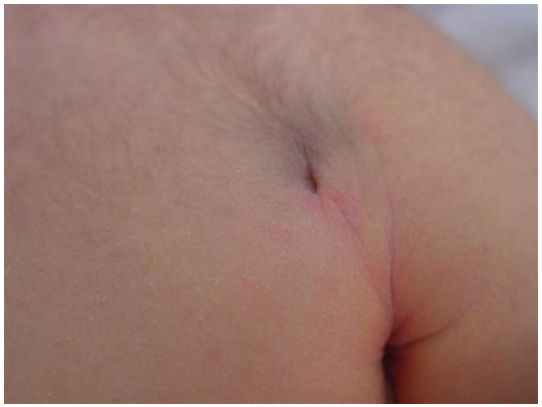
Case 1

A 13-year-old child is brought by her distressed mother with complaints of wetting her bed every night

- Occurs at least 2-3 times at night, often in deep sleep
- The child does not have any daytime symptoms
- No past history UTI, no constipation
- Well-grown child, regular at school, good in her studies
- Has lots of friends, socially interacts well
- However, more recently, she seems withdrawn from her friends and avoids sleepovers….
- Her mother wet her bed till 12 years of age

EXAMINATION

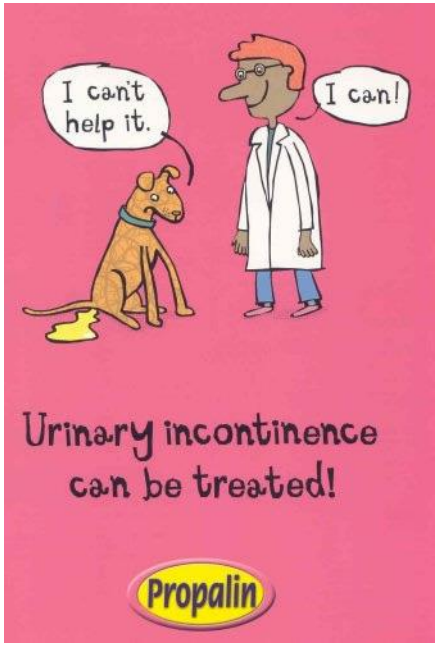
- spinal dysraphism
- bladder distention
- bladder tenderness
- fecal impaction
- rectal tone
- perineal reflexes
- pes cavus
- sexual abuse



Need to be carefully examined to rule out Neurogenic bladder

Approach

- **Voiding diary**
- Strict intake output chart
- Urine microscopy, culture
- Urine ph, sp gr, sugar
- **Urine and serum Osmolality**
- Urine calcium creatinine ratio
- Creatinine, electrolytes
- **Renal ultrasound with residual urine**
- Water deprivation test (if needed)
- MRI?



GOOD HISTORY AND CLINICAL EXAMINATION IS THE KEY

Frequency Volume Charting

Time	Urine	Fluids	Accident
0700	70		
0800	90	150	
0900	50		
1100	90	100	
1300	80	75	
1530	70		
1700	30	150	
2400	-	-	4
0200	-	-	
Total	650	525	

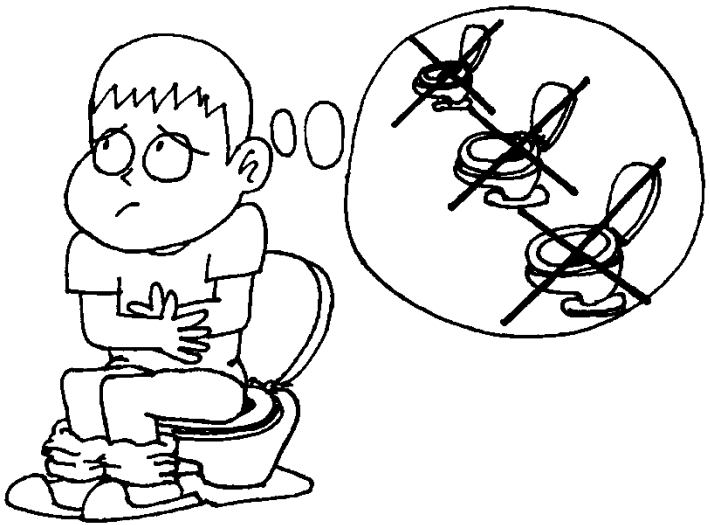
Frequent Voider/ Dribbler

Bladder Capacity (age in years + 2) x 30ml = expected volume

NOCTURNAL POLYURIA- when voiding volume exceeds 130% of FBC

Bowel dysfunction

- Bowel dysfunction may be silent or have
  - Painful defecation / Constipation
  - Fecal soiling
  - Encopresis



When to suspect a voiding disorder??

- Voiding disorders are commonly associated with enuresis ***and*** daytime incontinence

(Non-Monosymptomatic Enuresis)

- Enuresis ***refractive*** to therapy

? Detrusor instability

Bladder dysfunction may present with

Dribbling or Incontinence

Less obvious presentation

Recurrent UTI

Persistent reflux

Enuresis with daytime symptoms

MNE Vs N-MNE/Voiding disorder

- Primary
- No daytime Symptoms
- No UTI
- Good stream
- No constipation

No Further evaluation

<5%have organic basis

- Generally secondary
- Daytime symptoms
  - Frequency/Urgency
  - Holding maneuvers
  - Accidents
- UTI
- Poor stream/straining
- Constipation

Types of Voiding Disorders

Detrusor instability/Small Capacity

Phasic involuntary contractions of bladder during filling

Dys-synergistic bladder

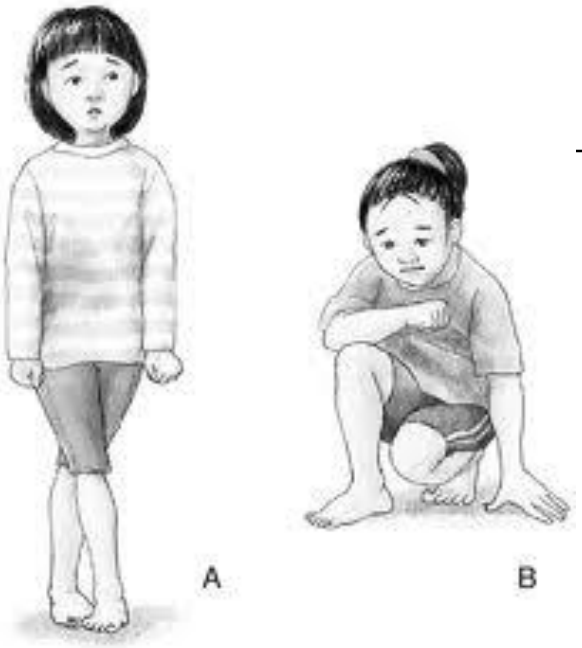
Obstruction by sphincter/pelvic muscles during voiding

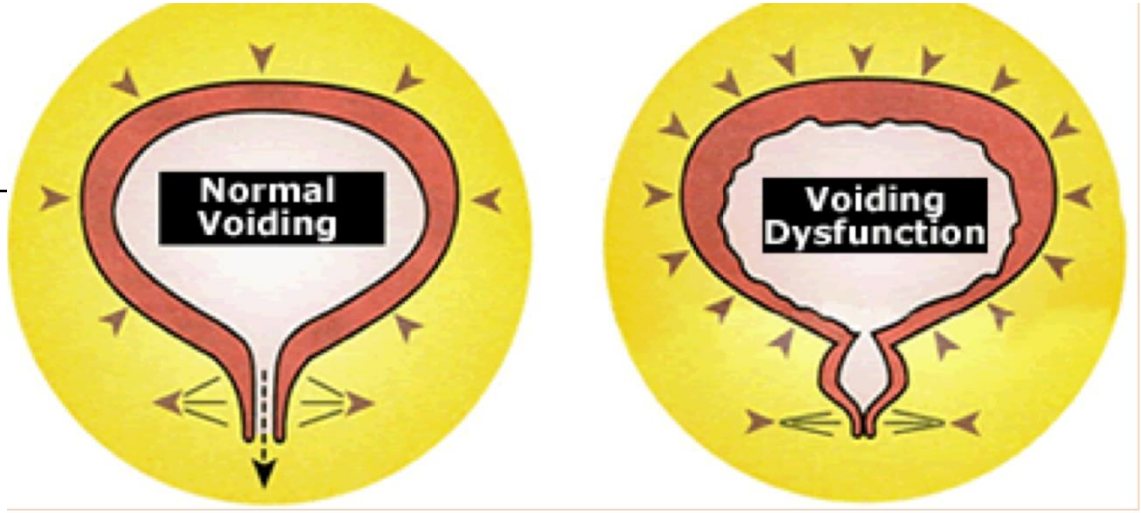
Lazy bladder

Capacious bladder with poor contractility

Expected bladder capacity (EBC) (mL)

Volume formula: 30 + [age (years) × 30] up to age 12. Adult EBC is approximately 400 mL
<65% of EBC is consistent with small bladder capacity
>130% of EBC overnight is consistent with nocturnal polyuria





Holding Maneuvers

Detrusor Sphincter Dyssynergia

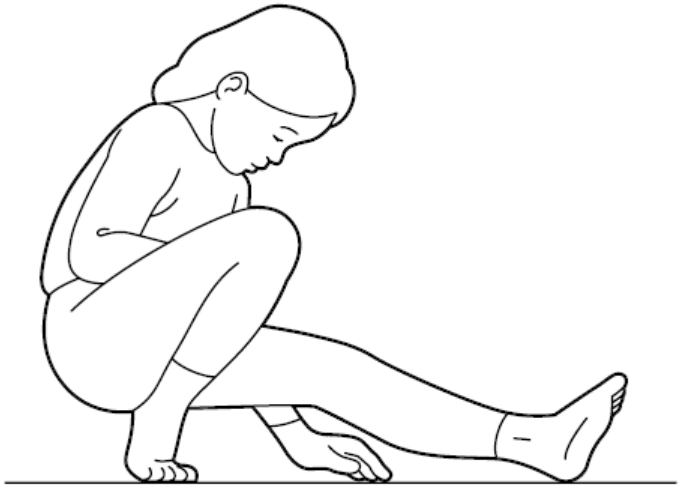
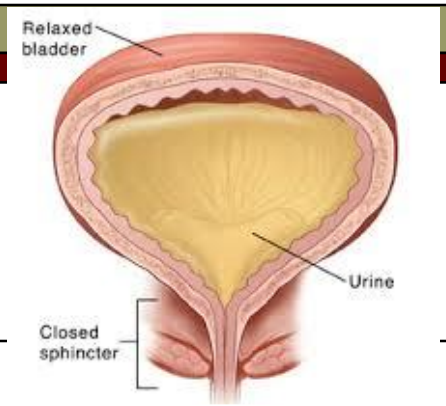
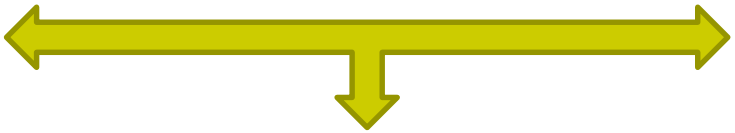
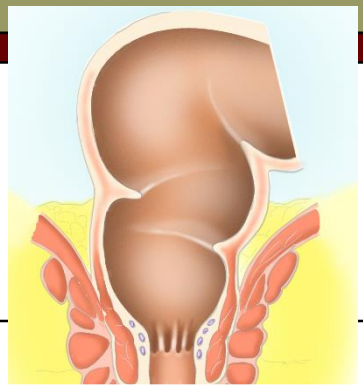


Figure 6.1 Vincent's curtsey







Postponement Of Urination	Avoiding Closet/defecation
Urge Incontinence	Standing To Stool
Day / Night Wetting	Hard Stools
Frequency	Encoperesis
Dysuria / Straining	Irregular Timings To Stool
Hesitancy	Fissure In Ano
Holding Maneuvers	Poor / Picky Eaters
Insignificant CFU In Urine	White Discharge

Causes of Voiding dysfunction

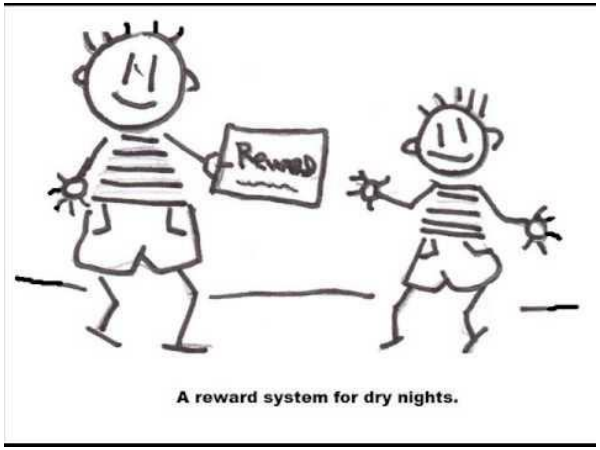
- Ano - rectal malformations
- lumbosacral anomalies
- bowel disturbance
- neurological deficits
- developmental disorders
- dysuria- hematuria syndrome

Additional Evaluation

If not recognized early UTI/VUR results

- Special Investigations:
  - Ultrasound abdomen - KUB
  - X-ray spine/MRI
  - MCU
  - IVU
  - UDS

- Rx: Bladder retraining
  - timed voiding
  - double void



A reward system for dry nights.

In our child:

- Symptomatic since early childhood
- Has a positive family history
- No precipitating/aggravating factors
- No daytime symptoms

Monosymptomatic Enuresis

Management options

- ICCS recommends treatment should be commenced when child reaches 6 yrs of age
- Key factor to eventual success- motivation of child and compliance of family
- Bladder diary – assesses the voiding pattern
- **Non-pharmacological treatment-**
  - behavioral therapy
  - star charts
  - optimize fluid intake (50 ml/kg)
  - treat constipation

General factors- important

- Child needs to be **brought to physician** by parents
- High degree of motivation- **Behavioral therapy: Star Charts**
- Regular toilet habits
- Parental age of attaining Bladder control
- Rule out Voiding disorders
- Conditioning therapy- dry bed training

Role of motivational therapy

- Providing reassurance
- Emotional support
- Eliminating guilt
- Reward for dry nights

- Changing sheets after bedwetting
- Avoidance of dairy products, fruit juices

- May resolve enuresis in 25% cases
- Reduction of wet nights by 70%

Treatment of Constipation/Encopresis

- This usually requires a consistent use of laxatives with behavioural modification
- A change is dietary habits to include more fibre and an adequate fluid intake is recommended
- Continue treatment for 6 months

Bed wetting Alarms

- First line of treatment
- Loud auditory or vibratory alarm attached to a moisture sensor in underwear, or below bedsheet
- **"Bell & Pad alarms" and "body worn alarms"**
- Trains the child to withhold urination or wake to void
- Worn till child experiences 14 consecutive dry nights
- Produce gradual but sustained improvement in wetting
- Success rate 30 to 60 % with significant relapse rate

Effectiveness of Alarm treatment

- Initial success: a minimum of 14 consecutive dry nights within 16 wks of Treatment
- Relapse: two wet nights in 2 weeks
- Continued success: no relapse within 6 months of continued success
- Complete Success: no relapse within 2 years of starting treatment

Pharmacological treatment

DESMOPRESSIN

- Used when alarm therapy has failed
- Synthetic analogue of *arginine vasopressin*
- Acts on renal collecting tubule- water reabsorption
- Helps to reduce **nocturnal polyuria** in 70% of children*
- Acts without permanently altering the associated causative factors
- Available as **Oral:** **Tablet 200-400µg**
  Melt : lyophilisate 120-240µg
  Nasal spray:10-40µg (not recommended)

* Glazener CM.Cochrane Database Sys review 2002

DESMOPRESSIN

- Risk of water intoxication and hyponatremia
- Available as tablet, Nasal spray and Melt
- Hence: restrict fluid intake to < 200 ml
  take 1 hour before bedtime
  and to be taken 2 hours after food
- Useful when a rapid response in required
- Could start with higher dose and taper down or vice versa
- If failure occurs- can be combined with Alarm clock

Skoog SJ, Stokes A, Turner KL. Oral desmopressin: J Urol. 1997

Clinical Trials

Canadian enuresis and evaluation (CESE) study:

Efficacy and safety of the long-term use of desmopressin .
Response rate remained constant : 74%

Continuous treatment reduced the median number of **wet nights from 5.7 5 to 1.00/week** during the period of 4 weeks.

Increasing the dose from 0.2 to 0.4 mg resulted in a further 31.1% response

Noresponse25.4% either dropouts, incomplete data from patient diaries, or relapses.

Only 0.8% patients reported possible drug-related adverse events, and there was no incidence of hyponatremia in this study.

Wolfish NM, Barkin J, Gorodzinsky F, Schwarz R. The Canadian Enuresis Study and Eval uation Short- and long-term safety and efficacy of an oral desmopressin preparation. Scan d J Urol Nephrol 2003;37:22-7.

Clinical Trials

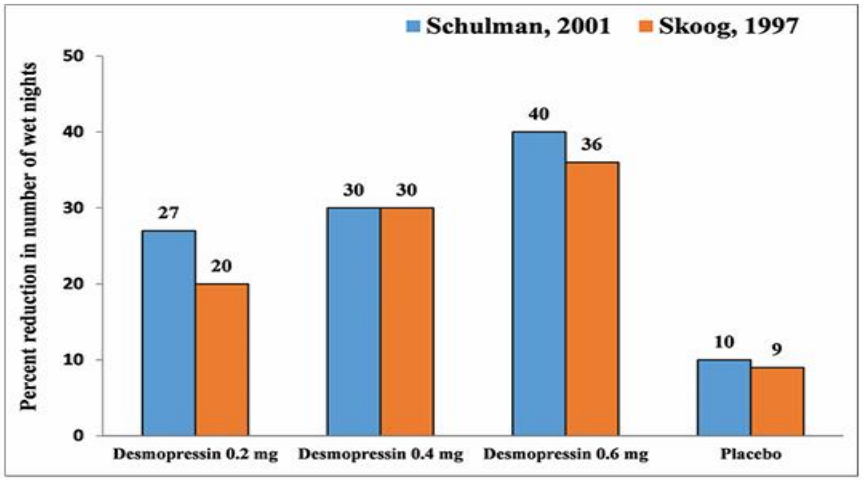


Figure 5: Decrease in number of wet nights after 2 weeks and 6 weeks of treatment with oral desmopressin

Table 3: Clinical trials with desmopressin

Author	Study design	Treatment	Results
Schulman *et al.* (*n*=193)	Double-blind, placebo-controlled, randomized, parallel group, multicenter trial	Phase 1: dose ranging for 2 weeks: oral desmopressin (0.2, 0.4 or 0.6 mg) or placebo at bedtime Phase 2: placebo washout for 2 weeks followed by dose titration for 8 weeks	Desmopressin significantly reduced wet nights compared to placebo ~44% of children treated with desmopressin achieved ≥50% reduction in the number of wet nights/2 weeks with doses of 0.2 and 0.4 mg Mild-to-moderate adverse effects unrelated to treatment
Skoog *et al.* (*n*=141)	Double-blind, placebo-controlled, randomized, parallel group trial	Oral desmopressin (0.2, 0.4, 0.6 mg) or placebo before bedtime	Desmopressin 0.6 mg significantly reduced wet nights compared to placebo ($P<0.05$) <50% decrease in wet nights was observed in 83%, 79%, 64%, and 61% of patients receiving placebo and 0.2, 0.4, 0.6 mg desmopressin, respectively

Schulman SL. J of Urol 2001, Skoog J of Urol 2001

Anticholinergics- 2nd line therapy

- Act by suppressing detruser over activity, inhibit bladder contractions
- Useful **in those with LUT symptoms**
- Exclude post-void residue, constipation and low voiding frequency
- Voiding diary, uroflowmetry and Ultrasound with PVR are pre-requisites
- **Oxybutynin 5mg or Tolteridine 2 mg**
- May take up to 3 months to respond
- Side effects - constipation, urine retention and risk of UTI, mood changes

Dosing

Table 2 Proposed dosage of anticholinergics in nocturnal enuresis.

Drug	Proposed dosage[a]
Oxybutynin	2.5–5 mg
Tolterodine[b]	2–4 mg
Fesoterodine[b]	4–8 mg
Solifenacin[b]	5–10 mg

[a] All doses are oral tablets given 1 h before bedtime.
[b] Not yet approved for label use in children.

Tricyclic antidepressants- 3rd option

IMIPRAMINE

- May help in those who have failed other therapy
- Reduction in wet nights by 20% but relapse rate is high
- Dose: 25-50 mg
- Life threatening side effects: Cardio toxic: arrthymias, heart blocks, convulsions
- Drug holidays for 2 weeks every 3 m to avoid tolerance

- If h/o palpitations or syncope or F/H of sudden cardiac death, long QT syndrome needs to be excluded

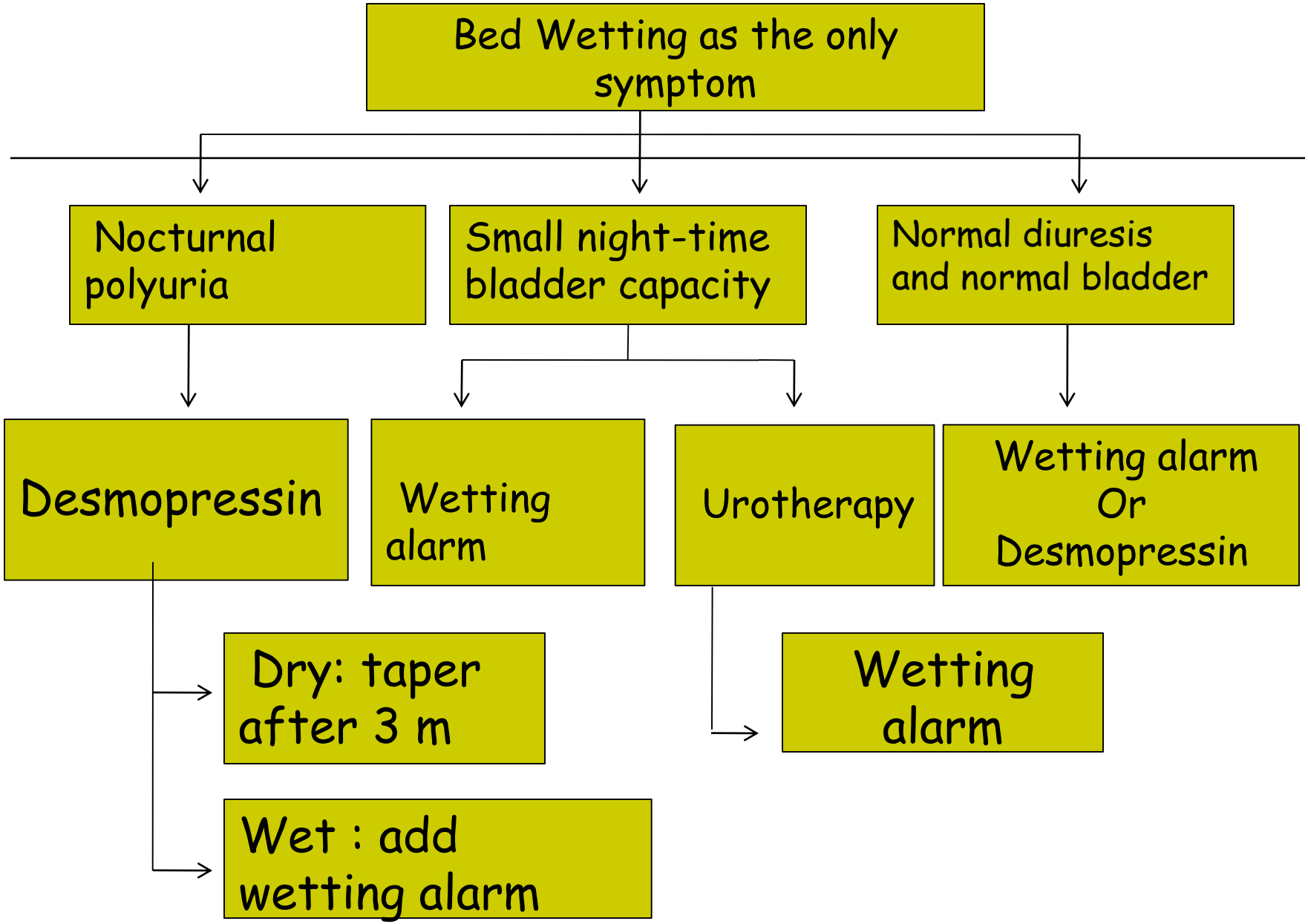
Which is the ideal treatment?

Table 5: Comparison of efficacy of nonpharmacologic and pharmacologic options for treatment of nocturnal enuresis

Therapy	Response (%)	Relapse rate (%)
Dry-bed training	50	40
Alarm	66	15-50
Motivational therapy	25	5
Desmopressin	60-70	60-80
Imipramine	40-60	82-100
Oxybutynin	47-71	83

In this Child- options

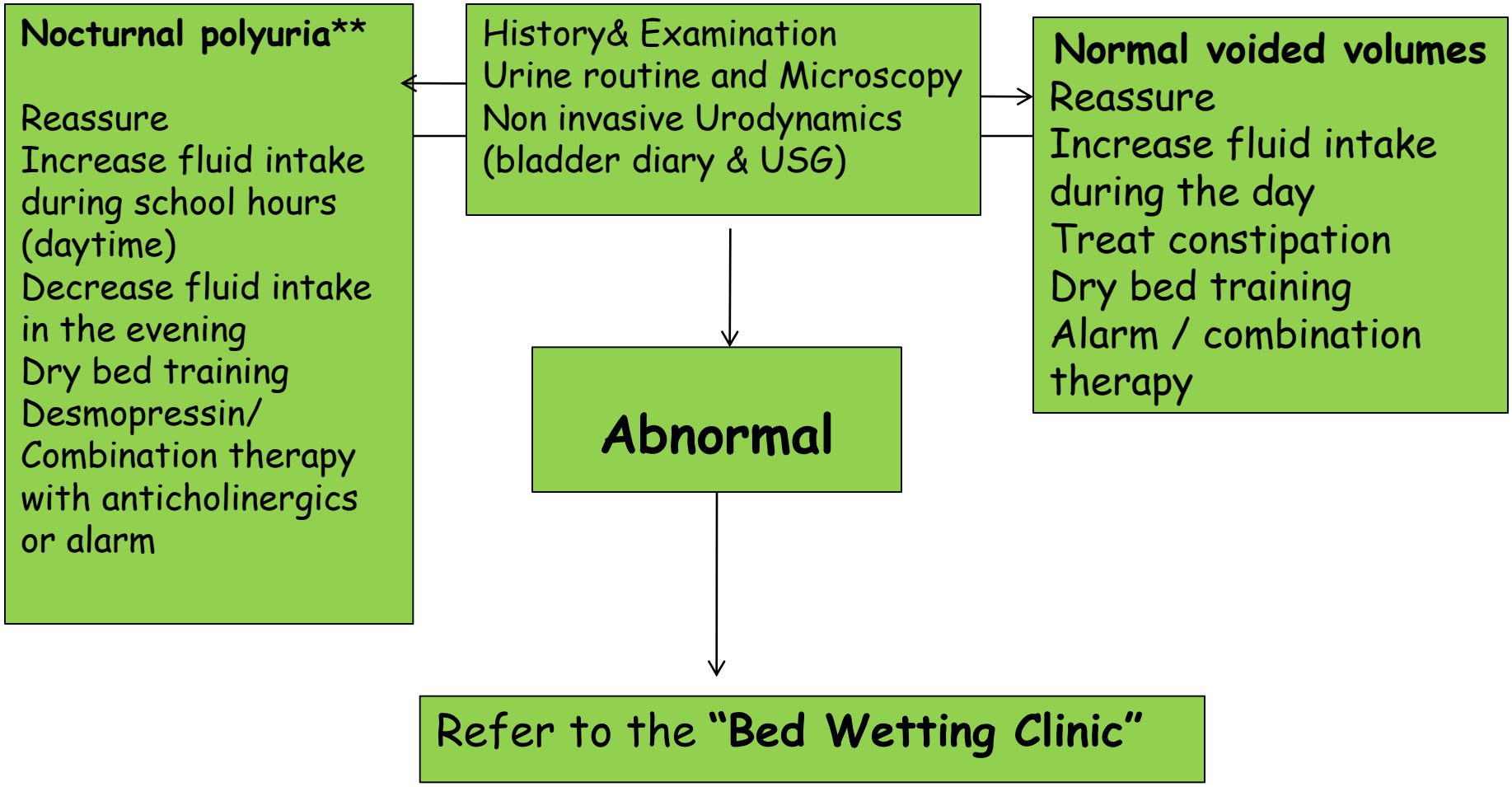
- Pre-adolescent
- No daytime symptoms
- Nocturnal urine output: 750ml
- Family history
- Behavioral changes


Bed Wetting as the only symptom
Nocturnal polyuria
Small night-time bladder capacity
Normal diuresis and normal bladder
Desmopressin
Wetting alarm
Urotherapy
Wetting alarm Or Desmopressin
Dry: taper after 3 m
Wet : add wetting alarm
Wetting alarm

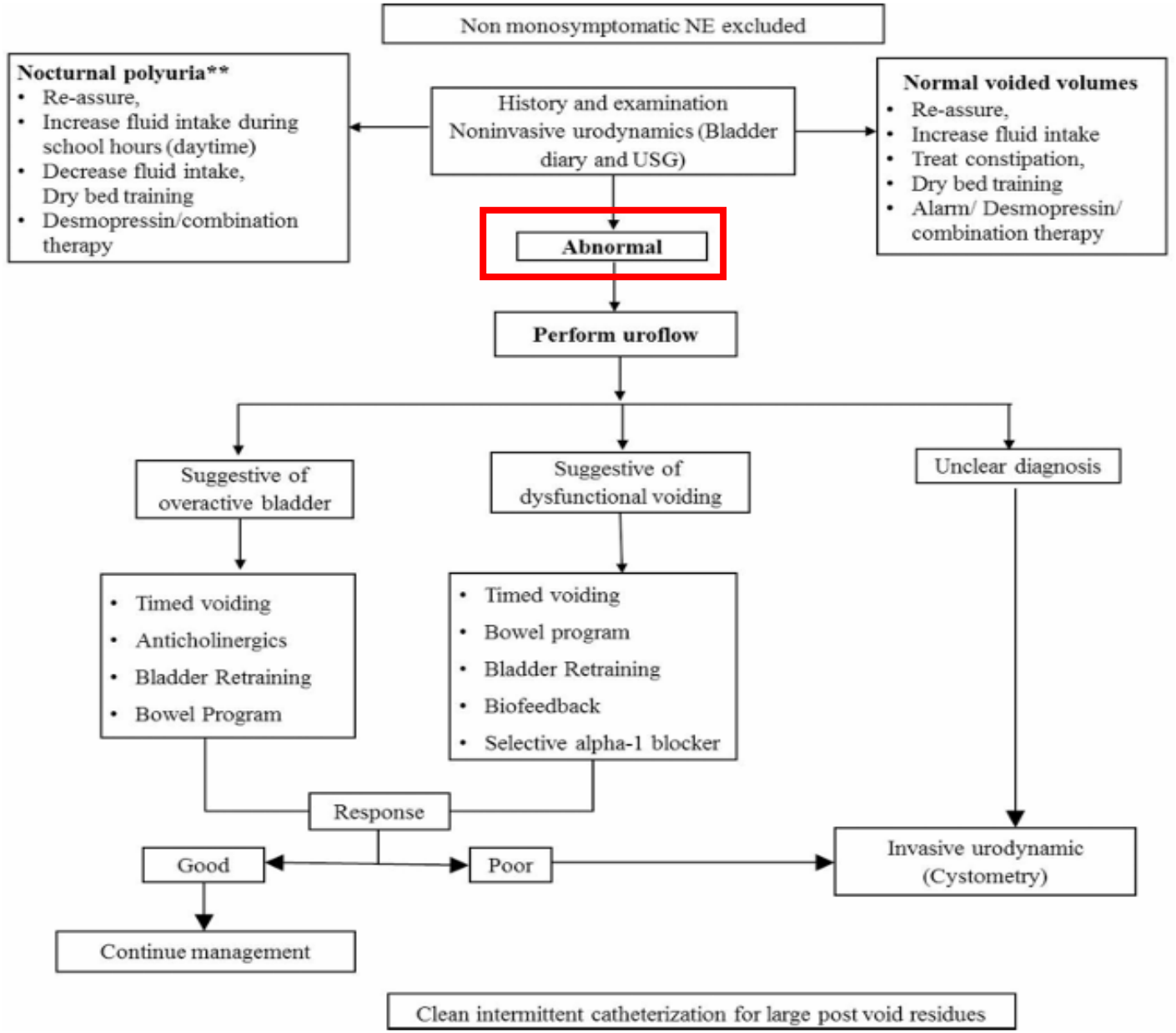
Response to therapy

- **Initial response**: at least 50% reduction in wet nights from baseline
- **Partial response:** a reduction of wet nights of 50-90%
- **Full response:** reduction of at least 90%
- **Delayed response:** wait for 2-3 months before new evaluation
- Some may respond to doubling of dose

Enuresis Treatment – Simple Algorithm



** Defined as urine output > 130% of expected bladder capacity for age during the night



re 4: Comprehensive management of functional voiding disorder

STUDY OF PSYCHOSOCIAL IMPACT OF ENURESIS ON PRIMARY SCHOOL CHILDREN USING A CHILD AND FAMILY IMPACT SCALE

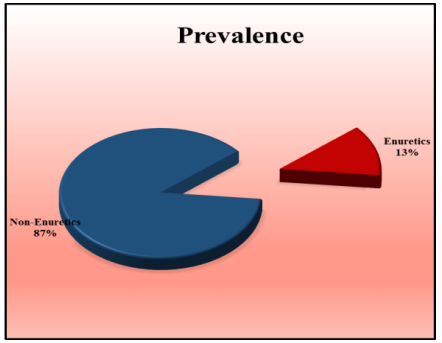
Esther Andrew*, Indira Agarwal, Manjusha Arumadi, Bijesh Yadav, Division of Pediatric Nephrology, Christian Medical College, Vellore, India **ACPN 2017 (PEMQOL)**

FAMILY IMPACT SCALE
Relatives are very understanding about the situation
Our family talks openly about my child's problem
I feel hopeful that my child's wetting will get resolved
I feel confident about the way I am managing the situation
My child's problem doesn't seem to limit our family
There's a lot of tension in our home due to my child's uncontrolled wetting
Relatives/family members are patient and tolerant about the problem
Others in our immediate family seem resentful toward this child because of his/her problems with wetting
I am frustrated that my child's wetting is unmanageable
We are embarrassed to have people in our home because of odor problems
There's a lot of turmoil and disruption in our home due to my child's problem
Family/relatives make a point to include this child in games and activities when we are together
I feel tired and worn out due to all the extra work (laundry, changing linen)
My child's problem with wetting controls my

CHILD IMPACT SCALE
My child feels pretty good about him/herself
My child is able to work to his/her potential in school
My child talks freely about issues with wetting
My child tries hard to control wetting
My child seems indifferent about the problem
My child seems to have less wetting episodes
My child doesn't play sports or gym because of wetting issues
My child seldom goes to overnight events because of problems with wetting
My child seems bothered and upset by wetting
My child's life seems limited because of problems with wetting
My child seems to enjoy life
My child hasn't let problems with wetting interfere with making friends or doing the usual things
My child seem comfortable among his/her peers
My child is at an age when he/she should take more responsibility for the problem but doesn't

RESULTS

The prevalence of enuresis was 12.7%



Parental perceptions	Yes(%)	No(%)
Could control if tried harder	20.6	11.8
Behavioural issue	44.1	20.6
Neurological basis	58	14.7
Significant health problem	58	20
Medications more helpful	50	23.5
Outgrow the problem	70	20.6
Serious medical issue	11	64
Sought medical care	64.5	36.5

THANK YOU!

CRRT IN CRITICALLY ILL CHILDREN

Dr. Muthu Kumar P

Clinical Lead and Senior Consultant Nephrologist

Kauvery Hospital – Radial Road, Chennai

BASICS

Why Perform Renal Replacement Therapy?

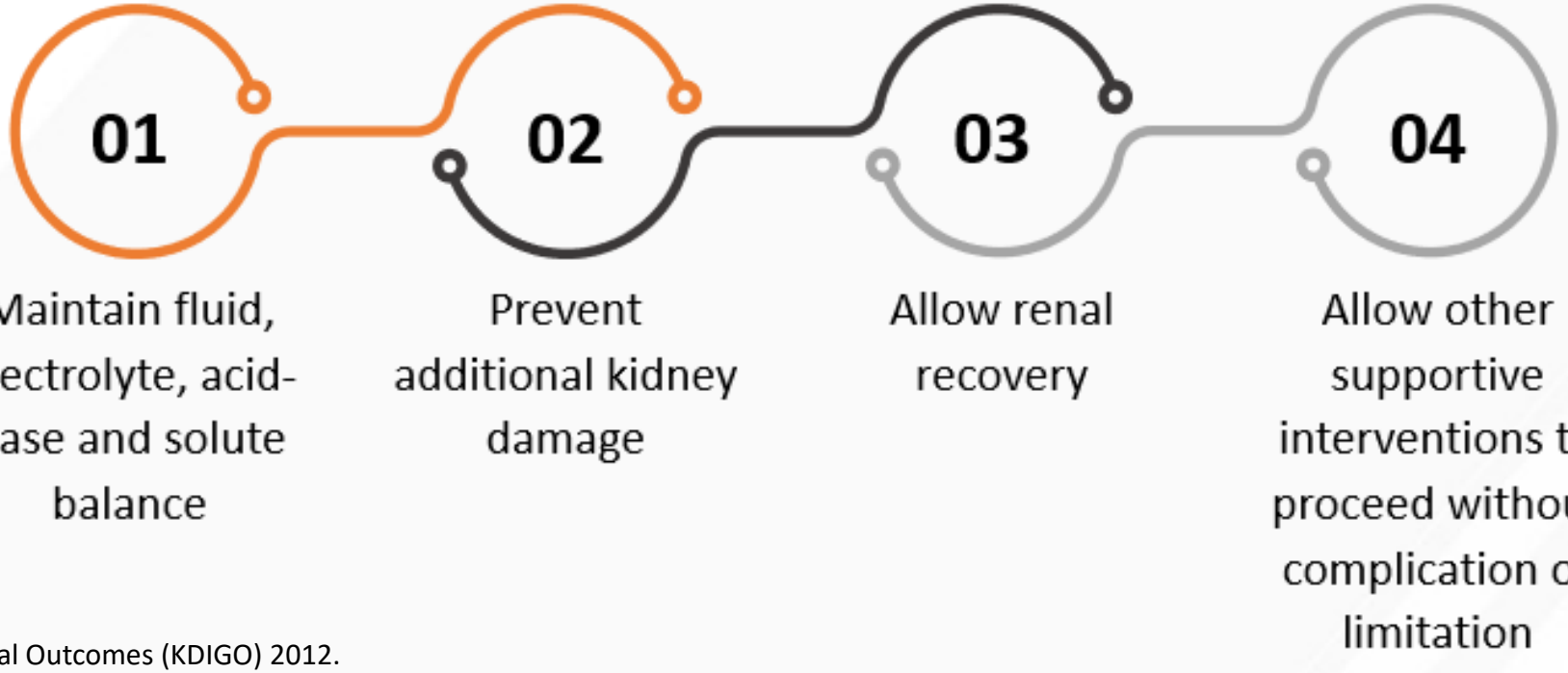
- Renal Replacement Therapy (RRT) is a generic term that refers to the various types of dialysis modalities used in the management of AKI.[1]
- RRT mimics the functionality of the native kidney and is the mainstay of therapy in patients with severe AKI. [2]

- Removal of waste products
- Regulation of acid-base balance
- Regulation of electrolytes
- Removal of fluid

1 Sharfuddin A et. al. Acute Kidney Injury. In *Brenner & Rector's The Kidney*. 9th ed. 2012.
2 Ronco C et. al. Renal Replacement Therapy in Acute Kidney Injury: Controversy and Consensus. 2015.

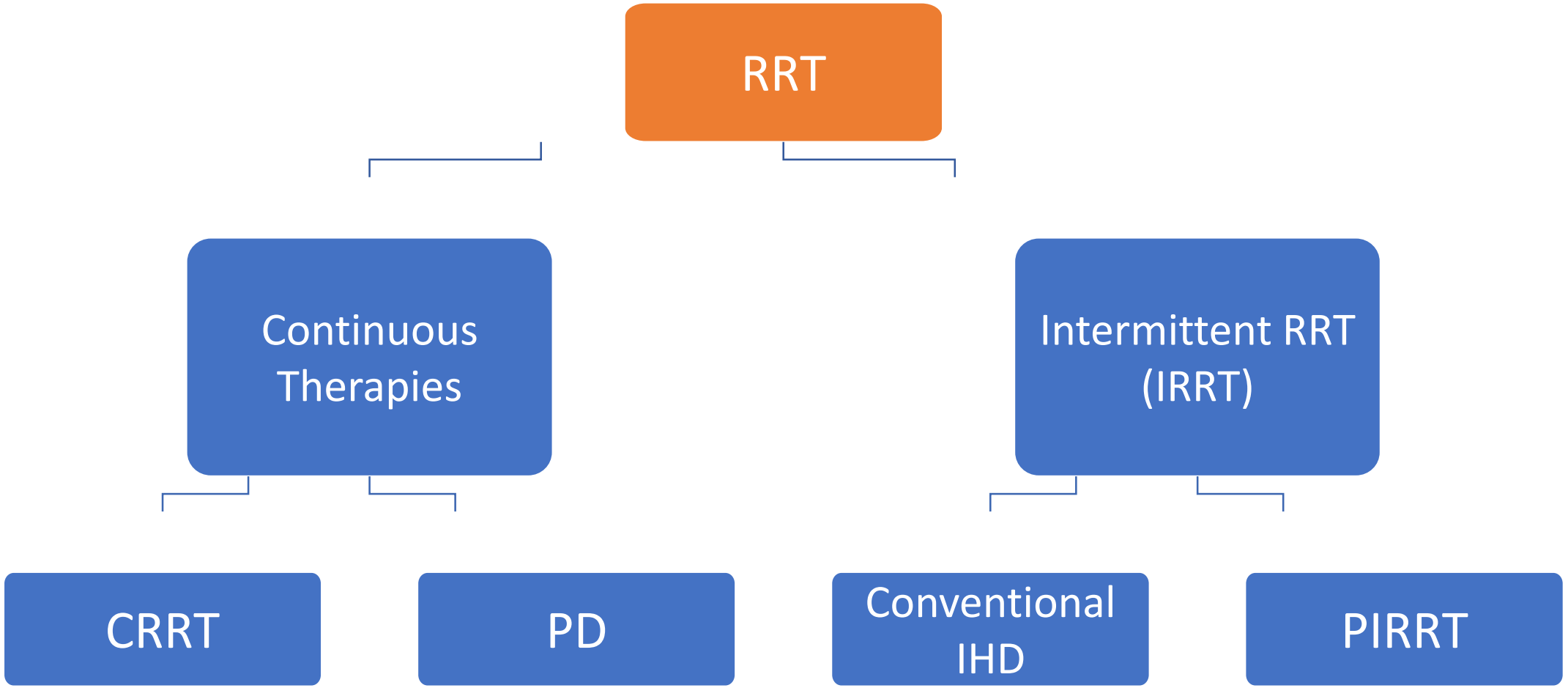
What Are the Goals of RRT in Patients With AKI?

- The goals of RRT in patients with AKI are to:



Kidney Disease: Improving Global Outcomes (KDIGO) 2012.

RRT Modalities



CRRT

- CRRT refers to any extracorporeal blood purification therapy intended to substitute for impaired renal function over an extended period of time and applied for, or aimed at, being applied for 24 hours per day.

- At present, CRRT is the preferred modality for AKI in ICUs throughout the world. [1]

1 Prowle J et. al. Clinical Review: Optimal Dose of Continuous Renal Replacement Therapy in Acute Kidney Injury. 2011.

CRRT Modalities

- Slow continuous ultrafiltration **(SCUF)**
- Continuous venovenous haemofiltration **(CVVH)**
- Continuous venovenous haemodialysis **(CVVHD)**
- Continuous venovenous haemodiafiltration **(CVVHDF)**

- The CRRT modalities differ mainly in terms of the mechanism of solute removal.

- Ultrafiltration in SCUF
- Convection in CVVH
- Diffusion in CVVHD
- A combination of convection and diffusion in CVVHDF

CRRT in AKI Patients

- CRRT tends to be the treatment of choice in critically ill patients with AKI. [1]
- In two large, multicentre randomised controlled trials, CRRT was either, used exclusively, or was the main modality used in haemodynamically unstable patients with AKI. [2,3]

01

The Veterans Affairs / National Institutes of Health Acute Renal Failure Trial Network (ATN) Study [2]

02

The Randomized Evaluation of Normal versus Augmented Level (RENAL) Replacement Therapy Study [3]

1 Prowle J et. al. Clinical Review: Optimal Dose of Continuous Renal Replacement Therapy in Acute Kidney Injury. 2011.
2 Palevsky P et. al. Intensity of Renal Support in Critically Ill Patients with Acute Kidney Injury. 2008.
3 Bellomo R et. al. Intensity of Continuous Renal Replacement Therapy in Critically Ill Patients. 2009.

INITIATION OF CRRT

When to initiate RRT in AKI?

EMERGENT INDICATIONS

- Severe azotemia (BUN >120, SCr > 6.0 and increasing)
- Severe acidosis (pH < 7.2)
- Pulmonary edema not responding to medical management
- Hyperkalemia (>6.5 meq/L)

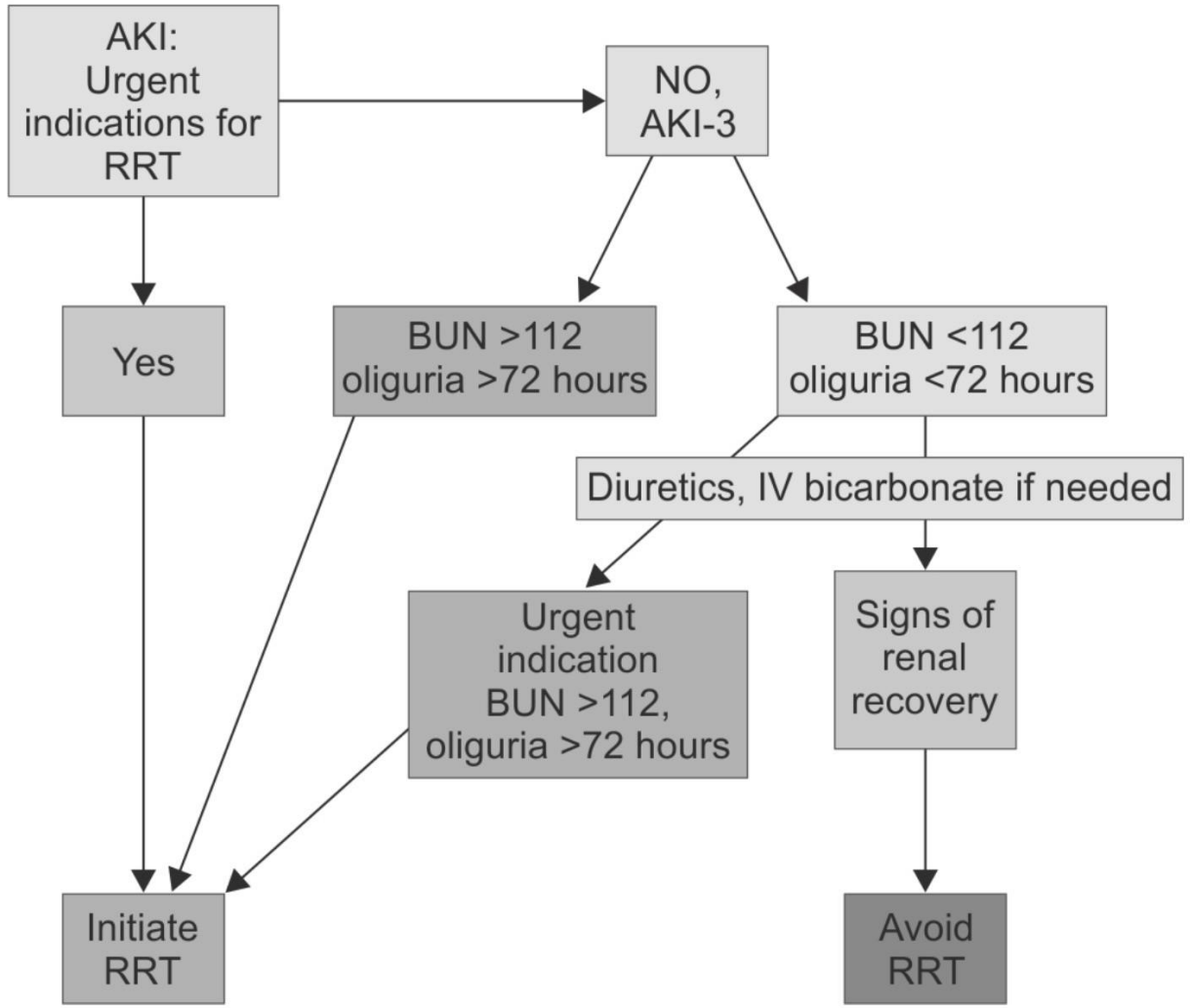
NON-EMERGENT INDICATIONS

- Metabolic and fluid demand

Comparison of studies of early vs. late RRT initiation

	ELAIN	AKIKI-1	IDEAL-ICU	STARRT-AKI	AKIKI-2
Study populations	Surgical	Mixed	Sepsis with AKI	Mixed	Mixed
No. of patients	231	620	488	2,866	278
Early RRT	KDIGO stage 2	KDIGO stage 3	KDIGO stage 3	KDIGO stage 2 or 3	KDIGO stage 3 with BUN >112 mg/dl or oliguria >72 hours
Delayed RRT	KDIGO stage 3	Specific criteria	48 hours	Specific criteria	BUN >140 mg/dl or specific criteria
Primary outcome	90-day mortality	60-day mortality	90-day mortality	90-day mortality	60-day mortality
Mortality	39% (early), 55% (late), p=0.03	48.5% (early), 49.7% (late, p=NS	58% (early), 54% (late), p=NS	43.9% (early), 43.7% (late), p=NS	44% (Early), 55% (late), p=0.07
RRT initiation in delayed group	100% vs. 91%	98% vs. 51%	97% vs. 62%	97% vs 62%	100% vs. 78%
Conclusions	Early initiation of CRRT in surgical patients is beneficial	Early initiation of RRT has no benefits	Early initiation of RRT has no benefits	Early initiation of RRT is associated with delayed renal recovery and RRT related complications	More-delayed initiation of RRT is potentially harmful

Flowchart 1: Algorithm to guide the timing of initiation of RRT in AKI.



(AKI: acute kidney injury; BUN: blood urea nitrogen; RRT: renal replacement therapy)

ISCCM Update 2021

Initiation - Summary

- Individualize the timing of initiation of CRRT.
- The timing of initiation of CRRT should include the clinical setting and metabolic demand
- Post-surgical and septic patients may benefit from early CRRT.

PRESCRIPTION OF CRRT

Initial prescription of CRRT: Issues to consider.

- Vascular access.
- Blood flow rate (Qb).
- **Dose**: Effluent volume (ml/hour).
- Diffusion (Qd) and Convection(QR) (replacement fluid) and fluid removal (Quf).
- Pre-dilution vs. Post-dilution
- Composition of fluids.
- Additives to fluids: potassium and sodium bicarbonate.
- Fluid removal (per hour and cumulative).
- Temperature settings.

Vascular access

- Internal Jugular Vein
- Femoral Vein
- Subclavian Vein

Catheter size:

- 7F/ 8F/ 10F/ 11.5F Dialysis Catheter

- Blood flow rate (QB):

•4-5 ml/kg/min
•Start at lesser flow and reach 50 – 100 ml/min

Priming: Albumin VS PRBC

Choice of Filter

® disposable sets

	Type of membrane	Filter surface area	Application
M60	AN 69	0.6 m^2	CRRT above 11 kg
M100	AN 69	0.9 m^2	CRRT incl. high flow above 30 kg
M150	AN 69	1.5 m^2	CRRT incl. high flow above 30 kg
ST60	AN 69 ST	0.6 m^2	CRRT above 11 kg
ST100	AN 69 ST	0.9 m^2	CRRT incl. high flow above 30 kg
ST150	AN 69 ST	1.5 m^2	CRRT incl. high flow above 30 kg
HF20	PAES	0.2 m^2	CRRT above 8 kg
HF1000	PAES	1.1 m^2	CRRT incl. high flow above 30 kg
HF1400	PAES	1.4 m^2	CRRT incl. high flow above 30 kg
oXiris	Surface-treated and heparin-grafted membrane	1.5 m^2	CRRT above 30 kg
septeX	High cut-off PAES membrane	1.1 m^2	CVVHD with removal of high molecular weight solutes (
TPE1000	Polypropylene	0.15 m^2	TPE above 9 kg
TPE2000	Polypropylene	0.35 m^2	TPE–adults
Adsorba 150 kit	Coated activated charcoal column	–	Hemoperfusion
Adsorba 300 kit	Coated activated charcoal column	–	Hemoperfusion
	PAES (MARSFLUX) PAES (diaFLUX)	2.1m^2 (MARSFLUX) 1.4m^2 (diaFLUX)	Albumin dialysis

Dialysate & Replacement Flow (QD & QR)

- Effluent dose = [QD + QR] – Patient Removal per hour
- **Target Effluent Dose = 25 - 35 ml/Kg/ hour**
- **QD: QR = 1: 1 proportion [conventional]**
- **QR = Pre-filter & Post Filter**

ANTICOAGULATION

Anticoagulation

- Heparin 20 U/Kg loading followed by 5 - 10U/Kg/hour

- APTT Target: 50 - 90
- ACT Target: 180 – 220

If Heparin Free:
- NS Flush 50 – 100 ml once in 2 hours

(to be removed in patient UF)

REGIONAL CITRATE ANTICOGULATION (RCA)

- CITRATE DOSE: 2- 3 mmol/L (Regiocit, Citrate concentration 18mmol/l)
- CALCIUM COMPENSATION: We use Calcium Gluconate – Undiluted
- FILTRATION FRACTION: Target Less than 25%

- EFFLUENT DOSE: ALWAYS LESS THAN 35ml/kg/hr unless specifically mentioned (reduce dialysate and replacement fluid accordingly)

RCA (Contd.)

- REGIOCIT - used as a replacement(pre- filter only)
- Post filter ionized calcium (ABG) – monitored regularly
- A separate systemic infusion of calcium must be administered during use of REGIOCIT to prevent or treat hypocalcemia.
- Blood calcium concentrations (ionized and total) must be monitored throughout CRRT.

- Contraindications for the use of REGIOCIT include:

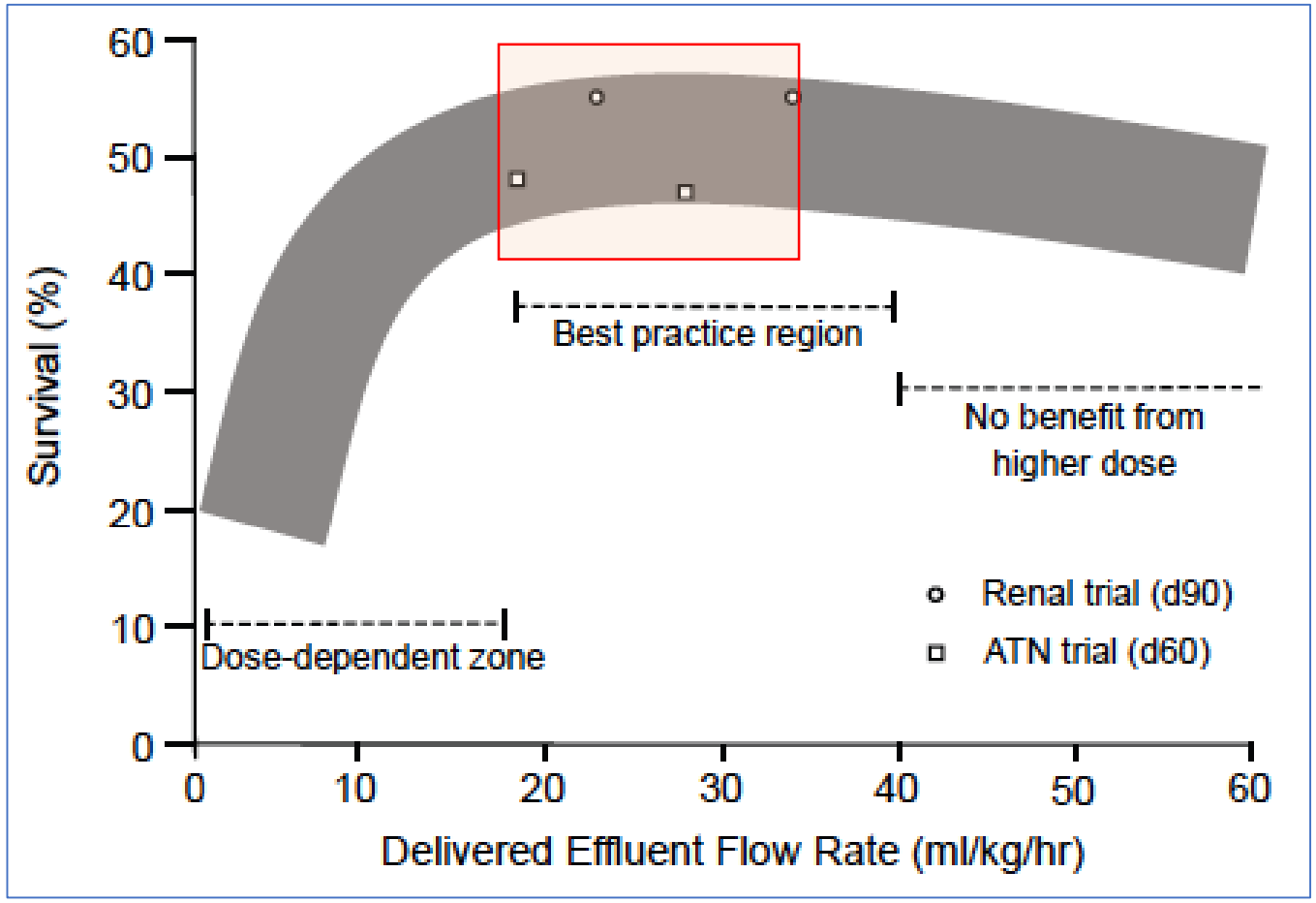
* Severe liver failure
* Shock with muscle hypoperfusion
* Known hypersensitivity to any component of REGIOCIT

Sliding Scale of Calcium Infusion

Patient ionized calcium	Starting Calcium Compensation flow rate
Less than 0.9 mmol/L	15ml/hr & give 30ml of undiluted Calcium Gluconate over 30 mins before starting
0.9 - 1.1 mmol/L	12.5 ml/h
Greater than 1.1 mmol/L	10 ml/hr

THERAPEUTIC GOALS

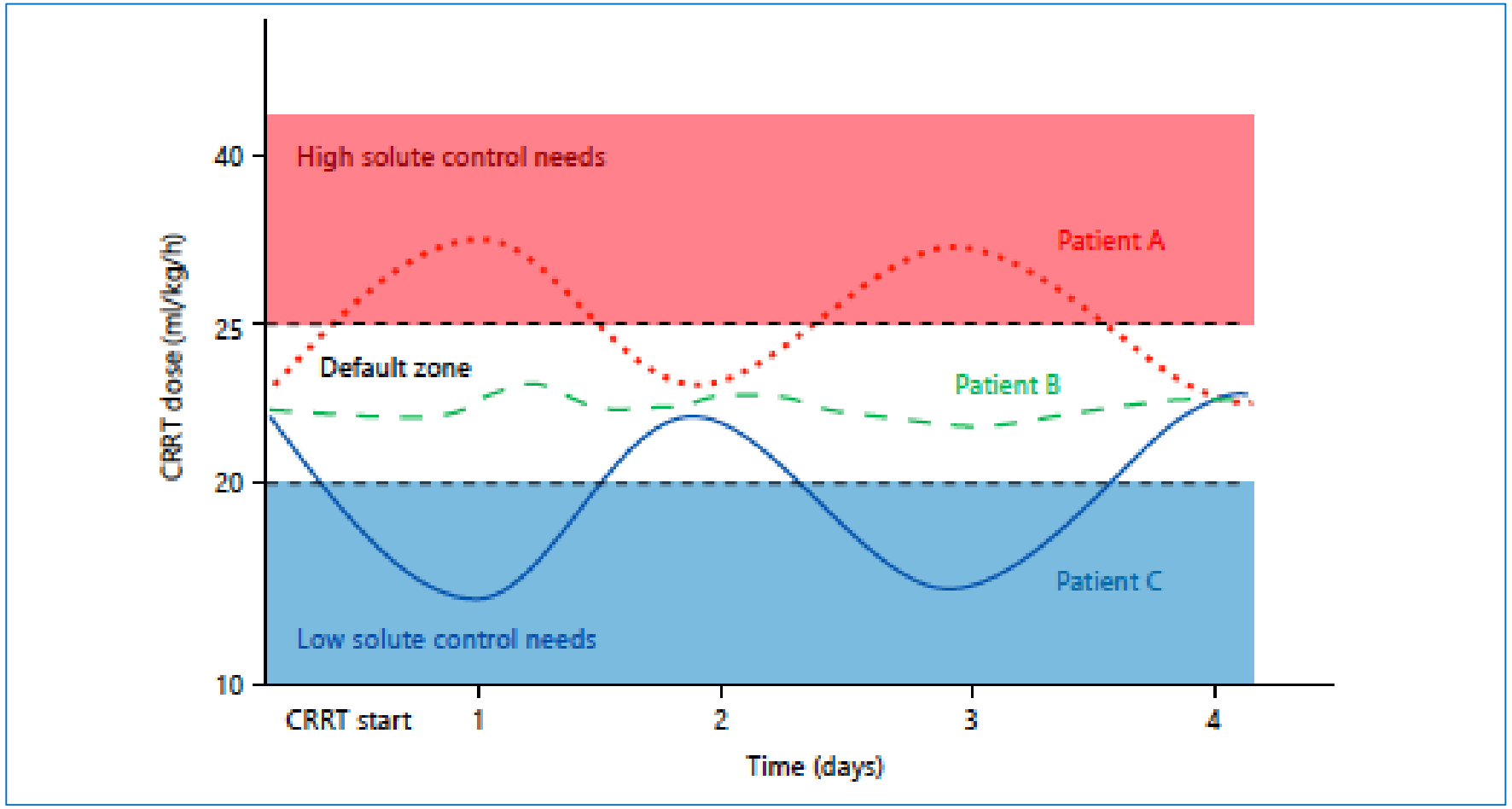
Relationship between delivered dose of CRRT and survival.



Prowle et al, Crit care 2011

Dynamic CRRT prescription.

Initial CRRT dose: Effluent volume 25-30 ml/kg/h (delivered: 20-25 ml/kg/h)



Therapeutic goals of CRRT in ICU

Azotemia	• BUN < 60mg/dl (Blood urea < 120 mg/dl).
Acidosis	• pH > 7.2-7.25.
Electrolytes	• Serum electrolytes within normal range.
Fluid balance	• Fluid removal to achieve volume closer to normal.
Anticoagulation	• Optimize anticoagulation, if used

Therapeutic goals (contd.)

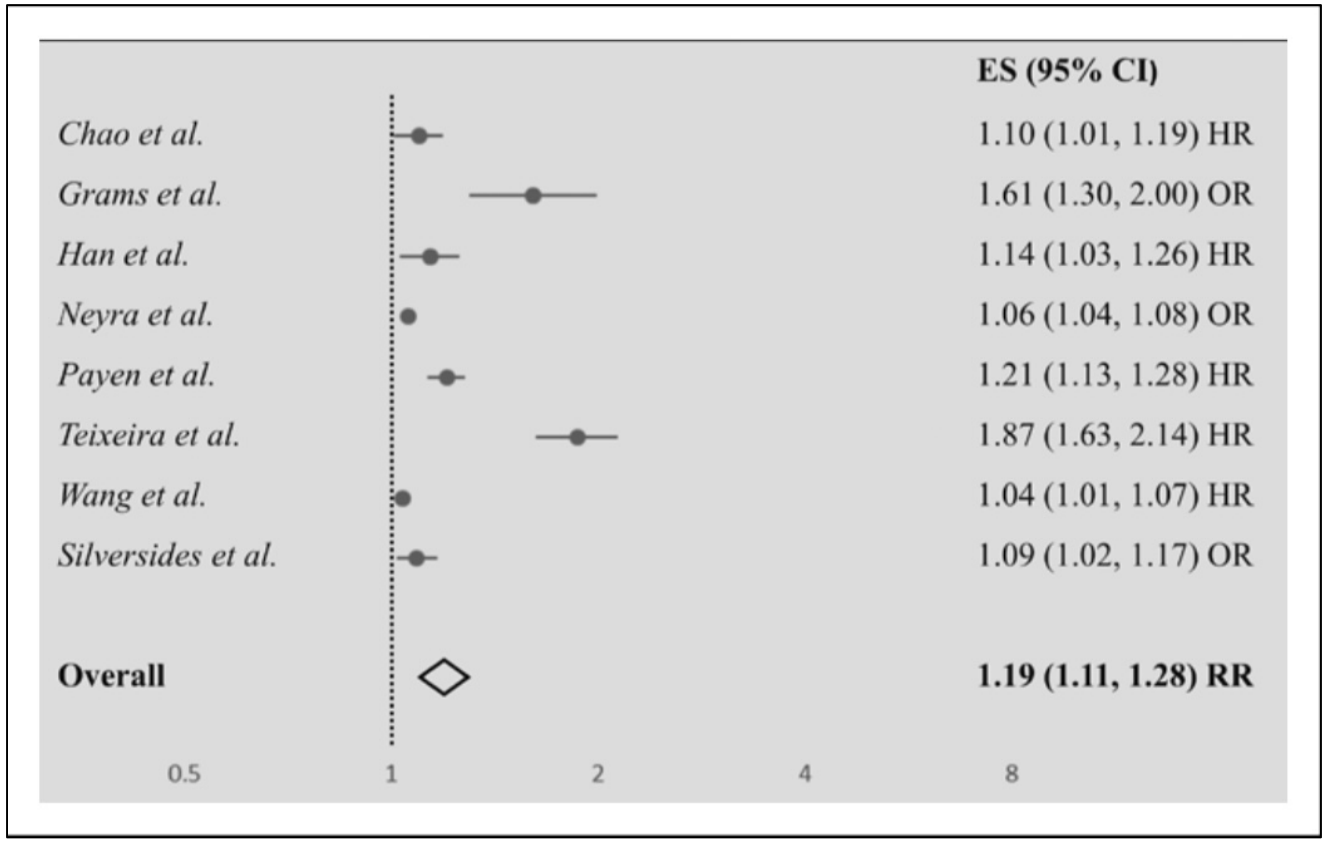
- Efficient clearance of uremic toxins (small and middle molecules)
- Correction of metabolic derangements
  - Acid-base balance
  - Electrolyte, divalent irons
  - Control of volume
- Facilitate renal and patient survival

FLUID OVERLOAD

Fluid overload: Why does it matter?

- The epidemic of fluid overload started in the early 2000s with the over-enthusiastic use of goal-directed fluid therapy
- First warning bells from Pediatric ICU
- Later confirmed in the analysis of the SOAP study (2006) in adults
- Current understanding:
  - Fluid overload > 5% of body weight increased risk , and >10% is strongly associated with hospital mortality and AKI

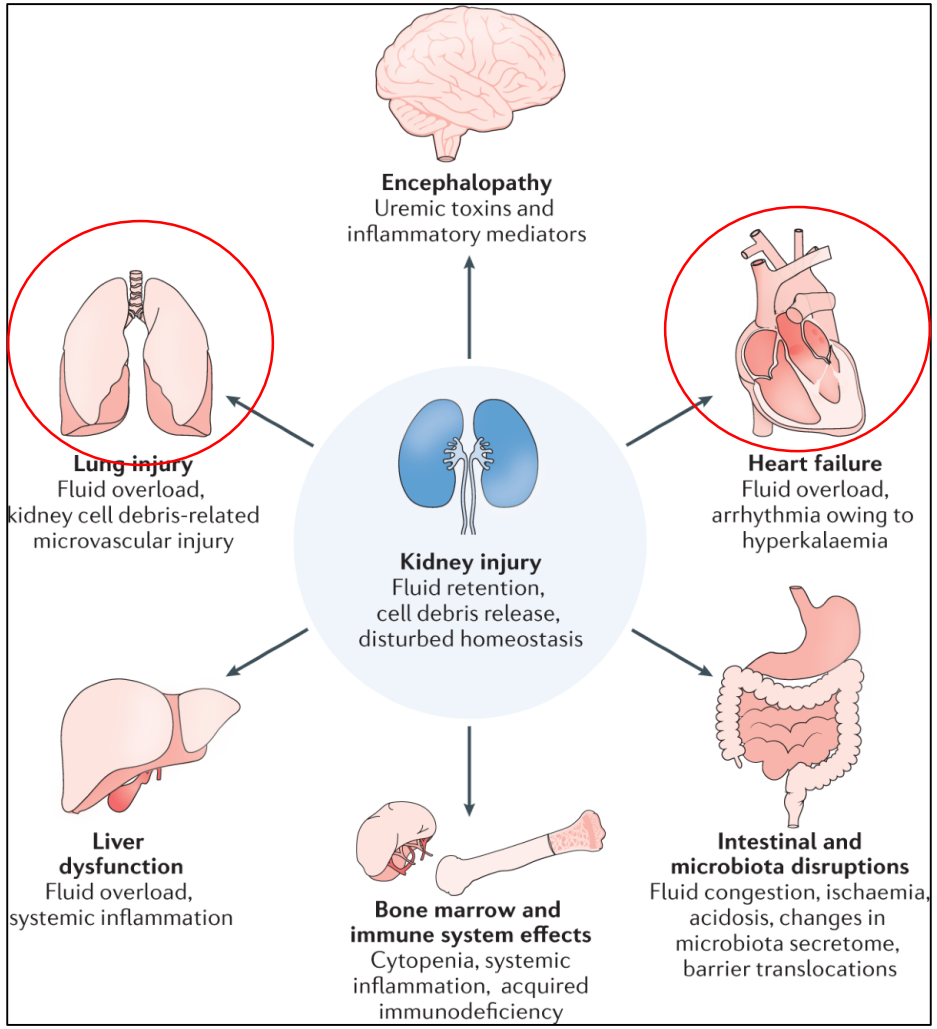
Fluid overload and mortality in critically ill



19% increase in mortality for every 1 L of excessive fluid accumulation

Messmer et al, Crit Care Med 2020 (meta-analysis)

Fluid overload in AKI: adverse effects



Kellum J A et al, Nat Rev Dis Primers, 2021

Management of fluid balance during CRRT

Assessment of volume status

- **Cumulative fluid balance**
- Change in weight
- Bio-impedance analysis
- Point of care Ultrasound
  - Lung B lines
  - IVC
  - Venous access
  - Stroke volume

Integrated fluid balance (iBalance): CRRT balance and net fluid balance of patient on CRRT

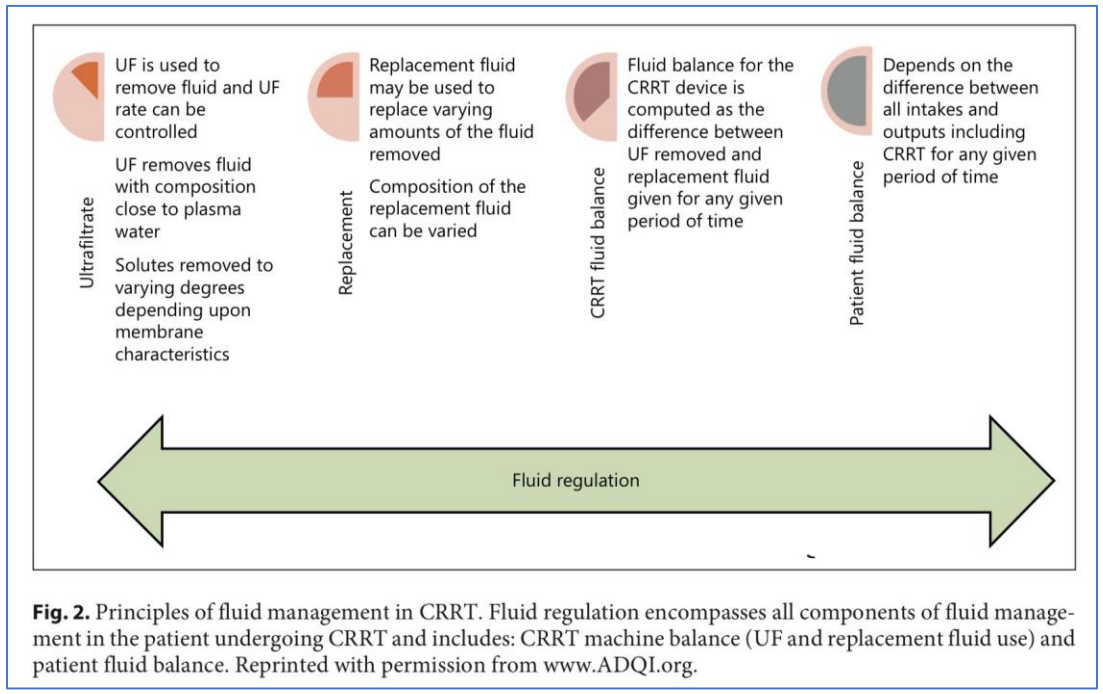
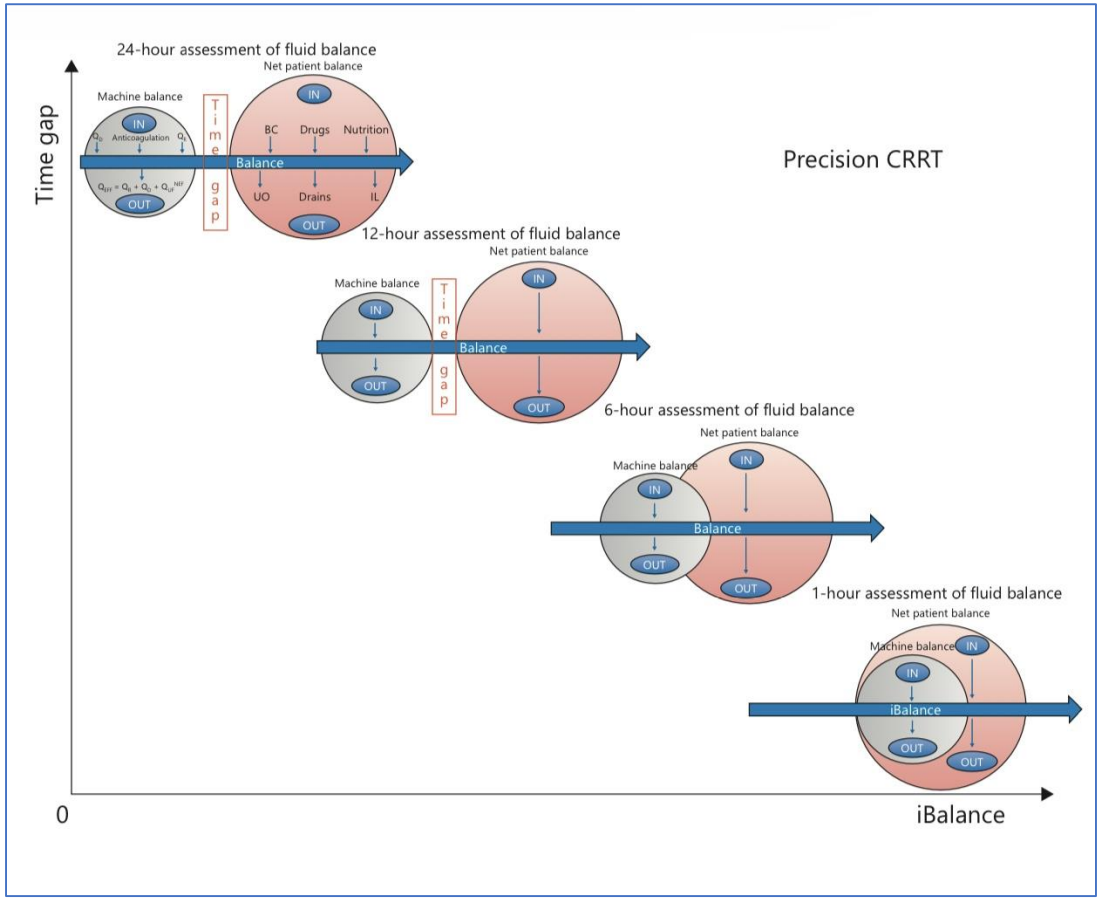


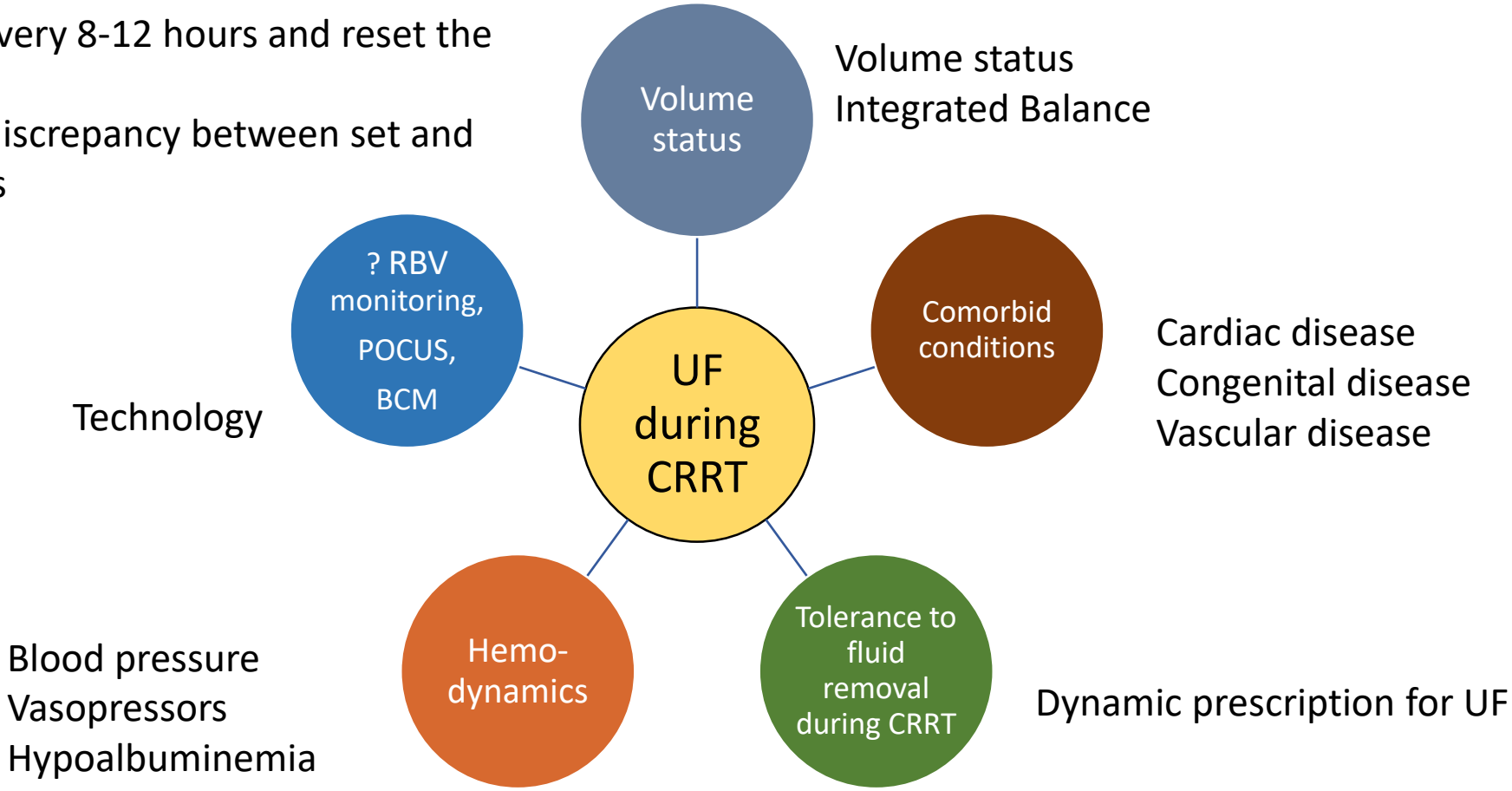
Fig. 2. Principles of fluid management in CRRT. Fluid regulation encompasses all components of fluid management in the patient undergoing CRRT and includes: CRRT machine balance (UF and replacement fluid use) and patient fluid balance. Reprinted with permission from www.ADQI.org.



Murugan R et al, Blood Purif 2016

Factors to consider during fluid removal during CRRT

- Assess iBalance every 8-12 hours and reset the goals
- Address the the discrepancy between set and achieved UF goals



Acidosis & Electrolyte Abnormalities

Impact of dialysis practice patterns on outcomes in acute kidney injury in Intensive Care Unit.

Table 4: Results of univariate and multivariate logistic regression analysis showing variables affecting hospital mortality

	Univariate analysis			Multivariate analysis		
	OR	95% CI	P	OR	95% CI	P
Age	1.0	0.98-1.02	0.97	0.99	0.96-1.02	0.51
Gender (male)	2.13	1.01-4.49	0.046	2.27	0.85-6.1	0.10
CRRT versus others	2.87	1.41-5.8	0.004	0.95	0.34-2.68	0.92
Anuria	2.38	1.07-5.23	0.032	1.97	0.69-5.6	0.2
Serum creatinine	0.69	0.56-0.85	<0.001	0.85	0.65-1.1	0.22
BUN	0.98	0.97-0.99	0.02	0.99	0.98-1.01	0.55
pH	0.001	0.0001-0.84	<0.001	0.001	0.000-0.14	0.005
MAP	0.96	0.94-0.99	0.009	0.99	0.96-1.04	0.95
Inotropes	2.12	1.4-3.22	<0.001	1.39	0.8-2.4	0.24
Ventilator	4.62	1.97-10.8	<0.001	2.15	0.73-6.3	0.16

CRRT: Continuous renal replacement therapy; BUN: Blood urea nitrogen; MAP: Mean arterial pressure; OR: Odds ratio; CI: Confidence interval

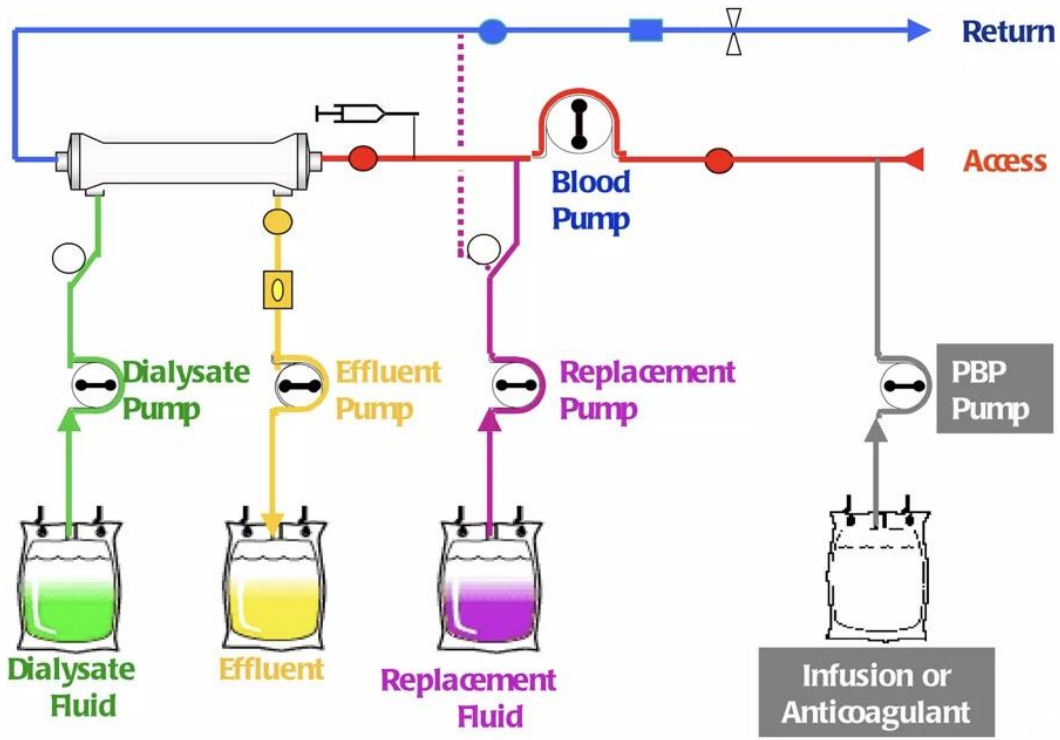
Metabolic acidosis is strongly associated with increased mortality

Correction of acidosis during CRRT

Increase the effluent volume
D=1250 ml/h
RF= 1250 ml/h

CVVH with post-dilution

Don’t add NAHCO3 to Dialysate



Prismasol
1000 ml/h

Prismasol
1000 ml/h

0.9% Saline
5000 ml/h

IV Soda bicarbonate
7.5% 30-50 ml/h

Add Soda bicarbonate
7.5%, 100-150 ml/5L of RF

Replace with 0.45% saline
465 ml+35 ml Soda bicarbonate

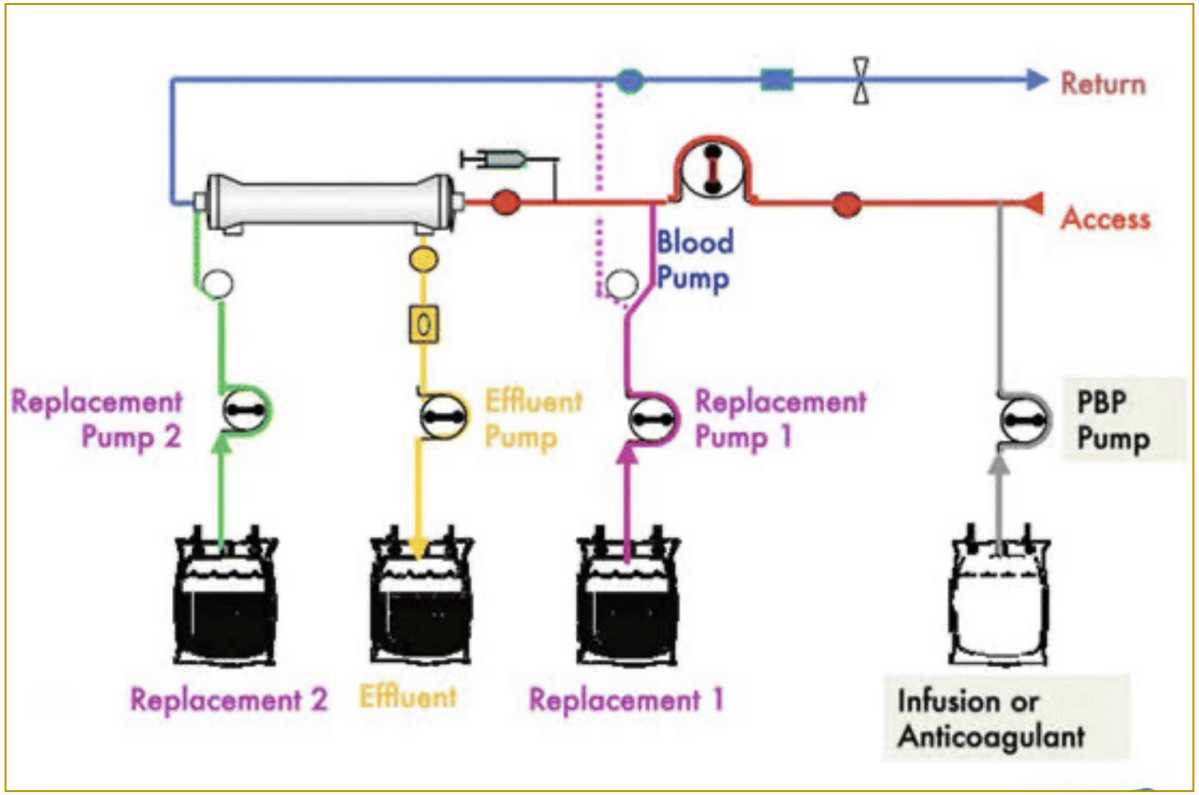
Hyponatremia and hypernatremia: principles of correction

- Serum sodium < 120 meq/L and > 160 meq/L are associated with increased mortality.
- The rate of correction depends on
    - Degree of imbalance of serum sodium
    - Acute or chronic
    - Symptoms
- In chronic (> 48 hours) hypo- or hypernatremia, the correction rate should not exceed > 10 meq/L per day.

Hyponatremia and hypernatremia: correction

- It is easier to manage in CRRT than SLED/IHD
- If sodium imbalance is the predominant indication for CRRT, using low-volume CVVH instead of standard CVVHDF is better.
- The RF can be customized to the required sodium concentration.
- If the patient has a concurrent need for correction of acidosis or severe azotemia, then the most life-threatening uremic complication should be addressed first.

CVVH with customized CRRT fluids



S. sodium	Target S. sodium	RF	PBP
110	120	120-122	120-122 (add 20-25 ml of 7.5% soda bicarbonate to 500 ml 0.45% saline) or Ringer lactate (130 meq/L)
165	155	154-156	154 (0.9% saline)

Modifications of RF to achieve desired sodium concentrate

To lower the sodium concentration of RF						
Volume of free water (5% dextrose) added to 5 L of RF	0	150 ml	250 ml	500 ml	750 ml	1000 ml
The final volume of RF	5 L	5.15 L	5.25 L	5.5 L	5.75 L	6L
The final sodium concentration in the RF	140	136	133	127	122	116.6
To increase the sodium concentration of RF						
The volume of 3% saline added to 5 L of RF	0 ml	50 ml	100 ml	150 ml	200 ml	250 ml
The final volume of RF	5 L	5.05 L	5.1 L	5.15 L	5.2 L	5.25 L
The final sodium concentration in the RF	140	144	147	150	154	158

MONITORING

Monitoring during CRRT

Patient	CRRT efficacy	Circuit patency
• Blood pressure • Cardiac rhythm • Organ failure (SOFA, qSOFA) • Urine output • Temperature • Organ edema	• Solute clearance • Filter efficacy • Electrolyte balance • Acid-base balance • Fluid balance	• Vascular access • Anticoagulation • Circuit pressures • (TMP, arterial pressure) • Filter clots

Lab monitoring in patients on CRRT

- Blood sugar - every 4-6 th hourly
- S.Electrolytes,-every 8-12 th hourly

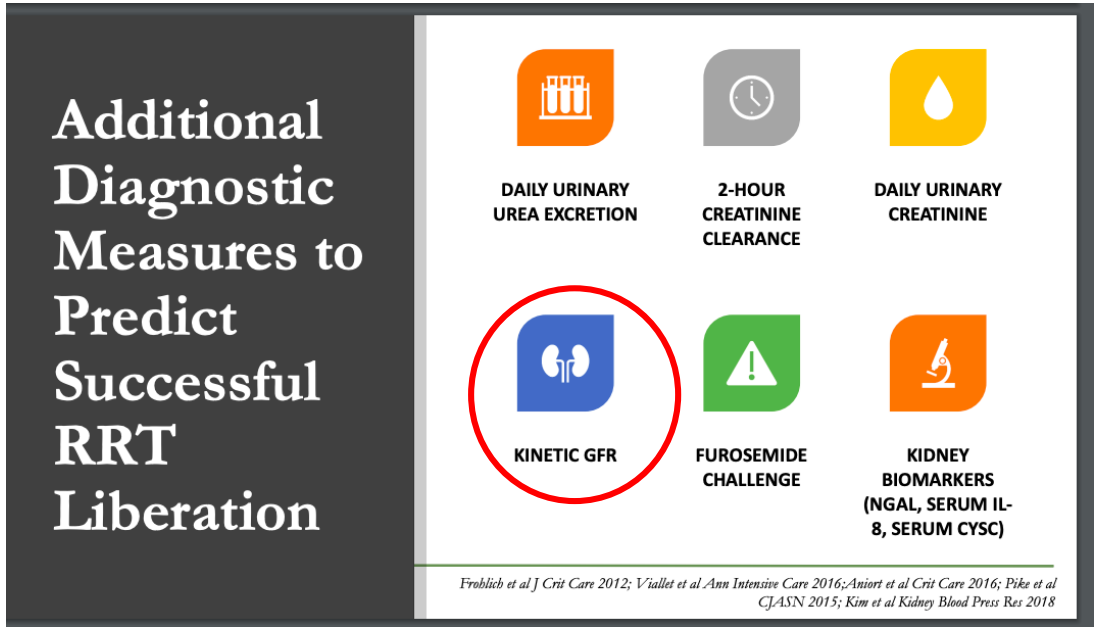
- S.calcium , Phosphorous and magnesium -12 th hourly if abnormal or 24 th hourly
- Blood urea, S.creatinine - Every 24 hourly
- ACT/Aptt -1-2 hourly during initiation and after a stable dose is established, every 12-24 th hourly

Weaning of CRRT

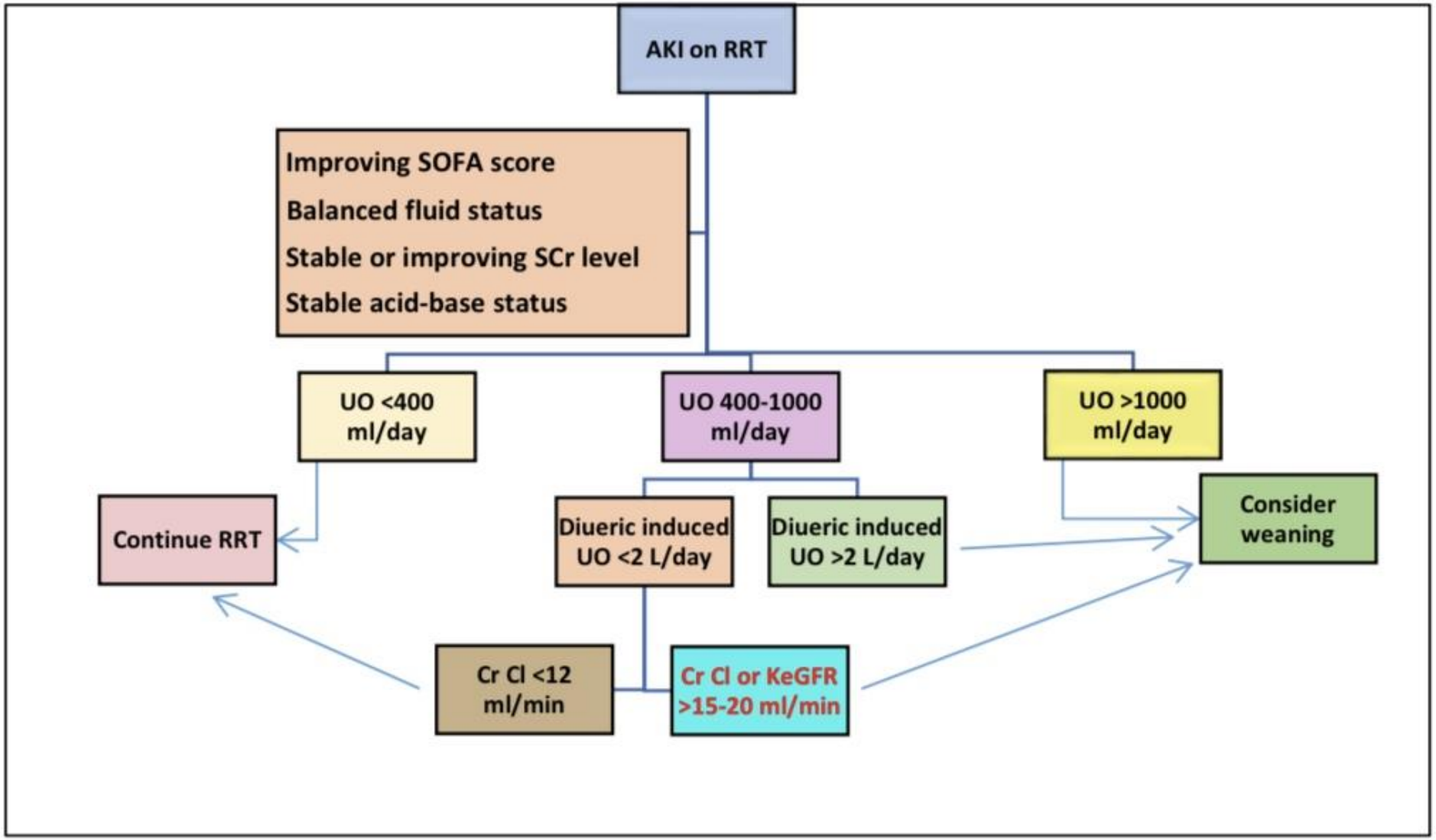
Weaning of CRRT

- Evidence of renal recovery
- Improvement in hemodynamics: transition to other modalities of RRT
- Futility of therapy

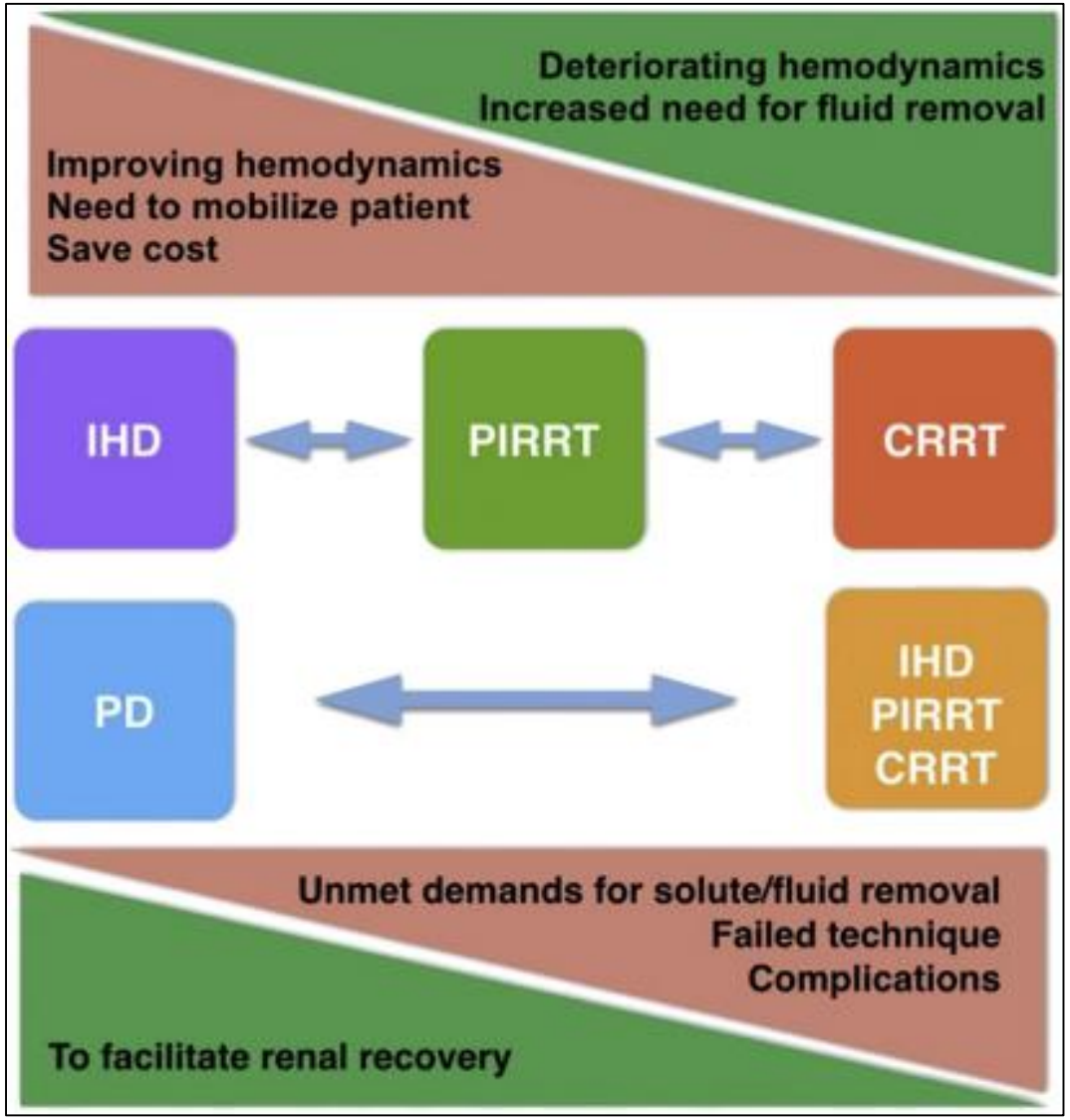
Urine output >450 ml/day, or >2000ml/day diuretic induced



Weaning from CRRT



Transition from CRRT to SLED



To summarize:

- Initiate CRRT when the said indications are met
- Set goals for CRRT to achieve
- Individualize the prescription of CRRT (personalized CRRT) to achieve the set goals
- Monitor CRRT and modify the prescription as needed (dynamic prescription)
- When the time is conducive, wean CRRT or transition to another RRT mode

THANK YOU

Antenatal renal anomalies

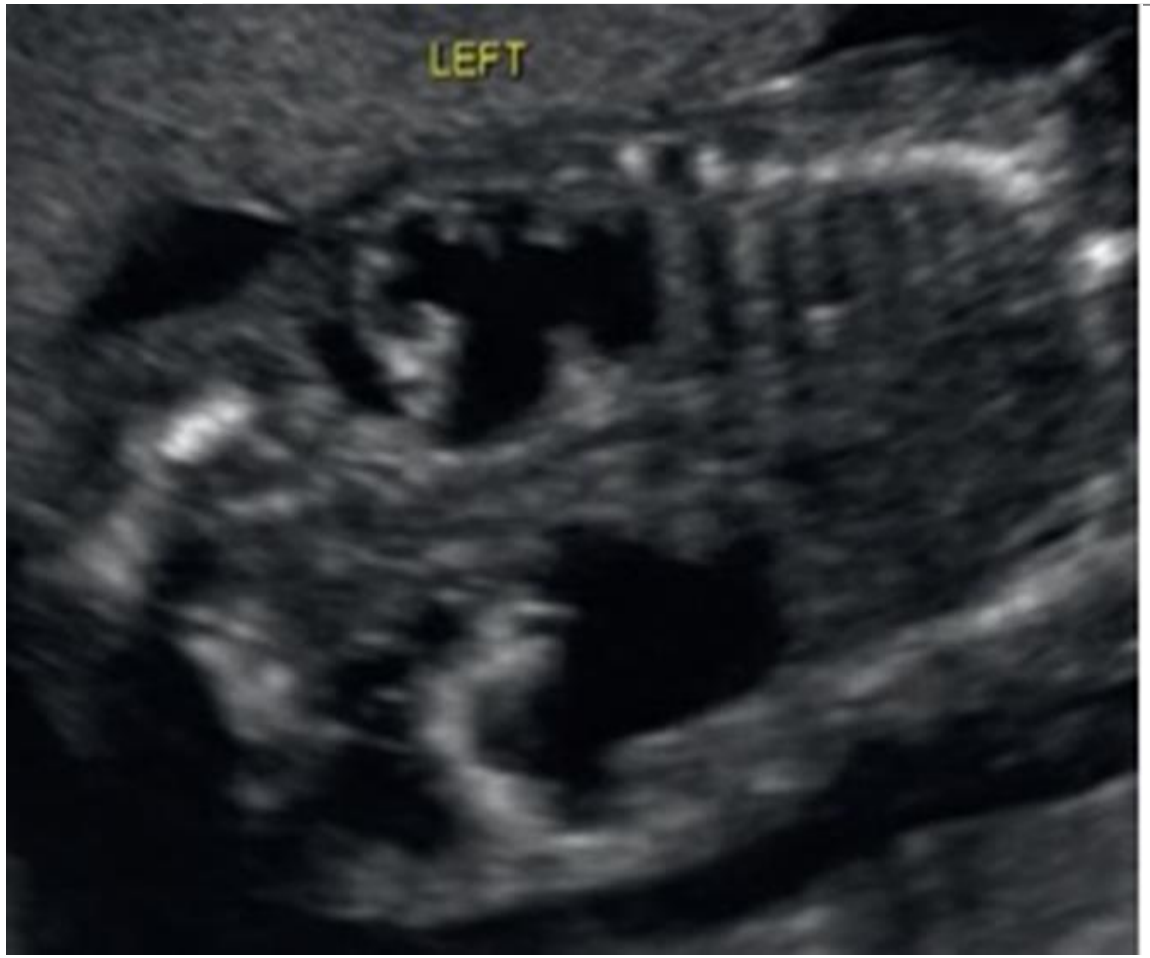
PANEL DISCUSSION

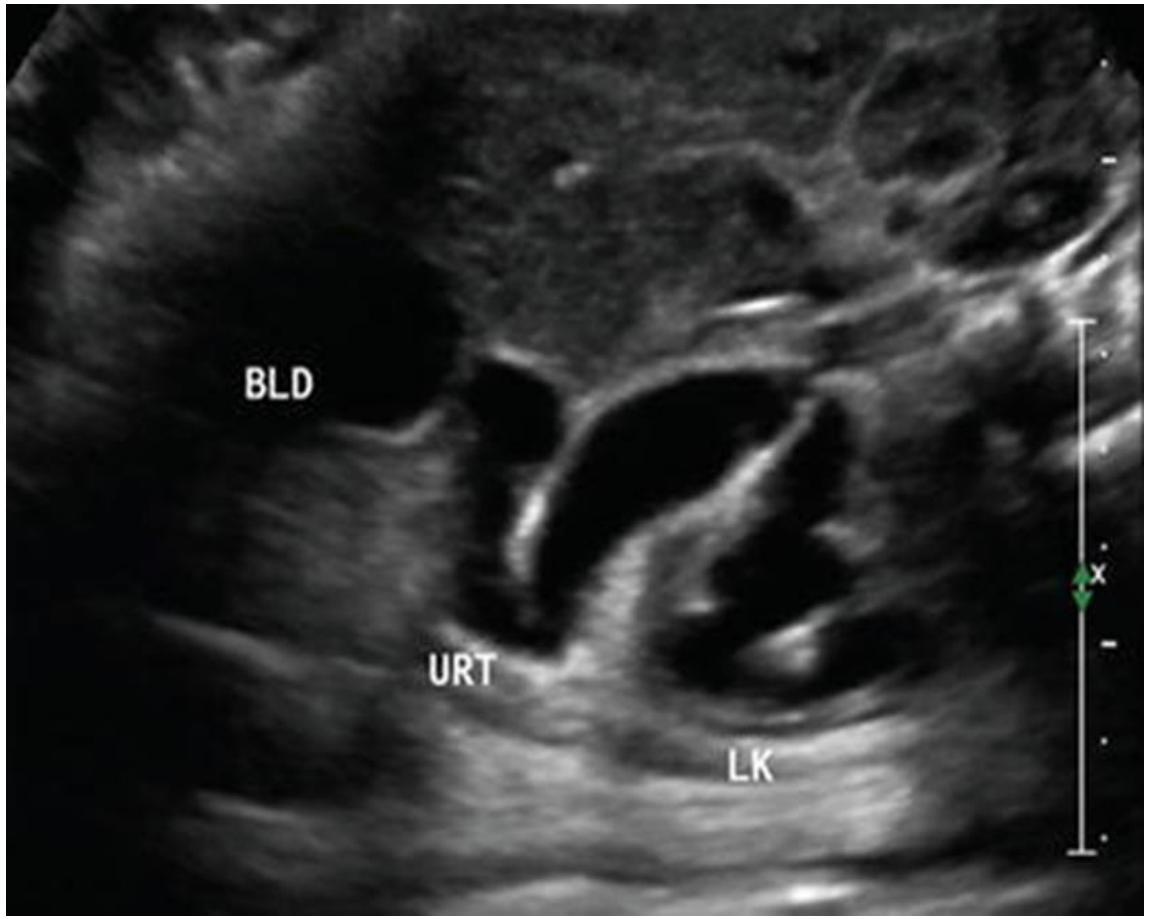
Case 1

30-year-old primigravida referred at 30 weeks' gestation"
Antenatal Ultrasound Findings
Bilateral renal pelvic dilatation (APD 12 mm left, 10 mm right)
Bilateral calyceal dilatation
Normal parenchymal echogenicity
Thick-walled bladder
Ureters are dilated
Amniotic fluid index: 10 cm (normal)

There is no family history of renal anomalies or consanguinity. The obstetrician refers for counseling and anticipatory guidance.

Fetal hydronephrosis





Dr Vidhya

How do you—as a pediatric nephrologist

approach risk stratification,prognosis, and counseling?

What are the causes of antenatal hydronephrosis?

What parameters in the fetal report are most prognostically significant, and what are your recommendations for monitoring and delivery planning?

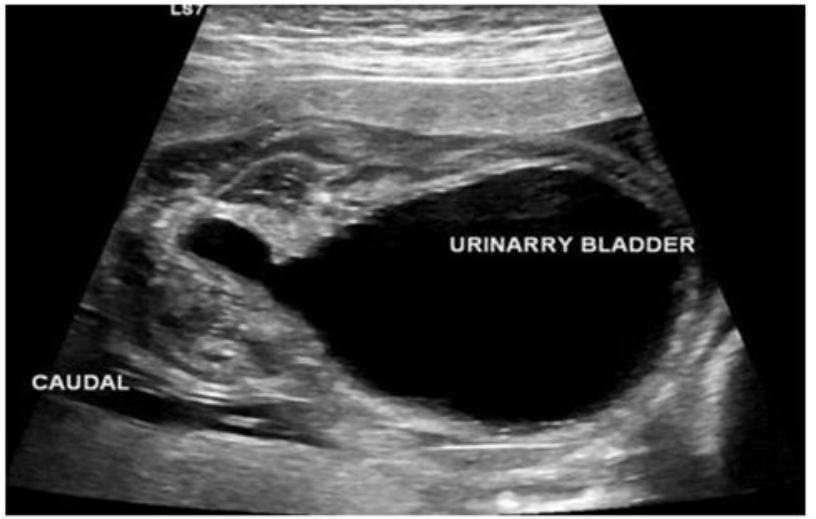
- Antenatal Hydronephrosis(ANH) is dilatation of the Renal Pelvi calyceal system detected antenatally through USG
- APD diameter: 2nd trimester ≥4 mm, and 3rd trimester ≥7mm

Etiology	All Cases(%)
Transient Hydronephrosis	41-88
PUJ Obstruction	10-30
VUR	10-20
VUJ Obstruction/Megaureter	5-10
MCDK	4-6
Duplex kidneys(+/- Ureterocele)	2-7
PUV	1-2
Others: Ureteral atresia, Prune Belly Syndrome, Tumours	Uncommon

- Need to distinguish infants requiring long-term follow-up or surgery from those with transient hydronephrosis and minimum need for invasive investigations

Classification of ANH based on renal antero posterior diameter(APD)

Classification	Second Trimester -APD	Third Trimester- APD
Mild	4-6mm	7-9mm
Moderate	7-10mm	10-15mm
Severe	>10mm	>15mm



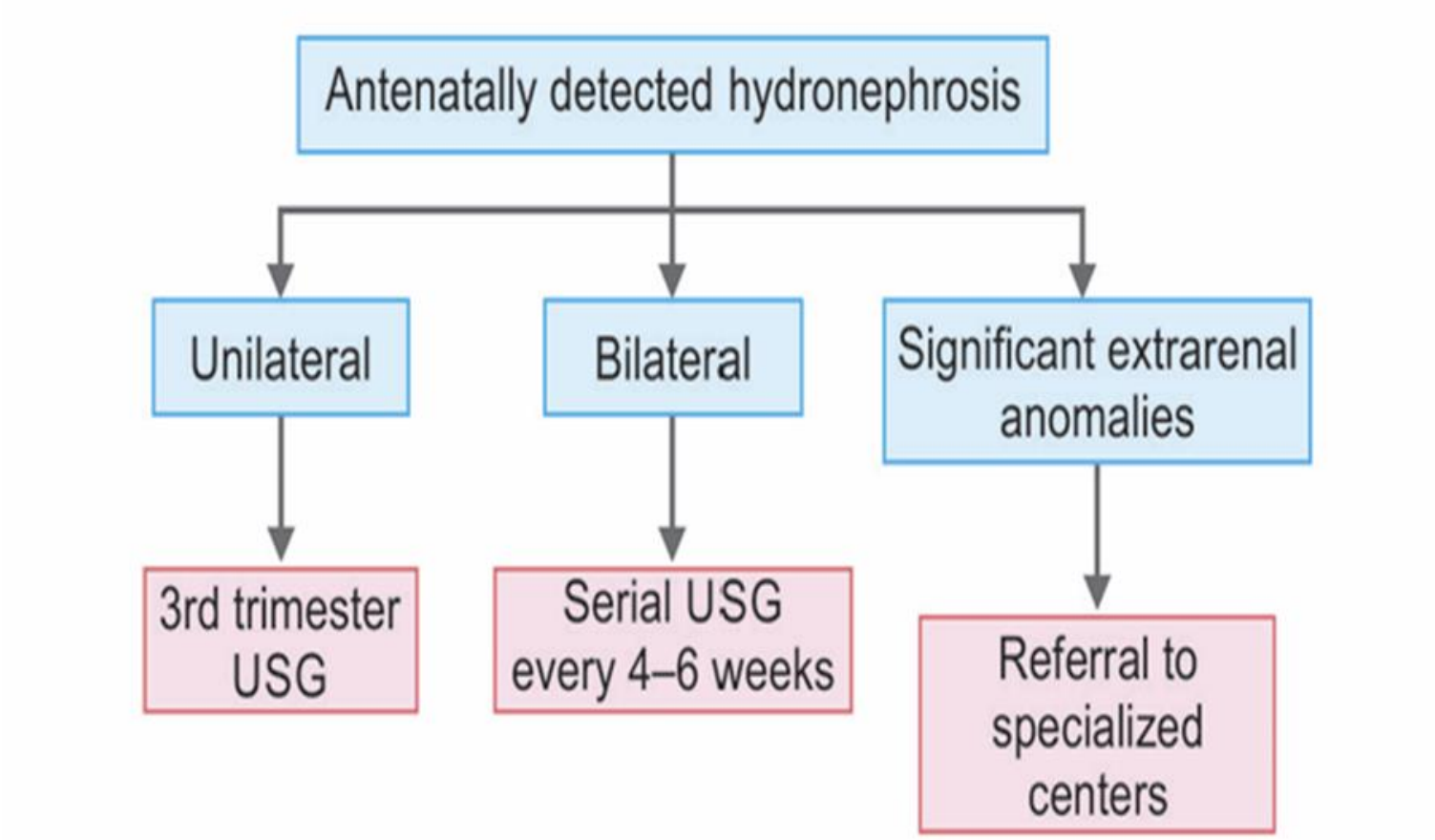
AN USG- Findings

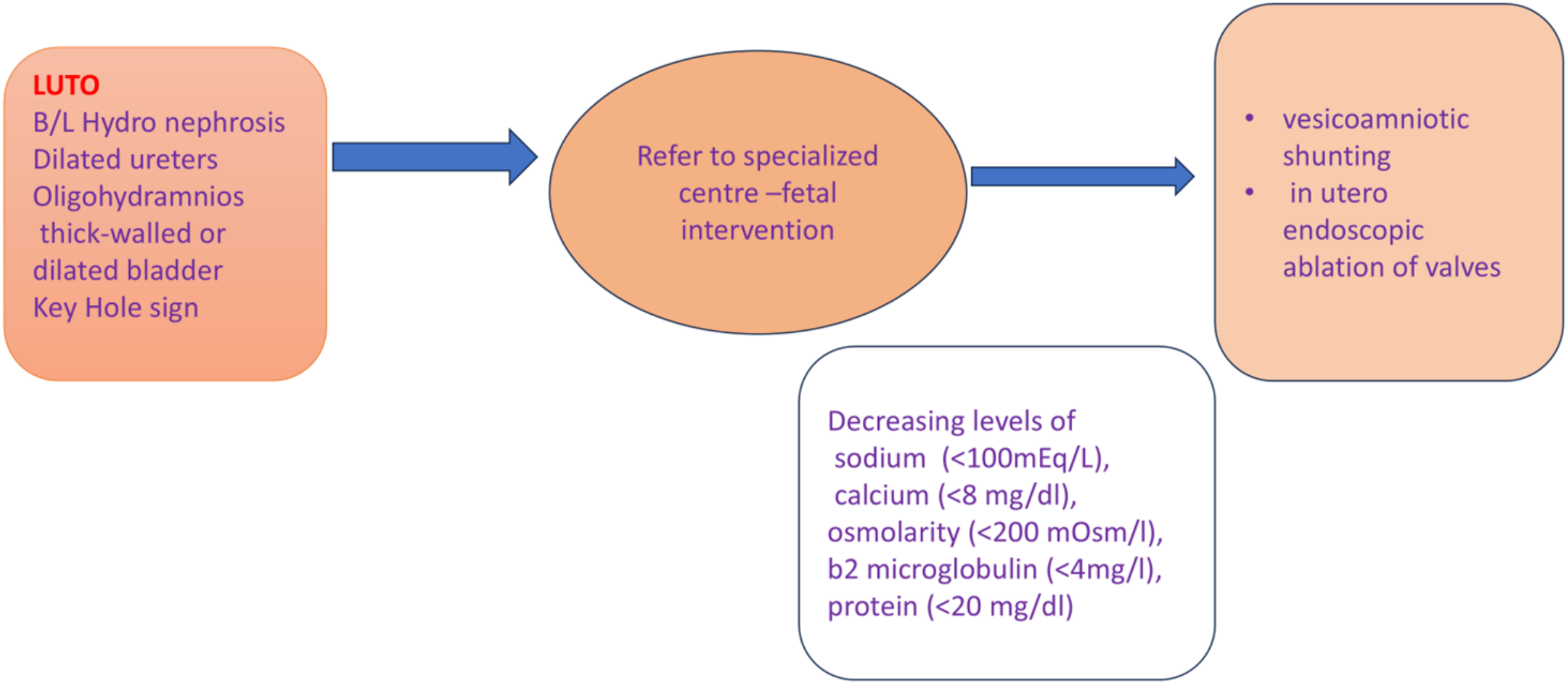
Renal Abnormalities
Calyceal dilatation Perinephric urinoma Ureteral dilatation Dilated /thick walled bladder Key hole sign Oligohydramnios
Loss of renal Parenchyma -cortical thinning -poor CMD -Increased renal echoes -renal cysts Renal Size

GESTATIONAL AGE(WEEKS)	KIDNEY LENGTH(mm) -50th %
15	12.5
20	20
25	26
30	33
35	38
40	44

Renal size in mm = Gestational age(weeks)

Antenatal Monitoring-with Ultrasound




LUTO
B/L Hydro nephrosis
Dilated ureters
Oligohydramnios
thick-walled or dilated bladder
Key Hole sign
Refer to specialized centre –fetal intervention
vesicoamniotic shunting
in utero endoscopic ablation of valves
Decreasing levels of sodium (<100mEq/L), calcium (<8 mg/dl), osmolarity (<200 mOsm/l), b2 microglobulin (<4mg/l), protein (<20 mg/dl)

Delivery planning

- Termination of pregnancy is not recommended in fetuses with unilateral or bilateral ANH, except in presence of extrarenal life threatening abnormality.
- Pregnancy should be carried out in a tertiary care centre with neonatal intensive care facilities
- Early delivery is not indicated, and carries risks of prematurity and low birth weight.

Postnatal management

The infant is delivered at 38 weeks/3.2 kg, passes urine within 12 hours of life

Ultrasound done on day 2 reveals

- Bilateral renal pelvic dilatation with APDs of 14 mm and 11 mm
- Moderate calyceal dilatation
- Thick-walled bladder, partially distended
- Mild ureteral dilatation
- Normal renal parenchymal echotexture
- Normal corticomedullary differentiation

Serum creatinine on Day 2 is 1.8 mg/dL.

Dr Manjusha

Given the case scenario, what is the likely diagnosis and how would you plan management?

LUTO – immediate postnatal care

Physical examination – palpable bladder

Catheterise the bladder to relieve obstruction → diuresis → dehydration, hyponatremia, hypokalemia

Strict intake output chart, monitor electrolytes

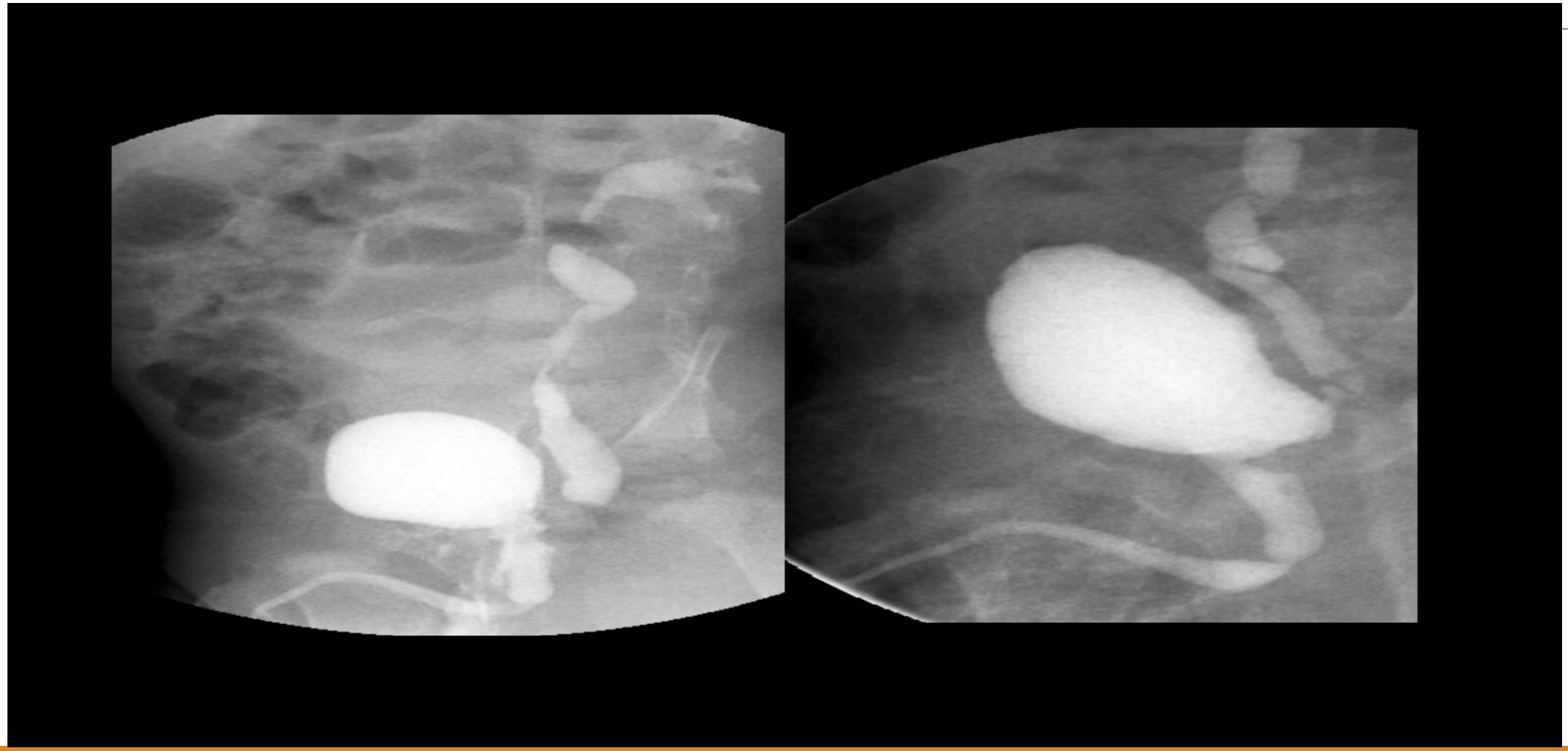
Fluid management: replacement of urine output in excess of 4ml/kg/hr with fluid containing sodium and potassium as per losses

MCU for diagnosis

Prophylactic antibiotics to prevent UTI

Stabilise and transfer for definitive correction by surgery

MCU – dilated posterior urethra with left grade 3 VUR



LUTO – PUV

The postnatal findings suggest lower urinary tract obstruction – PUV

Dr Moorthy

As a pediatric surgeon, what would be your approach to this neonate with confirmed PUV?

How would you prognosticate parents?

Case 2

30 year old primi with antenatal scan at 28 weeks showing right kidney 6cm with multiple thin walled non-communicating cysts of various sizes with non dilated pelvicalyceal system.

Left kidney is 3 cm and appears normal

Bladder wall normal. Normally emptying

Dr Vaishnavi

What are the differentials?

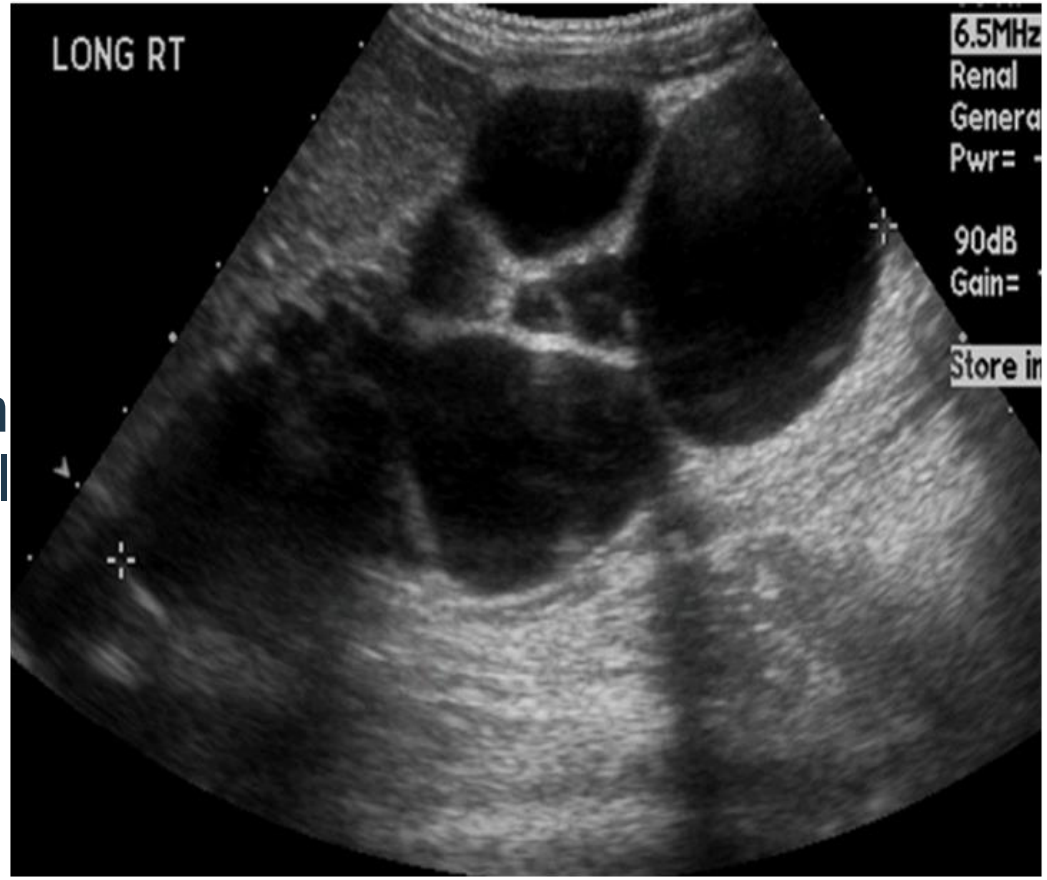
How would you evaluate postnatally?

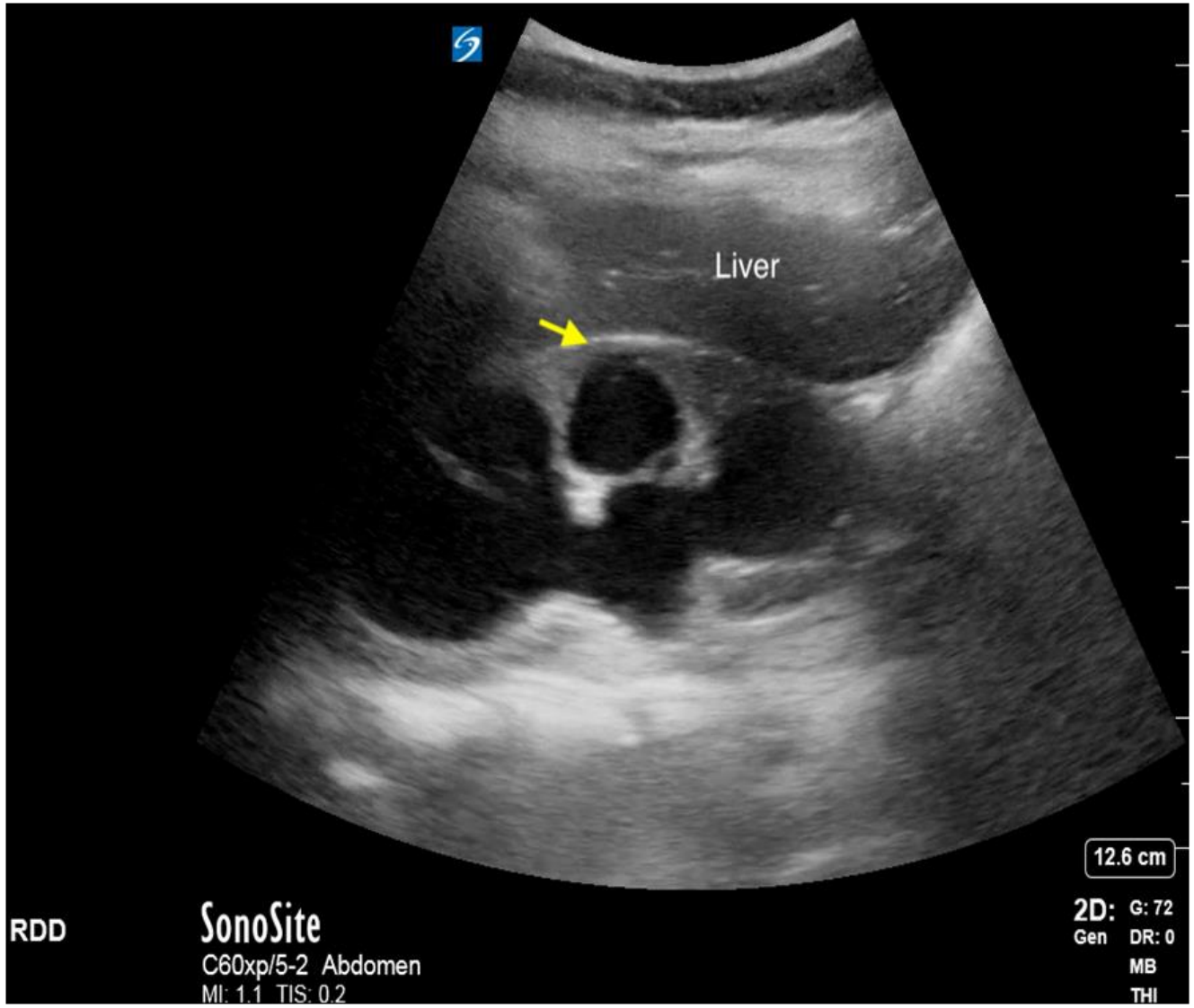
Kidney with

- smooth-walled cysts
- varying size
- not communicating with a renal pelvis,
- Abnormally echogenic intervening strom
- No cortex or collecting system identifiabl
- Other kidney Normal

classical of

MultiCystic Dysplastic Kidney





Cysts (Dilated calyces)

Communicating with pelvis

Thinned Cortex visible

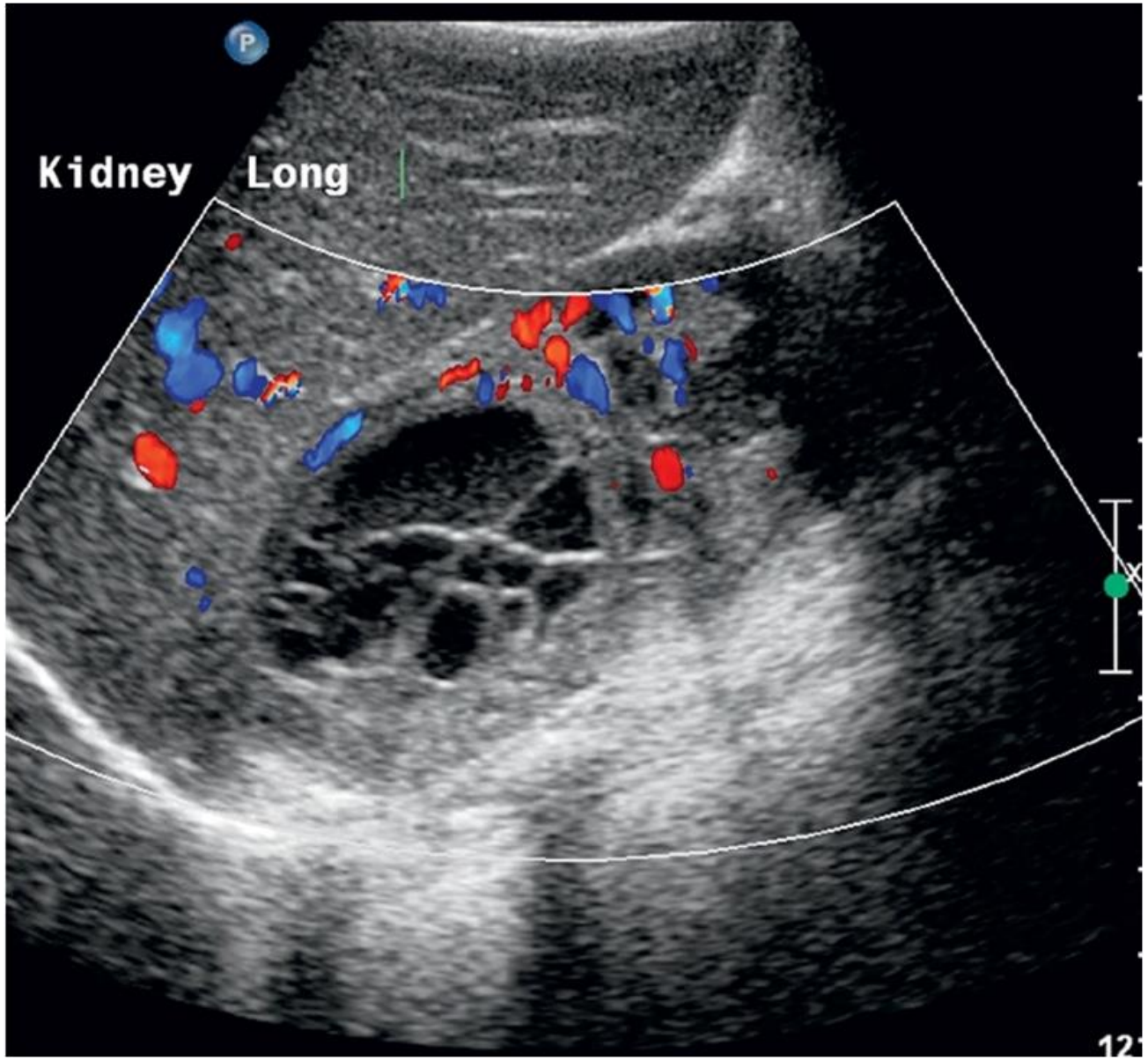
Severe hydronephrosis

DDs

1. Severe hydronephrosis
2. Cystic nephroma
3. Cystic renal dysplasia
4. ADPKD
5. ARPKD

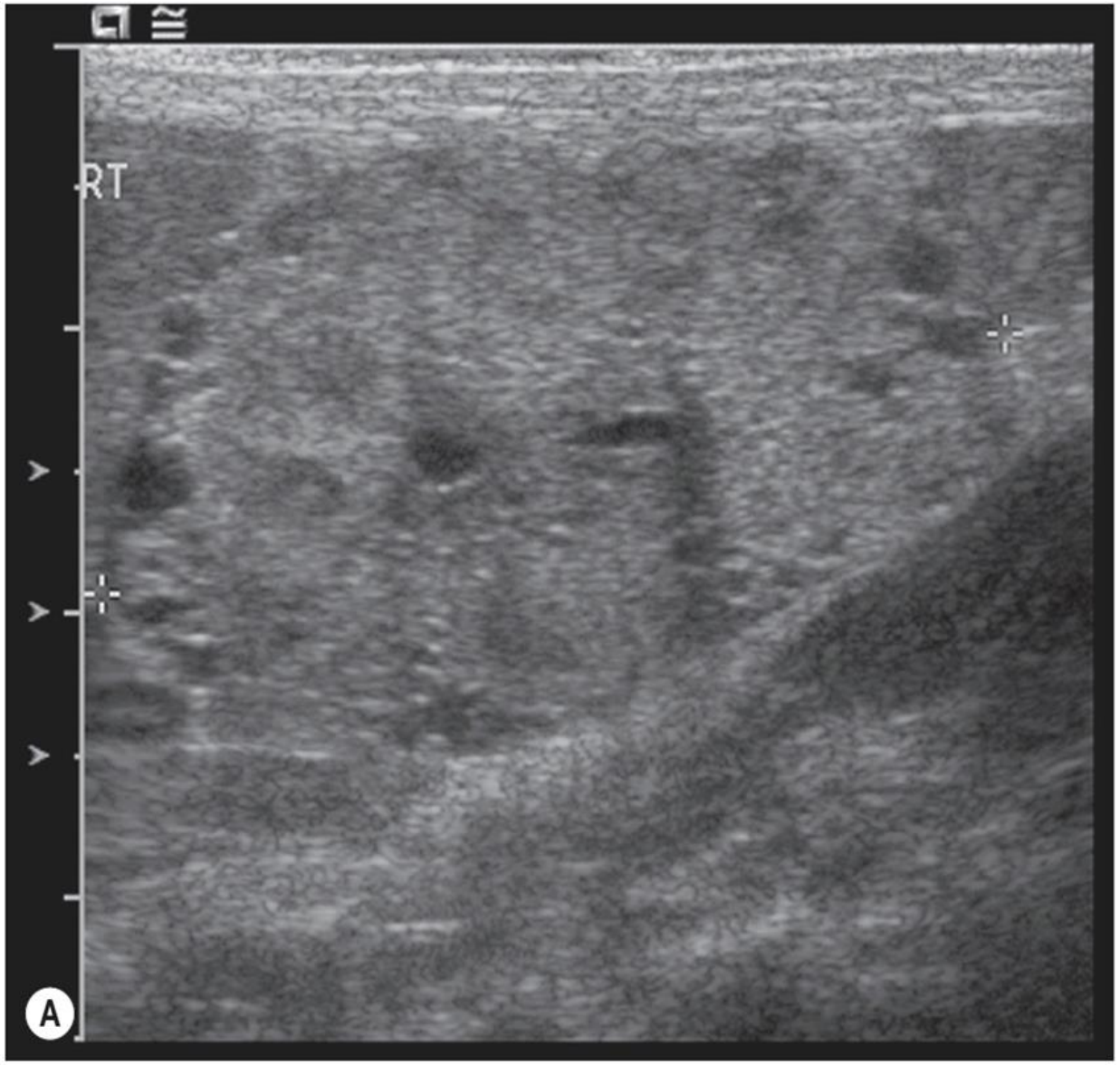
Unilateral	Bilateral
Multicystic dysplastic kidney[a] Simple cyst Multilocular cystic nephroma Cystic renal dysplasia[b]	Autosomal recessive polycystic kidney disease (ARPKD) Autosomal dominant polycystic kidney disease (ADPKD) Juvenile nephronophthisis Glomerulocystic disease Medullary cystic disease Syndromic renal cystic disease Medullary sponge kidney

[a]*Bilateral disease is not compatible with life.*
[b]*Often bilateral.*



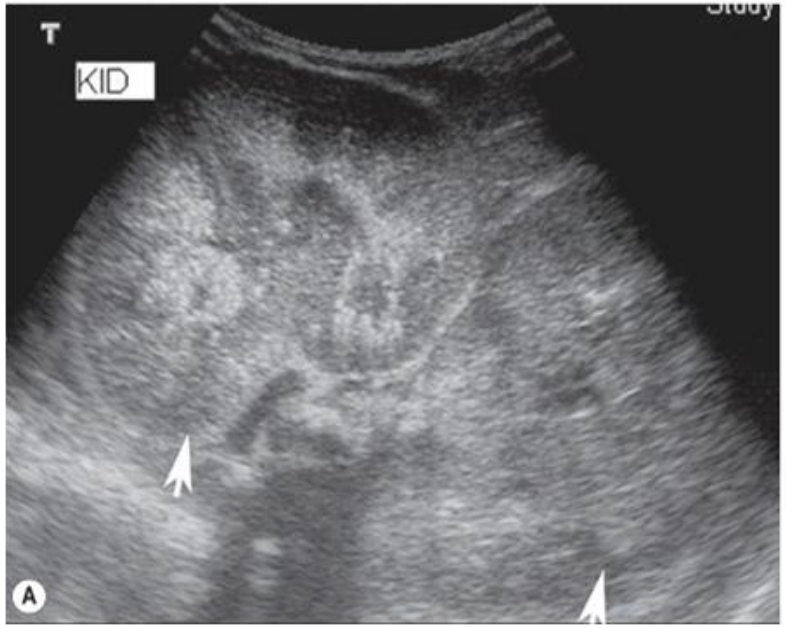
Multicystic mass lesion in one pole

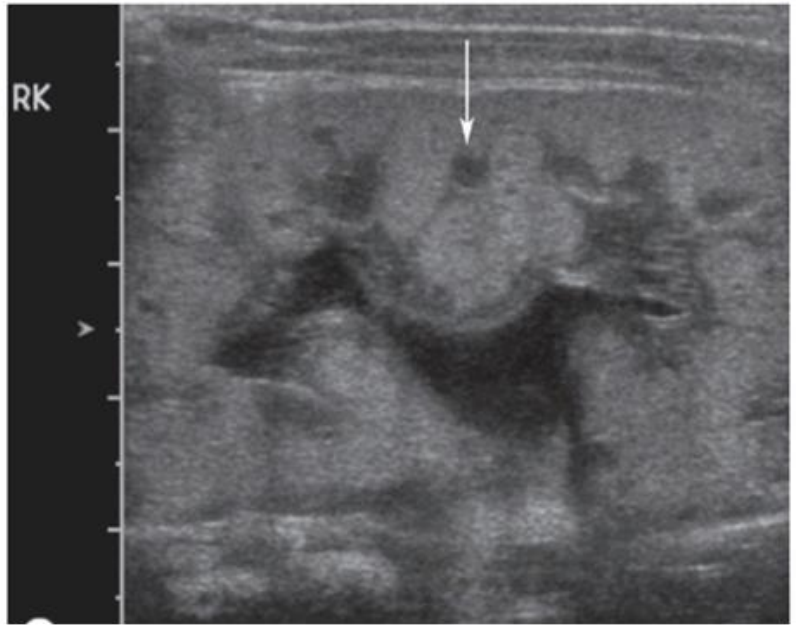
Multilocular cystic nephroma



Echogenic kidneys loss of CMD with small renal subcortical cyst – due to obstructive or reflexive nephropathy

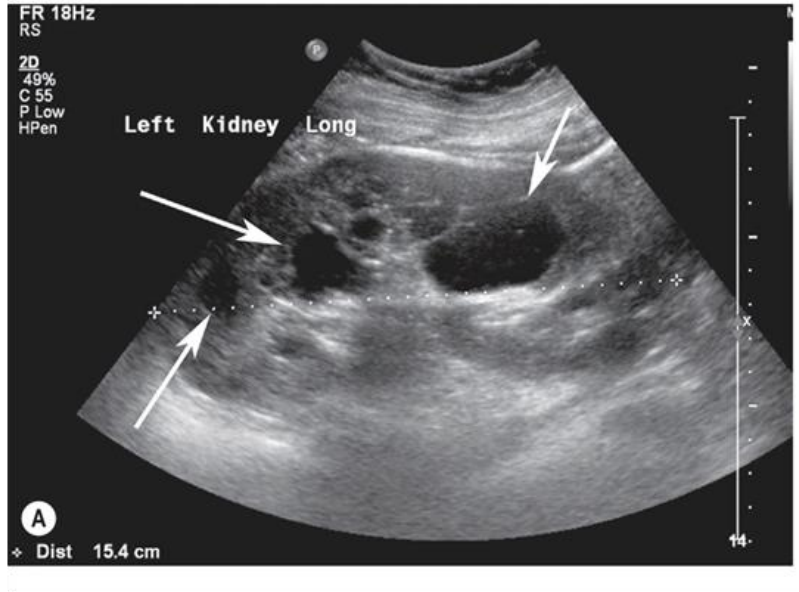
Cystic dysplasia

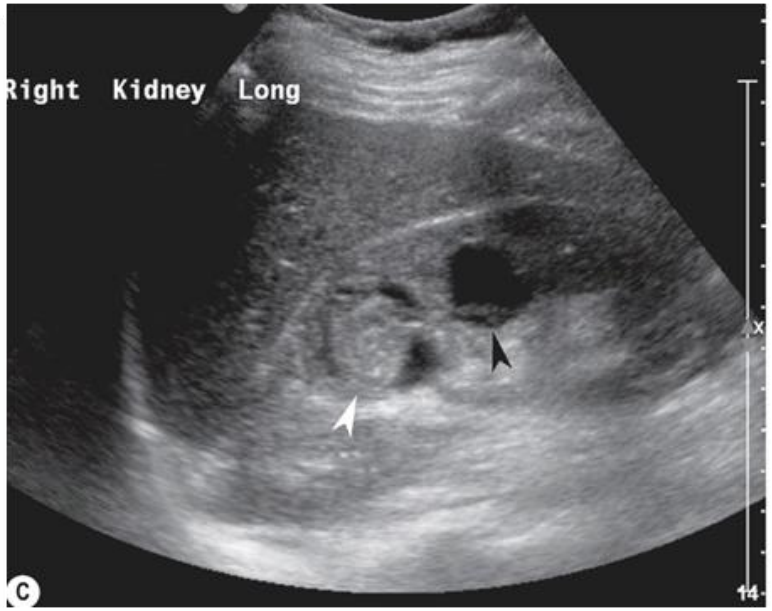




B/L Echogenic kidneys loss of CMD with small cyst - **ARPkD**

B/L Echogenic kidneys loss of CMD with multiple cyst varying size - **ADPKD**

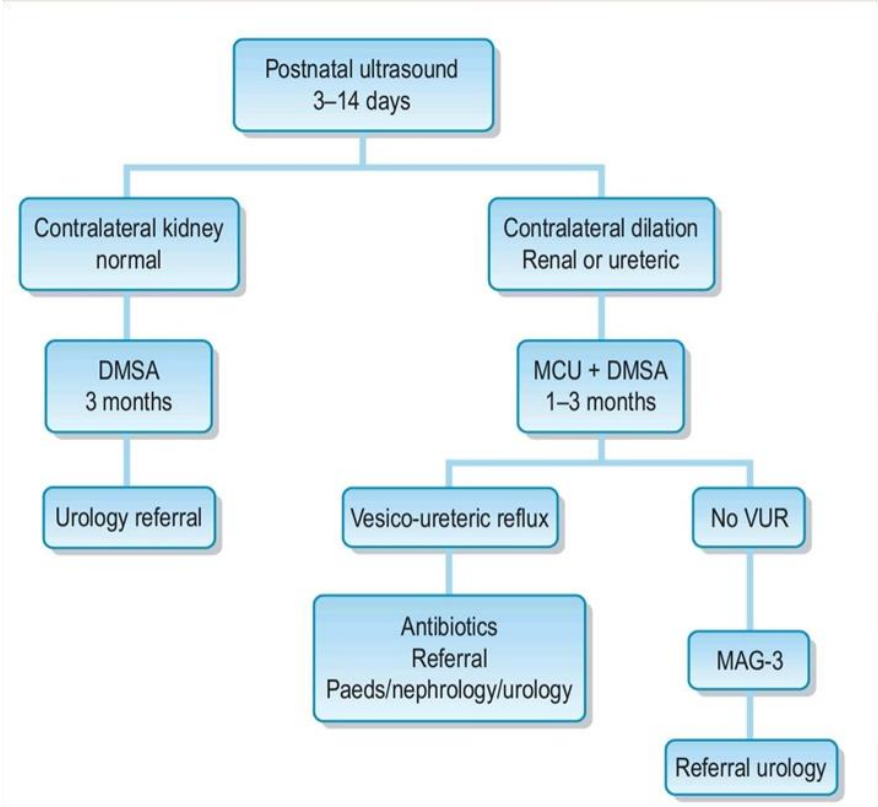




Dr Vaishnavi

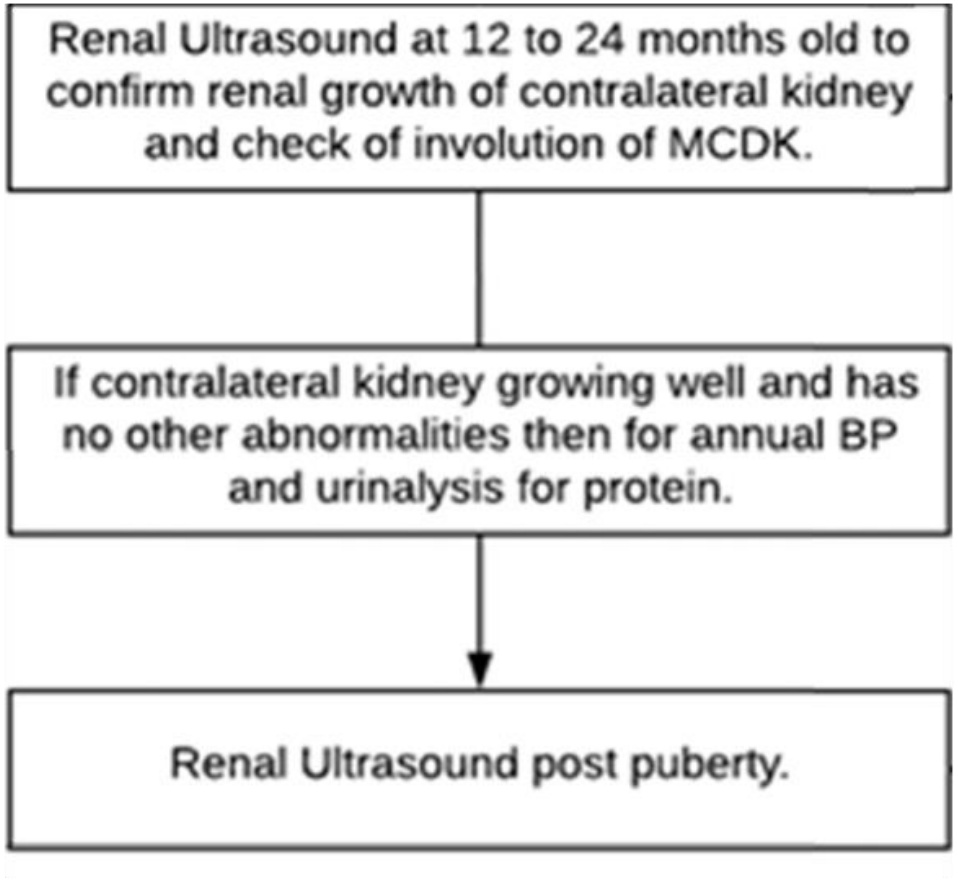
What would be the follow up plan?

Post natal evaluation



30-40% of cases have contralateral involvement Pujo/vur

Follow up plan



Complications
Hypertension
Proteinuria
Malignancy (rarely)

Dr Moorthy

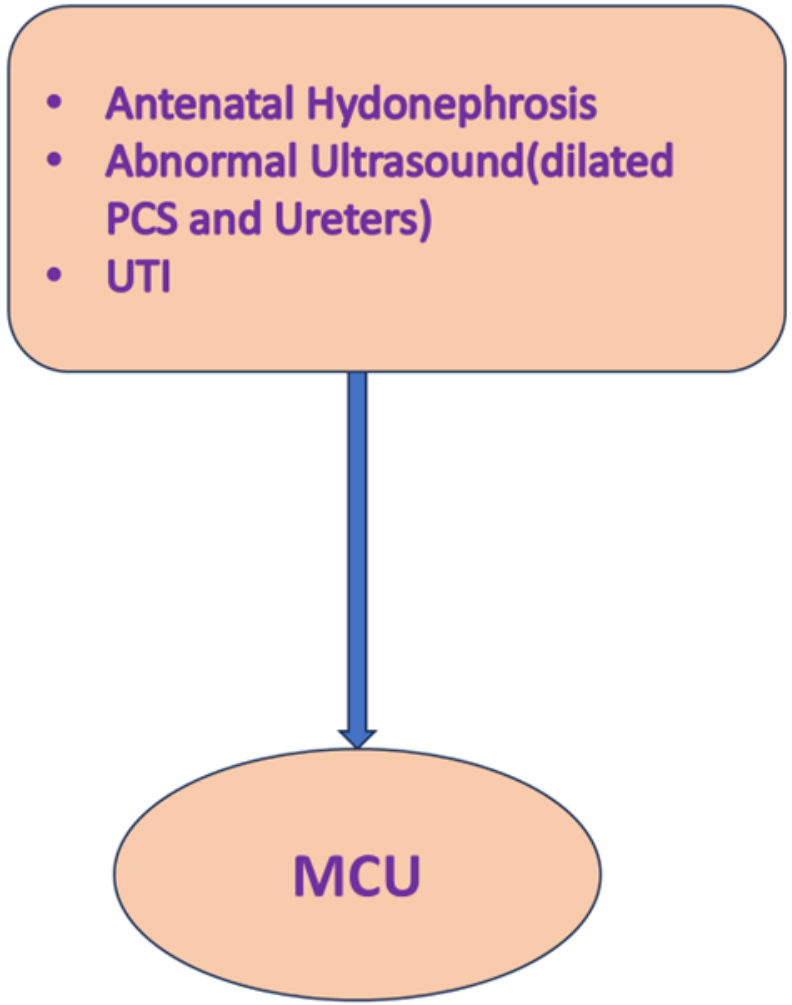
Any role of nephrectomy?

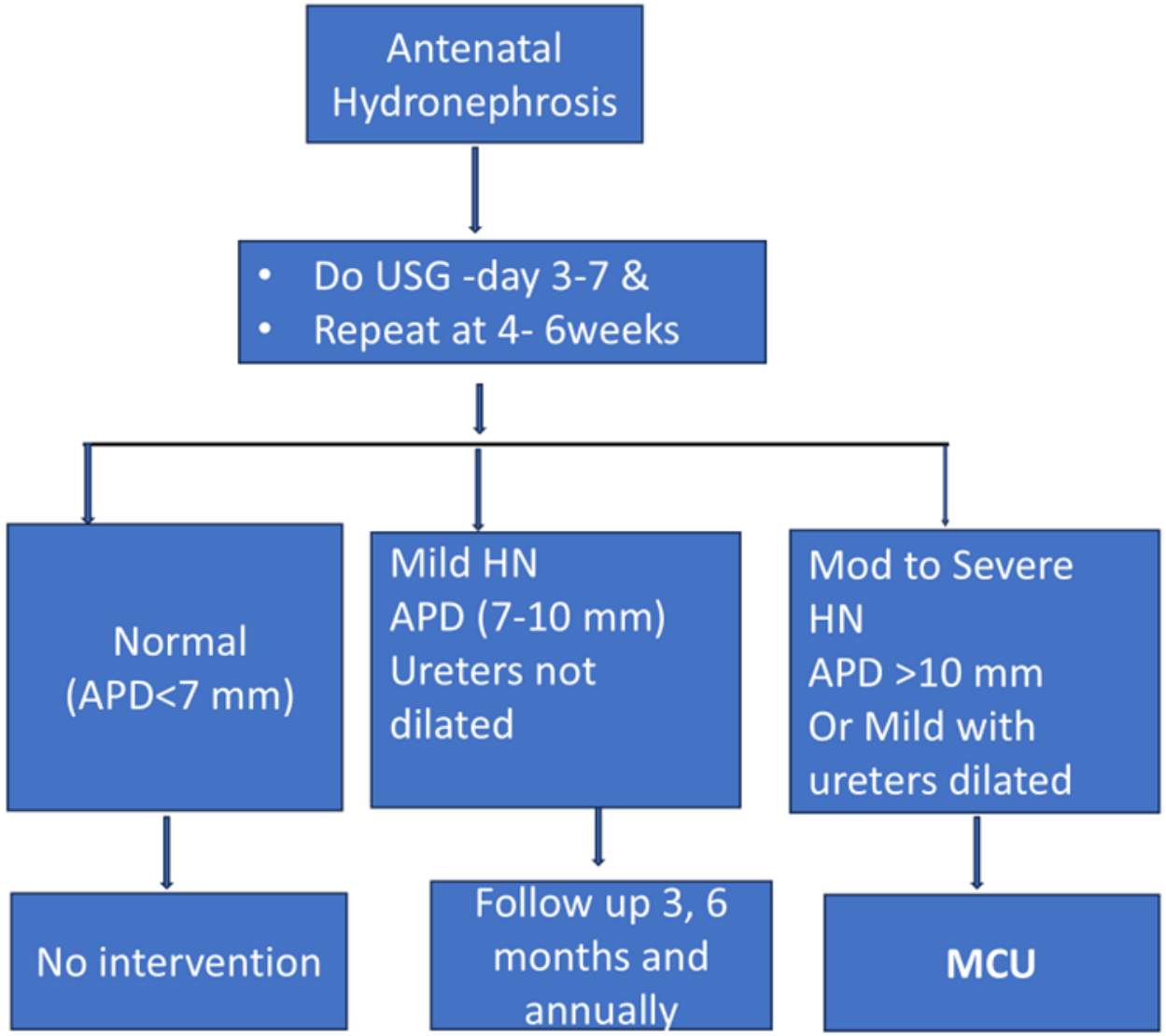
Case 3

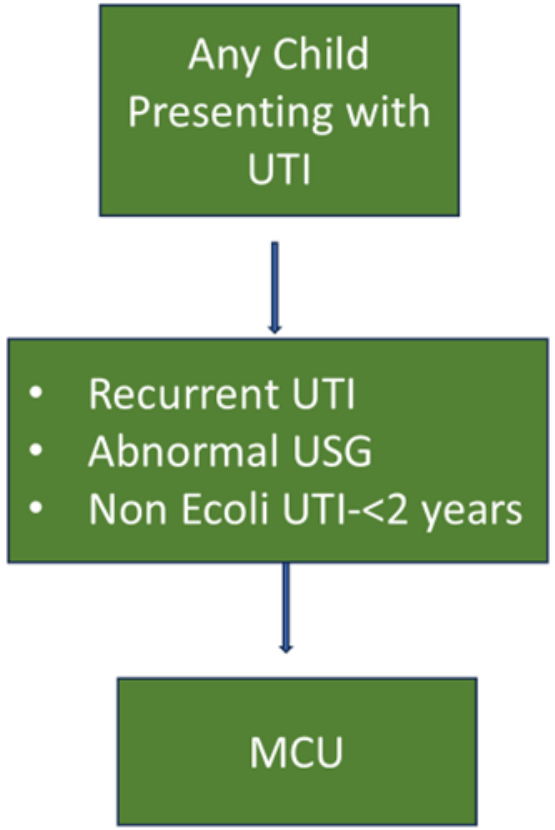
1.5 months old baby girl with history of left mild hydronephrosis detected in 3rd trimester USG, lost to follow up is now on treatment for 1st episode of febrile UTI. USG done now shows Left renal pelvicalyceal dilatation, Renal pelvis APD of 12mm with visualized distal ureters. RK is normal. UB is also normal.

What will be the next step in evaluating this patient?

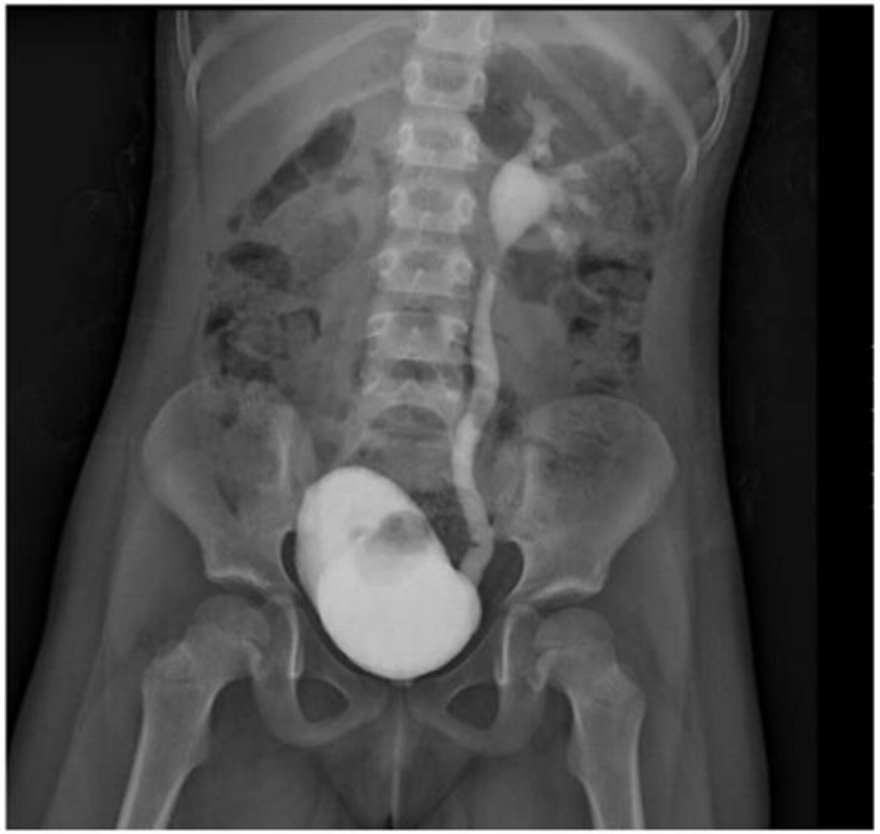
Dr.Vidhya


Antenatal Hydonephrosis
Abnormal Ultrasound(dilated PCS and Ureters)
UTI
MCU


Antenatal Hydronephrosis
Do USG -day 3-7 &
Repeat at 4- 6weeks
Normal (APD<7 mm)
Mild HN APD (7-10 mm) Ureters not dilated
Mod to Severe HN APD >10 mm Or Mild with ureters dilated
No intervention
Follow up 3, 6 months and annually
MCU


Any Child Presenting with UTI
Recurrent UTI
Abnormal USG
Non Ecoli UTI-<2 years
MCU

MCU



Left Grade 3 VUR

Management- Antibiotic Prophylaxis

Indications

- VUR (Gr 3-5)
- Low Gr VUR+ BBD
- Infants with recurrent febrile UTI

Dr Moorthy

How would you approach this case?

How can we prevent UTI? Circumcision?

Surgical options

Case 4

3rd trimester USG of 32 yrs old Primi showed right sided hydronephrosis with renal pelvis APD of 15mm, LK normal in size and appearance, ureters not visualised, UB normal. AFI normal. Now she has delivered a boy baby at term, with birth weight of 3.5kg, feeding well, passed urine and motion normally.

How will you evaluate this baby further?

Dr Vaishnavi

What are the possibilities

How should be the follow up approach?

Possibilities

- Transient hydronephrosis
- PUJO
- Low grade VUR

Follow up approach

Serial USG –APD, Renal cortical thickness

If APD > 1.5 cm -2cm or if cortical thinning +

Diuretic renogram – to check obstructive drainage And split renal function

If Non obstructive drainage and if UTI + MCU to r/o VUR

Dr Moorthy

How would approach PUJ?

When should surgery be planned?

Case 5

28yr old Primi was referred to the Pediatric nephrologist in view of increased echogenicity of bilateral normal sized kidneys on the 20 weeks antenatal scan. Ureters and urinary bladder normal. AFI normal. There was mild ventriculomegaly and a choroid plexus cyst.

What will be your plan on further evaluation of the fetus?

What is the importance of the extra renal findings in this case?

Dr Manjusha

In case of antenatal renal anomalies…

Look for:

Major systemic structural anomalies

Soft signs:

increased nuchal translucency

absent nasal bone

echogenic bowel

shortened long bones (humerus/femur)

choroid plexus cyst

Ventriculomegaly

Suggest increased chance of genetic syndromes

Causes of increased fetal renal echogenicity

Dysplastic kidney

ARPKD – Large kidneys

ADPKD with cysts

Syndromes like Bardet Biedl syndrome / BWS

Aneuploidy like Trisomy 13,18

Normal variant

In this case..

Assess the risk of an underlying aneuploidy

Offer genetic testing – 2nd trimester maternal serum screening – amniocentesis

Genetic counselling

Help in informed decision making

Take home messages

Introduction

- Previously healthy 8 year old child, weighing 19 kg,
- Climbed a stone wall which collapsed on him on 5/10/2020.
- Distended, tender abdomen with guarding
- Complete anuria for 8 hours after the event.
- Received around 1000 ml of crystalloid at the time of evacuation.
- Admitted in the PICU at KEM Hospital
- BP = 76/40 mm of Hg, RR 26/min, heart rate 170/min, GCS 15/15.
- Right internal jugular cannula inserted - CVP of 4 cm.
- Other Systems – Unremarkable.
- Further fluid resuscitation and Noradrenaline infusion did not improve urine output
- Hb = 14.8g%, TLC = 16400/mm^3, Plt = 1.64 lacs
- BUN = 92, Creat = 2.7 S. Bil = 0.7, LDH = 1174, SGPT = 734, GOT = 342, Amylase 2371 I U
- CXR – Bilateral small effusions
- USG:- Minimum hemoperitoneum. Mild perisplenic collection.
- Distended bowel loops. Liver normal
- Lt kidney – Normal appearing with 2X 2 cm collection at lower pole, Rt kidney not visualized.

Case 1 contd…

- **CECT abdomen:**
  - solitary left kidney, a non visualized renal artery,
  - splenic lacerations,
  - multiple lacerations in the body and tail of pancreas
  - numerous large & small intraperitoneal collections.

- **Exploratory laporotomy** showed
  - hemoperitoneum
  - widespread intra & retroperitoneal fat necrosis,
  - liquefaction of the jejunal wall, edematous pancreas with slough collection,
  - a thrombosed left renal artery with cyanotic kidney
  - Splenic laceration

- Desloughing, necrosectomy, drain insertion for pancreas
- Splenectomy , nephrectomy & feeding jejunostomy done.
- Post operatively received antibiotics, noradrenaline infusion, intravenous fluids @ 20 ml/hour,
- Elective ventilation.

Case 1 contd…

- **POD-2**: sudden bleeding from the abdominal drain
- Hb: 2.6g%, Platelets- 47000/mm^3, PT & aPTT - prolonged.

- Despite transfusions, developed shock with a systolic BP of 60, hypoxia, bradycardia, & a cardiac arrest.
- Resuscitated

- Circulation was stabilized with
  - Noradrenaline at 0.5 mcg/kg/min
  - Vasopressin at 2.4 U/hr.
  - TPN , RBC & platelet concentrates and fresh frozen plasma given
  - Patient was anuric

  - **What will you do?**
- Restrict fluids
- Start Frusemide
- Initiate CRRT
- Start SLED
- Need more information

Case 1 contd…

- Hb = 5.6g%, TLC = 31,200,Plt =64000/mm3, PT =18/13, aPTT = 54/34
- Blood urea= 167mg%, Creatinine= 7.3mg%,
- Sr. Potassium= 6.5mmol/L. Sodium = 132, Chloride 110mmol/L
- pH= 7.00, pCO2 = 29 mm of Hg, pO2 = 61 mm of Hg, Bicarbonate= 7.3mmol/L,

- CXR – Pulmonary Edema

- BP = 96/52 on Noradrenaline & vasopressin
- Daily Intake (TPN, blood products, drugs & vasopressor infusions) = 1300 ml

- **What are the indications for RRT**
- Hyperkalemia
- Metabolic Acidosis
- Pulmonary Edema
- Uremia
- Anuria with requirement for nutrition, blood products, antibiotics and pressors.

- **What abnormalities will be corrected by RRT?**
- **All of the above**

Planning RRT

- **What difficulties are posed by RRT in this patient?**
- **Multiple pressors with risk of hypotension.**
- **Pulmonary edema needing negative fluid balance.**
- **Coagulopathy and risk of bleeding if anticoagulated**

- **Aims of RRT**
- Achieving a negative balance - Difficulty in ultrafiltration as patient is on 2 pressor agents
- How much fluid should an anuric patient be given keeping in mind pulmonary edema and How should he be monitored?
- Managing lactic (metabolic) acidosis
- How does one ensure that all essential medications and nutrition are given without compromising circulation and ventilation

Planning RRT

- **What information will we require when planning our prescription of RRT ?**
- **Daily obligatory intake**
- **Cumulative fluid balance**
- **Timings of antibiotics**
- **Catabolic state – Rise of BUL**

- **What modality of RRT should such a patient receive?**
  - **Peritoneal Dialysis**
  - **Intermittent Hemodialysis**
  - **CRRT**
  - **Sustained Low Efficiency Dialysis**

  - **What modality of RRT will you choose?**

Prescription for SLEDD

- **Goals**
- The volume of blood products, TPN, antibiotic and pressor infusions, and intravenous fluids amount to 54 ml/hour.
- Within 36 hours he will gain 10% of his dry weight.
- He also has Pulmonary edema and is on Noradrenaline and Vasopressin infusions.
- Needs daily negative balance, correction of acidosis & hyperkalemia.

- **Components**
- *Vascular Access*
- *Dialyzer:-* His body surface area is 0.8m^2,
- *Blood Flow*
- *Dialysate Composition and Flow*
- *Ultrafitration rate and Duration*
- *Anticoagulation*
- *Convection (Optional)*

Prescription for SLEDD

- **What vascular access is ideal in this situation?**
- Central line in Rt IJV being used for antibiotics TPN, Noradrenaline and Vasopressin.
- Femoral line – dedicated
- Catheter should be at least 15 to19 cm long.

- **KDIGO**
- Right internal jugular -first option,
- Femoral site - second option,
- Left internal jugular (LIJ) - third option,
- Avoid subclavian insertions

Selecting A Dialyzer for SLED/SLED-f

Parameter	Sureflux 5N (Nipro)	FX40 (Fresenius)	FX ped (Fresenius)	Polyflux 6H (Gambro)	F4HPS	F3
Surface Area (m^2)	0.5	0.6	0.2	0.6	0.8	0.4
Priming Volume (ml)	34	53	18	52	51	28
Ultra filtration Coefficient	2.7	20	7	33	8	1.7
Urea Clearance	130*	170#	76!	50§	170	125
Creatinine Clearance	109*	144#	64!	50§	143	95
Phosphate Clearance	62*	138#	57!	49§	123	50
Material	Cellulose triacetate	Helixone	Helixone	Polyflux^	Polysulfone	Polysulfone
Blood flow (ml/min)	50 - 100	50 - 200	30 - 100	50 - 200	50 - 200	40 - 100
Sterilization	Gamma ray	Inline Steam	Inline Steam	Inline Steam	Inline Steam	ETO

* At Qb = 200 ml/min. # At Qb = 200 ml/min. ! At Qb = 100 ml/min § At Qb = 50 ml/min, ^ Polyflux is a blend of Polyarylethersulfone, Polyvinylpyrrolidone, Polyamide.

Case 2

- 10 year old boy diagnosed with IgA nephropathy in 2021 on renal biopsy was lost to follow up for 2 years .
- Creatinine was 1.4 mg/dl
- Came to ER in 2023 with decreased urine output, swelling of feet for 1 month and laboured breathing since 2 days.
- Ht = 124 cm, Wt = 23 kg, BSA = 0.94m^2, BP = 146/70, P = 102/min, RR = 27/min.
- Edema 4+ and pallor present
- Systemic examination:- Pericardial rub faintly heard on sitting up, few rales in chest, no organomegaly or free fluid on abdominal examination.
- Initial investigations:- Hb = 5.4 g/dl, TLC= 4800/mm^3, platelets 1.56 lacs.
- BUL = 278 mg/dl, creatinine = 13.2 mg/dl, Electrolytes – 129/5.5/108
- Venous bicarbonate = 9.3 mmol/L
- 2 D Echo screening- Concentric LVH, thin non tappable rim of pericardial effusion.
- Few B lines on lung fields.

- *What should be his dialysis prescription when initiating RRT ?*

Selecting A Dialyzer for HD

Parameter	Sureflux 5N (Nipro)	FX40 (Fresenius)	F4 (Fresenius)	Polyflux 6H (Gambro)	F4HPS	F40S
Surface Area (m^2)	0.5	0.6	0.7	0.6	0.8	0.7
Priming Volume (ml)	34	32	32	52	51	42
Ultra filtration Coefficient	2.7	20	2.8	33	8	20
Urea Clearance	130*	170#	155	50§	170	165
Creatinine Clearance	109*	144#	128	50§	149	140
Phosphate Clearance	62*	138#	78	49§	123	138
Material	Cellulose triacetate	Helixone	Polysufone	Polyflux^	Polysulfone	Polysulfone
Blood flow (ml/min)	50 - 100	50 - 200	40 - 200	50 - 200	50 - 200	50 - 200
Sterilization	Gamma ray	Inline Steam	Inline Steam	Inline Steam	Inline Steam	Inline Steam
Fibre inner diameter (mic)	200	185	200		200	200
Fibre wall thickness (mic)	15	35	40		40	40

* At Qb = 200 ml/min # At Qb = 200 ml/min ! At Qb = 100 ml/min § At Qb = 50 ml/min ^ Polyflux is a blend of

Selecting A Dialyzer for HD

Parameter	FX 50	F 50S	F5 (Fresenius)	F5HPS
Surface Area (m^2)	1.0	1.0	1.0	1.0
Priming Volume (ml)	53	63	63	63
Ultra filtration Coefficient	33	30	4.0	10
Urea Clearance	189	178	170	179
Creatinine Clearance	170	160	149	162
Phosphate Clearance	165	158	103	155
Material	Helixone	Polysufone	Polysufone	Polysulfone
Blood flow (ml/min)	200 - 300	200 - 300	200 - 300	200 - 300
Sterilization	Inline Steam	Inline Steam	ETO	Inline Steam
Fibre inner diameter (mic)	185	200	200	200
Fibre wall thickness (mic)	35	40	40	40

* At Qb = 200 ml/min. # At Qb = 200 ml/min. ! At Qb = 100 ml/min § At Qb = 50 ml/min,

Case 2 cont'd

- Was taken for a 2 hours HD session from a left femoral 10F 2-lumened catheter. Blood flow = 150ml/min, Dialysate flow = 300 ml/min
- F4HPS dialyser used.
- No heparin used. No UF done
- Started feeling uneasy 15 minutes after HD was completed.
- Appeared restless and did not want to eat.
- Lab reports sent:- BUL = 124, creatinine = 7.1 mg/dl, Elec – 135/4.3/103 mmol/L, bicarb = 17.8 mmol/L
- Patient had a sudden seizure.

- *What is the possible cause?*
- *What is the treatment?*
- *How can such events be avoided?*

Case 3

- An 8 year old boy CKD -5D secondary to P-U valves initiated CAPD in 2019,
- 6months later had to switch to HD following a non resolving peritonitis.
- Rt temporary IJV 2LC initially used, converted to TCC in September 2019.
- In Feb 2020 had CRBSI with suspicion of IE and MRSA on blood culture, so catheter was removed and 2 weeks of dialysis done through Lt femoral temporary catheter .
- Received Vancomycin and gentamicin,
- After 2 negative cultures Lt TCC was inserted, 8F 19 cm long catheter.
- A-V fistula not possible as artery and vein in both UL were too small
- (Patients height was 118 cm , weight = 19.5 kg)
- Catheter gave a blood flow of 200 ml/min, Kt/V was > 1.4 always.
- Fathers donor workup put on hold because of Covid – 19.

Case 3 cont'd

- In March 2021, had another episode of CRBSI, resolved with systemic antibiotics and antibiotic catheter lock.
- Following this episode had decreased blood flow between 130 to 160 ml/min. (Nurses frequently interchanged bloodlines and lumens)
- In April 2021, no flow from the catheter – Urokinase 5000 units instilled in each lumen flow obtained from blue port so dialysis started at 120 to 125 ml/min.
- One more such episode so catheter was locked with Urokinase.
- On 18th May 2021, no flow from both catheter lumens, no improvement with Urokinase.
- Easy passage of saline if injected, but no blood could be aspirated.

- *What is the likely cause?*
- *What are the treatment options?*

Case 4

- A 13 year old boy CKD – 5D initiated HD in 2014 through Rt IJV – 2LC.
- CAPD not possible owing to prior multiple abdominal surgeries in ealy childhood & functioning Lt ureterostomy.
- Lt radiocephalic AVF constructed in 2013 – Primary failure.
- Lt brachiocephalic A-V fistula constructed in June 2014. Bruit and faint thrill.
- Fistula thrombosed after 1 week. Could not be salvaged by thrombectomy.
- Lt IJV TCC inserted in June 2014 and 3/week MHD done.
- In September 2019, CRBSI due to Pseudomonas led to catheter removal and use of Lt femoral temporary catheter.
- Evaluated for Rt radiocephalic AVF- Radial artery calibre too poor.
- Offered loop graft in Rt forearm – declined by patient.
- Rt IJV TCC inserted- 19 cm 14.5F hemosplit.
- Had 2 additional episodes of endotoxic shock, suspected catheter biofilm. (All cultures negative)
- In Jan 2025, declining flow from TCC, underwent thrombolyis with transient improvement.
- Jan 2025 – CRBSI with Enterococcus fecalis and no flow from arterial lumen.
- Venous lumen – good inflow but poor outflow, 100 ml/min on bllod pump with arterial pressure of – 160 mm of Hg.
- 2D- Echo – No vegetations
- Treated with Vancomycin and gentamicin and taken for catheterogram

Case 5

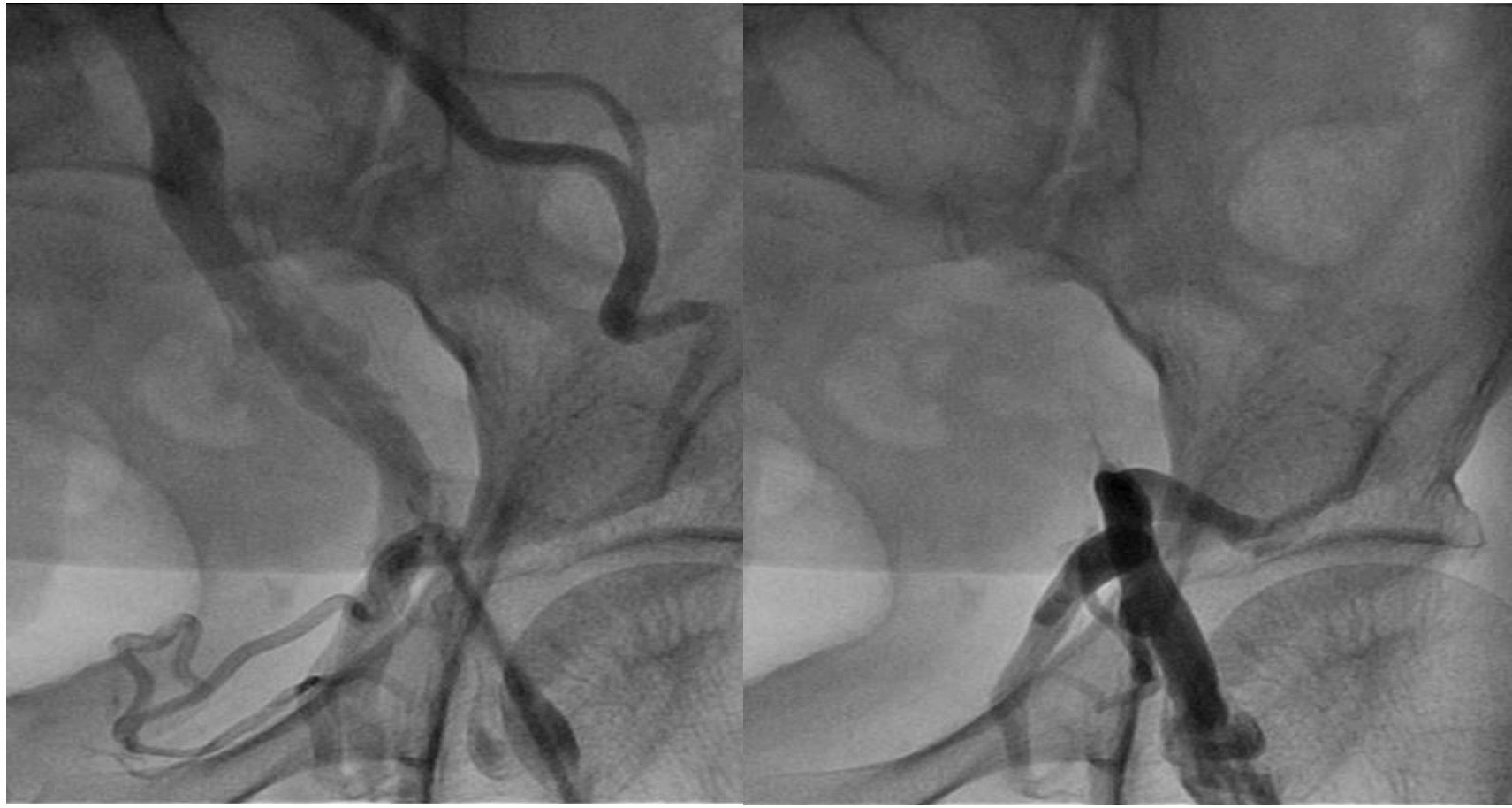
- A 12 year old boy with ESRD secondary to FSGS started MHD in 2014,
- Initially left femoral temporary, then right internal jugular temporary catheter for 6 months
- Left radiocephalic A-V fistula used from November 2014.
- April 2015 - came to KEM hospital with severe pain, redness and swelling of the left upper limb
- Diagnosed cellulitis and severe thrombophlebitis of the fistula veins.
- Blood culture - Enterococcus.
- Treated with Vancomycin weekly, and post HD gentamicin.
- Cuffed tunnelled catheter inserted in the Left internal Jugular vein
- Used for a period of 3 month till cellulitis and thrombophlebitis resolved
- Resumed HD through the AVF.
- 2 further episodes of swelling and pain, treated at dialysis center with antibiotics and dialyzed from temporary catheters.

Case 5

- August 2015 - swelling of the fistula arm with prolonged bleeding after needle removal
- Inability to completely extend his elbow.
- Angiography - normal anastomosis and cephalic vein in the forearm and arm
- Complete thrombotic occlusion of the left brachiocephalic vein at origin. Angioplasty attempted – failed.
- Reinforced corrugated necklace PTFE graft placed between the right and left axillary veins.
- Venous hypertension resolved within 48 hours and the fistula used for HD.
- March 2017, - recurrence of swelling in both upper limbs left > right
- Increased bleeding from needle punctures , elbow contracture
- Inability to use the AVF for dialysis.
- Facial swelling and dyspnoea.
- No improvement with aggressive ultrafiltration

Case 5 – cont’d

- Doppler studies - Normal graft flow
- CT venogram - Stenosis of the right brachiocephalic and subclavian veins
- Both Internal Jugular and Lt Brachiocephalic veins thrombosed with absence of flow.



Renal tubular disorders: Beyond the basics: A case-based approach

Moderator

Prof Sriram Krishnamurthy

JIPMER, Puducherry

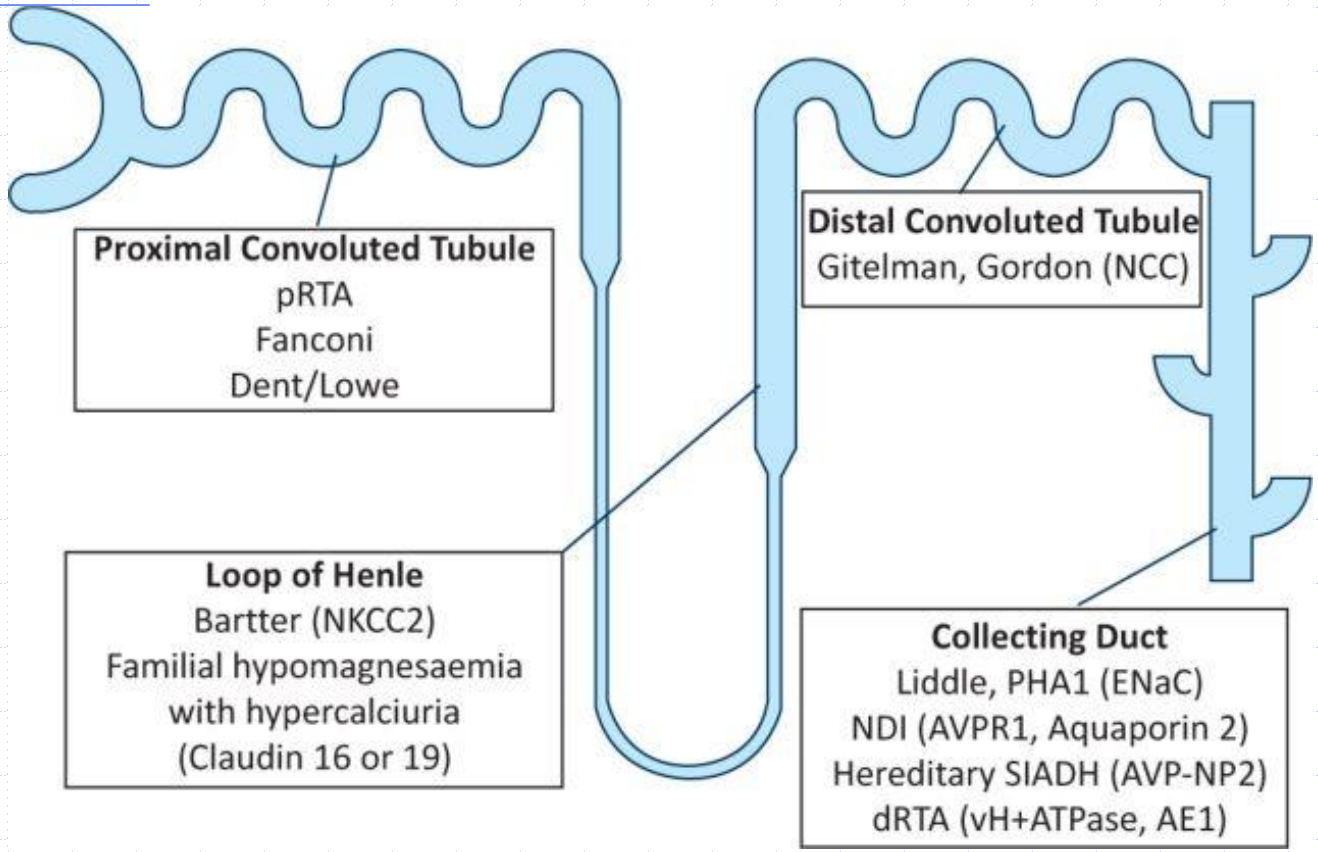
Panelists:

- **Dr Kalaivani Ganesan, Mehta Children's Hospital, Chennai**
- **Dr Manasi Garg, MGMCRI, Puducherry**
- **Dr Sunil Reddy, CMC, Vellore**
- **Dr M Suresh, Kauvery Hospital, Trichy**

OBJECTIVES

- Algorithmic diagnostic approach to a child with renal tubular diseases
- Identify diagnostic clues to children with renal tubular diseases e.g., rickets, polyuria, nephrocalcinosis, FTT, hypokalemia, metabolic acidosis/ metabolic alkalosis, etc
- Learning through Case vignettes

Hereditary renal tubular disorders along various segments of the nephron



- Distal RTA, Fanconi syndrome and Bartter syndrome more common among tubular disorders in children
- Gitelman syndrome more common in adolescents and adults

Clinical Medicine (London, England), 01 Oct 2012, 12(5):476-479 https://doi.org/10.7861/clinmedicine.12-5-476 PMID: 23101152

- What are the diagnostic clues for renal tubular disorders? (Dr Suresh)

Diagnostic clues for renal tubular disorders

- Failure to thrive
- Polyuria/polydipsia/salt craving/ recurrent dehydration
- Hypokalemia with metabolic acidosis/alkalosis
- Nephrocalcinosis/ renal stones
- Ocular problems, GDD, cholestasis, hepatosplenomegaly with rickets/hypokalemia/FTT/polyuria
- Family history of rickets, with consanguinity setting
- Craniosynostosis, Dental pulp abnormalities, Predominantly lower limb involvement with lack of hypotonia- Hypophosphatemic rickets
- Hypomagnesemia (hypocalcemic tetany)
- Hypertension rarely- e.g., Liddle syndrome

Case 1

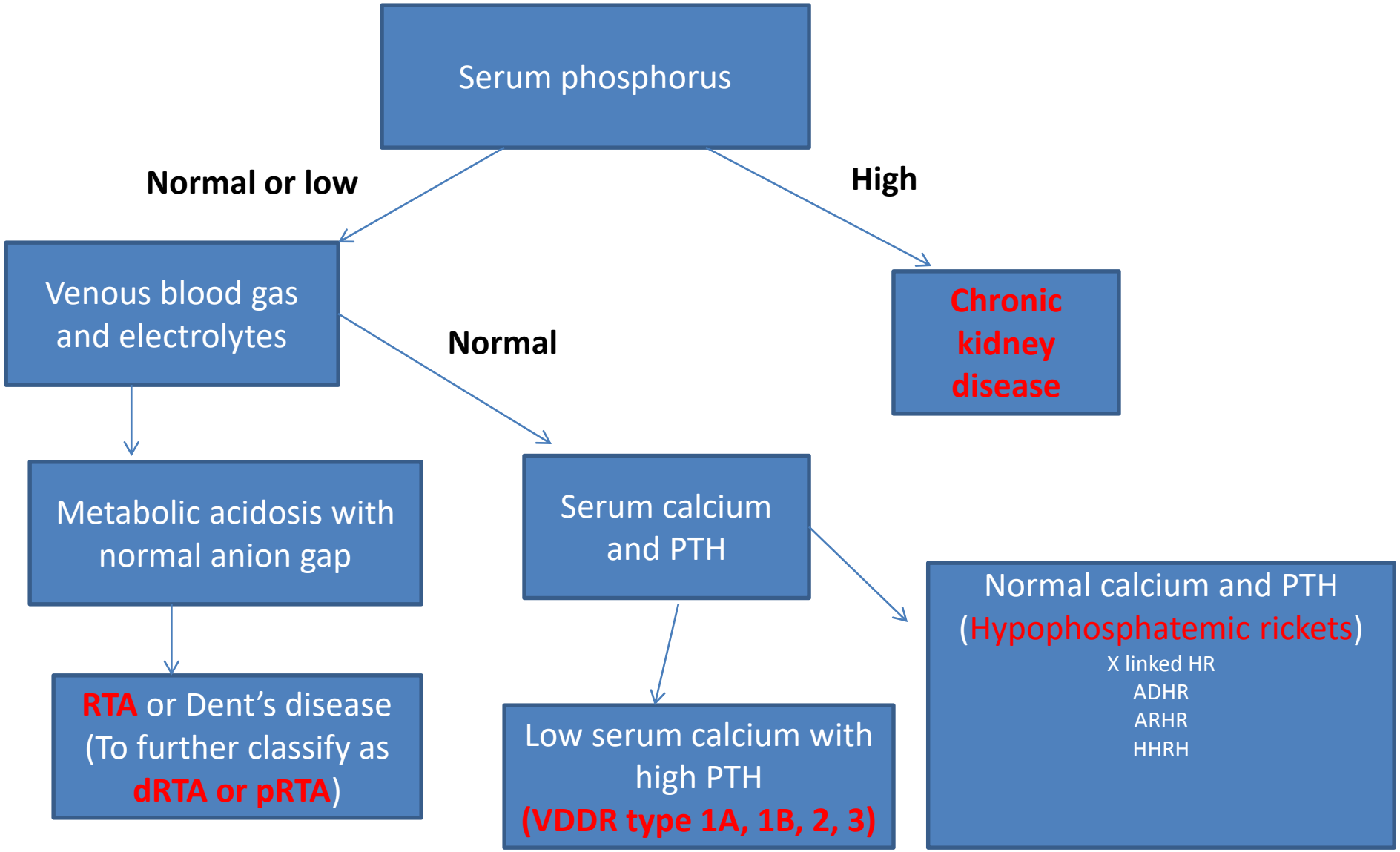
- A 7-month-old girl child born of 2nd degree consanguineous marriage
- Polyuria (6 ml/kg/hour) and failure to thrive
- No antenatal history of polyhydramnios; term baby- birth weight 2.9 kg
- On examination- Weight 3.1 kg (-2.8 z), length 56 cm (-2.1 z), HC 42 cm
- Wrist widening, **rachitic rosary**, AF wide (vitamin D level 35 ng/ml)
- Serum bicarbonate 12 mEq/L, chloride 113 mEq/L, creatinine 0.18 mg/dL
- Serum sodium 135 mEq/L, potassium 2.8 mEq/L
- Serum anion gap 10, urine anion gap +, blood glucose (random)- 80 mg/dL
- USG s/o medullary nephrocalcinosis, Urine Ca: Cr ratio 1.2

- **What is refractory rickets? What is the algorithmic approach to a child with non-nutritional rickets (refractory rickets)? (Dr Kalaivani)**

Refractory rickets: Definition

- Two large (or large cumulative) doses of vitamin D have been given 4 weeks apart
- No radiological healing or resolution of biochemical abnormalities even after 2-4 months of vitamin D administration
- Non-nutritional in nature

Approach to refractory rickets



- What investigation should be done next in this case? (Dr Manasi)

Next step

- FeHCO3% = $\frac{\text{urine HCO3}}{\text{serum HCO3}} \times \frac{\text{serum creatinine}}{\text{urine creatinine}} \times 100$

- In this case, after bicarbonate loading test, the FeHC03 was 3%

Further evaluation

- Oral potassium chloride supplements started
- Bicarbonate dose to titrate serum bicarbonate levels to 22 mEq/L was 2 mEq/kg/day
- Hearing evaluation-normal
- Homozygous Mutation detected in the *ATP6V0A4 gene* (encodes α4 subunit of H+ATPase)

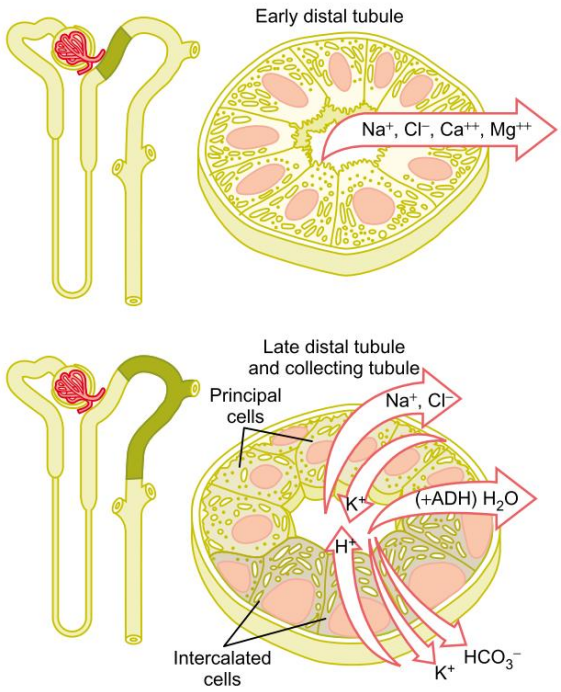
PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

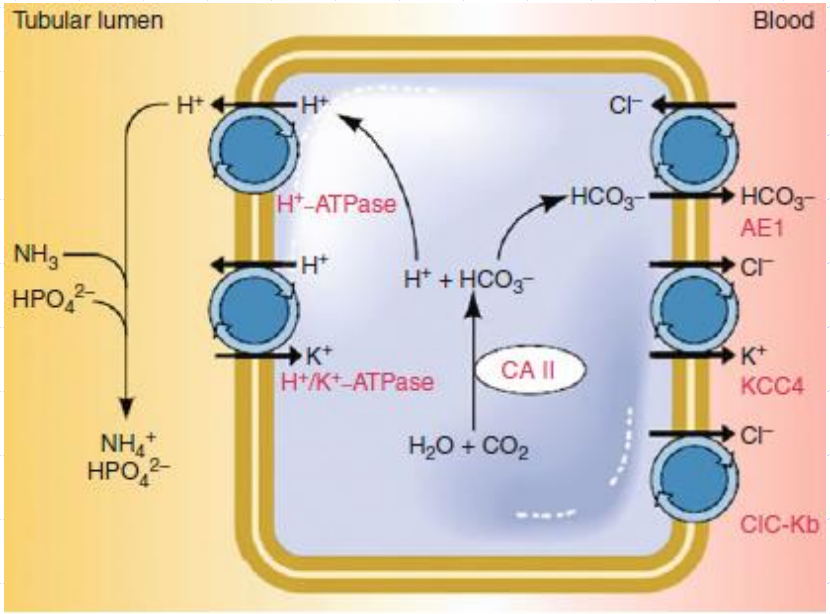
Gene (Transcript) #	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
***ATP6V0A4* (-)** (ENST00000310018.7)	Intron 10	c.816+1G>A **(5' Splice site)**	Homozygous	Distal renal tubular acidosis-3 with or without sensorineural hearing loss	Autosomal recessive	Pathogenic

- FINAL DIAGNOSIS
- **Distal Renal tubular acidosis (dRTA) due to ATP6V0A4 gene mutation; now on potassium citrate**

- What are the pathophysiological mechanisms of dRTA? (Dr Sunil Reddy)

Distal RTA: urine acidification





- **The intercalated cells reabsorb potassium and bicarbonate ions from the lumen and secrete hydrogen ions into lumen**

- **dRTA: mutations in the H+ATPase (AR) or Cl-/HCO3- exchanger (AD)**

- What are the causes of dRTA?

(Dr Suresh)

Primary and secondary dRTA

Primary (most common in children)	Secondary
Autosomal dominant (associated with HS)/ Autosomal recessive (SEAO) (Anion exchanger)	Lupus nephritis, Sjogren syndrome, Wilson disease
Autosomal recessive (with early Hearing loss) [β1 subunit of H+ATPase)	Amphotericin B, lithium, foscarnet, melphalan
Autosomal recessive (with late hearing loss) [α4 subunit of H+ATPase]	Glue sniffing, acquired distal RTA during treatment of hypophosphatemic rickets

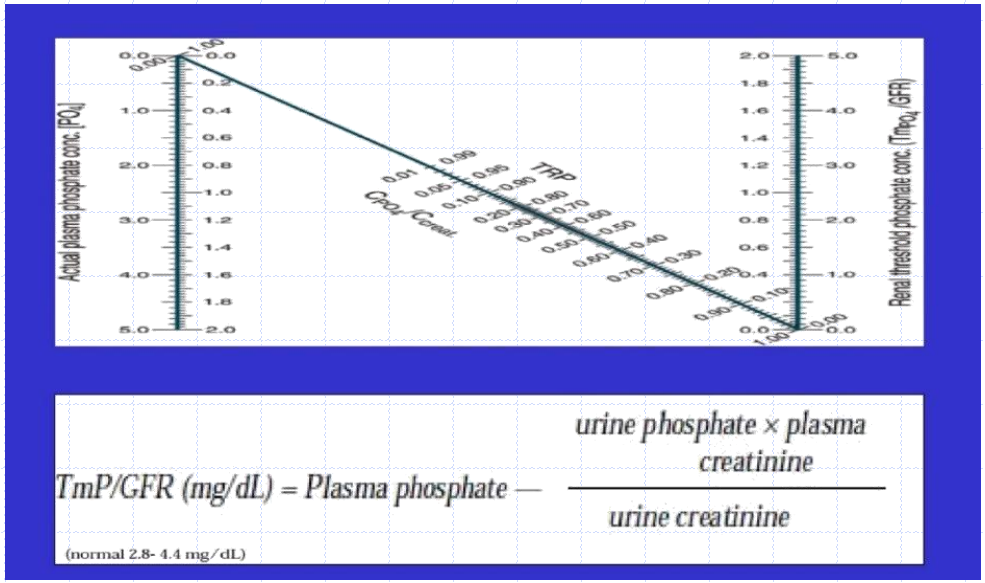
Other genes- **WDR 72,** FOXI1, C2 subunit of H+ATPase

Case 2

- H, 2 year old boy; Failure to thrive (weight 7.2 kg); Birth weight 3.4 kg
- Third child of 2nd degree consanguineous parents
- Now presented with acute flaccid paralysis; **Polyuria (7 ml/kg/hour)** x 1 year
- Hepatomegaly (liver 4 cm, span 9 cm)
- Rickets; mostly gross motor developmental delay
- Severe hypokalemia (1.46)
- Metabolic acidosis (Bicarbonate 13.2) with normal anion gap
- Hypophosphatemia (2.1), calcium 8.8 mg/dL
- Serum creatinine 0.21 mg/dL, alkaline phosphatase 725 U/L

Further investigations

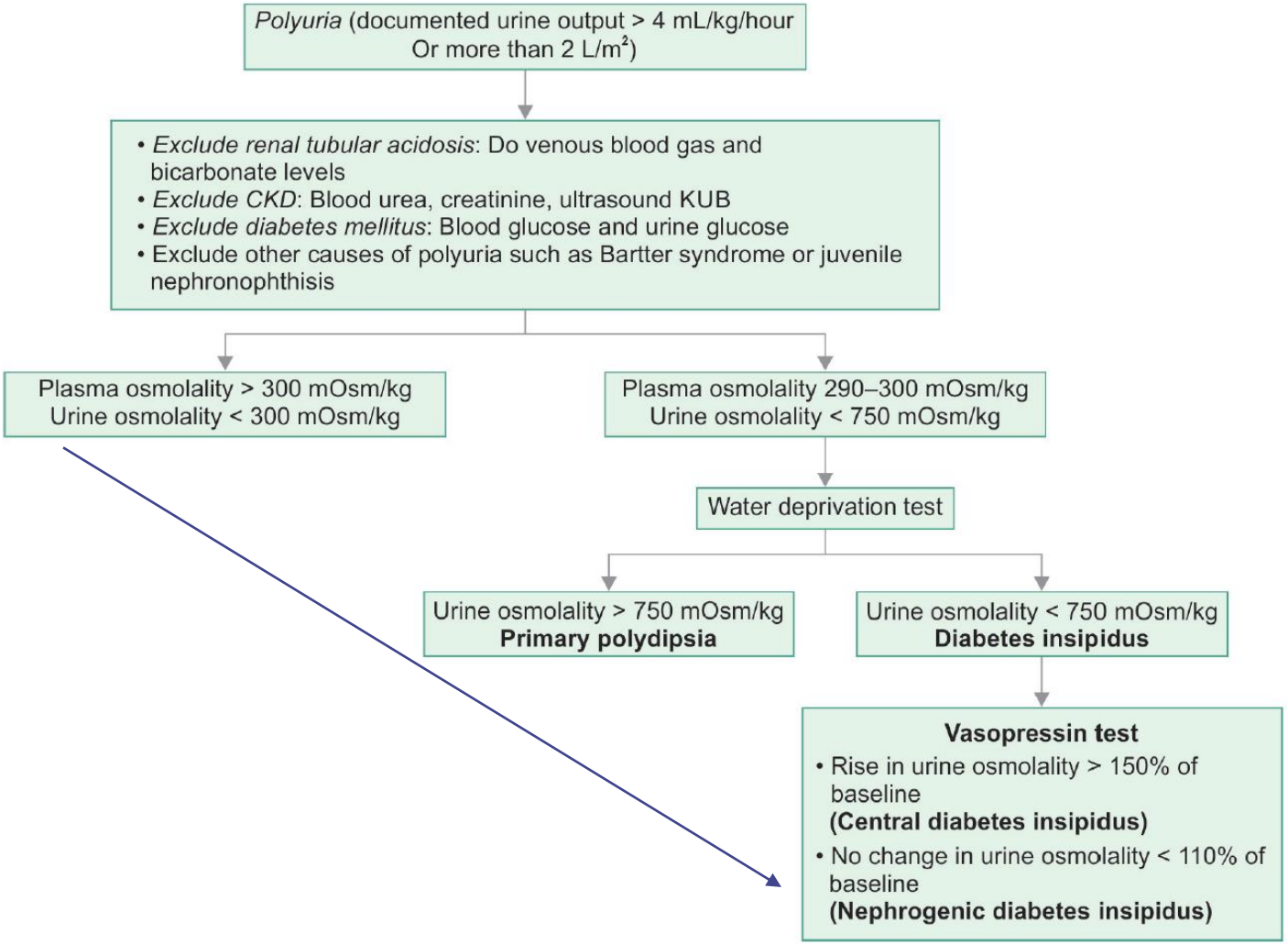
- Blood glucose normal, urine for galactose negative.
- Glycosuria present
- FEHC03- 15%



- FeP04 80%; TmpGFR 1.2 mg/dL.
- Aminoaciduria present.

- What is the approach to a child with polyuria? **(Dr Sunil Reddy)**

Algorithmic approach to polyuria



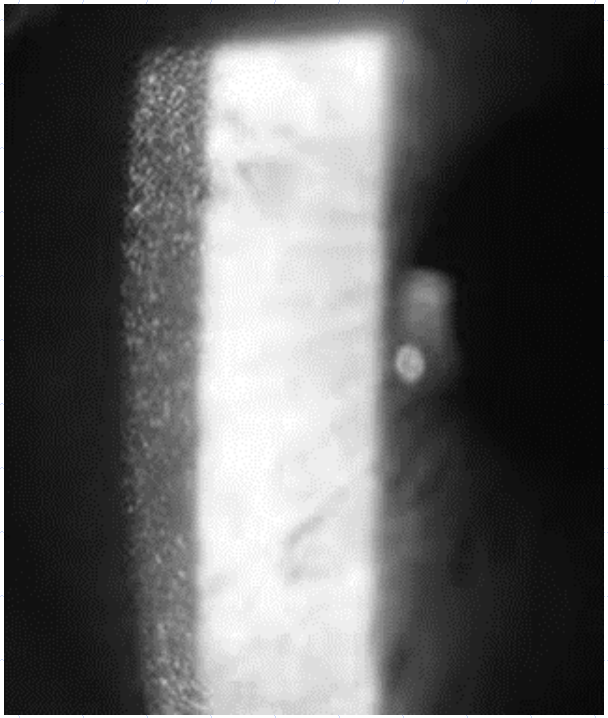
(CKD: chronic kidney disease; KUB: kidneys, ureters, bladder)

Source: Bagga A. Sinha A, Gulati A. Polyuria. In: Bagga A, Sinha A, Gulati A (Eds). Protocols in Pediatric Nephrology, 1st edition. New Delhi: CBS Publishers and Distributors Pvt Ltd; 2012. pp. 73-7.

- This child has failure to thrive with polyuria NAGMA with hypokalemia with
- Bicarbonaturia
- Phosphaturia
- Glycosuria
- Aminoaciduria

- What is this constellation of symptoms known as? (Dr Suresh)
- Which investigation should be done next? (Dr Suresh)

Ophthalmological evaluation: Corneal shiny crystals



Final diagnosis

- Cystinosis with Fanconi syndrome

LIKELY PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

Gene (Transcript) #	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
***CTNS* (+)** (ENST00000381870.8)	Exon 10	c.807_809del **(p.Ser270del)**	Homozygous	Nephropathic cystinosis; Ocular nonnephropathic cystinosis	Autosomal recessive	Likely Pathogenic

Management

- Potassium citrate (7 mEq/kg/day)
- Sodium bicarbonate (8 mEq/kg/day)
- Neutral phosphate (50 mg/kg/day)
- Cysteamine

- What are the causes of inherited Fanconi syndrome? (Dr Manasi)

Inherited causes of Fanconi Syndrome

Disease	Gene defect	Inheritance	OMIM
Cystinosis	Cystinosin (*CTNS*)	AR	219800
Tyrosinemia	Fumarylacetoacetase	AR	276700
Fanconi–Bickel syndrome	*GLUT 2*	AR	138160
Hereditary fructose intolerance	Fructose-1-phosphate aldolase (*ALDOB*)	AR	229600
Dent's disease type 1	CLCN5	X	300009
Dent's disease type 2	*OCRL1*	X	300555
Lowes syndrome	Phosphatidylinositol 4,5-bisphosphate 5-phosphatase deficiency (*OCRL1*)		309000
Galactosemia	Galactose-1-phosphate uridylyltransferase (*GALT*)	AR	230400
Fanconi renotubular syndrome 3	*EHHADH*	AD	615605
Wilson's disease	ATPase, Cu(2+)-transporting, beta polypeptide (*ATP7B*)	AR	277900

AD autosomal dominant, *AR* autosomal recessive, *X* x-linked

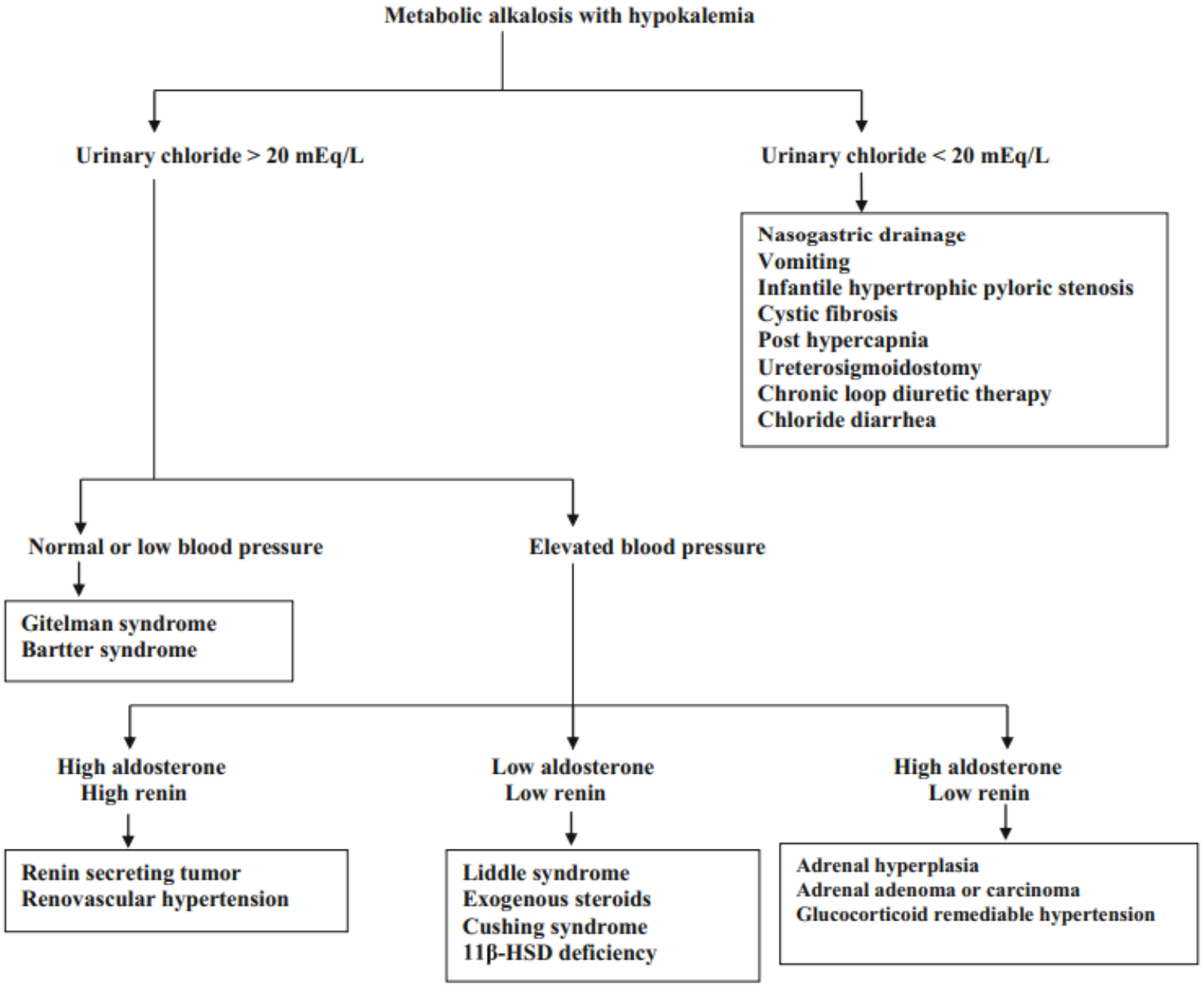
In addition, Mitochondrial disorders, Lysinuric protein intolerance, ARC syndrome, MLD and Von Gierke disease can cause Fanconi syndrome

Isolated proximal RTA (Lowe-like features) described in autosomal recessive SLC4A4 mutations (NBC1)

Case 3

- PJ, 8 month old girl; non-consanguineous parents; second born
- Poor weight gain since birth (birth weight 2.46 kg; now 4.2 kg)
- Antenatally, no polyhydramnios documented, term delivery at 37 weeks
- History suggestive of polyuria: documented as 6 ml/kg/h; dehydrated
- Serum sodium 129 mEq/L, potassium 2.6 mEq/L, chloride 95 mEq/L; Urine chloride 48 mEq/L
- Serum creatinine 0.15 mg/dL, bicarbonate 34 mEq/L; Serum phosphorus 4.2 mg/dL, calcium 9.4 mg/dL, Mg 1.9 mg/dL
- Plasma renin activity high; BP 64/30 mm Hg
- How to approach a child with hypokalemic metabolic alkalosis? (Dr Kalaivani)

Approach to a child with hypokalemic metabolic alkalosis



NGS

LIKELY PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS IDENTIFIED

VARIANT INTERPRETATION AND CLINICAL CORRELATION

Contiguous regions encompassing the *CLCNKB* gene (ENST00000375679.4) were not covered in the sequencing data of this sample. These regions are usually well covered and hence, could likely be due to homozygous deletion of these regions.

MLPA

PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS IDENTIFIED

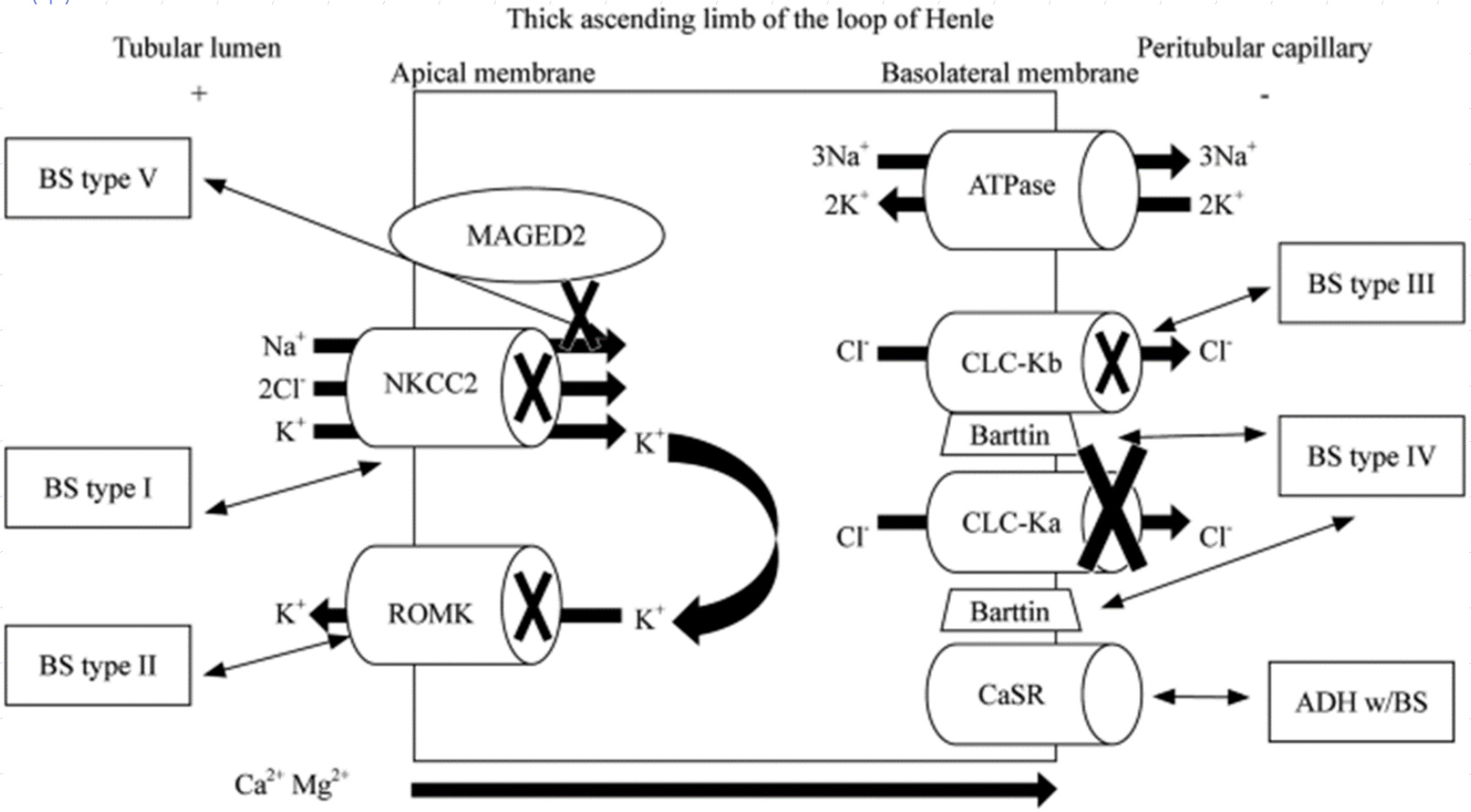
Sl. No.	Deletions /Duplications	No. of exons deleted/duplicated †	MLPA probe ratio (Dosage quotient) #	Disease (OMIM)	Inheritance	Classification
1.	Homozygous deletion	19 (Exons 1-19)	0.00	Bartter syndrome, type 3 (607364)	Autosomal recessive	Pathogenic

- **Final diagnosis: Bartter syndrome type 3**
- KCl supplements (6 mEq/kg/day) and indomethacin (1 mg/kg/day)
- Growth velocity 4.5 cm/year

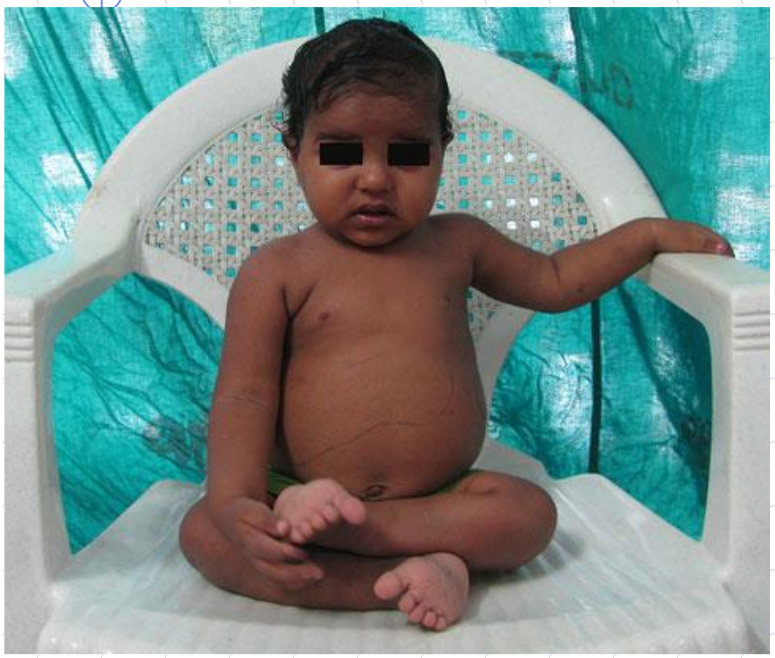
What are the 5 types of Bartter syndrome and the molecular mechanisms involved?

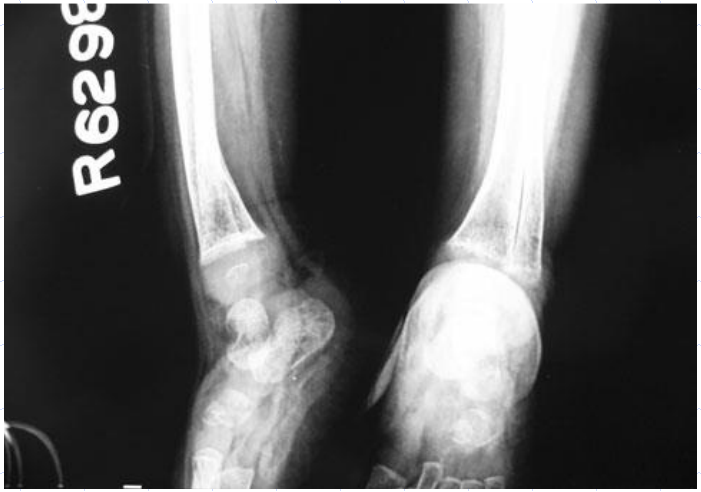
(Dr Sunil Reddy)

Bartter syndrome subtypes



Case 4





What is the likely diagnosis? (Dr Kalaivani)

Child with Fanconi syndrome, rickets, polyuria, hypoglycemia and hepatomegaly

Liver biopsy s/o GSD

Diagnosis?

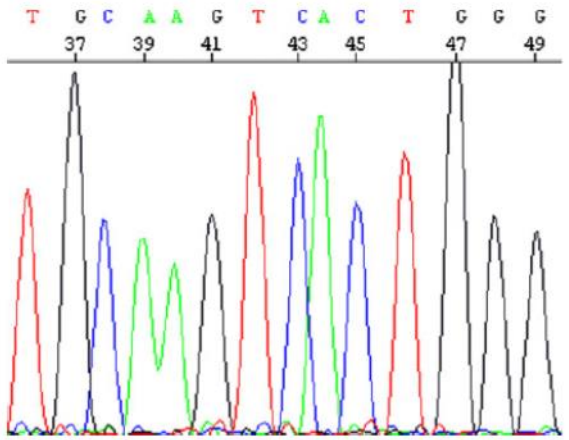


Fig. 4 Direct sequencing of genomic DNA revealing a G-to-A substitution at position −1 of the splicing acceptor site in intron 1 of the GLUT2 (*SLC2A2*) gene in a homozygous pattern (c.16-1G>A or IVS1-1G>A)

FANCONI BICKEL SYNDROME

- GLUT2 transports glucose in and out of hepatocytes, pancreatic beta cells, and the basolateral membranes of intestinal and renal epithelial cells.
- A functionally inactive GLUT2 , results in impaired glucose and galactose utilization, accumulation of glycogen in the liver and kidney and proximal renal tubular dysfunction.

Case 5

- V, 10 year old boy
- Polyuria, Polydipsia, refractory rickets, bony deformity in Lower limbs
- Weight 20 kg (<3rd centile), Height (110 cm) (<3rd centile), BP normal
- Serum bicarbonate 27 mEq/L, calcium 9.4 mg/dL, phosphorus 1.1
- Serum potassium 2.8 mEq/L, SAP 520 U/L
- Hypercalciuria (6 mg/kg/24 h), **nephrocalcinosis**
- FeP04 85%, TmPGFR 1.4 mg/dL, eGFR 92 ml/min/1.73 sq.m
- Urine albumin 2+, but 24 hour urine protein 3.1 g/24 hours
- What should be the next step? Possible diagnosis? (Dr Sunil Reddy)

Further investigations

- Urine beta2 microglobulin 10000 mcg/L

Gene	Gene/Locus MIM number	Disease (Inheritance)	Exon	Nucleotide change	Amino acid change	Zygosity	Type
CLCN5	300008	Dent disease (XLR)	-	c.933+1G>A	-	Hemizygous	Pathogenic

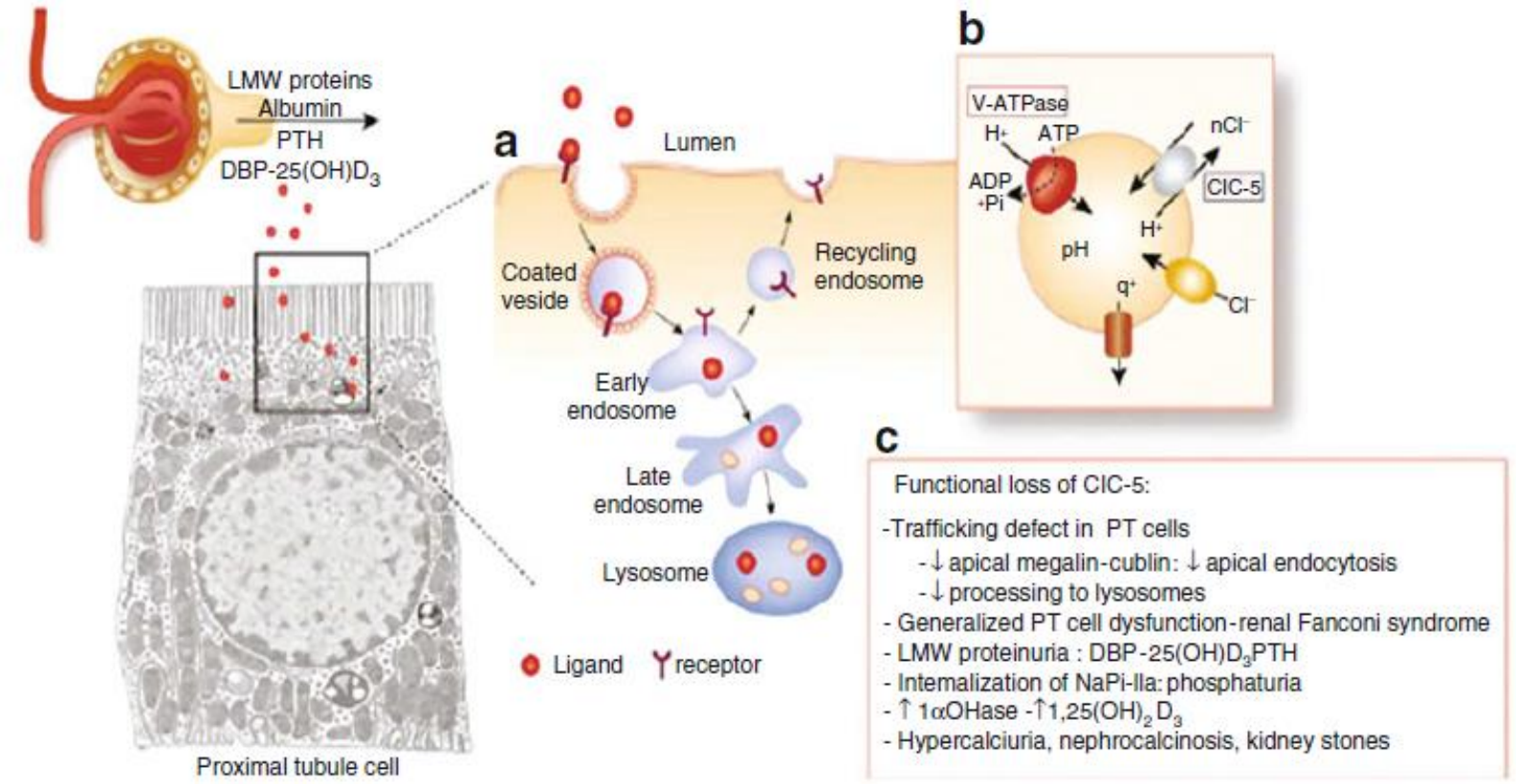
FINAL DIAGNOSIS

Dent disease Type 1

- Treated with neutral phosphate supplements, potassium chloride
- Thiazides added initially, but withdrawn later due to adverse effects
- Mechanism of polyuria: Nephrocalcinosis and hypokalemia

- What is the pathogenesis of Dent disease? (Dr Manasi)

Albumin and LMW proteins are filtered into the primary urine and endocytosed via the megalin-cubilin pathway

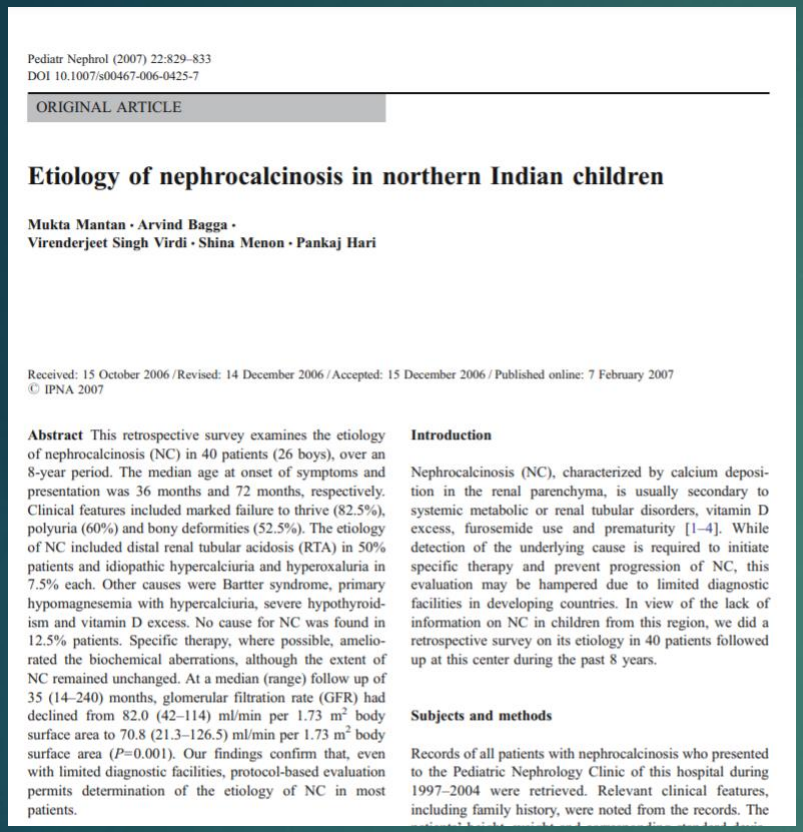


- The index case had nephrocalcinosis.

What are the causes of nephrocalcinosis?

(Dr Suresh)

Nephrocalcinosis: Distal RTA is the most common cause



Pediatr Nephrol (2007) 22:829–833
DOI 10.1007/s00467-006-0425-7

ORIGINAL ARTICLE

Etiology of nephrocalcinosis in northern Indian children

Mukta Mantan · Arvind Bagga · Virenderjeet Singh Virdi · Shina Menon · Pankaj Hari

Received: 15 October 2006 / Revised: 14 December 2006 / Accepted: 15 December 2006 / Published online: 7 February 2007

Abstract This retrospective survey examines the etiology of nephrocalcinosis (NC) in 40 patients (26 boys), over an 8-year period. The median age at onset of symptoms and presentation was 36 months and 72 months, respectively. Clinical features included marked failure to thrive (82.5%), polyuria (60%) and bony deformities (52.5%). The etiology of NC included distal renal tubular acidosis (RTA) in 50% patients and idiopathic hypercalciuria and hyperoxaluria in 7.5% each. Other causes were Bartter syndrome, primary hypomagnesemia with hypercalciuria, severe hypothyroidism and vitamin D excess. No cause for NC was found in 12.5% patients. Specific therapy, where possible, ameliorated the biochemical aberrations, although the extent of NC remained unchanged. At a median (range) follow up of 35 (14–240) months, glomerular filtration rate (GFR) had declined from 82.0 (42–114) ml/min per 1.73 m^2 body surface area to 70.8 (21.3–126.5) ml/min per 1.73 m^2 body surface area (P=0.001). Our findings confirm that, even with limited diagnostic facilities, protocol-based evaluation permits determination of the etiology of NC in most patients.

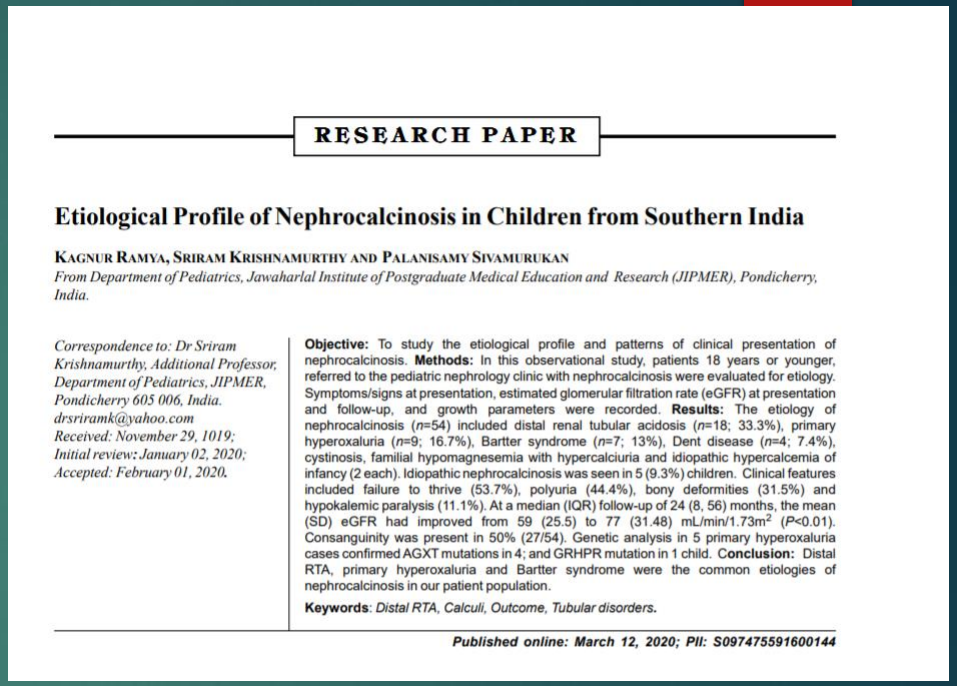
Introduction

Nephrocalcinosis (NC), characterized by calcium deposition in the renal parenchyma, is usually secondary to systemic metabolic or renal tubular disorders, vitamin D excess, furosemide use and prematurity [1–4]. While detection of the underlying cause is required to initiate specific therapy and prevent progression of NC, this evaluation may be hampered due to limited diagnostic facilities in developing countries. In view of the lack of information on NC in children from this region, we did a retrospective survey on its etiology in 40 patients followed up at this center during the past 8 years.

Subjects and methods

Records of all patients with nephrocalcinosis who presented to the Pediatric Nephrology Clinic of this hospital during 1997–2004 were retrieved. Relevant clinical features, including family history, were noted from the records. The

Pediatr Nephrol 2007; 22: 829



RESEARCH PAPER

Etiological Profile of Nephrocalcinosis in Children from Southern India

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Received: November 29, 1019; Initial review: January 02, 2020; Accepted: February 01, 2020.

Objective: To study the etiological profile and patterns of clinical presentation of nephrocalcinosis. **Methods:** In this observational study, patients 18 years or younger, referred to the pediatric nephrology clinic with nephrocalcinosis were evaluated for etiology. Symptoms/signs at presentation, estimated glomerular filtration rate (eGFR) at presentation and follow-up, and growth parameters were recorded. **Results:** The etiology of nephrocalcinosis (n=54) included distal renal tubular acidosis (n=18; 33.3%), primary hyperoxaluria (n=9; 16.7%), Bartter syndrome (n=7; 13%), Dent disease (n=4; 7.4%), cystinosis, familial hypomagnesemia with hypercalciuria and idiopathic hypercalcemia of infancy (2 each). Idiopathic nephrocalcinosis was seen in 5 (9.3%) children. Clinical features included failure to thrive (53.7%), polyuria (44.4%), bony deformities (31.5%) and hypokalemic paralysis (11.1%). At a median (IQR) follow-up of 24 (8, 56) months, the mean (SD) eGFR had improved from 59 (25.5) to 77 (31.48) mL/min/1.73m^2 (P<0.01). Consanguinity was present in 50% (27/54). Genetic analysis in 5 primary hyperoxaluria cases confirmed AGXT mutations in 4; and GRHPR mutation in 1 child. **Conclusion:** Distal RTA, primary hyperoxaluria and Bartter syndrome were the common etiologies of nephrocalcinosis in our patient population.

Keywords: *Distal RTA, Calculi, Outcome, Tubular disorders.*

Published online: March 12, 2020; PII: S097475591600144

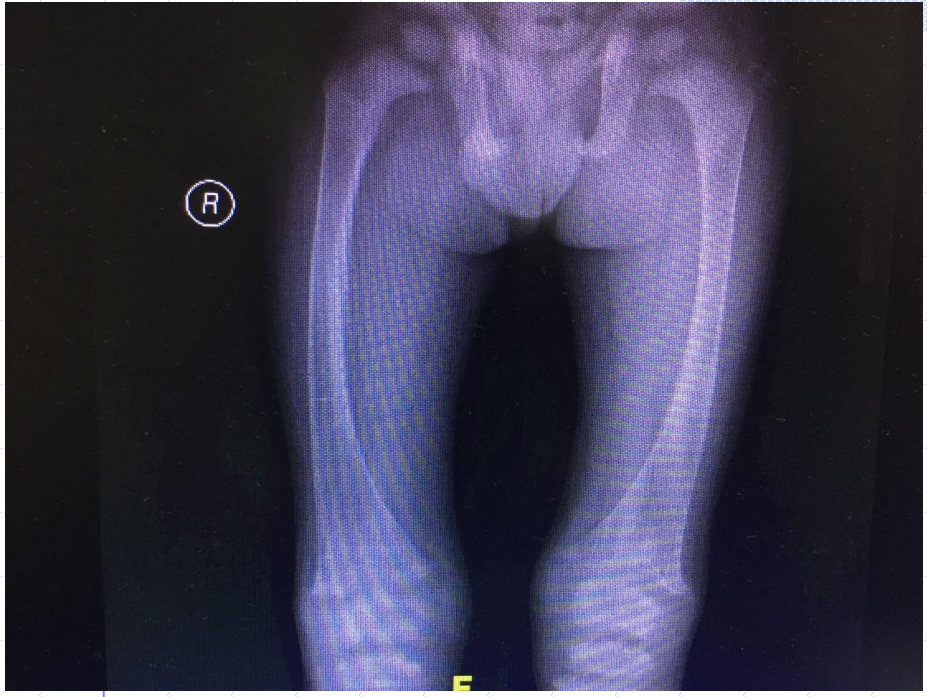
Indian Pediatr 2020; 57: 415-419

Most common causes of NC:

- **Distal RTA**
- **Bartter syndrome type 1, 2, 4, 5**
- **Dent Disease**
- **Primary hyperoxaluria 1, 2, 3**
- **Hypercalcemia**
- **FHHNC**

Case 6

- 6-year old girl with severely bowed legs
- Multiple T/t with Vitamin D
- Wt (- 0.3 SDS), Ht (- 2.4 SDS)
- Widened ankles and wrist along with genu varum
- No dental anomalies
- No history of polydipsia/pallor/jaundice/diarrhea
- Lower limbs more involved than upper limbs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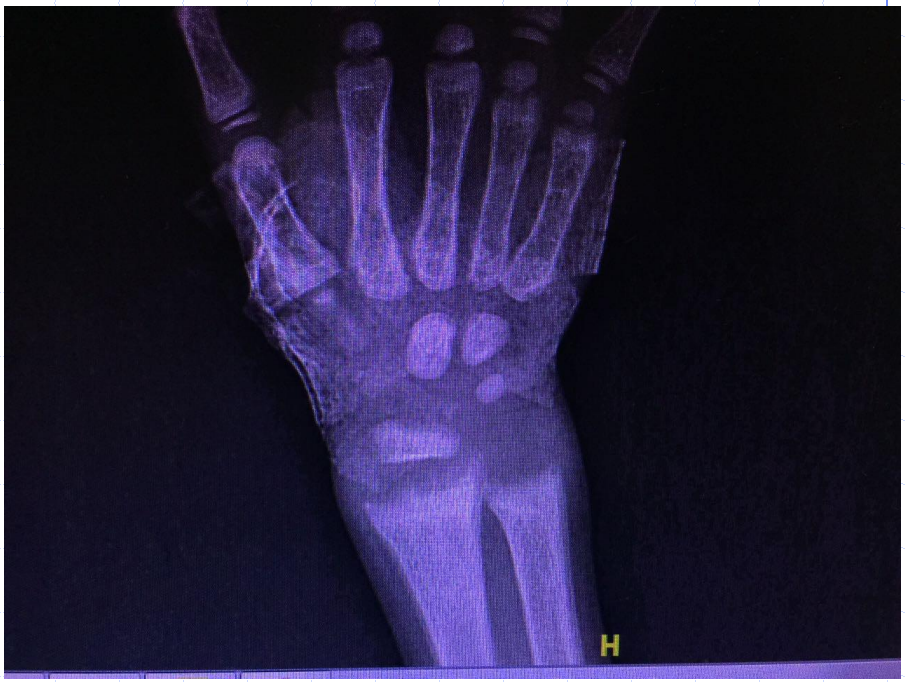
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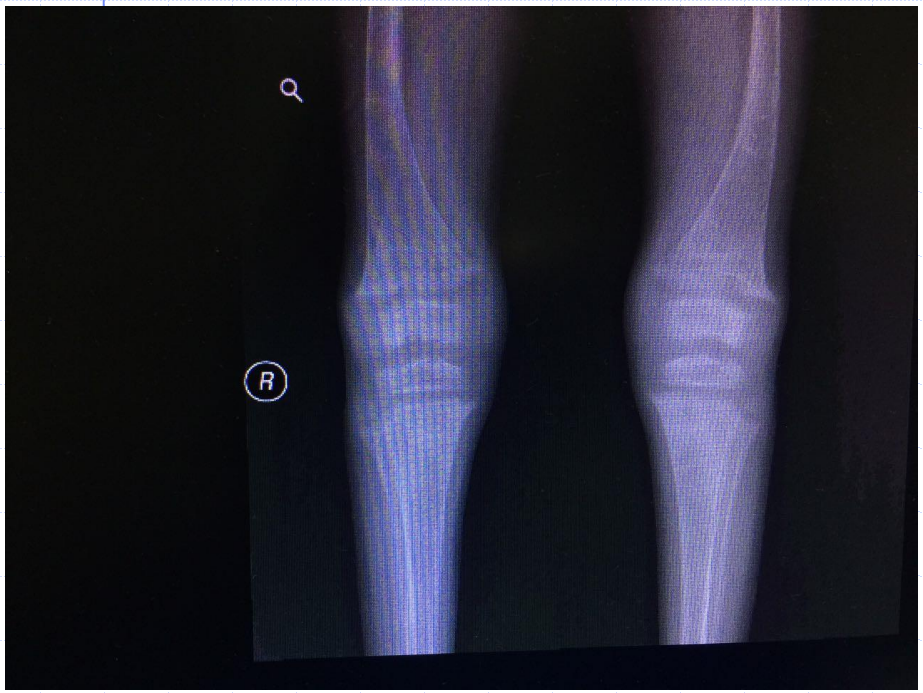
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Laboratory values

Biochemistry	Plasma
Calcium	9.1 mg/dl (normal)
ALP	989 IU(↑)
Phosphate	1.9 mg/dl (↓)
Creatinine	0.41 mg/dl
25 (OH) Vit D	45 ng/ml (Normal)

PTH-35 pg/ml (normal)

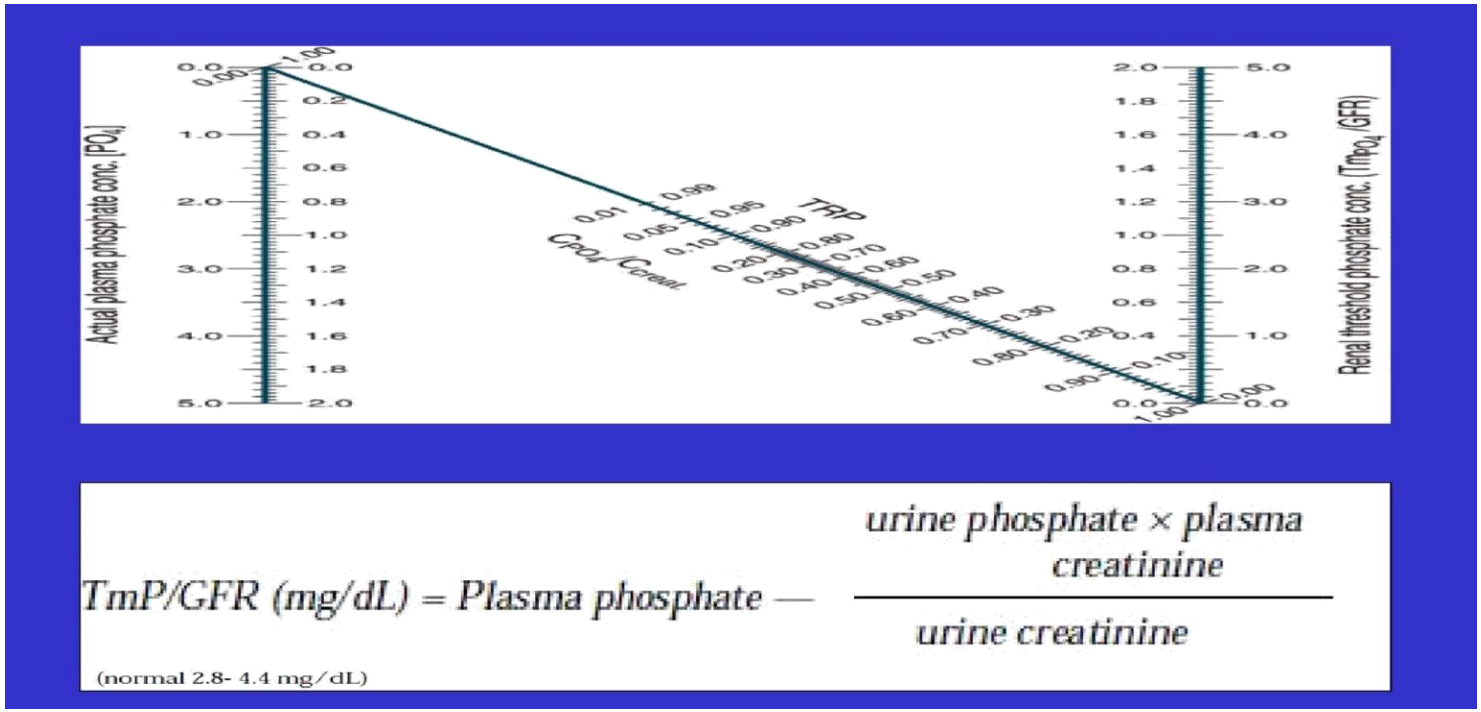
HCO3-24

Further investigations

Biochemistry	Plasma	Urine
Calcium	9.1 mg/dl	0.1 (spot Ca: Cr)
Phosphate	1 mg/dL	47.1
Creatinine	0.4 mg/dl	29.4
	FEP04- 34%	

Bijvoet normogram

- TRP 66%
- TmPGFR-1.4 mg/dL



What is the likely diagnosis? How do we confirm the diagnosis?

(Dr Kalaivani)

Final diagnosis: X-linked hypophosphatemic rickets

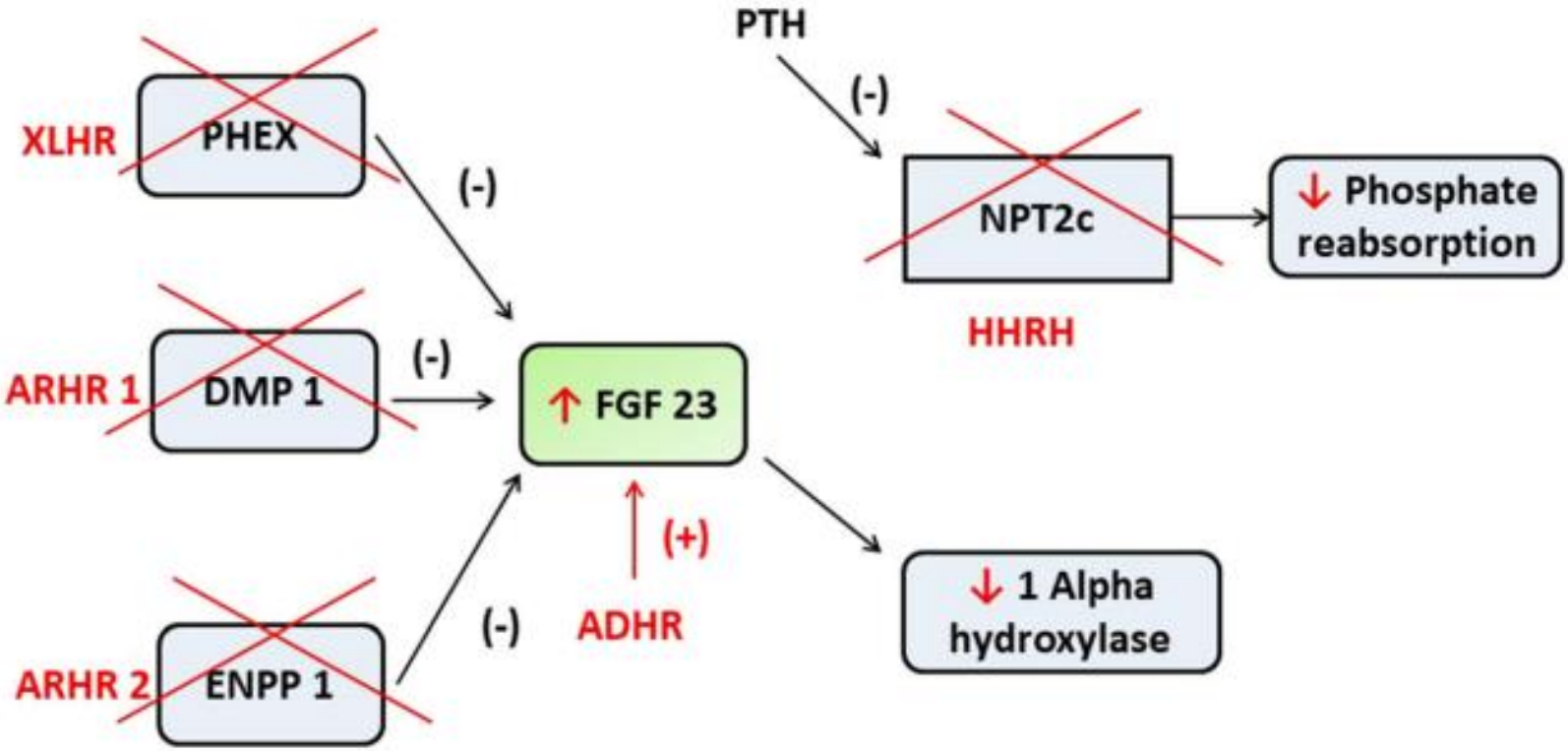
Gene	Gene/Locus MIM number	Disease (Inheritance)	Exon	Nucleotide change	Amino acid change	Zygosity	Type
PHEX	300550	Hypophosphatemic rickets, (XLD)	Ex3	c.345delG	p.K116fs*28	Heterozygous	Likely Pathogenic

Urine Calcium creatinine ratio 0.1
Neutral phosphate (30-50 mg/kg/day)
Calcitriol added (25 ng/kg/day)

What are the different types of hypophosphatemic rickets and mechanisms involved?

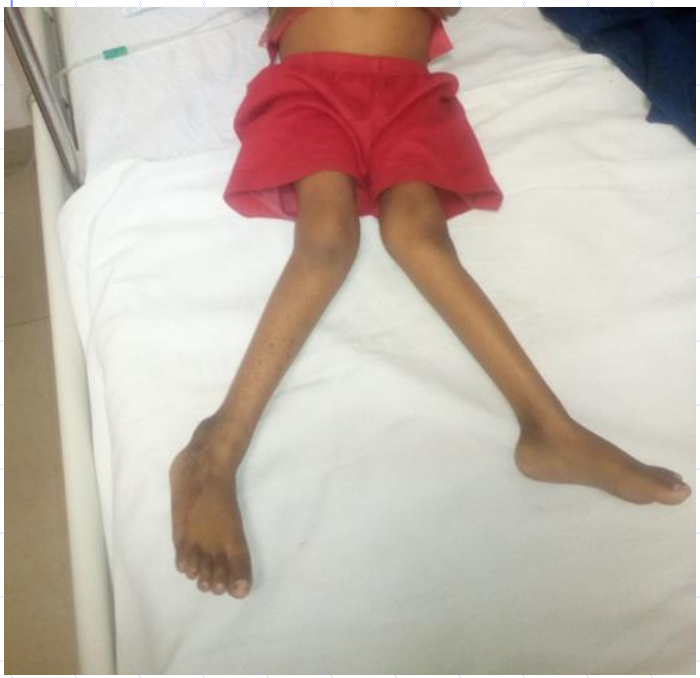
(Dr Manasi)

Mechanisms of hypophosphatemic rickets



Case 7

- 8 year old boy presented with deformity of lower limbs
- Height 102 cm (< -3 SDS)
- Ca 9.9 mg/dl, PO4 7.1 mg/dl (↑), ALP 1009 IU (↑)



- Treated with mega-doses of vitamin D followed by corrective osteotomy elsewhere
- Later, referred for short stature evaluation

Review of history

- Younger sibling: 6 years old taller than him (110 cm)
- Polyuria, nocturia observed for 4 years with secondary nocturnal enuresis
- Second degree consanguineous parents
- Poor appetite

Further investigations

- Hb 9.6 mg/dl (↓)
- **Urea 160 mg/dL**
- **Creatinine: 5.7 mg/dL**
- **PTH: 1421 pg/mL**
- **pH 7.3, Bicarbonate 12.1 mEq/L**
- Serum vitamin D levels 56 ng/mL

- USG-KUB: RK 7.1 cm, RK 7.2 cm, CMD Poor
- **Cysts noted at Corticomedullary junction in both kidneys**, bladder normal, no hydronephrosis

- What is the likely diagnosis? How do we confirm?

(Dr Sunil Reddy)

Final diagnosis: Nephronophthisis-1

PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

SNV(s)/INDELS

Gene[#] (Transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification[$]
NPHP1 **(-)** (ENST00000445609.7)	Exon 14	c.1305G>A **(p.Trp435Ter)**	Homozygous	Nephronophthisis - 1 (OMIM#256100); Senior-Loken syndrome-1 (OMIM#266900); Joubert syndrome 4 (OMIM#609583)	Autosomal recessive	Pathogenic

Calcitriol, sodium bicarbonate, calcium carbonate, EPO, iron supplements

Later initiated on mHD

Case 8: 10-year old boy

- Referred for evaluation of nephrocalcinosis and nephrolithiasis (4 mm calculi)- renal colic
- Hypomagnesemia (0.9 mg/dL)- cramps
- Hypercalciuria (6.5 mg/kg/day)
- Serum potassium-3.9 and bicarbonate-22.1 normal
- Born of 2nd degree consanguineous marriage
- Ophthalmological evaluation-normal
- FeMg- 7% (normal < 5%)

Gene (Transcript) #	Location	Variant	Zygosity	Disease (OMIM)	Inheritance
***CLDN16* (+)** (ENST00000264734.3)	Exon 4	c.437G>A **(p.Arg146His)**	Homozygous	Hypomagnesemia-3	Autosomal recessive

What is the diagnosis? How should we manage this child? (Dr Suresh)

Familial hypomagnesemia with hypercalciuria and nephrocalcinosis

THE SKELETON KEY

Rare autosomal recessive tubular disease

Mutations
- *CLDN16*
- *CLDN19*

Occurs early in childhood or before adolescence

Hypomagnesemia

Excessive renal Mg and Ca excretion

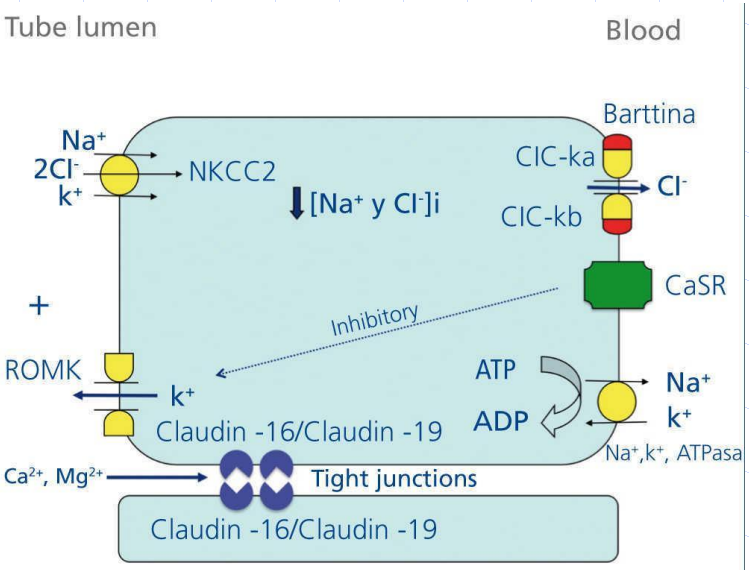
FHHNC

Bilateral nephrocalcinosis

Recurrent UTI | Nephrolithiasis | Polyuria | Polydipsia | Failure to thrive | CKD

Claverie-Martin F. (2015). Familial hypomagnesaemia with hypercalciuria and nephrocalcinosis: clinical and molecular characteristics. *Clinical kidney journal*, *8*(6), 656–664.

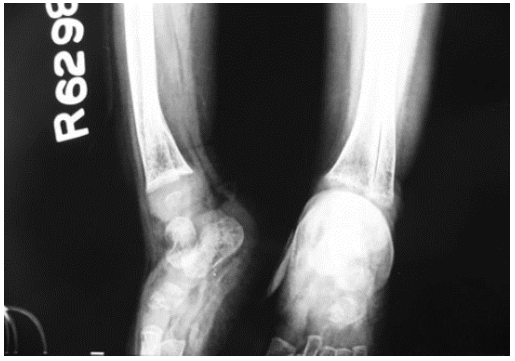
@deniise_am

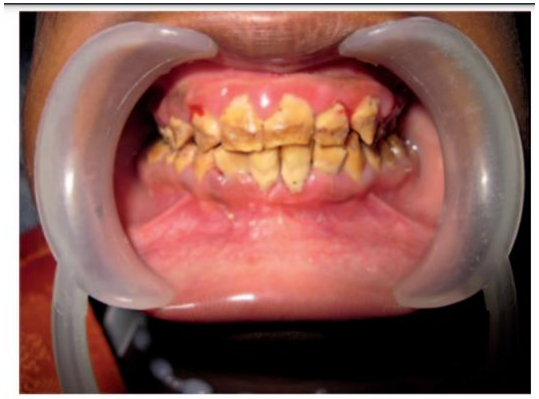


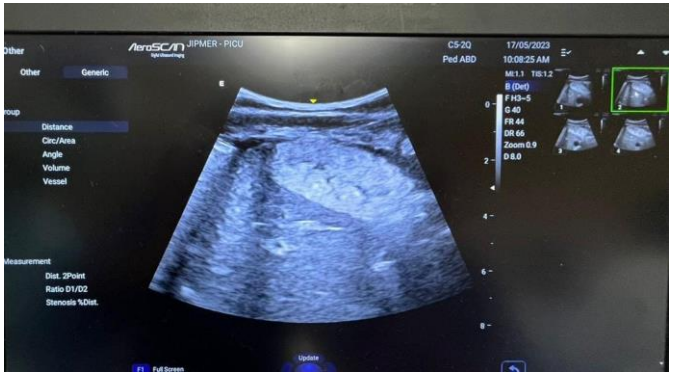
Diagnosis: Familial hypomagnesemia with hypercalciuria and nephrocalcinosis (FHHNC):

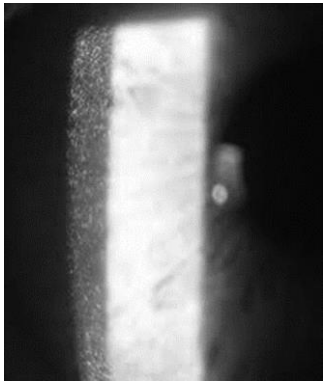
Rx potassium citrate, magnesium, plenty of fluids

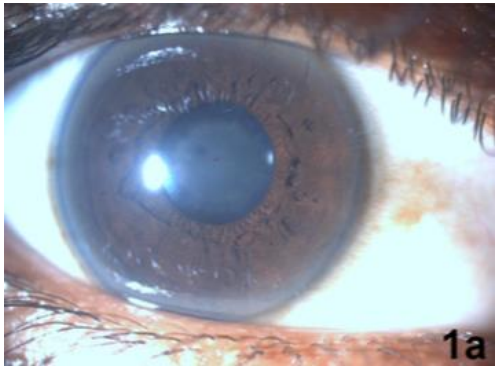
To summarise…..Clinical clues to tubular disorders

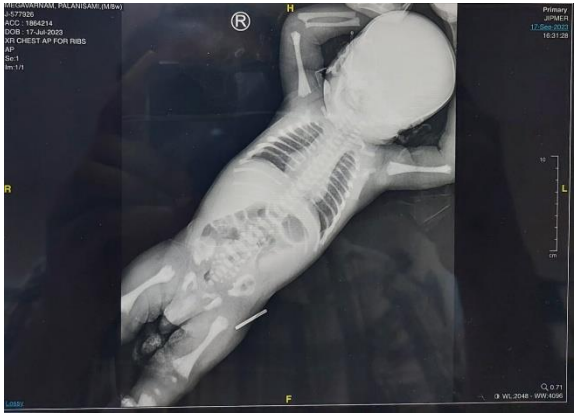


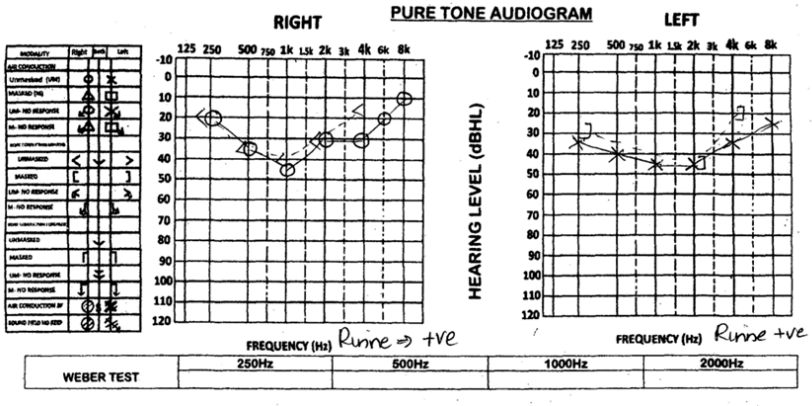


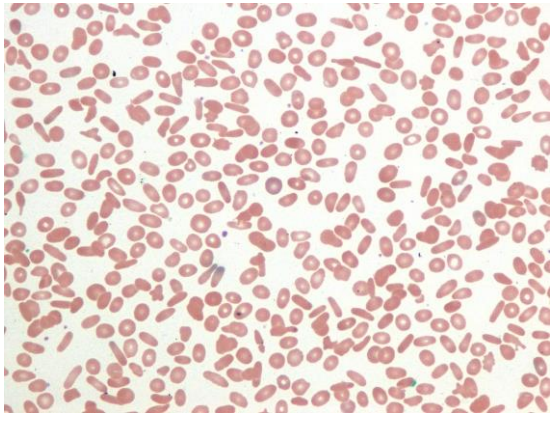












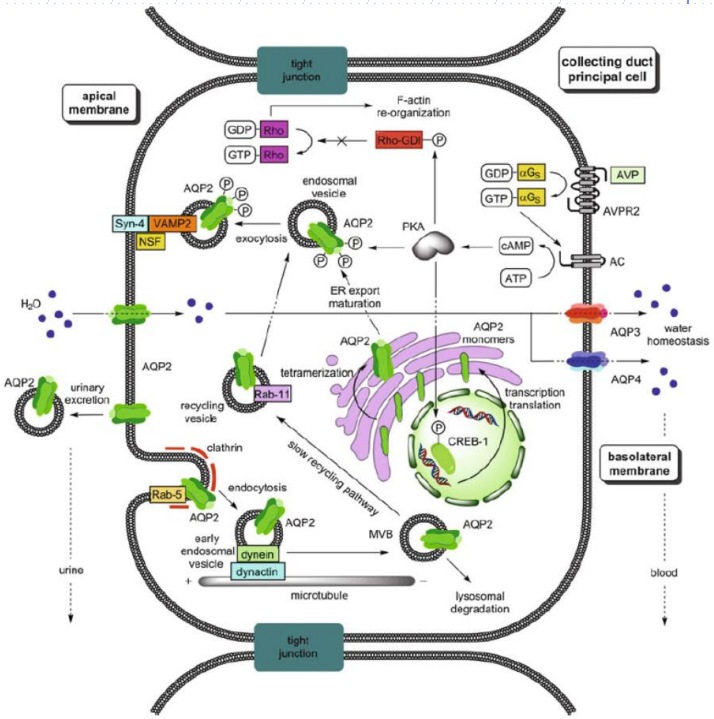
Tubular disorders can have surprising presentations!

Bartter Syndrome with Nephrogenic Diabetes Insipidus and Vitamin D Resistant Rickets

A 1-year-old boy presented with polyuria, polydipsia and poor weight gain noticed since three months of age. He weighed 5 kg (-3SD), Height 64 cm (-3 SD), and had features of some dehydration. Hypernatremia (165 mEq/L) and metabolic acidosis (pH 7.27, bicarbonate levels 17 mEq/L) were detected. Serum creatinine, potassium, calcium, magnesium and chloride levels were within normal reference ranges. Serum osmolality and urine osmolality were 355 mOsm/L and 145 mOsm/L, respectively. He was diagnosed as nephrogenic diabetes insipidus after a vasopressin challenge test failed to increase the urine osmolality levels. Renal ultrasonography was normal. He was treated with spironolactone.

At the age of 3 years, he presented with rickets and hypocalcemic tetany (ionized calcium 2.2 mg/dL) in association with hypophosphatemia (2.2 mg/dL) and secondary hyperparathyroidism (PTH levels 180.2 pg/mL). The rickets was refractory to therapy with Vitamin D; and the child developed fractures of bilateral ulnae and femur requiring hip spica and plaster casts. He was still showing poor weight gain (weight 7.9 kg, -3SD). Triangular facies, prominent eyes and forehead, and large ears were appreciated. Blood pressure was normal. At this juncture, he was found to have hypokalemia (2.5 mEq/L), metabolic alkalosis (pH 7.52, bicarbonate levels 35.2 mEq/L) and hypercalciuria (spot calcium: creatinine ratio 1.4). Serum magnesium and creatinine levels were normal; urine chloride was >20 mEq/L. Plasma renin activity was high (38.9 ng/mL/h), confirming Bartter syndrome. Wrist *X*-ray showed metaphyseal cupping and splaying. Serum 25 hydroxycholecalciferol levels were 31.4 ng/mL. He is currently on potassium chloride (8 mEq/kg/day), indomethacin (2 mg/kg/day), enalapril (0.5 mEq/kg/day), and calcium supplements. At the last follow up at age of 4 years, his serum potassium, sodium, creatinine, calcium and phosphate levels are normal, and he is showing satisfactory weight gain.

The presentation of this child with Bartter syndrome is unusual for two reasons. The first being the initial paradoxical presentation with hypernatremic dehydration and metabolic acidosis; the second being the association with vitamin D resistant rickets (leading to secondary hyperparathyroidism). The former presentation has been anecdotally reported in the literature [1,2]. Bettinelli, *et al.* [1] reported a child who presented with severe hypernatremia, who was initially diagnosed as nephrogenic diabetes insipidus, but on follow up was diagnosed as Bartter syndrome. They concluded that in a few cases of Bartter syndrome, hypokalemia and/or metabolic alkalosis may be absent during the initial few



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Clinical and laboratory parameters among various tubular disorders

	Clinical parameters	*Laboratory parameters*
Distal renal tubular acidosis	Polyuria, polydipsia, failure to thrive, rickets, features of hypokalemia (e.g. weakness, paralysis, neck flop)	Hyperchloremic metabolic acidosis, normal anion gap, hypokalemia, hypercalciuria, nephrocalcinosis
Proximal renal tubular acidosis	Polyuria, polydipsia, failure to thrive, rickets, features of hypokalemia (e.g. weakness, paralysis, neck flop), features of the underlying etiology, e.g. galactosemia, glycogen storage disorder, tyrosinemia, Wilson disease, etc.	Hyperchloremic metabolic acidosis, normal anion gap, hypokalemia
Bartter syndrome	Polyuria, failure to thrive, features of hypokalemia, triangular facies, dehydration *Other clues*: Polyhydramnios in fetal life; deafness (in type 4 Bartter syndrome); hypocalcemia features (e.g. tetany; rickets) in type 5 Bartter syndrome	Hypokalemic metabolic alkalosis, high urinar chloride, high plasma renin activity
Diabetes insipidus	*Nephrogenic*: Polyuria, polydipsia, X-linked variety seen in boys *Central*: Polyuria, headache, seizures	Hypernatremia, high serum osmolality, low-urine osmolality. Water deprivation test can differentiate nephrogenic diabetes insipidus (NDI) from central diabetes insipidus (CDI)

TAKE HOME MESSAGES

- Tubular disorders can have varied clinical manifestations
- Polyuria/polydipsia, hypokalemia, metabolic acidosis, metabolic alkalosis, failure to thrive, salt craving, nephrocalcinosis, refractory rickets, hypomagnesemia, recurrent dehydration can be useful diagnostic clues
- Distal RTA is generally primary in children, while Proximal RTA is generally secondary in nature
- Bartter syndrome and Gitelman syndrome present with hypokalemic metabolic alkalosis without hypertension, but Pseudo-Bartter conditions such as CF should be carefully ruled out
- Follow standard diagnostic algorithms for establishing the correct diagnosis
- Regular follow-up of these children is required and eGFR should be monitored along with other laboratory parameters

Thank You

Vascular access in KRT -POCUS

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Overview

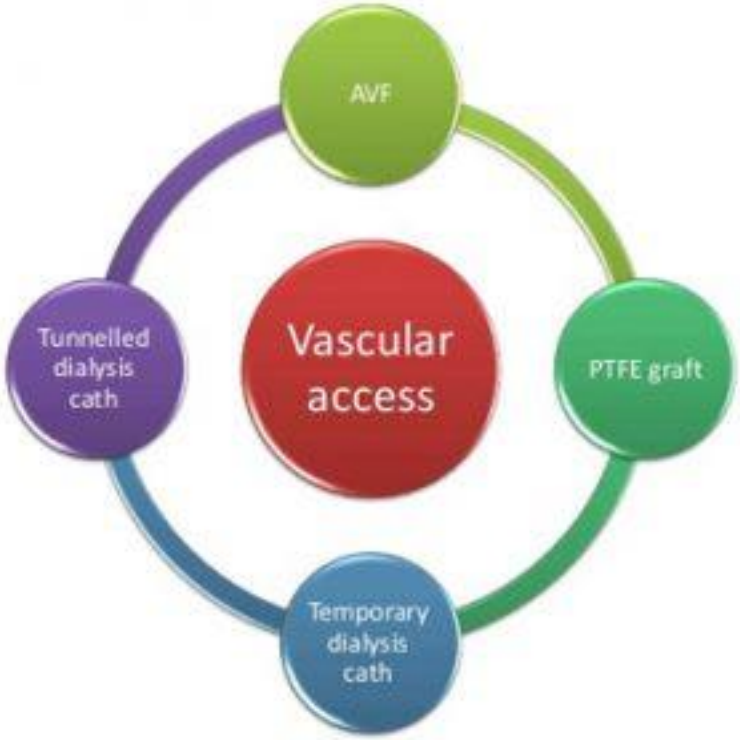
- Understand the type of vascular access for KRT
- Role of POCUS in vascular access
- Recognize key sonographic features of AVF,AVG and central veins
- Identify the complications using POCUS
- Role of US in endovascular intervention

Introduction

- Hemodialysis
  - Most prevalent form of KRT
- Vascular access
  - Achilles heel of Hemodialysis
- Success of vascular access depends diagnosis and monitoring of access related issues
- Clinical signs and physical examination strategies may help
- POCUS –Additional valuable skill to provide optimal access care

Dialysis vascular access

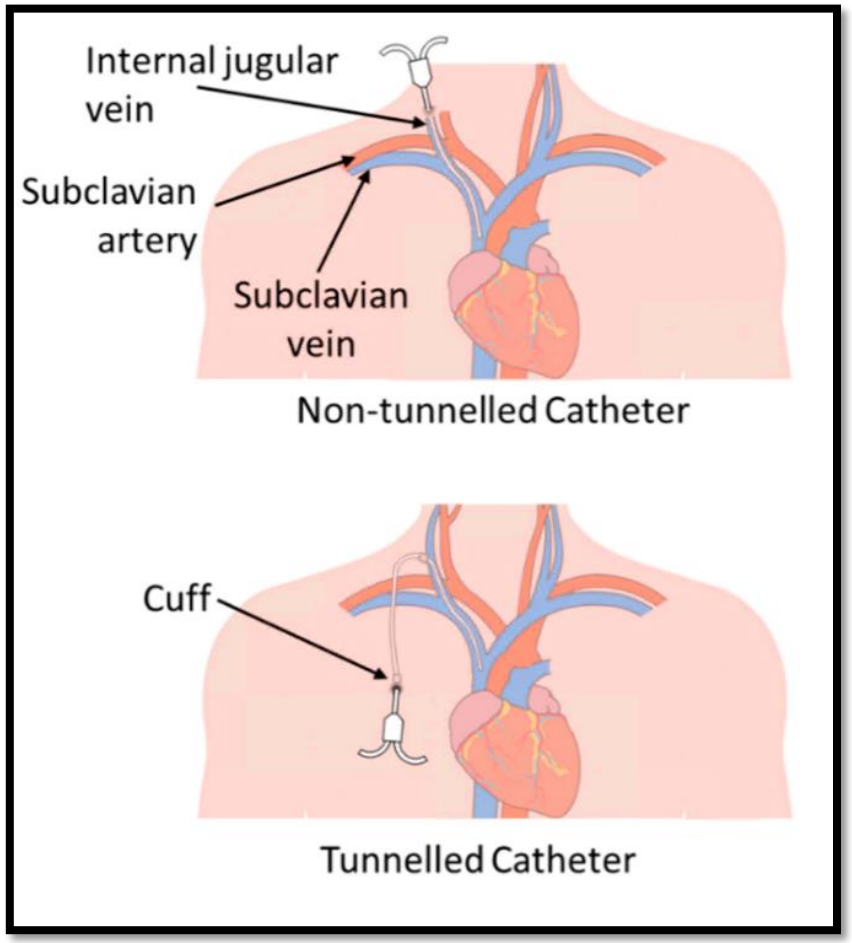
- AV fistula
- AV graft
- Central venous Dialysis catheter
  - Tunneled cuffed catheter
  - Temporary dialysis catheter



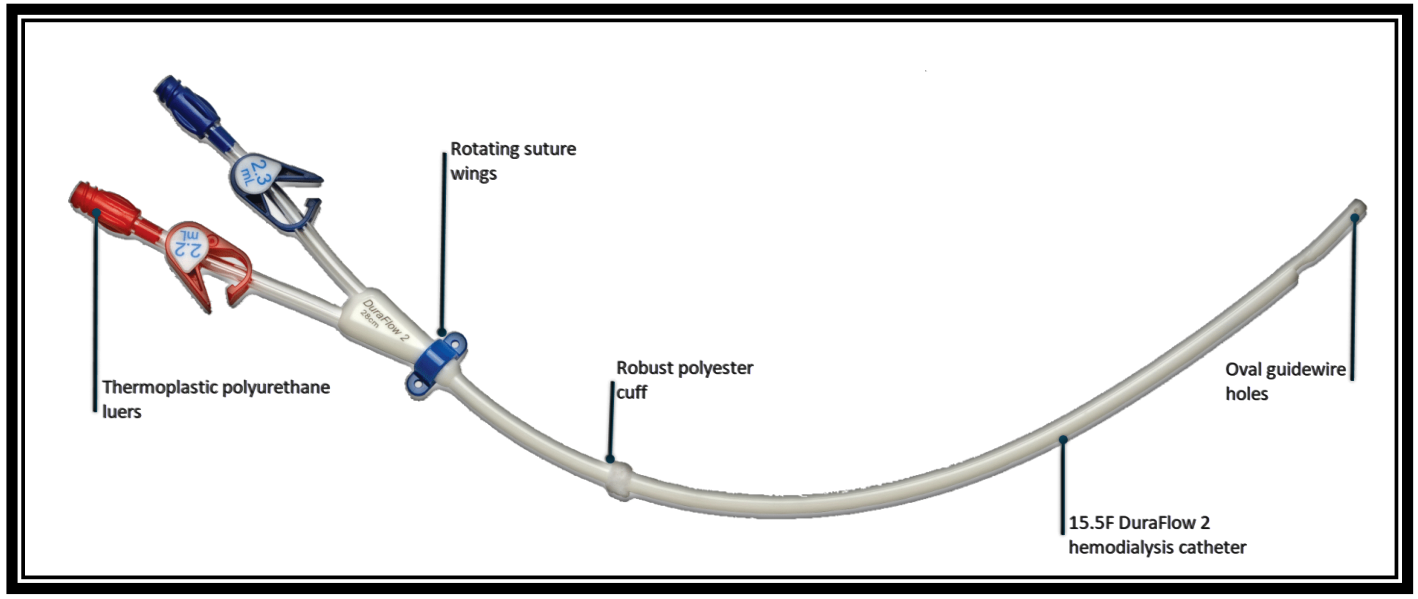
Tunneled vs non-tunneled catheter

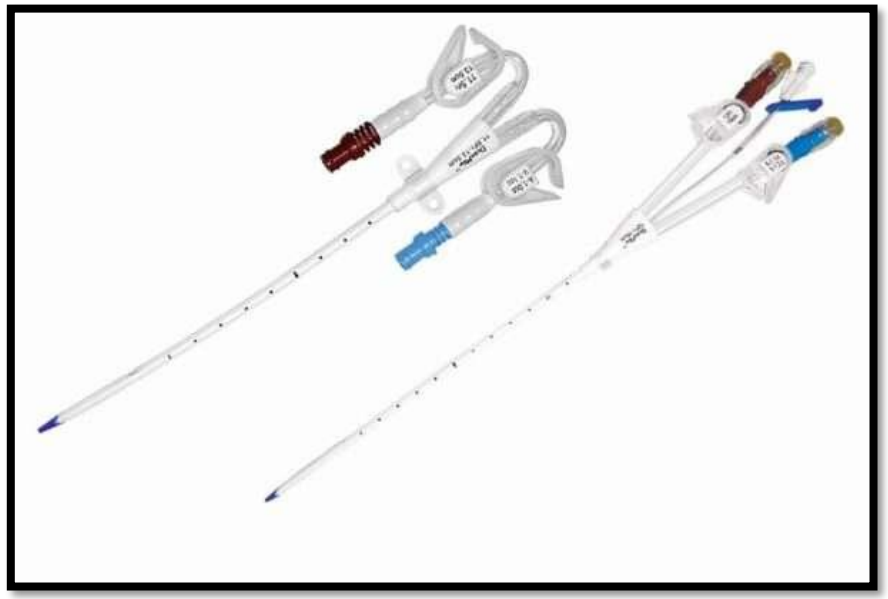
- Non-tunneled temporary dialysis catheter
  - Used for short-term dialysis (days to weeks)
  - Inserted directly into a vein without tunneling, increasing infection risk
  - Less secure, with a higher chance of displacement
  - Typically placed in emergencies or when immediate dialysis is required

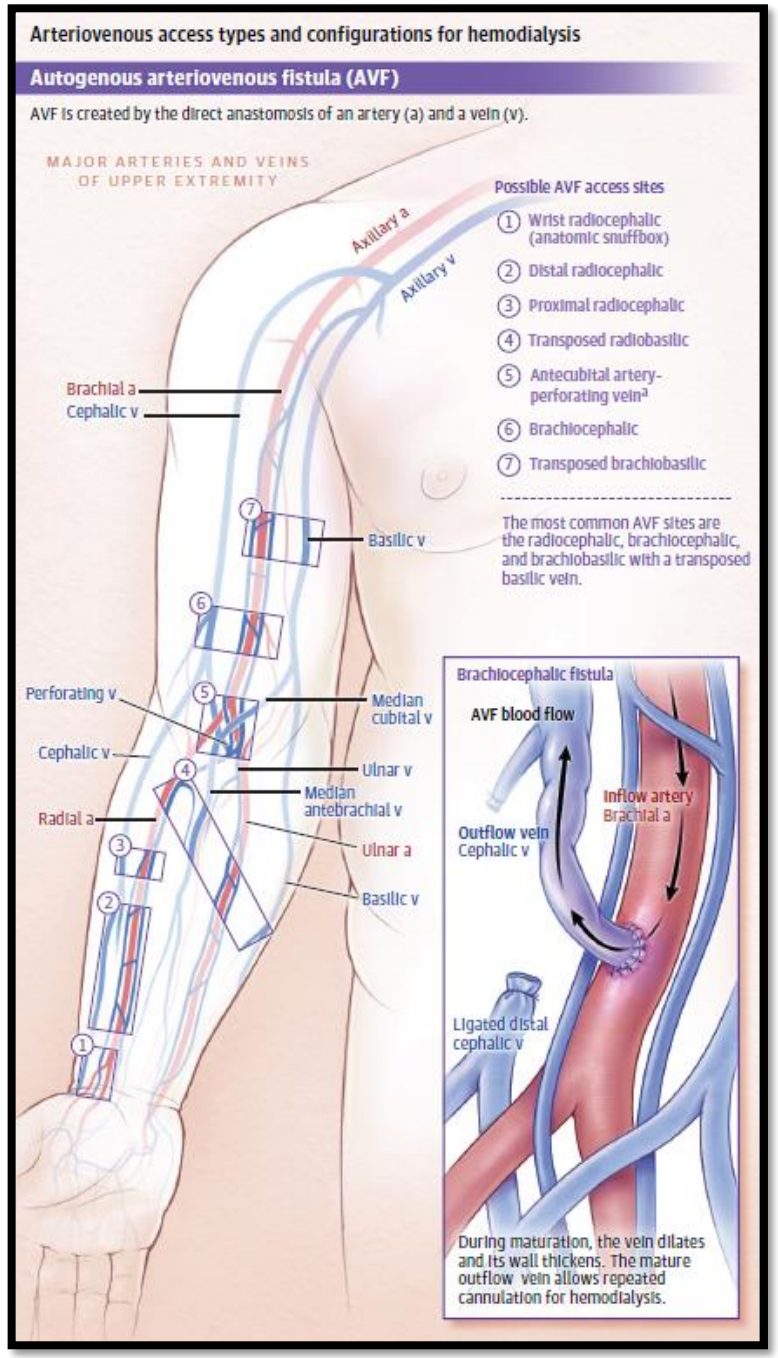
- Tunneled dialysis catheter
  - Designed for long-term use (weeks to months)
  - Inserted under the skin before entering the vein, reducing infection risk
  - More secure and less likely to be displaced
  - Commonly used when permanent vascular access (like an AV fistula) is not ready

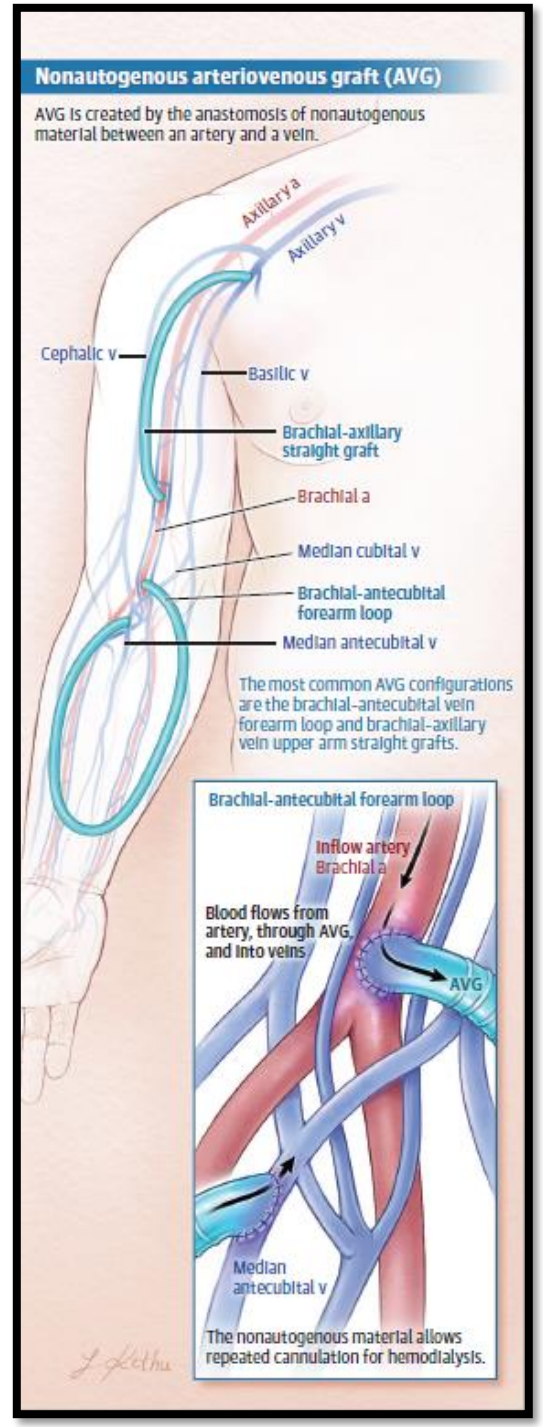


Tunneled cuffed catheter vs Temporary catheter





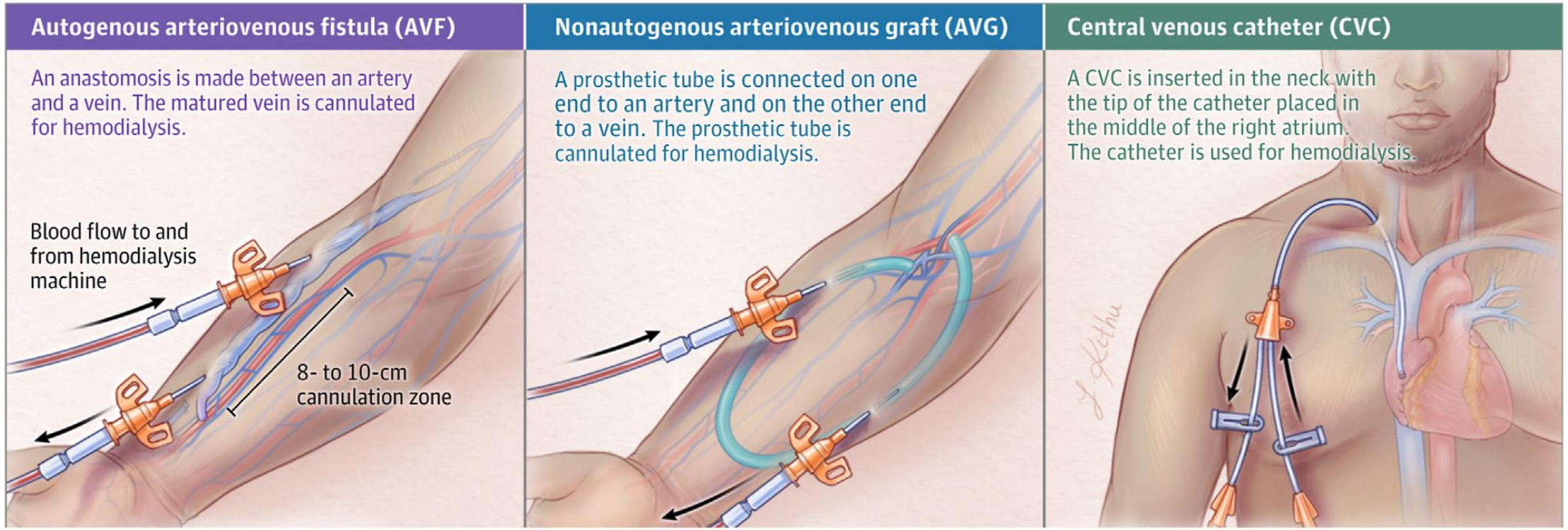

Arteriovenous access types and configurations for hemodialysis
Autogenous arteriovenous fistula (AVF)
AVF is created by the direct anastomosis of an artery (a) and a vein (v).
MAJOR ARTERIES AND VEINS OF UPPER EXTREMITY
Axillary a
Axillary v
Brachial a
Cephalic v
Basilic v
Perforating v
Median cubital v
Cephalic v
Ulnar v
Median antebrachial v
Radial a
Ulnar a
Basilic v
Possible AVF access sites
1 Wrist radiocephalic (anatomic snuffbox)
2 Distal radiocephalic
3 Proximal radiocephalic
4 Transposed radiobasilic
5 Antecubital artery-perforating vein[a]
6 Brachiocephalic
7 Transposed brachiobasilic
The most common AVF sites are the radiocephalic, brachiocephalic, and brachiobasilic with a transposed basilic vein.
Brachiocephalic fistula
AVF blood flow
Inflow artery Brachial a
Outflow vein Cephalic v
Ligated distal cephalic v
During maturation, the vein dilates and its wall thickens. The mature outflow vein allows repeated cannulation for hemodialysis.


Nonautogenous arteriovenous graft (AVG)
AVG is created by the anastomosis of nonautogenous material between an artery and a vein.
Axillary a
Axillary v
Cephalic v
Basilic v
Brachial-axillary straight graft
Brachial a
Median cubital v
Brachial-antecubital forearm loop
Median antecubital v
The most common AVG configurations are the brachial-antecubital vein forearm loop and brachial-axillary vein upper arm straight grafts.
Brachial-antecubital forearm loop
Inflow artery Brachial a
Blood flows from artery, through AVG, and into veins
AVG
Median antecubital v
The nonautogenous material allows repeated cannulation for hemodialysis.

Vascular access-comparison

Central venous catheter	AV Graft	AV fistula
• Highest infection rate • High Thrombosis risk • Highest mortality • Can be used immediately • Can be used for almost all patients • Primary failure rate is low	• Moderate infection rate • Moderate thrombosis risk • Mortality risk less than CVC • Can be used in a couple of weeks • Primary failure rate slightly higher than CVC	• Lowest infection rate • Lowest mortality rate • Maturation time 1-5 months • Primary failure rate is high • May not be possible in all patients

Vascular access -comparison



Ideal vascular access

- Adequate blood flow
- Easy cannulation
- Early use
- Low complication rate
  - Less failure rate
  - Less infection

Role of Ultrasound

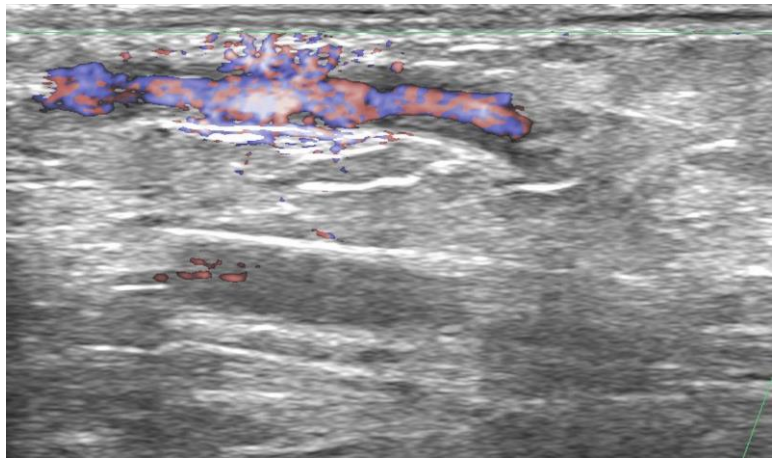
- Selecting best site VA creation- high risk patients(pre-procedure vascular mapping)
- For Temporary and TCC insertion
- Evaluation for non maturation
- Assisting Difficult cannulation
- Monitoring and Surveillance In high risk patients
- **Diagnostics - Vascular access problems**
- **In endovascular or surgical repair**
- **Post procedure evaluation**

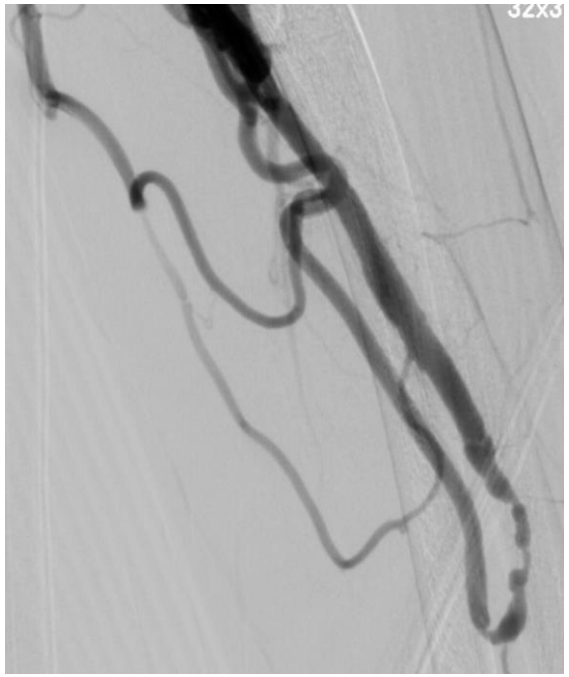
Advantages

- Non invasive
- Portable, easy set up, minimal space requirement
- No radiation - repeated exam harmless
- Structural evaluation
- Functional / Hemodynamic evaluation
- Real time information

Limitations

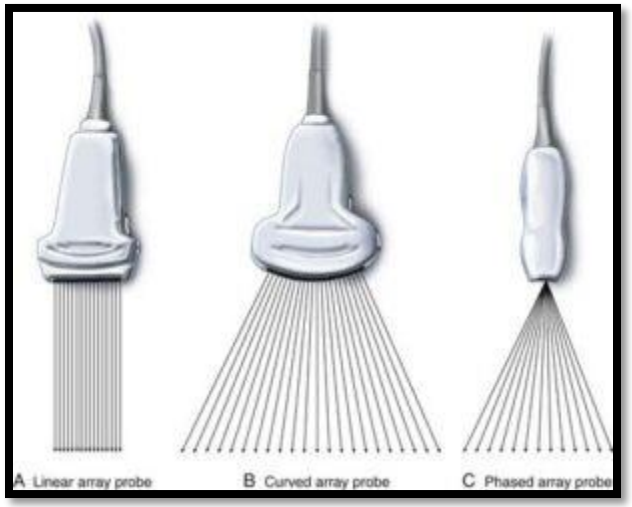
- Quality - Operator dependant
- Inter reader variability
- Central venous system can’t be evaluated
- Small field of view





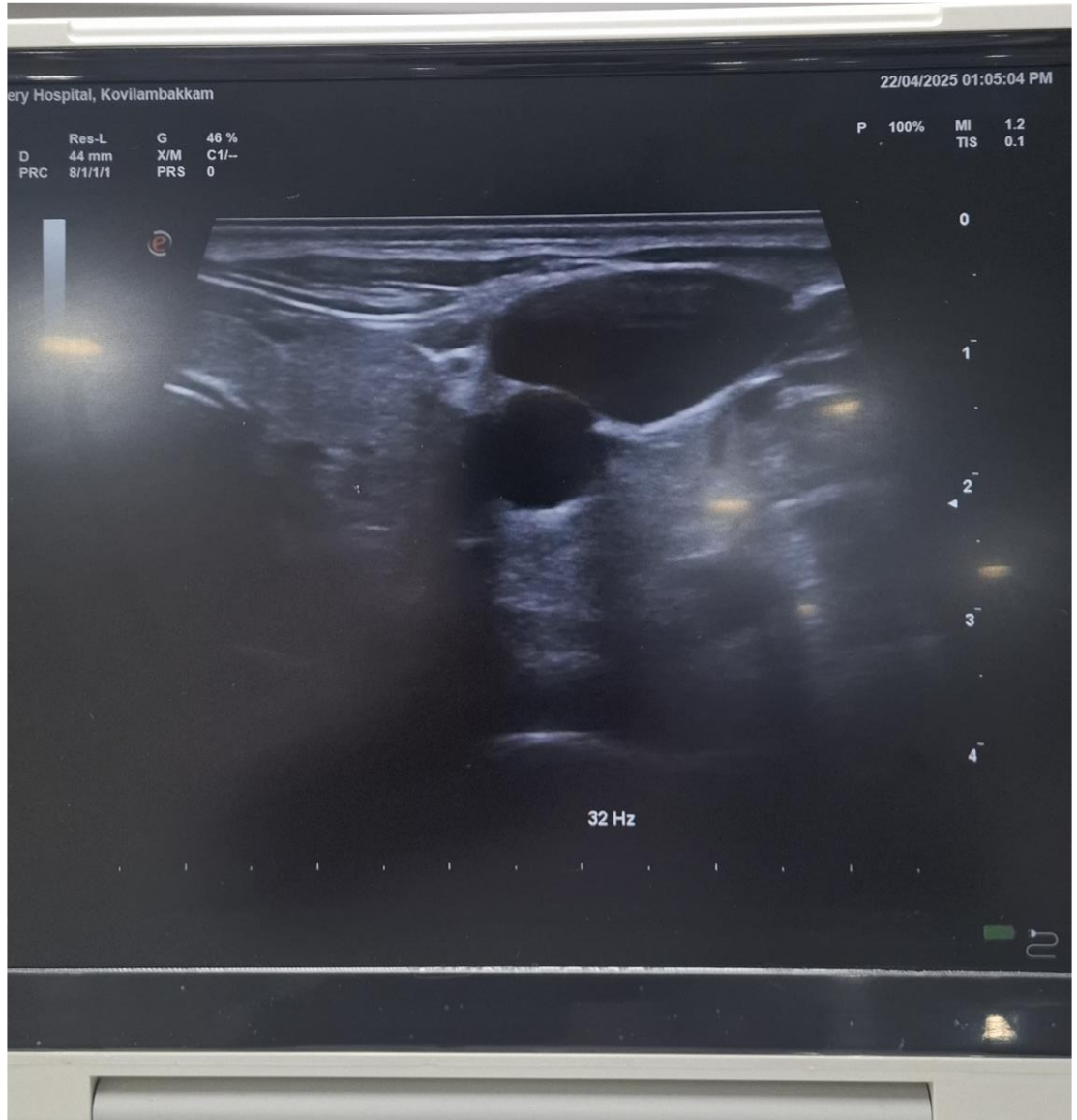
POCUS of vascular access

- Linear phased array probe is preferred(7-12 HZ)
- B mode
  - Identify the access and other surrounding structures such as blood vessels or fluid collections.
- Color doppler
  - To assist and confirm findings on the B-mode
  - To monitor the patency of the access.
- Pulse-wave doppler
  - To measure the blood flow



POCUS –during Catheter insertion

- Used for temporary and TDC insertion
- Minimizes the complications
- Can assess the patency of the veins


ery Hospital, Kovilambakkam
22/04/2025 01:05:04 PM
Res-L
D 44 mm
PRC 8/1/1/1
G 46 %
X/M C1/--
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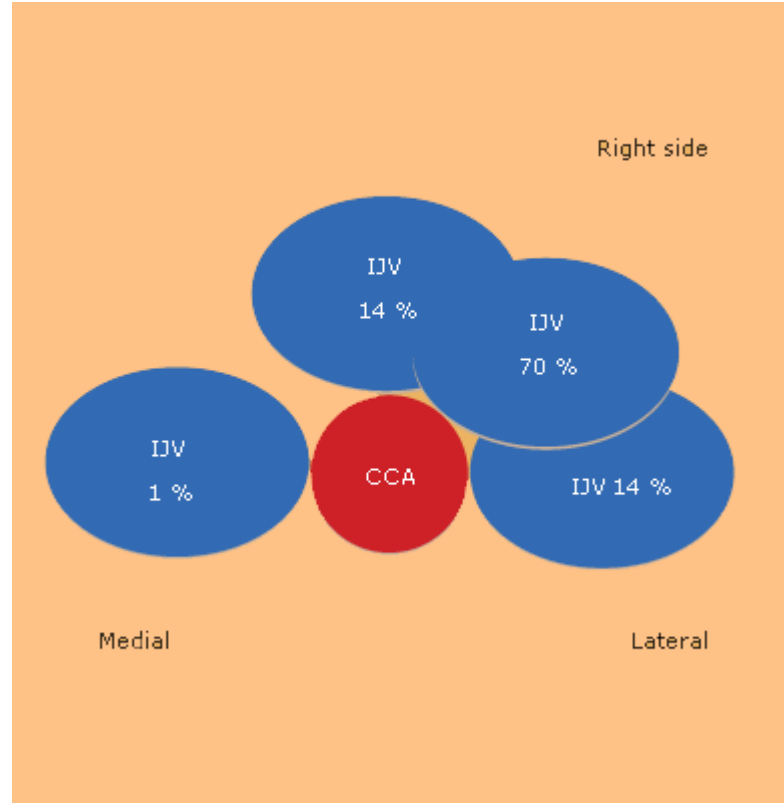
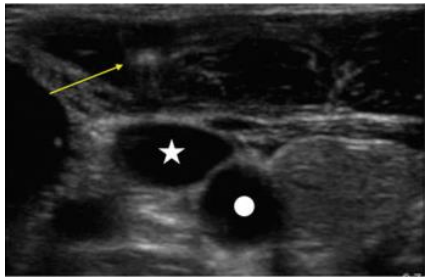
P 100%
MI 1.2
TIS 0.1
0
1
2
3
4
32 Hz


Right side
IJV
14 %
IJV
70 %
IJV
1 %
CCA
IJV 14 %
Medial
Lateral

Arterial puncture



Minimized with USG guidance

- Identify vein
- Compressibility
- Doppler (Color and PW doppler)

Arterial puncture if not recognized and dealt immediately –devastating

AVF and AVG –POCUS

- Clinical signs and Physical exam before POCUS
- History

Clinical parameters

Physical exam - see, touch, listen

- Abnormal thrill (weak and/or discontinuous)
- Failure of the fistula to collapse when the arm is elevated (outflow stenosis) and lack of pulse augmentation (inflow stenosis)
- Excessive collapse of the venous segment upon arm elevation
- Abnormal bruit (high pitched)

Clinical parameters

Physical exam - see, touch, listen

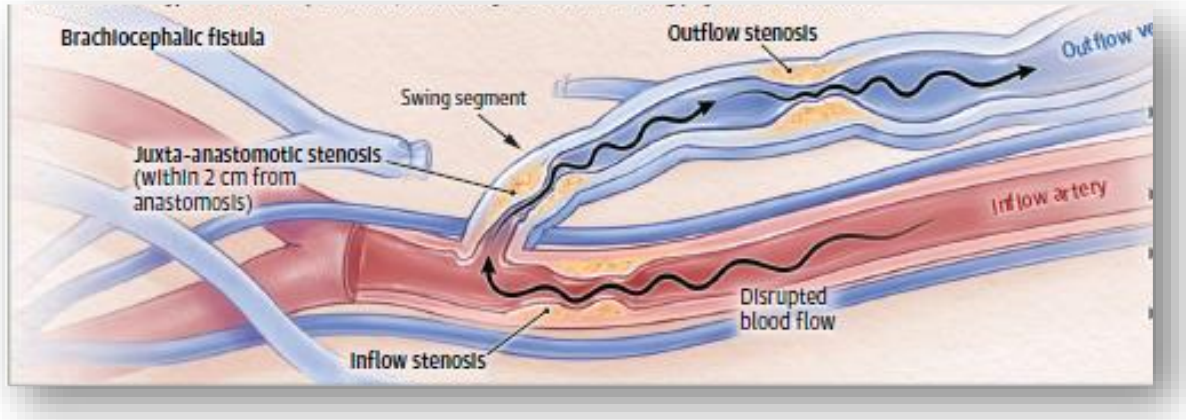
- Aneurysmal dilatation
- Ipsilateral Arm oedema
- Dilated veins on chest wall / upper arm
- Hand ischemia

Dialysis parameters

- Unable to maintain blood flow / Collapse of vein during dialysis
- High venous pressure / prolonged bleeding post needle removal
- New onset difficulty in cannulation
- Ineffective dialysis - Kt/V or URR
- Higher recirculation
- Aspiration of clots

POCUS on AVF and AVG

- Focus on 3 elements
- Inflow
  - Inflow artery
  - Arterial anastomosis
  - Juxta-anastomotic segment
- Conduit
  - Body of the fistula
- Outflow
  - After the venous anastomotic area in graft
  - Outflow veins beyond the cannulation zone



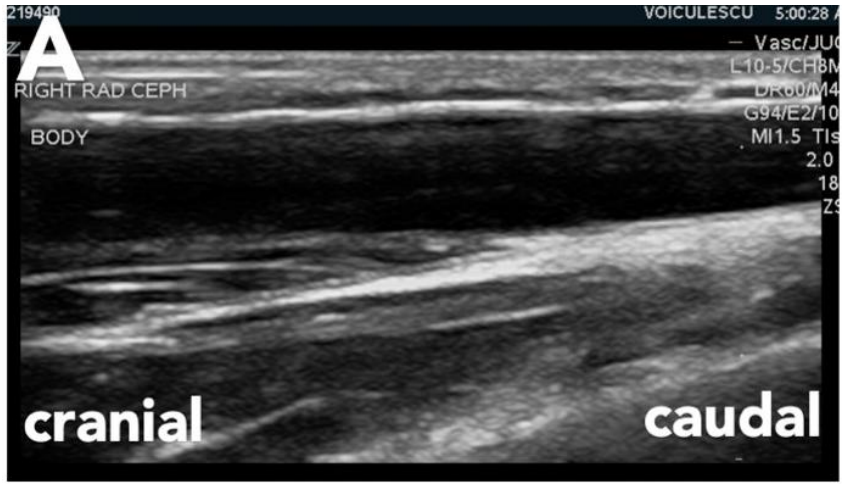
Protocol Based Approach

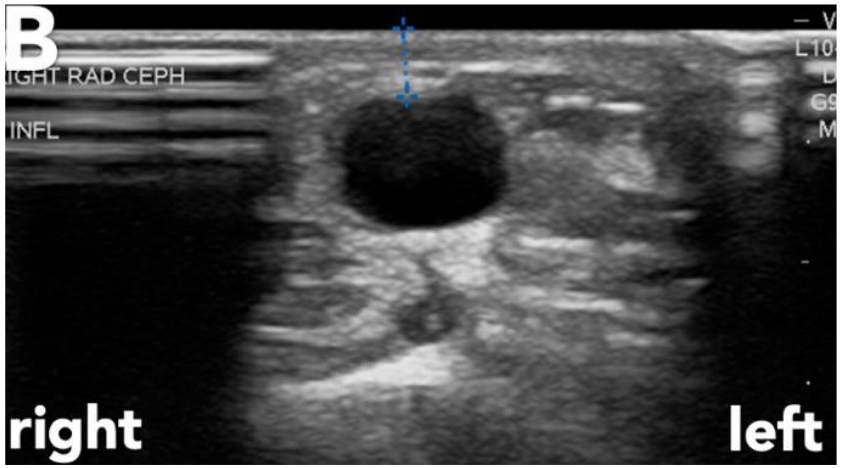
Arterial side - Inflow

1. By a transverse scan B mode:
   - Identify the brachial artery and radial artery
     Use M-mode to identify the average diameter in relation to the pulsatility.

2. By Longitude scan:
   - B mode and Colour doppler examination of arterial circuit
   - Estimated blood flow in the vascular access and the real resistance in the downstream according to the **morphology** of Doppler **velocity spectrum**.

- Longitudinal axis
- Transverse axis





Venous side - outflow

By short axis scan in B-mode (**venous outflow**):

- Describe the average diameter of the efferent vein/graft, its depth from the skin, its course.

By a longitudinal scan (**venous outflow**):

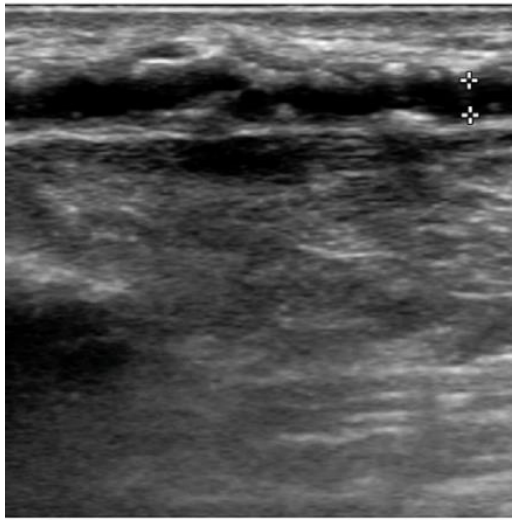
- Analyse the wall and the lumen of the access - aneurysm, pseudo-aneurysm, thrombosis, wall integrity
- Analyse also the soft tissue peri-access - hematoma, peri-access liquid film, oedema in the soft tissue
- Analyse the colour Doppler in order to identy stenosis, thrombosis, wall alteration with thrombosis

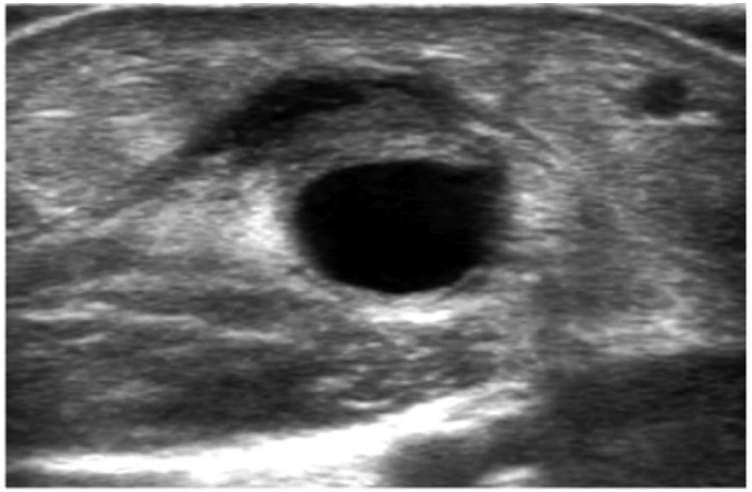
Describe the **anastomosis** between the graft and the vein: two diameters (mm) and maximum peak systolic velocity (cm/s)

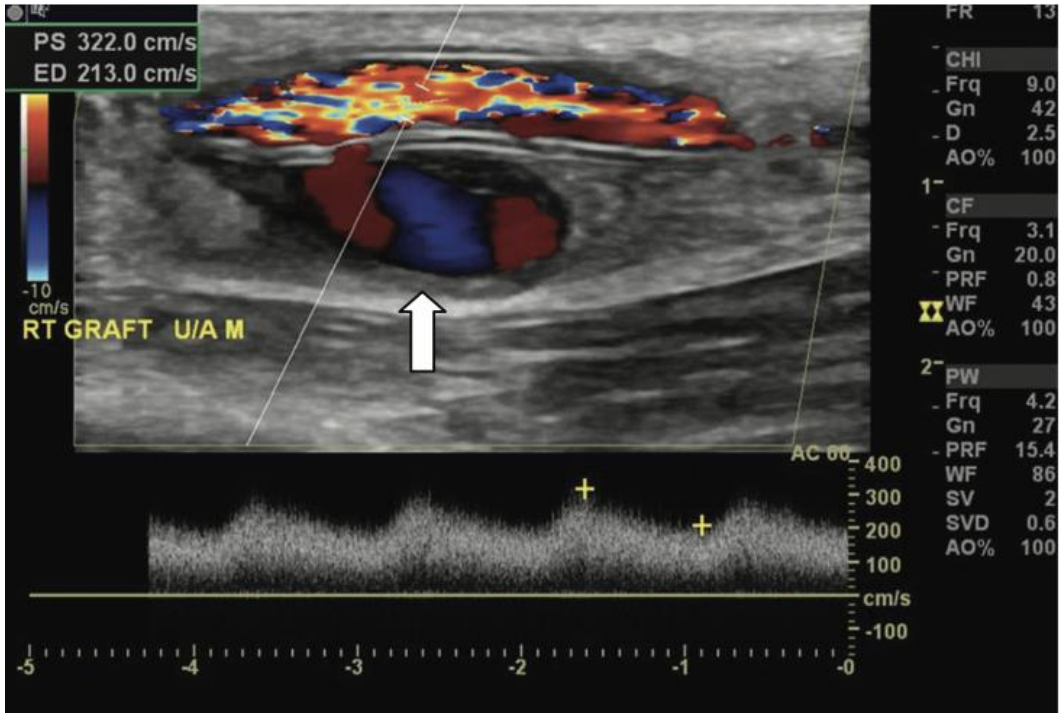
By a transverse and longitude scan of **Graft**:

- Identify the graft diameter
- Blood flow measurement
- Puncture site stenosis / thrombosis

Central vein evaluation - convex / phased array probe

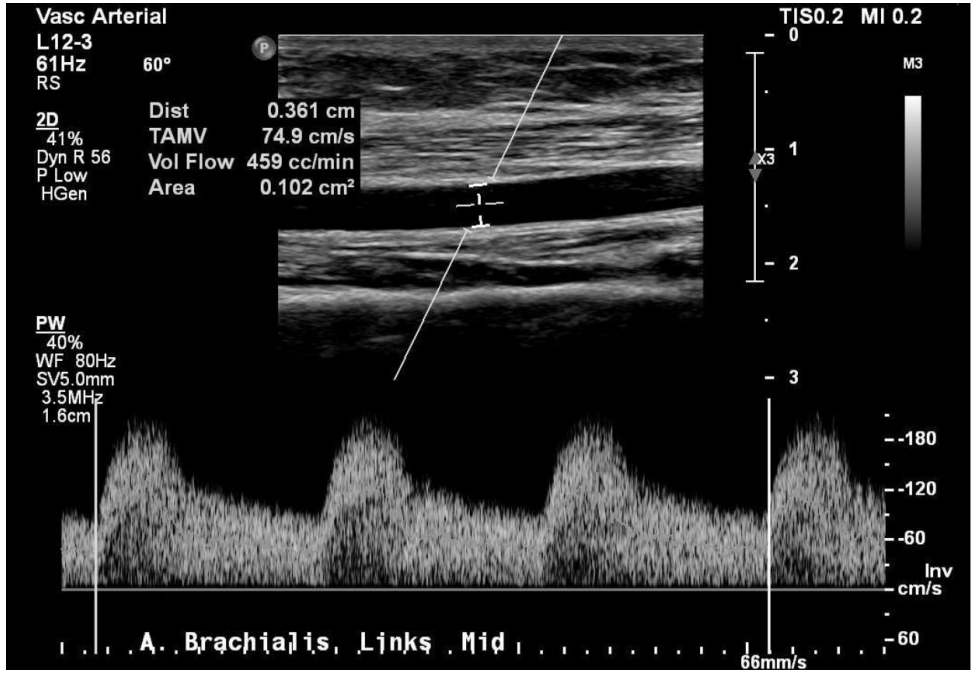






Blood flow measurement of AVF

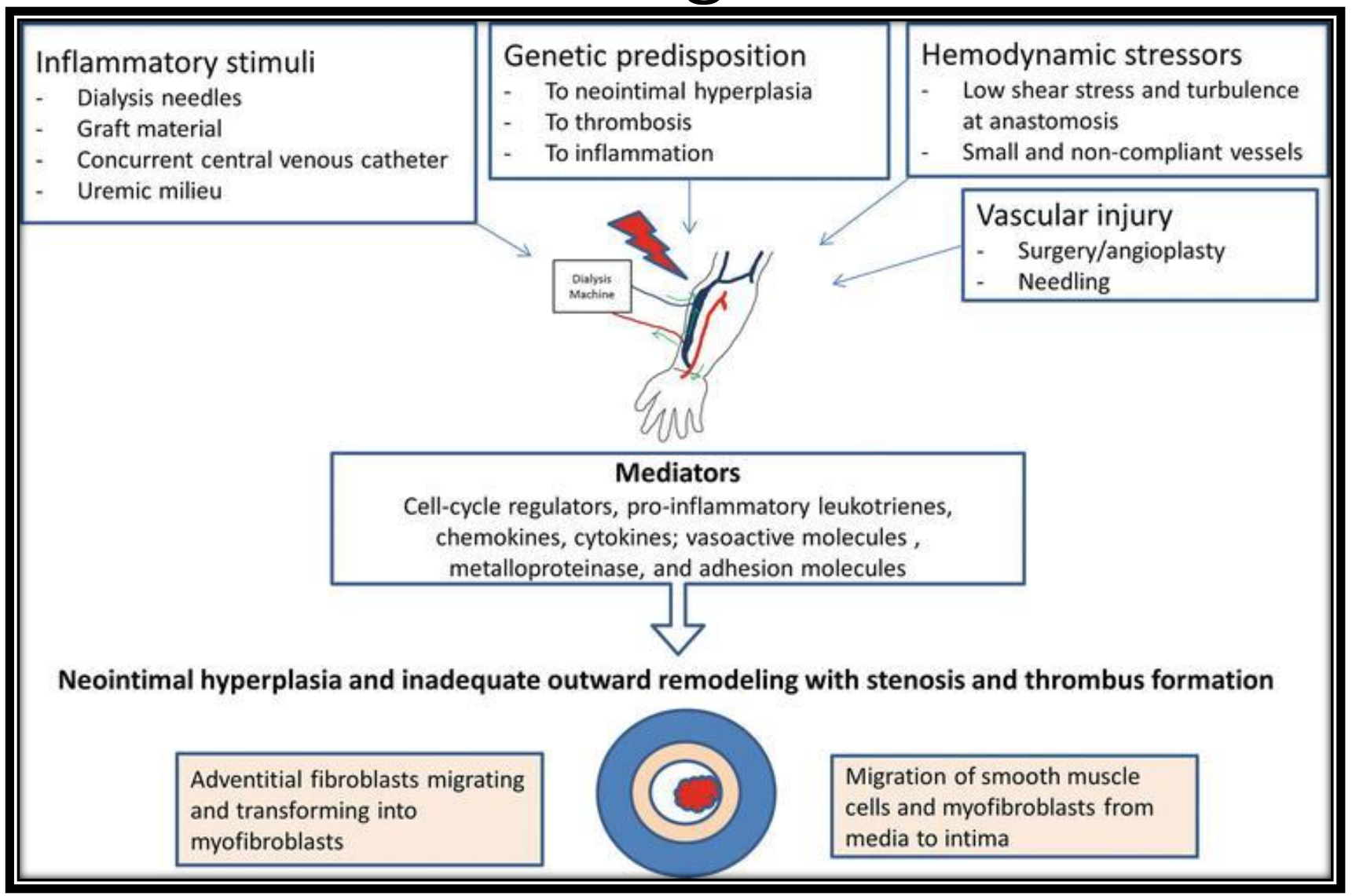
- To measured in Brachial artery
- Measured in Longitudinal view
- Why brachial artery is used?
  - Less prone for compression
  - Facilitates accurate diameter measurements
  - Laminar flow
  - Correlates with access flow
  - Can identify dysfunction



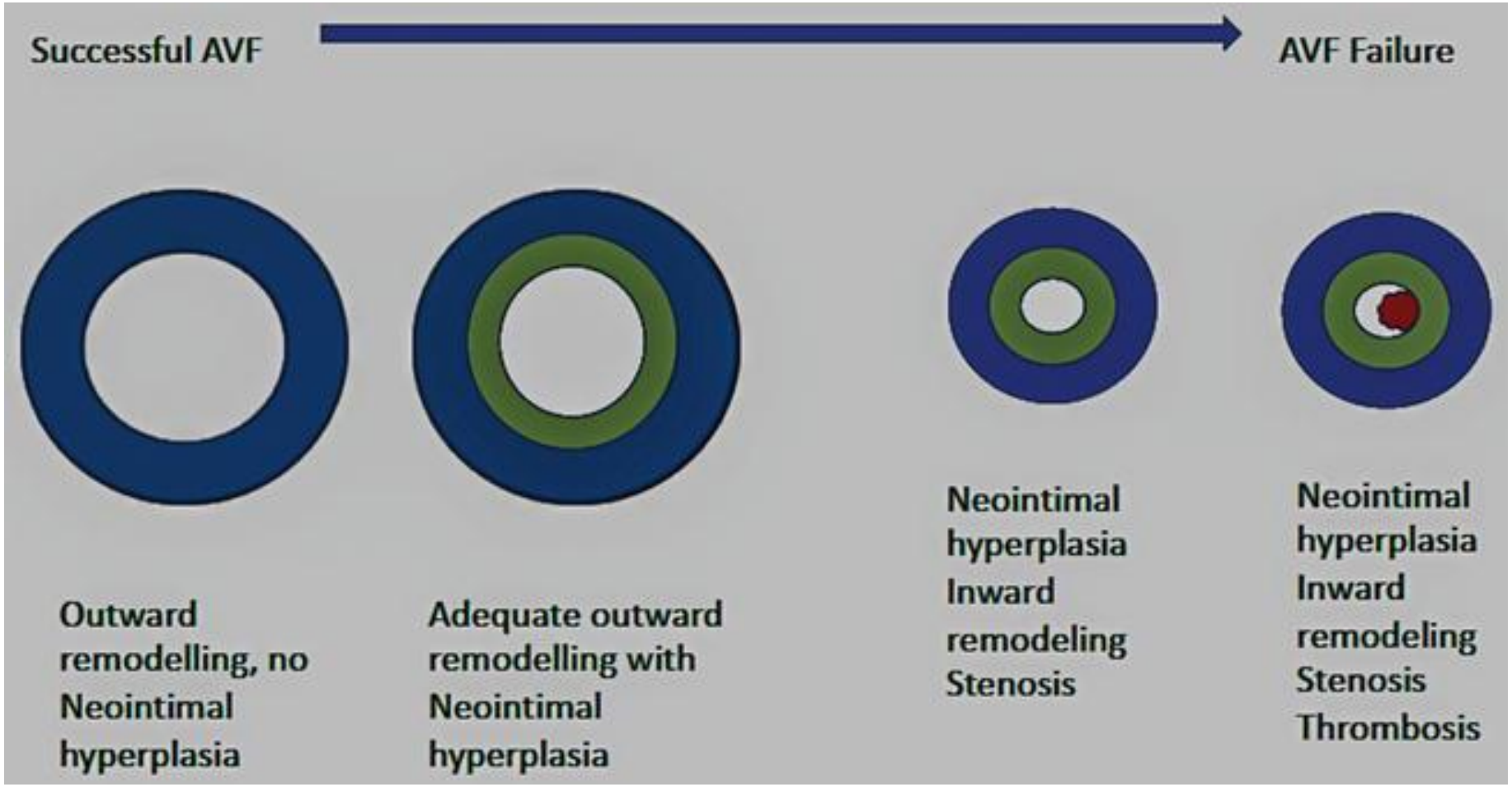
Monitoring and surveillance

- Why it is needed?
- Salvage may not be possible after cessation of flow
  - AVF – 72 hrs
  - AVG – 5 days
- Dialysis nurses and technicians, as well as patients, should monitor the arteriovenous access and various dialysis parameters to detect abnormalities before, during, and after dialysis that may indicate problems with the AV access

Factors affecting access health



Pathophysiology of AVF failure



Lesions in vascular access stenosis

- Inflow stenosis

- Lesion in the feeding artery
- Arterial anastomosis
- Juxta-anastomosis
- Combination

- Outflow stenosis

- Outflow vein
- Central vein
- Venous anastomosis of AVG

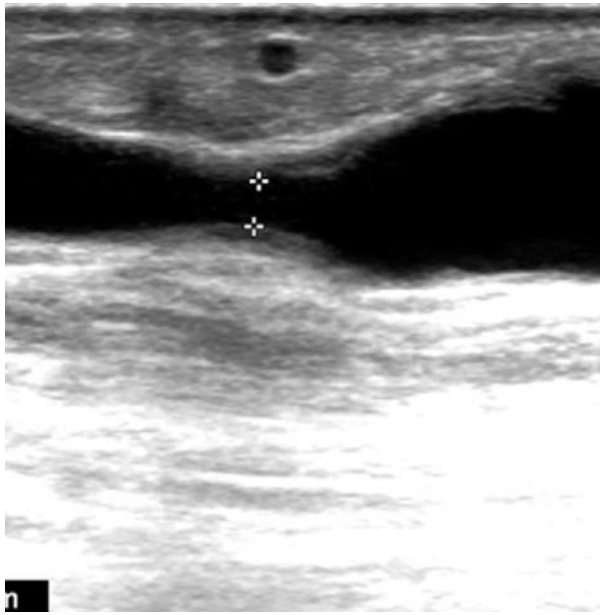
Findings	What it suggests
Head: Facial edema	 Superior vena cava stenosis
Neck: Scars (prior central venous catheters)	 Increased risk of central venous stenosis
Chest: Edema Breast swelling Collateral veins Implantable devices	 Central vein stenosis Central vein stenosis Central vein stenosis Increased risk of central vein stenosis
Arm: Edema Collateral vein(s) Aneurysms and pseudoaneurysms Visible pulsation	 Central vein stenosis Stenosis near the vein(s) Outflow stenosis Outflow stenosis
Hand: Cyanosis,pallor, skin necrosis, or dystrophic nails	 Vascular steal syndrome

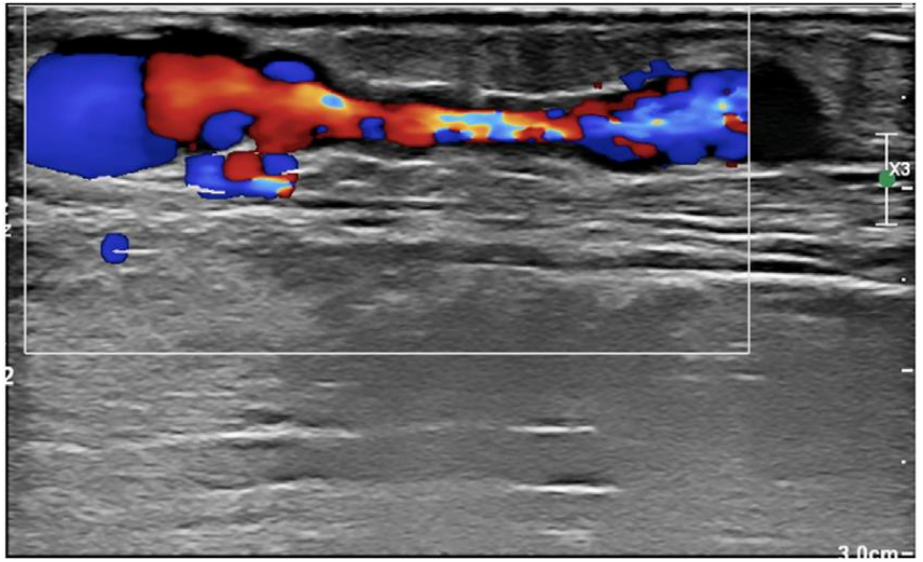
Inflow vs outflow stenosis

	Inflow stenosis	Outflow stenosis
Clinical findings	Difficult cannulation Poor flow Negative arterial pressure	Prolonged bleeding Poor flow High venous pressure
Inspection	Poorly defined	Distended AVF does not collapse on arm elevation
Palpation	Poor pulse augmentation Discontinuous and decreased thrill	Hyperpulsatile Thrill is discontinuous and accelerated at the site of lesion
Auscultation	Discontinuous and decreased bruit	Bruit is high pitched,discontinuous and accentuated at the site of lesion

Diagnosing - stenosis

1. **Anatomical** : reduced lumen on gray scale / colour doppler.
   - > 50 % reduction, **< 2mm - critical**
2. **Turbulence** on colour doppler
3. **Blood flow value** - > 25% reduction from baseline or
   1. AVF: Less than 350 ml/min, or < 400 - distal AVF / < 500 - proximal AVF
   2. AVG: Less than 500ml/min or < 600 ml/min
   3. High flow - > 1500 ml/min and > 20% of CO





Pathology

Diagnosing - Stenosis

4. Resistive index (**RI**)

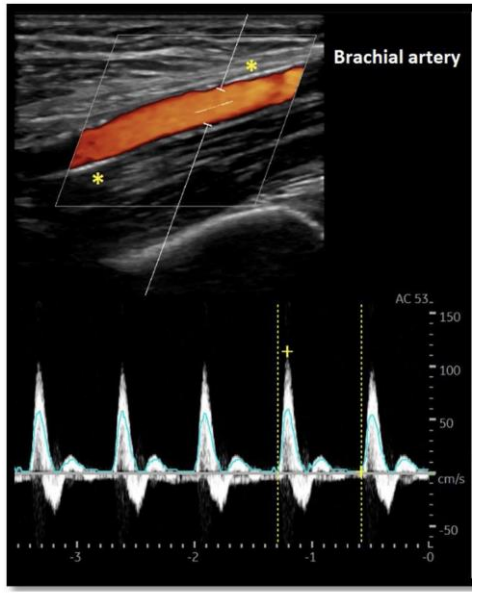
> 0.6 - significant, > 0.7 - higher risk of thrombosis

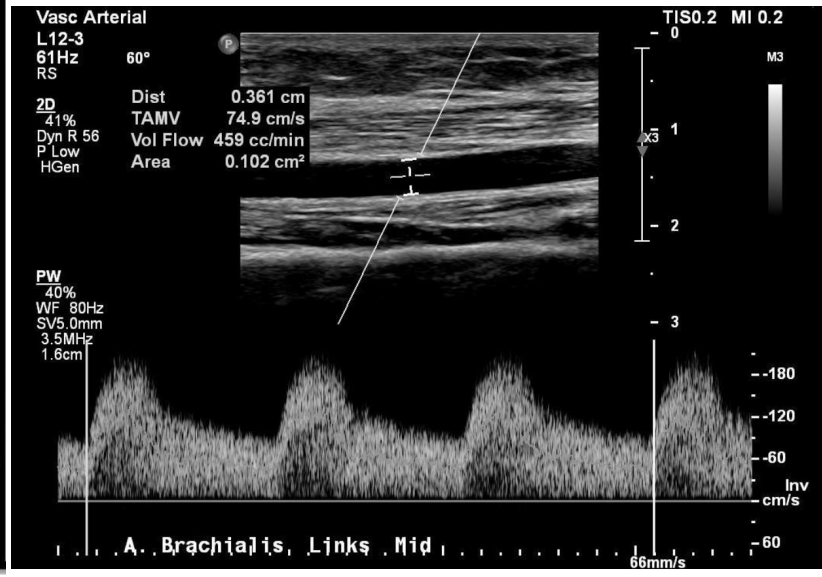
5. **PSV and PSV Ratio** - only vaguely defined

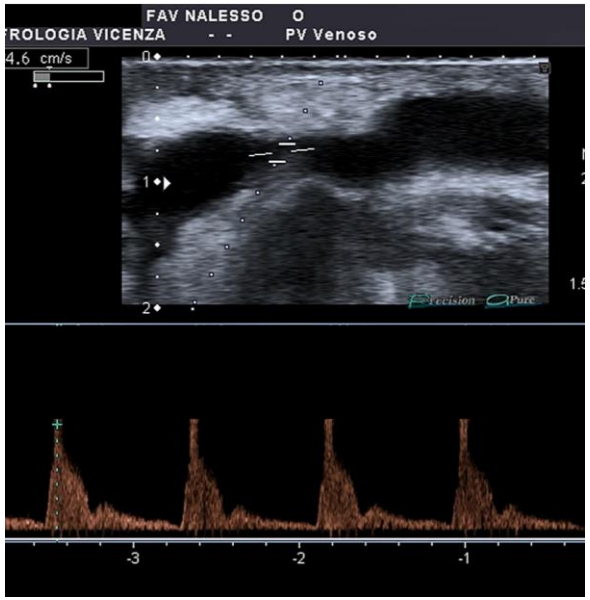
Anastmosis : PSV > 400 cm/sec and PSV ratio > 3

Venous : PSV > 375 cm/sec and PSV ratio > 2

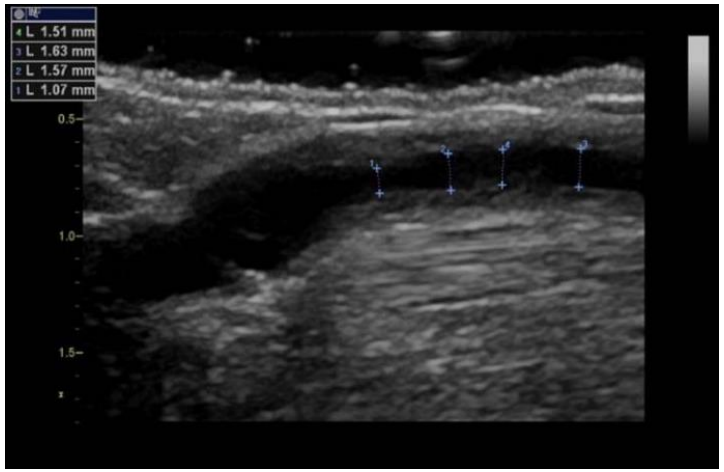
6. Serial Measurements (**Trends**) more important

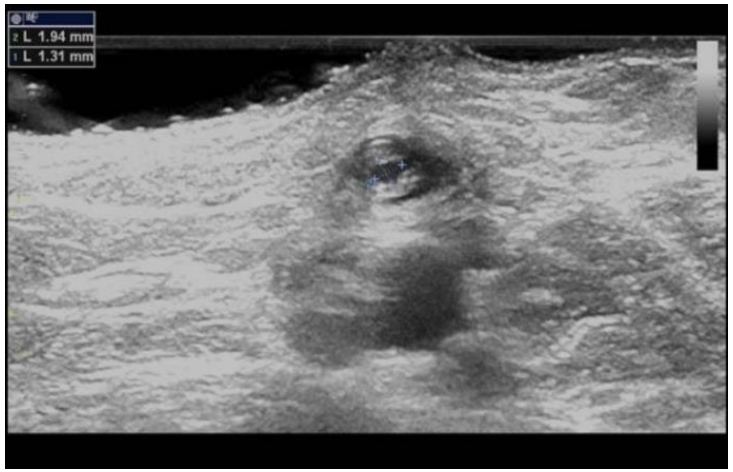


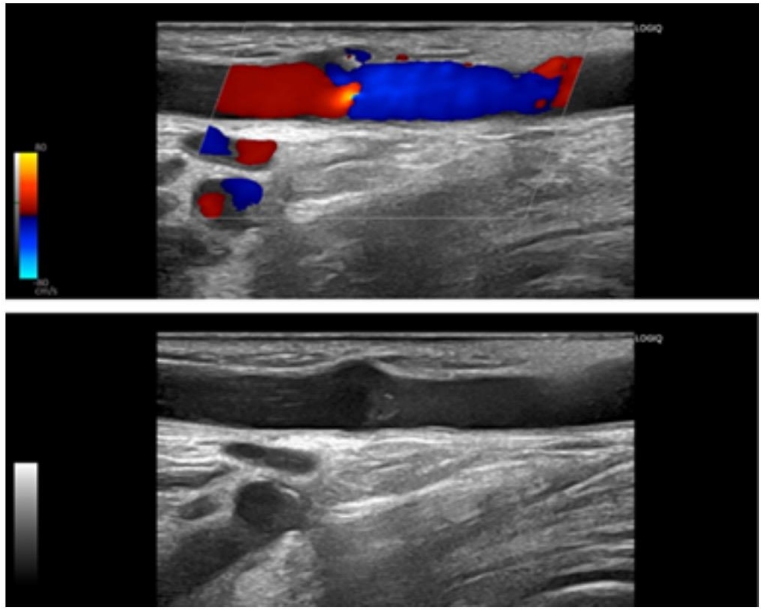


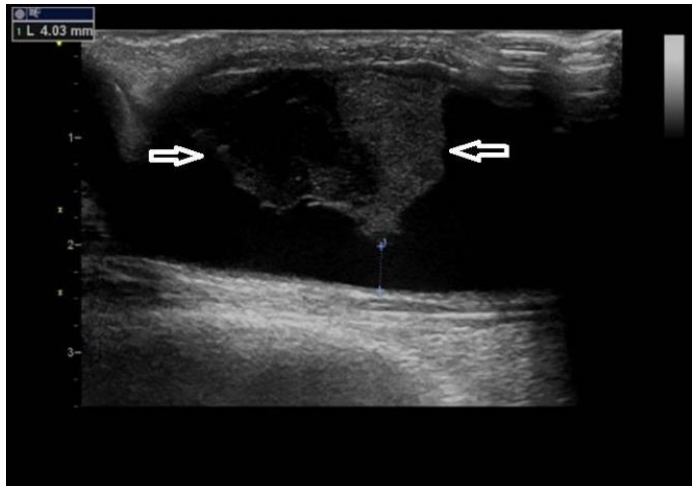


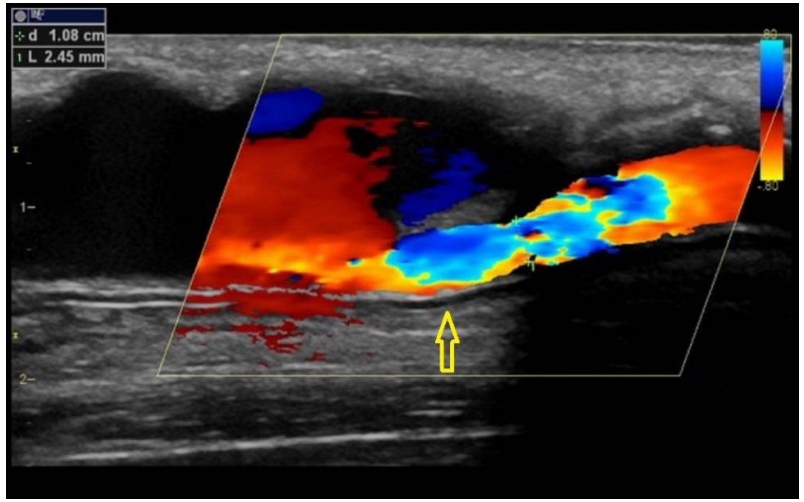
Stenosis


4 L 1.51 mm
3 L 1.63 mm
2 L 1.57 mm
1 L 1.07 mm


2 L 1.94 mm
1 L 1.31 mm




1 L 4.03 mm

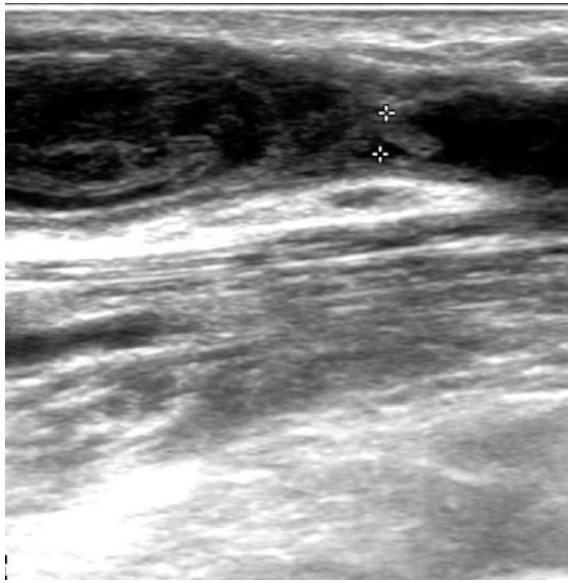

d 1.08 cm
1 L 2.45 mm

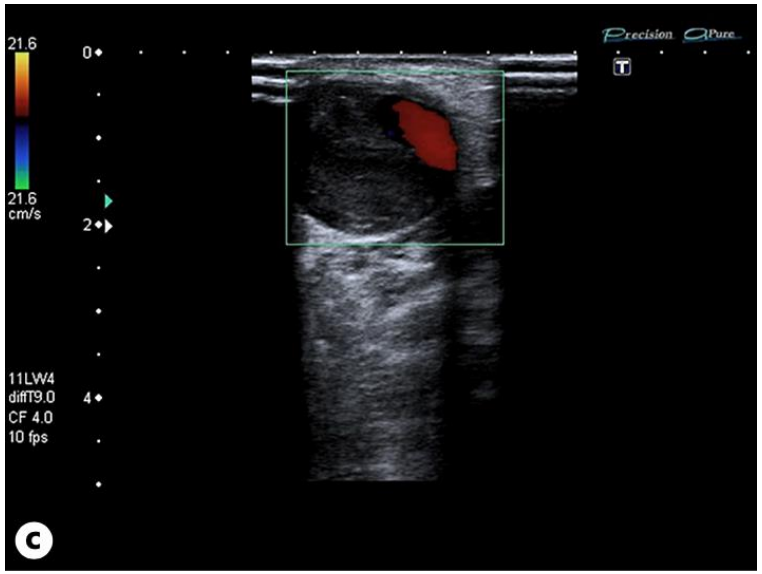
Ultrasound

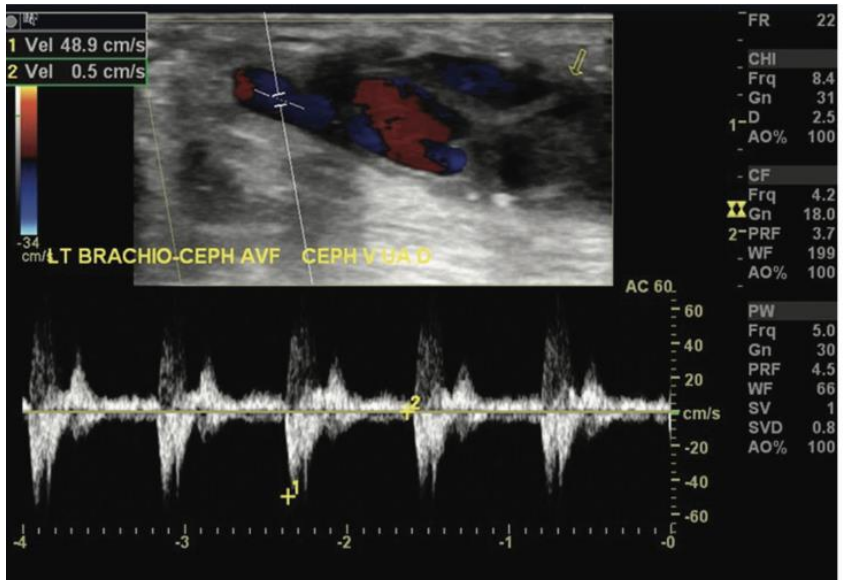
Diagnosing - Thrombosis

- General features
  - non occlusive or occlusive filling defect, typically in outflow vessel.
  - non-compressible venous segment
  - loss of phasic flow on Valsalva manoeuvre
  - absent colour flow if completely occlusive
- Acute thrombus
  - increased venous diameter
  - soft/deformable intraluminal material
  - smooth surface
  - occasionally free-floating proximal propagation at risk of detachment

- **Chronic post-thrombotic change**
  - normal or decreased venous diameter
  - rigid intraluminal material
  - irregular surface
  - synechiae or bands
- DUS helps to determine the exact **location and extent** of the thrombosis.
- The characteristics of the **stenosis underneath** the thrombosis.
- In the case of a globally fibrotic vein, may guide the choice of a new AV access site.

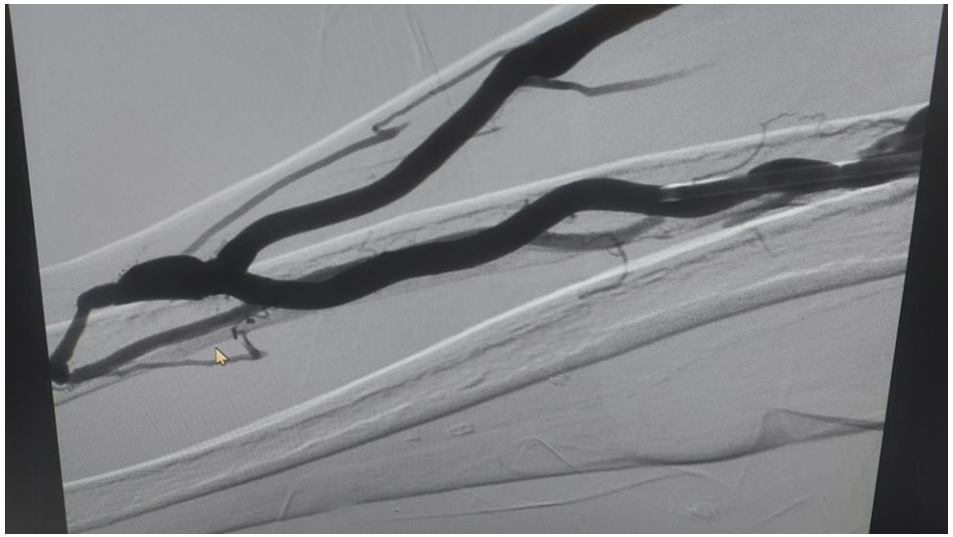


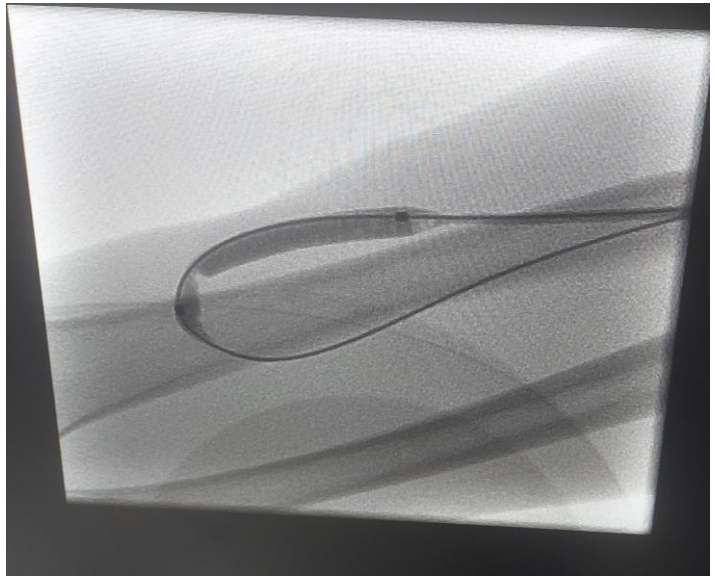


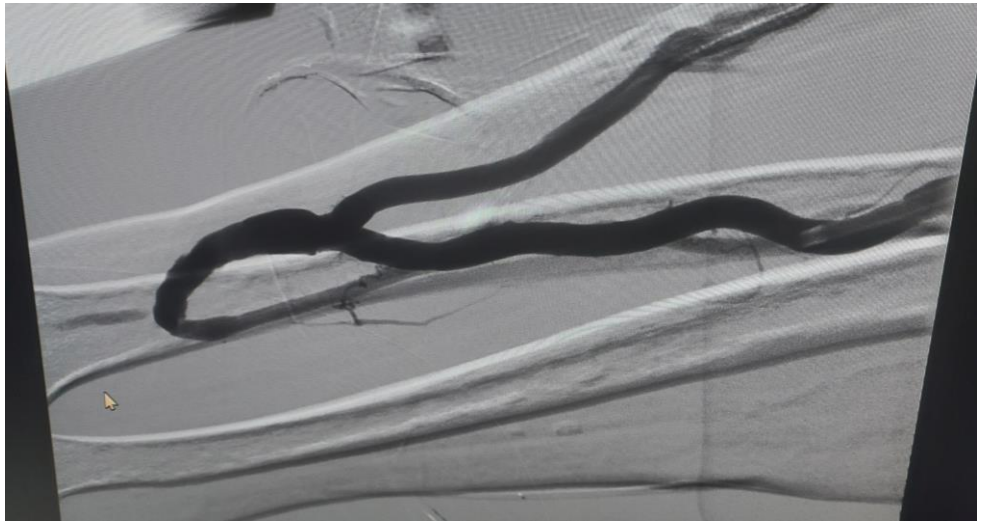


Case 1

- 65 yr old female
- CKD stage 5 on regular MHD through Right permcath
- Right RCF created 1 yr back
- Not able to cannulate AVF; poor blood flow; aspiration of clots
- Advised to create another fistula
- But due to poor veins, she continued to do HD through permcath

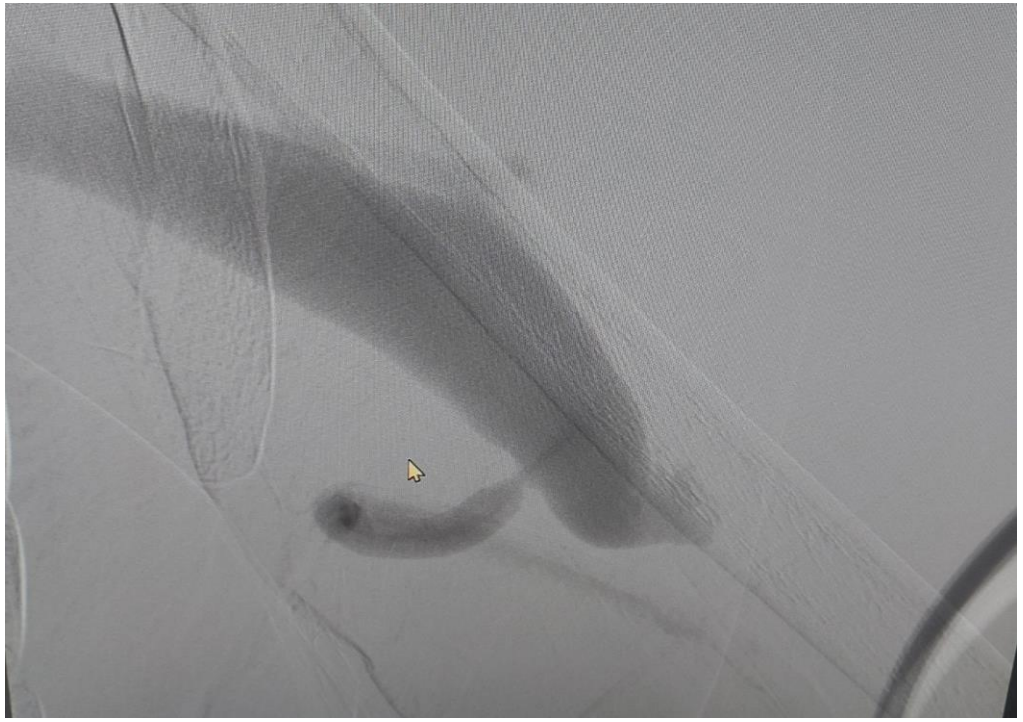


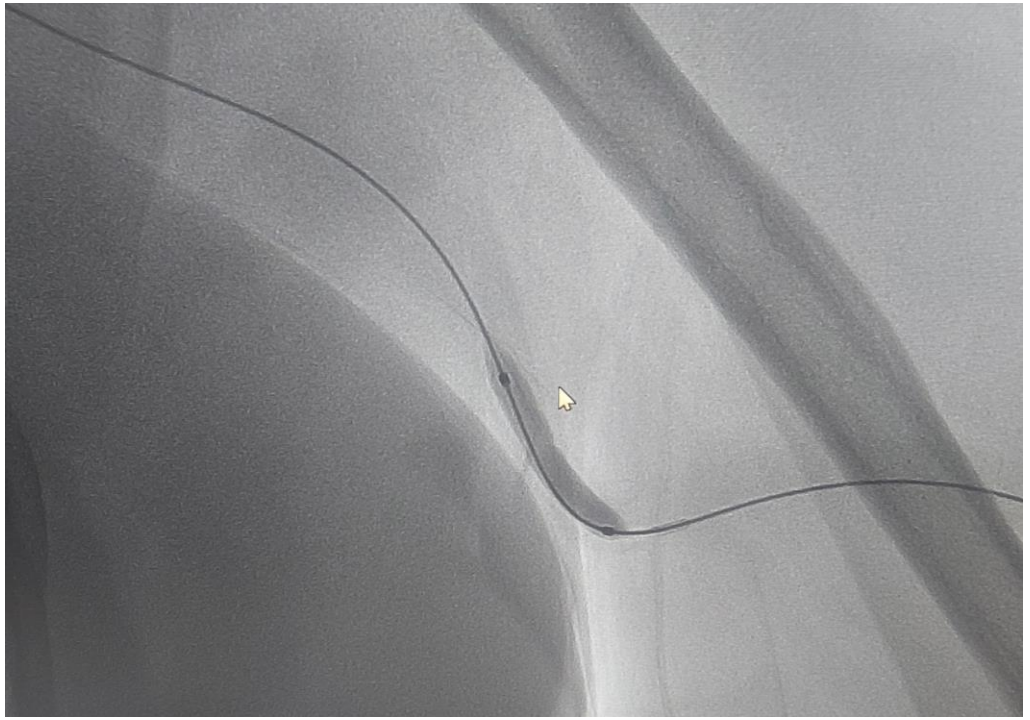


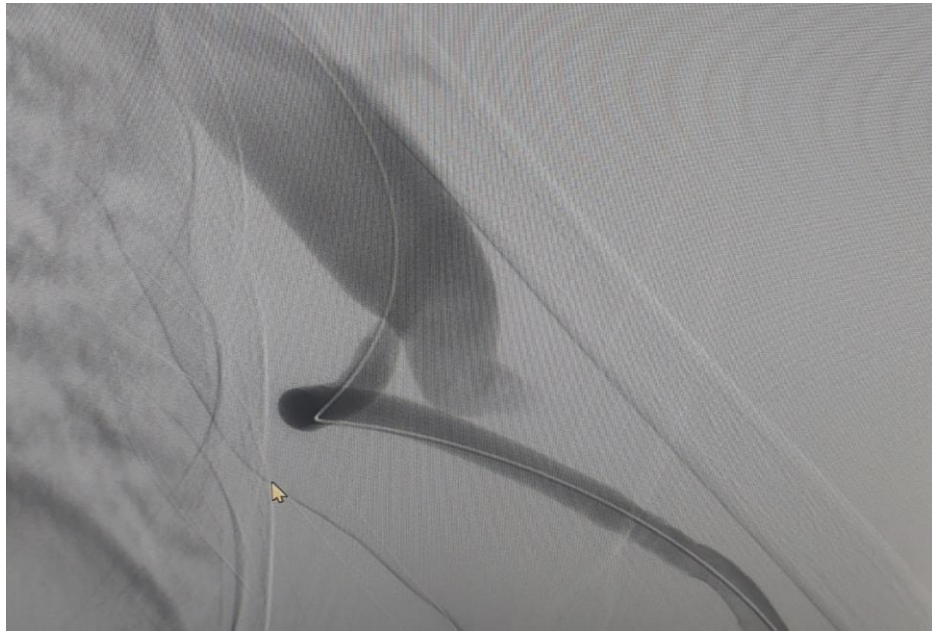


Case 2

- 56 yr old female CKD 5D on MHD
- Getting dialysis through upper arm AV graft
- Facial edema
- Dialysis tech noted difficulty in doing HD and high venous pressure during HD
- One episode of clotting of dialysis circuit and hence dialysis has to be stopped at 2hrs





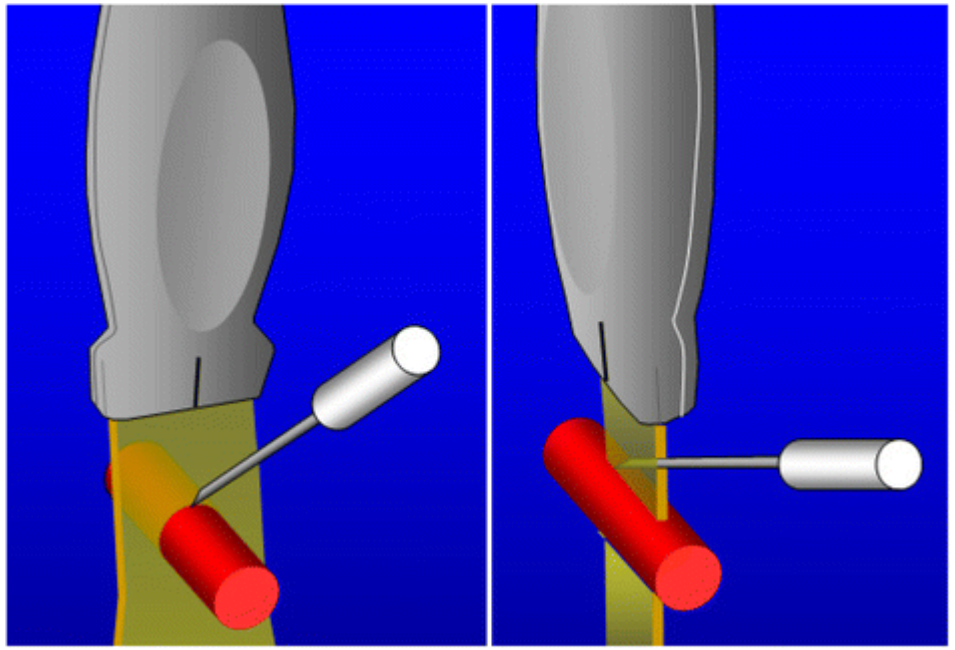


POCUS after endovascular procedure

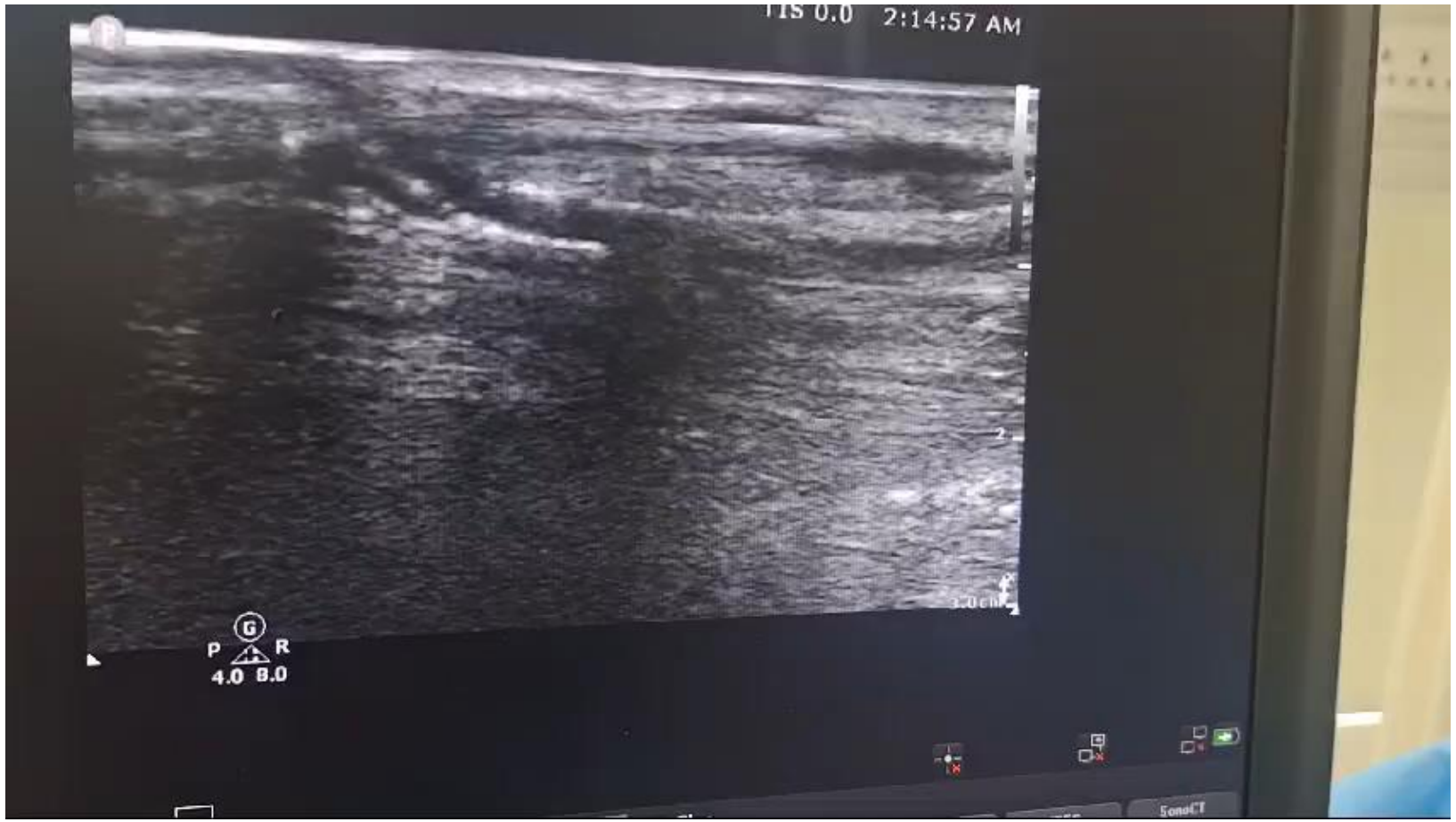
- Helps in measuring improvement in blood flow and RI after procedure
- Helps in evaluating the correction of stenosis
- Can access the presence of residual stenosis and thrombosis after procedure
- Detection of complications like post procedure blood leak,hematoma

AVF Cannulation guidance

- Helps in guiding cannulation of AVF in patients with difficulty in cannulation
- Increased success rate
- Reduce complications
- Improves staff confidence in cannulating difficult fistulas
- Patient satisfaction by minimizing needle attempts



USG guided interventions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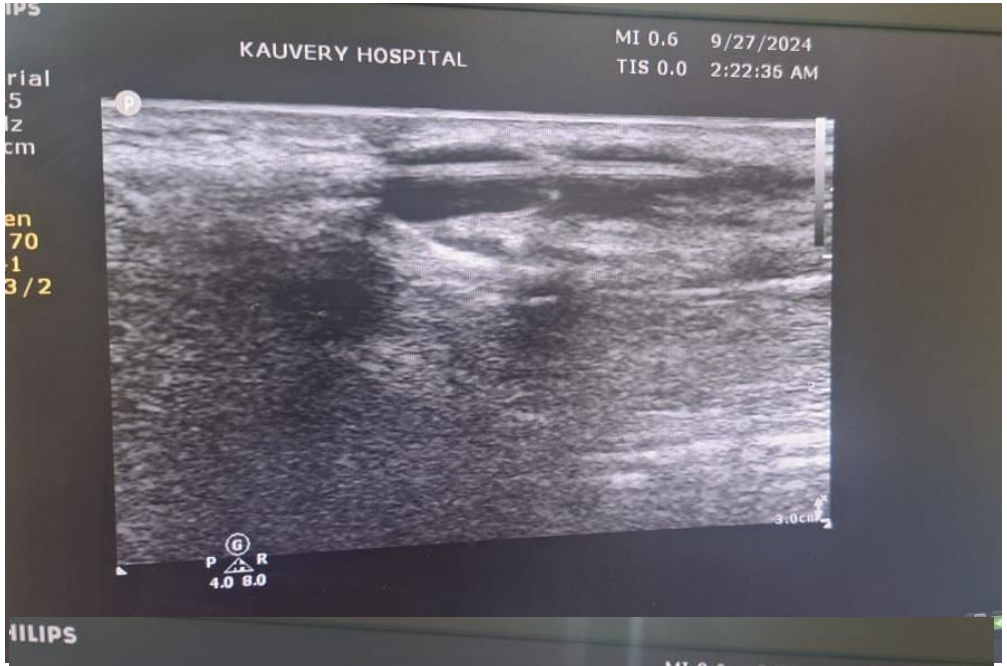
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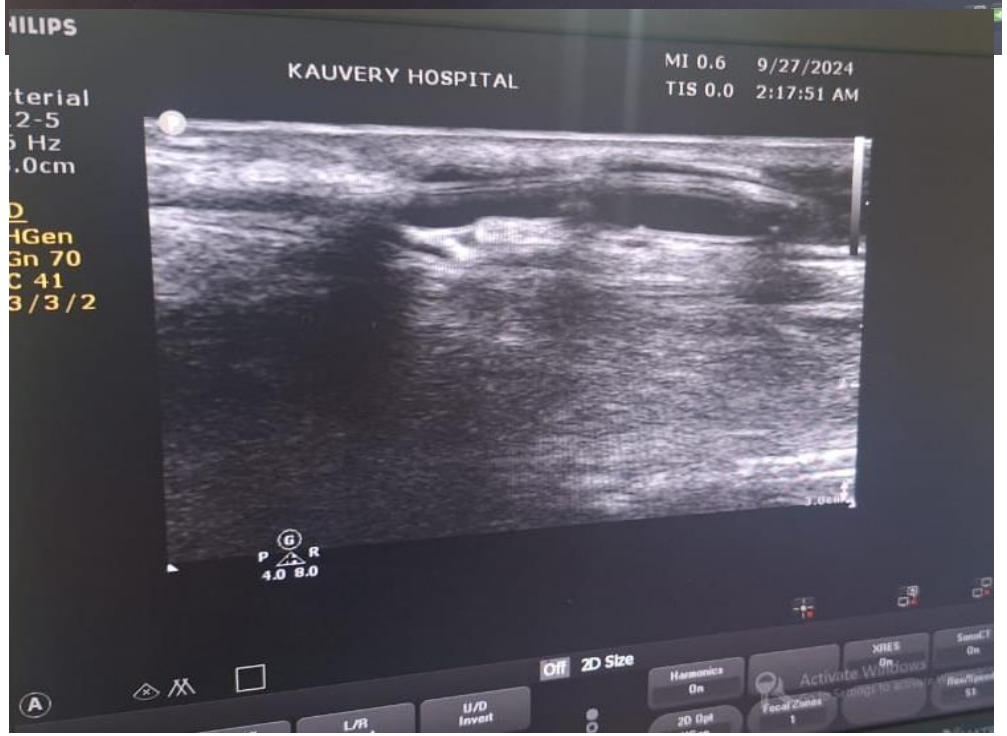
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2D Size

EndoAVF creation –Ellipsys

- US guided imaging is crucial for AVF creation with Ellipsys device
- Helps in pre-procedure vessel assessment and during procedure for vessel guidance
- Creates AVF using thermal energy and pressure to fuse arterial and venous walls
- Relies heavily on USG to ensure accurate placement and success

Ellipsys Vascular Access:

Faster, Less Invasive Access for Hemodialysis

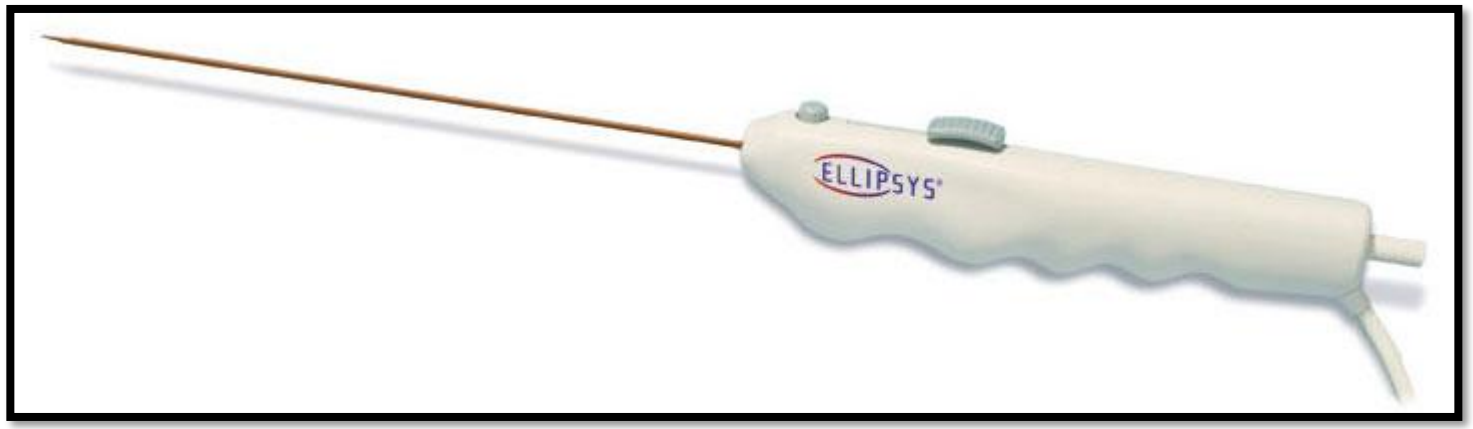
For the nearly half-million U.S. patients who suffer kidney failure and require hemodialysis to survive, the new Ellipsys® procedure offers an easier way to access their bloodstream for treatment. This revolutionary procedure **replaces surgery with a needle stick** - no incisions, no scars and no lengthy recovery. **Quicker recovery means patients can begin their life-saving dialysis sooner**. Here's how it works.

1 Directed by ultrasound, a doctor inserts a small needle into the vein and advances it to an adjacent artery, then inserts a wire to introduce the Ellipsys catheter and guide it into place.

2 Once it's inside the artery, the catheter is closed and activated. This creates a permanent connection between the vein and artery.

3 The catheter is removed and blood begins to flow through the newly created "super vein" (also known as a fistula). No sutures or implant required.

4 The patient leaves with just a band aid and can return to normal activities the next day.



Key takeaways

- Vascular access –Achilles heel of HD
- Vascular access types- Temporary HDC,TCC,AVF and AVG
- POCUS is essential in planning, guiding and maintaining vascular access in KRT
- Enhances safety, accuracy and outcomes
- Should be a standard skill for Nephrologist and dialysis staff
- USG guided interventions for AVF can be done
- Newer techniques –Endo AVF creation in pipeline

Thank you

Panel discussion

A balancing act,your kidneys and electrolytes

Dr T S Ekambaranath

Dr Prasanna R

Dr Balaji C

Dr Lakshmi Prashanth

Dr Divyashree Shetty

Introduction

- Kidneys play a crucial role in maintaining fluid and electrolyte balance

- Renal dysfunction can produce various electrolyte imbalances thereby affecting other organ systems

Osmolality vs Volume

Water balance ⟺ Osmolality

Sodium balance ⟺ Volume

Maintenance of volume takes precedence over osmolality

Volume depletion stimulates ADH secretion and thirst, even when osmolality is low

Volume (Na)balance

Kidney regulates Na balance

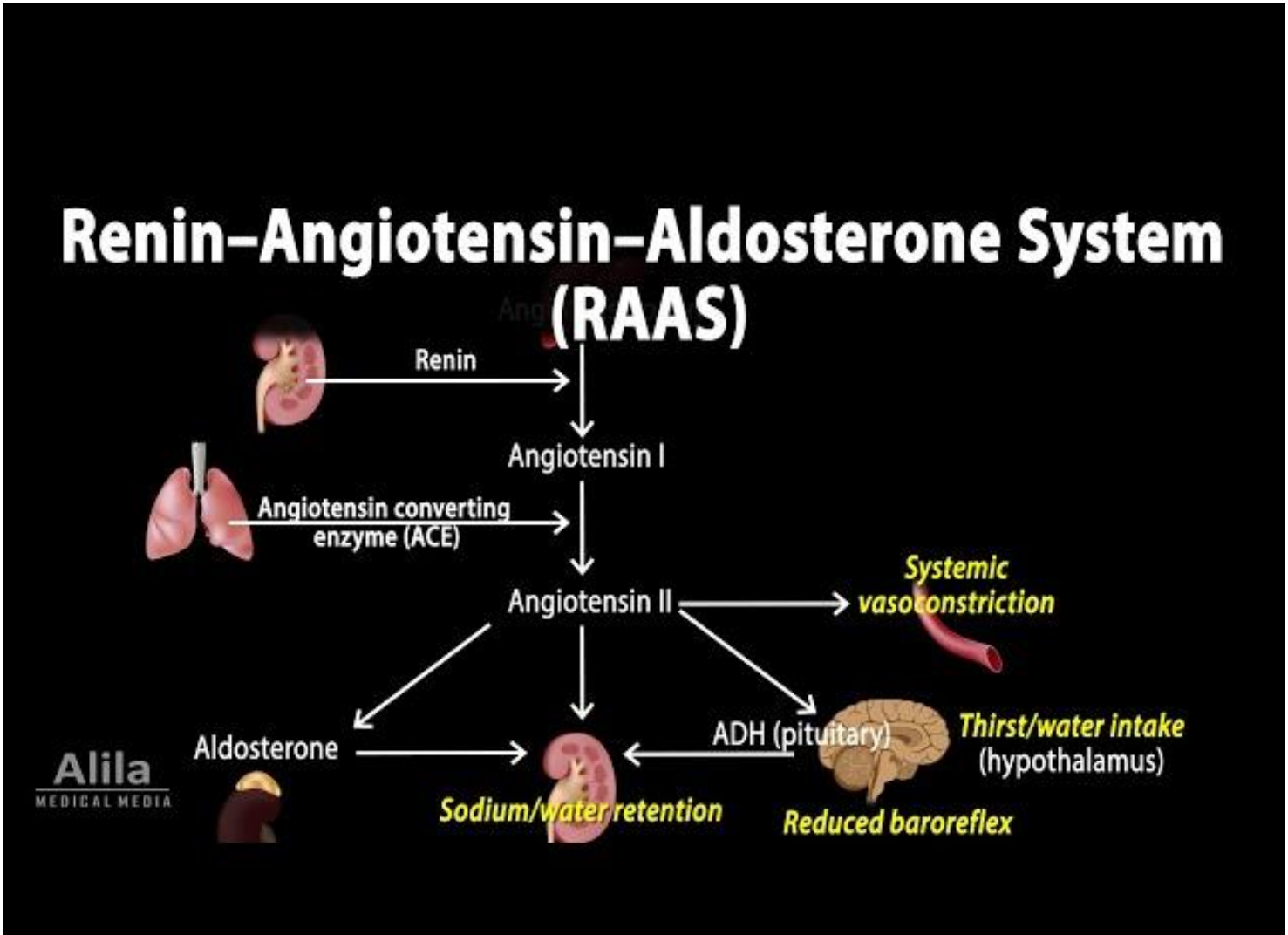
<1% of filtered Na is excreted, normally.

But renal Na excretion can vary from undetectable to dramatic levels,

And it depends on *effective intravascular volume*

Na intake  loss(extrarenal +*renal*)

Renin–Angiotensin–Aldosterone System (RAAS)



Volume (Na)overload states

Na intake > output

Renal failure

Primary hyperaldosteronism,Renal A stenosis

AGN

Volume(Na)depleted states

Na loss > intake

AGE,burns, cystic fibrosis

Tubulopathy,diuretics, preterms

CAH

Renal retention of Na-NS,CCF,Liver failure(reduced effective circulating volume)

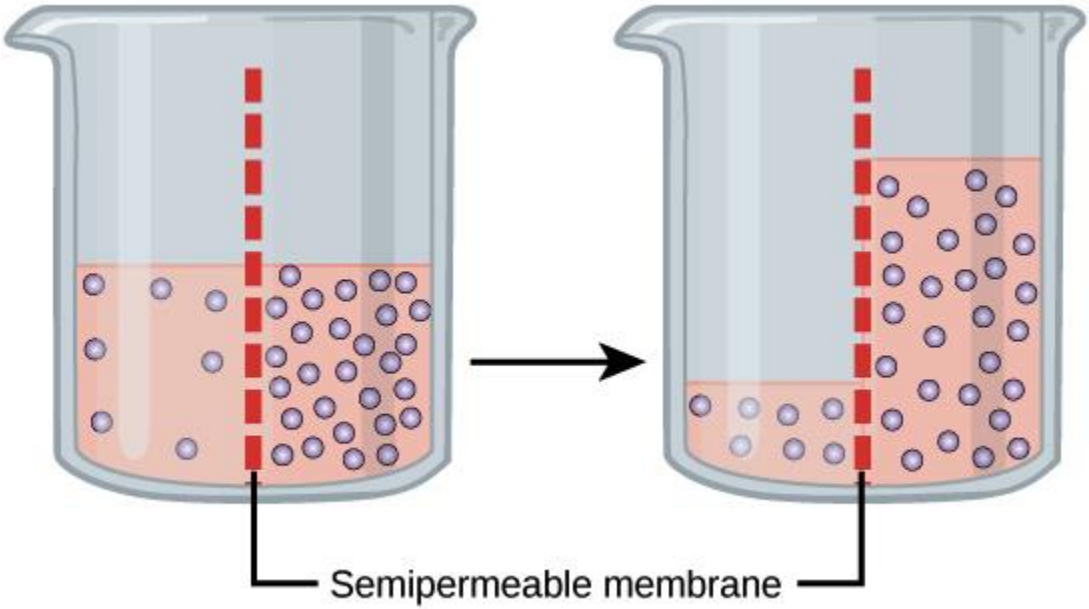
Pure water loss(DI)

Increased urine Na -SIADH, water intoxication

Reemphasizing control of intravascular volume takes precedence over control of osmolality

Osmotic equilibrium

ICF = ECF



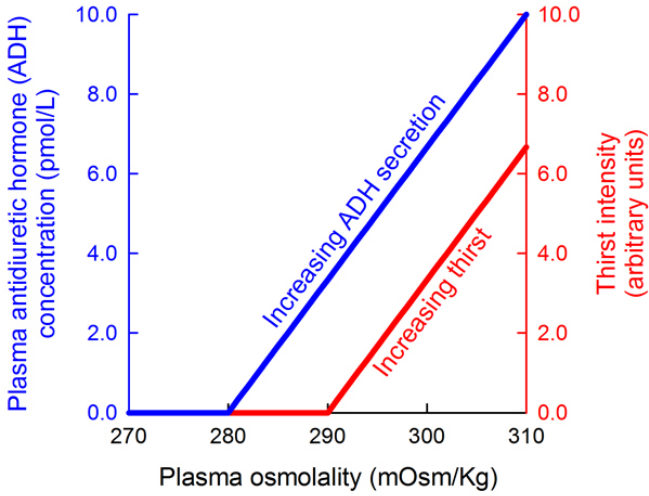
Osmotic (water) balance

Water intake+produced in body=water loss(*renal*, skin,GIT,lungs)

Urine osmolality:

30-50 mOsm/kg to 1200mOsm/kg

Polydipsia,DI SIADH



Road map

- Few case scenarios with common electrolyte disorders
- Approach
- Investigations
- Management

Case 1

- A 4 yr old boy a known case of Nephrotic syndrome, now admitted with relapse.
- H/o low grade fever for 2 days, reduced urine output
- O/E : conscious, oriented.
- Anasarca +, no pallor ,icterus.
- HR 110/min,RR 24/min,BP 94/70 mm Hg
- Abd- soft, distended
- RS-Air entry reduced R side, no added sounds
- CVS, CNS -normal

Case 1 -cont'd

- Inv: CBC-TC 12300,P64L30M6,Hb 9.4,Plt 220000
- Urea 38,creatinine 0.8,sugar 104
- Na 123, K 3.8,Cl 105,Hco3 22
- Urine protein 4+, spot PCR 3.1
- Ser albumin 1.8

Case 1 -cont'd

- How severe is the hyponatremia and how will you classify it?

Dr Divya

Case 1 -cont'd

- How severe is the hyponatremia and how will you classify it?
- Moderate (120-125)
- Hypervolemic hyponatremia(in spite of reduced “effective circulatory volume”)
- Reduced “effective circulatory volume”results in renal conservation of water and sodium. Water >sodium

Case 1 -cont'd

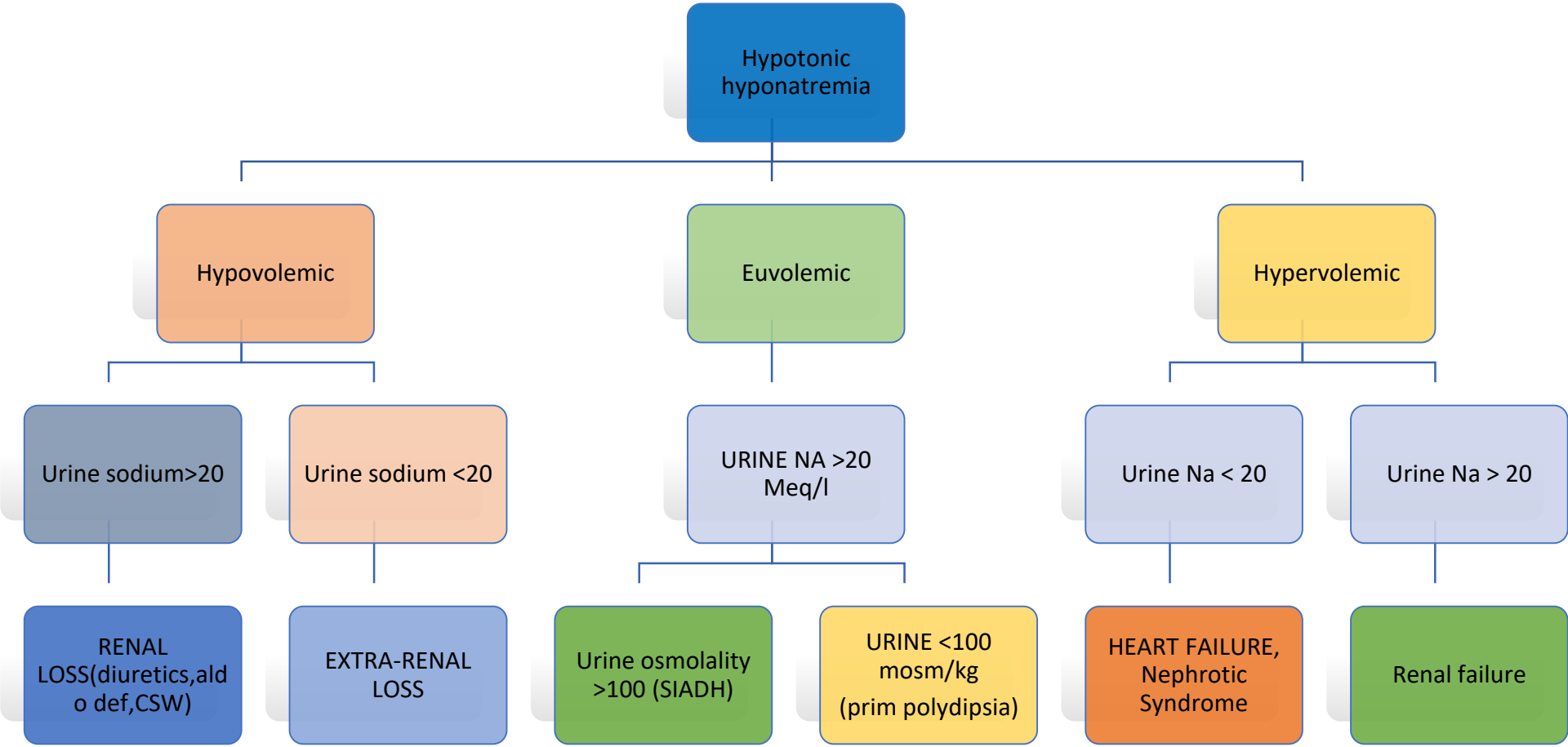
- What will be the approach to hyponatremia?

Dr Prasanna

Case 1 -cont'd

- What will be the approach to hyponatremia?

- Acute(12-24 hrs) or chronic (>48hrs)
- Symptomatic or not
- Volume status


Hypotonic hyponatremia
Hypovolemic
Euvolemic
Hypervolemic
Urine sodium>20
Urine sodium <20
URINE NA >20 Meq/l
Urine Na < 20
Urine Na > 20
RENAL LOSS(diuretics,ald o def,CSW)
EXTRA-RENAL LOSS
Urine osmolality >100 (SIADH)
URINE <100 mosm/kg
(prim polydipsia)
HEART FAILURE, Nephrotic Syndrome
Renal failure

Case 1 -cont'd

- How will you treat hyponatremia in this scenario?

Dr Lakshmi

Case 1 -cont'd

Management of asymptomatic hyponatremia in nephrotic syndrome:

Dilutional hyponatremia

- Fluid restriction - depending on the degree of edema/Na.
- Albumin transfusion with a loop diuretic.
- Relapse management : Steroids
- Rate of increase not more than 0.3 -0.4mEq/L per hr

Case 2

- A 6 year old child with craniopharyngioma, was operated for the same and was shifted to PICU postoperatively on ventilatory support.

12 hours postoperatively, child's vitals were

Heart rate-155/min

Respiratory rate-34/min

Arterial Blood pressure -80/46 mmHg

Child was under sedation in view of ventilatory support

Urine output- 10 ml /kg/hr last 3 hours

Case 2-cont’d

- Investigations done revealed :

CBG-80 mg/dl

Serum sodium-159 mEq/L

Serum potassium-3.8 mEq

Urea-55 mg/dl

Creatinine-1 mg/dl

Serum osmolality -346 mosm/Kg

Case 2-cont’d

- What is the inference from the above case scenario?
- Is this common post neurosurgeries?
- What type of hypernatremia is this?

Dr Balaji

Case 2-cont'd

- Children with craniopharyngioma are expected to have associated endocrine abnormalities due to its location near the pituitary and hypothalamus.

- 8-35% of patients with craniopharyngioma have Diabetes insipidus preoperatively
- Postoperatively 70-90% of children develop Diabetes Insipidus
- It may be transient or permanent.

This is hypovolemic hypernatremia

Case 2-cont’d

- How do we differentiate Central from Nephrogenic diabetes insipidus?

Dr Lakshmi

Diabetes Insipidus

	Central DI	Nephrogenic DI
Defect	Decreased ADH release from Pituitary	ADH resistance in V2 receptors in kidney
Etiology	• Idiopathic • Trauma • Intracranial surgeries • Ischemic Encephalopathy	• Drugs (Lithium, cidofovir, Foscarnet) • Electrolyte abnormalities (hypercalcemia,Hypokalemia)
Clinical features	Polyuria Nocturia	Polyuria Polydipsia Nocturia
Response to Desmopressin	Increased urine osmolality (> 50% from baseline 1 to 2 hours after administration)	Little or no change

Case 2-cont’d

- What are the conditions which cause hypernatremia?

Dr Divya

Case 2-cont’d

Sodium and water balance are interdependent

Hypernatremia occurs when

1) **Excess Sodium**

Improperly Mixed Formula

Excess sodium bicarbonate

Ingestion of seawater or sodium chloride

Intentional salt poisoning (Munchausen Syndrome)

Intravenous hypertonic saline

Hyperaldosteronism

Case 2-cont’d

2) **Water deficit**

Nephrogenic DI

Central DI

Increased insensible loss: Premature infants

Radiant warmers

Phototherapy

Inadequate intake

Case 2-cont’d

3) **Water and Sodium Deficit**

a) Gastrointestinal losses

Diarrhea

Emesis/Nasogastric suction

Osmotic cathartics(lactulose)

b) Cutaneous losses

Burns

Excessive sweating

c) Renal losses

Osmotic diuresis(mannitol)

Diabetes mellitus

Chronic Kidney Disease(Dysplasia and Obstructive Uropathy)

Polyuric phase of acute tubular necrosis

Postobstructive uropathy

Case 2-cont’d

- What are the clinical manifestations of hypernatremia?

Dr Prasanna

Case scenario 2-contd

- Clinical manifestations are related to neurological system.
- Children manifest hypernatremic symptoms when sodium level approaches 165 mEq/L .
- Acute onset hypernatremia (< 48 hours) present with irritability ,high pitched cry, altered sensorium, increased muscle tone or frank seizure.
- Death due to Respiratory failure with serum osmolality >400 mOsm/Kg.
- In chronic hypernatremia(>48 hours) rapid fluid resuscitation will lead to cerebral edema
- Sudden changes in serum osmolality can lead to Osmotic Demyelination Syndrome.

Case 2-cont’d

- How would you manage Hypernatremia?

Dr Divya

Case 2-cont'd

- Correct the precipitating cause
- Replace free water deficit and correct dehydration over 48-72 hours.
- Formula for free water correction:
- 0.6 xpatient's weight in kg.[Patients Na. -1]

$$\frac{\text{0.6 xpatient's weight in kg.[Patients Na. -1]}}{140}$$

- Where 0.6 xweight is estimated total body water and 140 is desired Na
- Frequent monitoring of patient' progress with treatment adjustment as it is difficult to accurately determine patient's hydration status.
- Monitor serum sodium Q2-4 H
- Irrespective of serum sodium level, in patients with shock isotonic fluid(normal saline) is given.

Glucose 2.5% & Sodium Chloride 0.45% 500mls

Case 2-cont'd

- Once hypovolemia is corrected,½ NS with 2.5 % or 5 % D is used. depends on the rate of infusion and change in osmolality required based on acute or chronic hypernatremia

- Adrogue Madias equation for correction
- This estimates the change in serum Sodium by 1 Litre of any intravenous fluid

- $= \{(\text{Na content of IVF}) + \text{K content of IVF}\} - \text{Patient serum Sodium}$
- $\frac{}{0.6 \times \text{weight(TBW in litres)} + 1}$

- Do not decrease > 10 m Eq /L of sodium over 24 hours.
- If sodium fall >0.6, decrease the infusion rate
- If sodium fall <0.5, increase the rate
- During therapy, if sodium falls too rapidly and/or neurological symptoms develop, consider a short infusion of 3% NS over 1-2 hours
- Dialysis may be required in extreme cases, especially when associated with metabolic acidosis.

Case 3

5 yr old Radha

- k/c/o MPGN(conservative Rx)
- Breathlessness
- Decreased Urine Output 2days
- Diarrhoea 5 – 7 episodes
- O/E

No pedal edema, dehydration +

RS – B/L A/E Normal

31/7/20	11:30pm
pH	7.18
PCO2	21.00
PO2	90
Actual HCO3	7.80
Base Excess	-18.80
SO2	95
Na	140.6
Chloride	102
T.Protein	6
Albumin	2.4

Case 3-cont’d

- 1. What do you infer from history and blood gases?

Dr Divya

31/7/20	11:30pm
pH	7.18
PCO2	21.00
PO2	90
Actual HCO3	7.80
Base Excess	-18.80
SO2	95
Na	140.6
Chloride	102
T.Protein	6
Albumin	2.4

- STEP 1 – Acidemia
- STEP 2 – pH ↓ PCO2 ↓

  Metabolic
- STEP 4 – PCO2 expected (Winters formula)

  PCO2 exp = (1.5 x HCO3)+8±2

  (1.5X7.80)+8±2 19.7±2= 17.7 – 21.7

➢ Compensated metabolic acidosis

Case 3-cont’d

- 2. What do you infer from anion gap?

Dr Lakshmi

Case 3-cont'd

- Reflects the difference between the major measured cations and anions in serum.

Anion Gap(AG) = Na – (HCO_3 + Cl)

Normal Value = 8 to 12 mEq/L

- Helps categorize metabolic acidosis by identifying the presence of unmeasured anions.
- NAGMA - Bicarbonate is lost (GI/renal losses)
- HAGMA - Unmeasured anions increase due to accumulation of acids like lactate, ketoacids, or toxins

HAGMA

M	METHANOL
U	UREMIA - ARF/CRF
D	DIABETIC KETOACIDOSIS & other KETOSIS
P	PARALDEHYDE, PROPYLENE GLYCOL
I	ISONIAZIDE, IRON
L	LACTICACIDOSIS
E	ETHANOL, ETHYLENE GLYCOL
S	SALICYLATE

Case 3-cont'd

Adjusted Anion Gap = Observed AG +2.5(4- S.Albumin)

50% ↓ in S. Albumin → 75% ↓ in Anion Gap !!!

Hypoalbuminemia : Lowers the measured anion gap because it reduces the unmeasured anion pool.

This can mask the presence of an elevated anion gap metabolic acidosis, leading to underdiagnosis of occult tissue anions like lactate and other organic acids.

31/7/20	11:30pm
pH	7.18
PCO2	21.00
PO2	90
Actual HCO3	7.80
Base Excess	-18.80
SO2	95
Na	140.6
Chloride	102
T.Protein	6
Albumin	2.4

- STEP 5 – ANION GAP

  = Na – (HCO3 + Cl)

  = 140.6-(7.80+102)

  = 30.8

✓ AG corrected for albumin =

30.8+5.25 AG = 36.05

High AG Met. Acidosis

Case 3-cont’d

- 3. Are there any other added problems in this child ?

Dr Prasanna

Co existent metabolic disorder – "**Gap Gap**"?

C/O HAG metabolic acidosis,another disorder?

- **Δ Anion Gap =** Measured AG – Normal AG

  Measured AG – 12

- **Δ HCO_3 =** Normal HCO_3 – Measured HCO_3

  24 – Measured HCO_3

Ideally, ΔAnion Gap = ΔHCO_3

For each 1 meq/L increase in AG, HCO3 will fall by 1 meq/L

$\Delta AG/\Delta HCO_3^-$ = 1-2 ⍰ Pure High AG Met Acidosis

$\Delta AG/\Delta HCO_3^-$ > 2 ⍰ Assoc Metabolic Alkalosis

$\Delta AG/\Delta HCO_3^-$ < 1 ⍰ Assoc NAG Met Acidosis

31/7/11	11:30pm
pH	7.18
PCO2	21.00
PO2	90
Actual HCO3	7.80
Base Excess	-18.80
SO2	95
Na	140.6
Chloride	102
T.Protein	6
Albumin	2.4

- STEP 6 – GAP GAP
  = (AG-12)/(24-HCO3)
  = 36.05-12/24-7.80
  = 24.05/16.2
  = 1.48

Gap/gap 1-2 = Pure HAGMA

Δsis – Primary Metabolic Acidosis

High Anion Gap, compensated Cause- CRF

Though there is diarrhea it didn't cause any additional issues here . It may be insignificant

Case 3 -summary

- History and physical examination most important.
- In ABG look at the pH. < 7.35 in acidemia.
- Look at HCO3 and PCO2. HCO3 ↓and PCO2 ↓in metabolic acidosis.
- If metabolic acidosis, then look at Anion Gap: Normal anion Gap or High Anion Gap
- Is the Compensation adequate (Winter's formula)?
- If anion gap is elevated, then calculate the **Delta-Ratio** (Δ/Δ) for other simultaneous disorders.

Case 4

- History:
  - 2-year-old boy, recurrent vomiting, failure to thrive, polyuria, polydipsia
  - No significant perinatal history; normal development until 18 months
- Examination:
  - Weight and height below 3rd percentile, mild dehydration, normotensive
- Investigations:
  - Serum K+: 2.4 mmol/L, Na+: 136 mmol/L, Cl-: 93 mmol/L, HCO3-: 30 mmol/L
  - Urine: high K+, high Cl-, specific gravity 1.010
  - Renin and aldosterone elevated

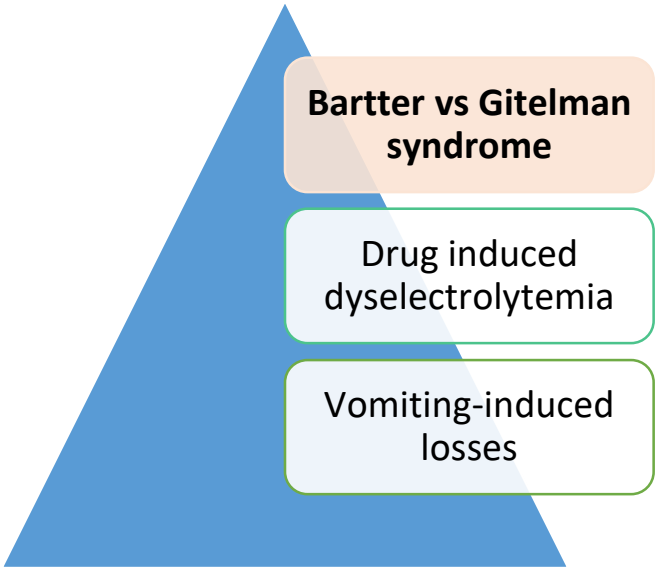
Case 4- cont’d

- What metabolic abnormalities are evident in this scenario?
- What are the DDx for such a biochemical presentation?
- What is the likely diagnosis in this particular toddler?

Dr Divya

Case 4- cont’d

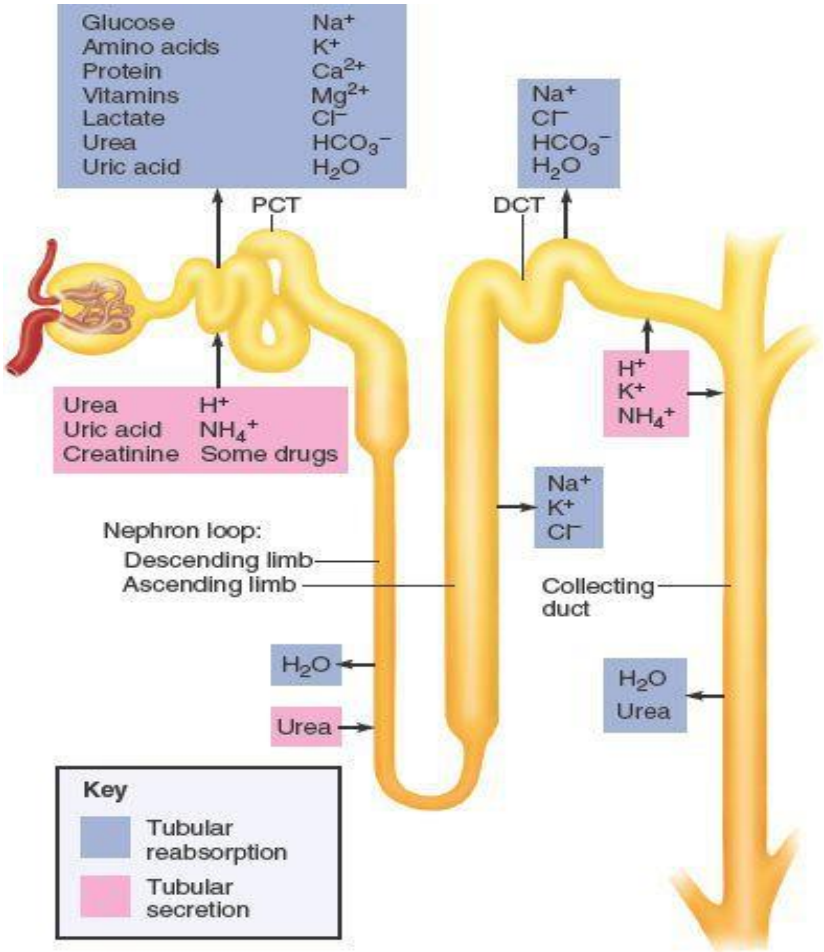
DDx for Hypokalemia with Metabolic alkalosis



- This toddler has classic features of a salt-wasting renal tubular disorder.
- Notice the high urinary potassium, which indicates renal potassium loss.
- Elevated renin and aldosterone reflect volume depletion.
- Gitelman syndrome differs from Bartter by hypomagnesemia and hypocalciuria.

Case 4- cont’d

- Given the non-specific clinical presentations of tubulopathies, can biochemical changes help localize the tubular segment involved?



Tubular Reabsorption and Tubular Secretion

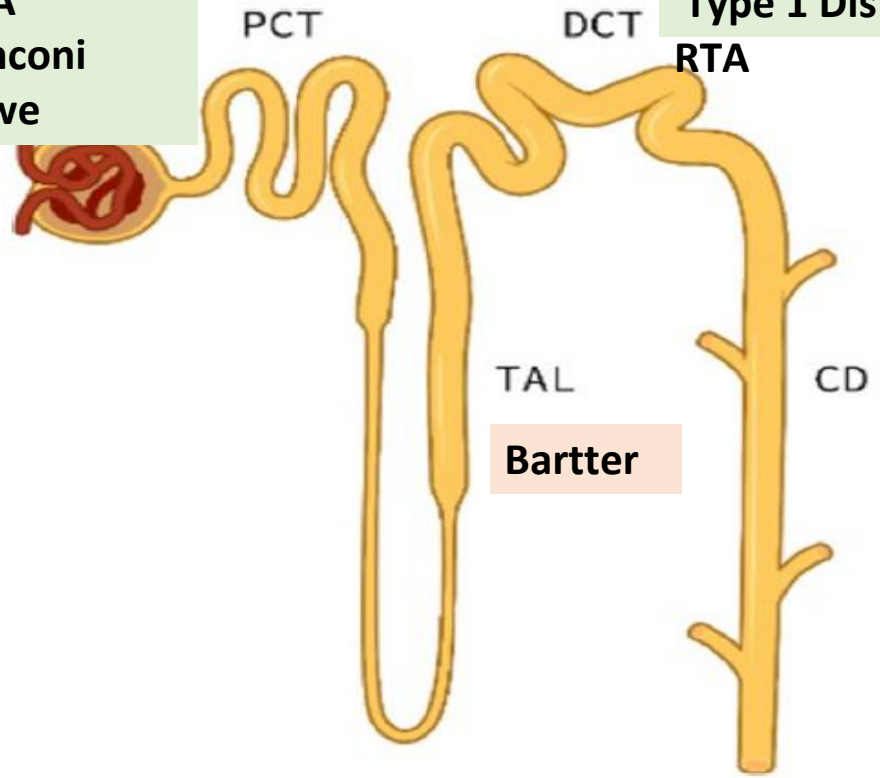
The image comprehensively describes different components absorbed and secreted in different parts of nephron

Image via: https://socratic.org/questions/how-does-the-functional-unit-of-kidney-works-nephron-give-a-detailed-explanation

Proximal
RTA
Fanconi
Lowe

Gitelman

Type 1 Distal
RTA



Bartter

Primary
Hyperaldosteronism
Liddle' Syndrome
Apparent
mineralocorticoid
excess

Type 4 RTA
Pseudo-
hypoaldosteronism

Hypokalemia
Metabolic
alkalosis

Hypokalemia
Metabolic
acidosis

Hyperkalemia
Metabolic
acidosis

Case 4- cont’d

- What is the approach to tubular syndromes with hypokalemia?

- Clinical clues, investigations and diagnostic pathway?

Dr Lakshmi

Case 4- cont'd

Clinical

- Polyuria, polydipsia; preference for savory foods
- Dehydration
- Growth retardation, failure to thrive
- Refractory rickets
- Renal calculi, nephrocalcinosis
- Unexplained hypertension

Bagga A, Bajpai A, Menon S. Approach to renal tubular disorders. Indian J Pediatr. 2005 Sep;72(9):771-6.

Case 4- cont'd

Investigations

Bloods	Urine	Imaging
Venous blood gas	Urinary dipstick for glucose	Kidney ultrasound
Biochemical profile	Urine microscopy	
+/–	Urine protein:creatinine ratio	
Osmolality	Urine calcium:creatinine ratio	
Renin/aldosterone	+/–	
	Urine B2 microglobulin	
	Urine osmolality	
	Urine metabolic screen	

Biochemical Profile

Na, K, Cl, HCO3
Urea, Creatinine
Ca, Mg, PO4

*Kermond, R., Mallett, A. & McCarthy, H. A clinical approach to tubulopathies in children and young adults. Pediatr Nephrol **38**, 651–662 (2023).*

Case 4- cont'd

Assessment of Tubular Handling of Salts

	Formula	Normal value	Interpretation
FeNa	$= \frac{Na\ (urine) x\ Creatinine\ (serum)}{Na\ (serum) x\ creatinine\ (urine)} x100$	FeNa <1% *(with normal salt load and normal GFR)*	If >1% suggests: – Kidney salt wasting – Appropriate naturesis in the context of salt load
FeMg	$= \frac{Mg\ (urine) x\ Creatinine\ (serum)}{Mg\ (serum) x\ creatinine\ (urine) x\ 0.7} x100$	FeMg < 4%	> 4% suggests – Kidney wasting magnesium in setting of hypogmagnesaemia
TTKG	$= \frac{K\ (urine) x\ Osmlality\ (serum)}{K\ (serum) x\ Osmolality\ (urine)} x100$	TTKG 4–6% *(Interpretation dependent on kalaemic state)*	In hypokalaemic states – <2% suggests appropriate kidney handling – >4% suggests kidney losses
TmP/GFR	$= PO4\ (serum)\left[\text{PO4 (urine)} x\ \text{Creatinine}\ \frac{\text{serum}}{\text{urine}}\right]$	Varies with age	< lower limit of range – Kidney phosphate wasting Ranges: Birth: 1.43–3.43 mmol/L 3 mths: 1.48–3.30 mmol/L 6 mths: 1.15–2.60 mmol/L 2–15 years 1.15–2.44 mmol/L

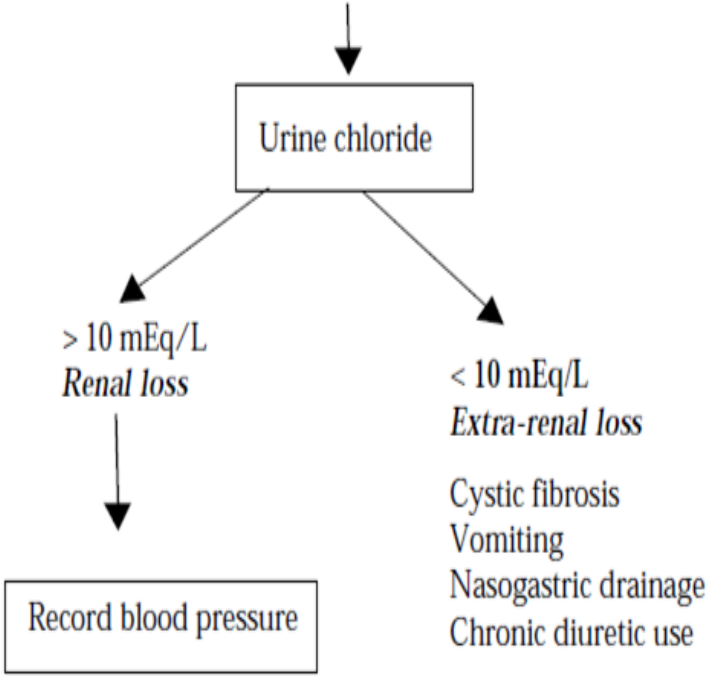
Case 4- cont’d

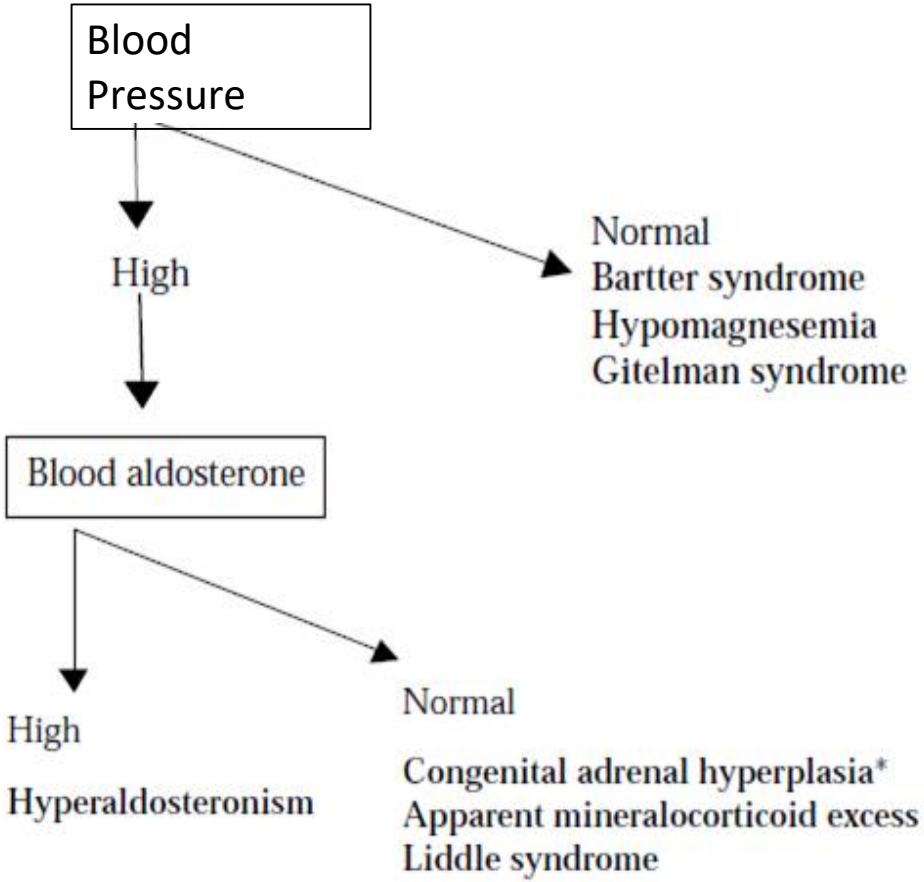
Diagnostic Pathway

- Hypokalemia with Metabolic Alkalosis
- Hypokalemia with Metabolic Acidosis

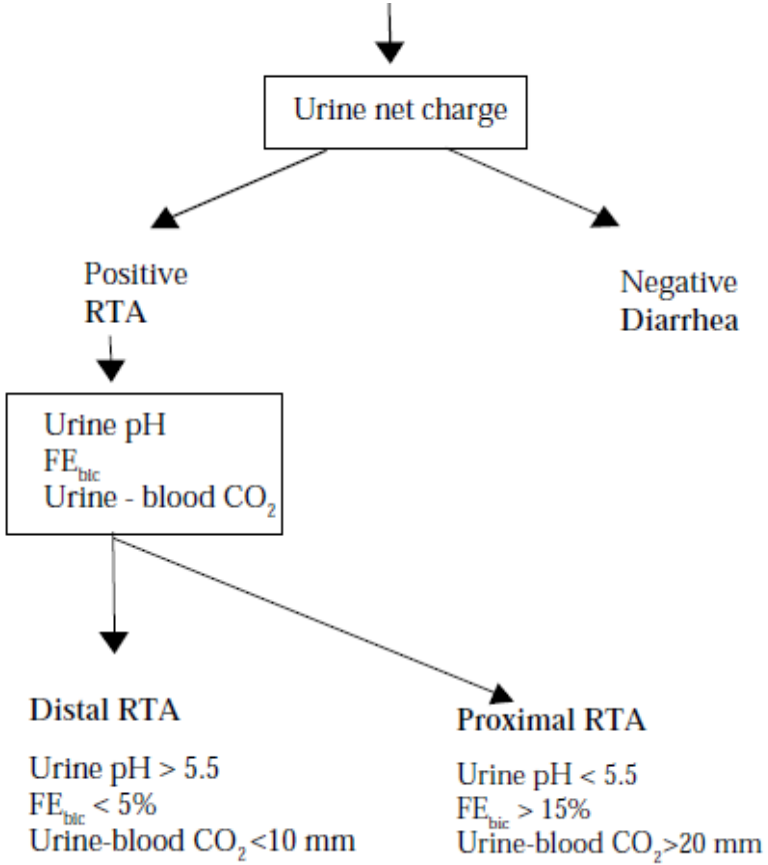
Bagga A, Bajpai A, Menon S. Approach to renal tubular disorders. Indian J Pediatr. 2005 Sep;72(9):771-6.

Hypokalemia/Metabolic Alkalosis





Hypokalemia/Metabolic Acidosis



Urine anion gap (net charge)

Urine $(Na^+ + K^+) - Cl^-$

Provides an estimate of urinary ammonium ($NH4^+$)

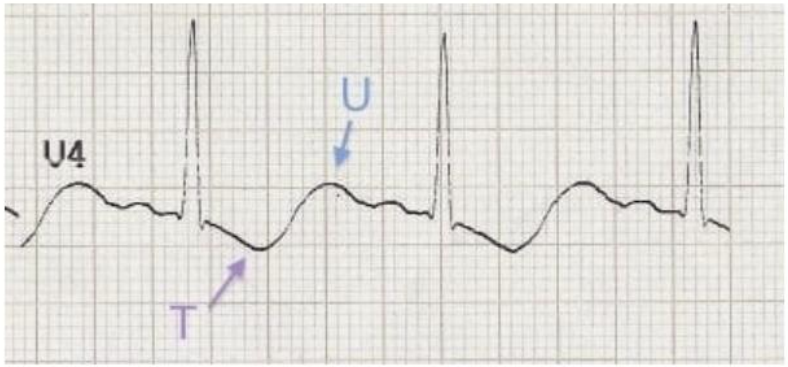
Case 4- cont’d

- What are the clinical manifestations of hypokalemia?
- How do we manage hypokalemia?
- What are the principles of using IV potassium?
  Any ICU specific considerations?

Dr Prasanna

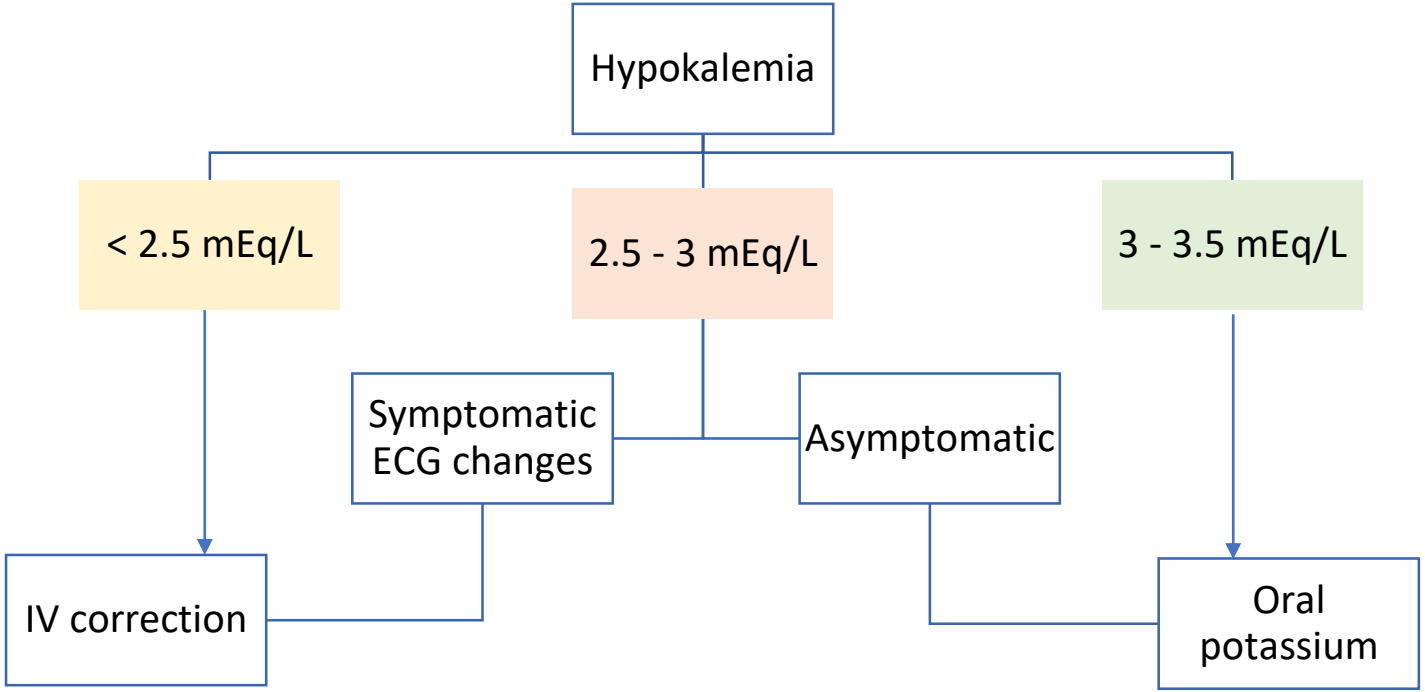
Case 4- cont’d

- Muscle weakness
- Cramps
- Paralysis
- Arrhythmias



ST depression
PR prolongation
T wave inversion
U waves

Case 4- cont’d


Hypokalemia
< 2.5 mEq/L
2.5 - 3 mEq/L
3 - 3.5 mEq/L
Symptomatic ECG changes
Asymptomatic
IV correction
Oral potassium

Case 4- cont’d

- Never give a bolus of potassium
- Always label potassium and keep it separately
- All potassium orders should be checked by 2 doctors before administration
- IV correction with ECG monitoring

- **Maintenance fluids** in peripheral line – Increase up to 60 mEq/L
- > 60 mEq/L – Central line

- Oral Syrup Potklor 15 ml= 20 mEq (oral dosing 1 to 2 mEq/kg/dose upto 5 mEq/kg/day)

Case 5

An 15-month-old male child, previously healthy, presented to emergency department with dullness, decreased oral intake, multiple episodes of vomiting, and diarrhea of two days duration.

Upon clinical examination, the patient was hypoactive, ill-looking. He had tachycardia, fever, dry mucous membranes, tearless crying, sunken eyes, depressed anterior fontanel, and delayed capillary refill (three seconds). His blood pressure was 93/54 mmHg.

Lab investigations

Creatinine (Cr): 2.1 mg/dL

Blood Urea Nitrogen (BUN): 60 mg/dL

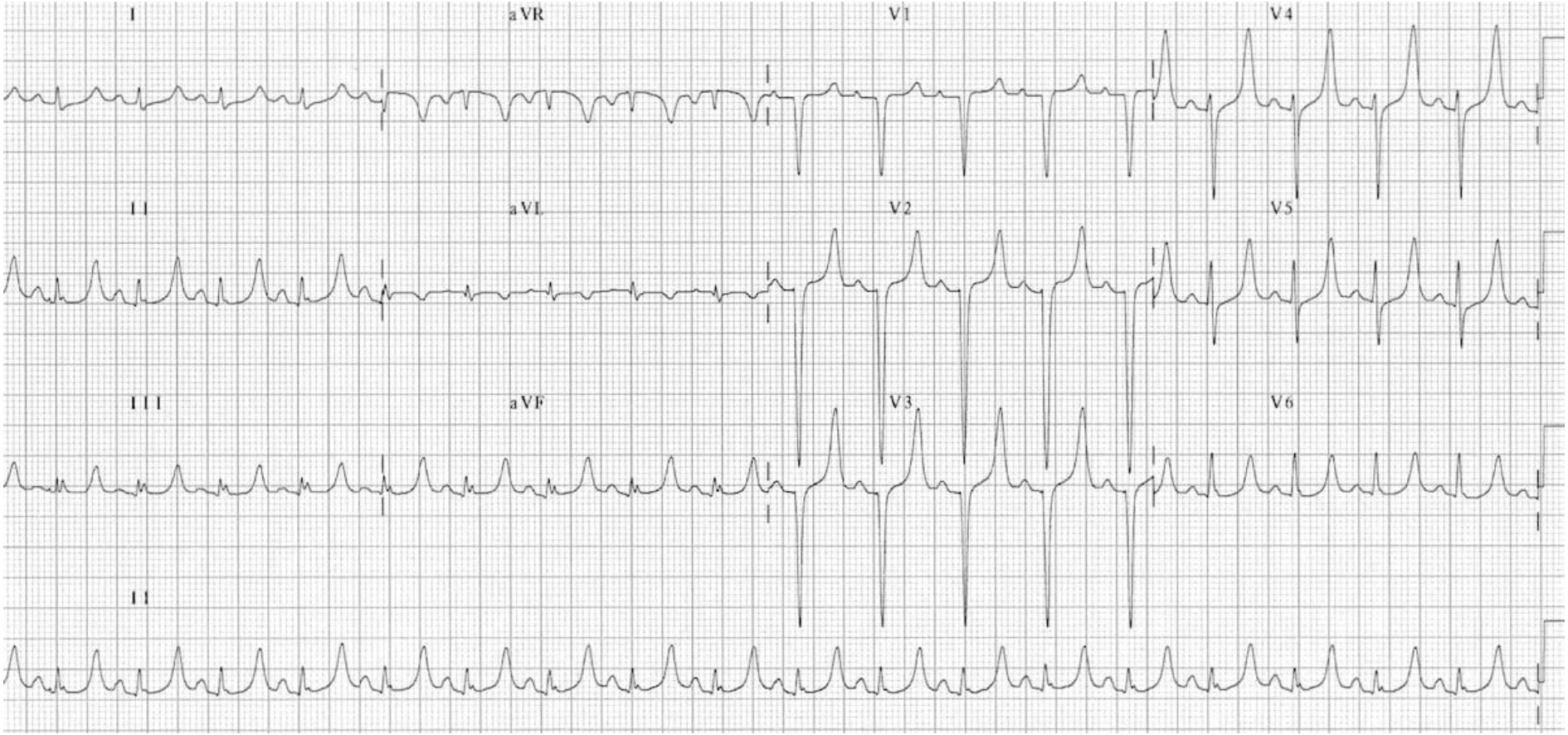
Sodium (Na^+): 148 mmol/L

Potassium (K^+): 7.25 mmol/L

Chloride (Cl^-): 96 mmol/L

Random Blood Sugar (RBS): 111 mg/dL

Calcium (Ca^{2+}): 9 mg/dL


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

Question to panelist

- What do you interpret from the investigation & history ? What specific aspect is worrying you the most ?

Dr Divya

- 15 mth old child presenting with acute onset diarrhoea and vomiting. There is clinical evidence of severe dehydration. Also the renal parameters are elevated suggesting Acute Kidney injury. What is alarming is the elevated potassium levels. Hyperkalemia is defined as potassium greater than 5.5 mEq/l. However, the upper limit of normal in infants may be as high as 6.5 mEq/L. Severe hyperkalemia (potassium level ≥7 mEq/L [mmol/L]) is a serious medical problem and potentially life-threatening.
- We should first rule out pseudohyperkalemia which happens due to hemolysis often when syringe is used instead of vacuum device, arm restraining and limb movements releasing muscle cell potassium.

- **ECG** - tall symmetrical peaked T waves suggestive of hyperkalemia. (Usually seen at 5.5 - 6.5)

- We are worried about hyperkalemia because of the potentially life threatening disturbances in cardiac conduction. At 6.5-7.5 - Loss of P wave, widening QRS, At 7.0- 8.0 - progressive widening of QRS and eventually merges with T wave to form a sinusoidal pattern followed by ventricular fibrillation at 8.0-10.0

A word about pathophysiology of hyperkalemia. Transcellular movement of potassium due to metabolic acidosis is the most common cause of hyperkalemia in children. Also in children with Acute/Chronic Kidney disease urinary potassium excretion may be reduced due to decrease in GFR.

Question to panelist

- How will you decide the urgency of treatment of hyperkalemia in this scenario ?

Dr Balaji

Urgency in treatment is needed to children at risk of life threatening cardiac conduction disturbances.

1.Patients with clinical signs and symptoms of hyperkalemia – Children with electrocardiographic changes, including widening of the QRS complex, loss of P waves,or arrhythmias, and those with muscular weakness or paralysis. However, emergent therapy is not initiated for isolated peaked T waves, which is typically associated with levels between 5.5 to 6.5 mEq/L.

2. Asymptomatic children with potassium level ≥7 mEq/L.

3. Patients with potassium level between 6 and 7 mEq/L who are at-risk for continued rapid rise in extracellular potassium due to ongoing intracellular potassium release (eg, tumor lysis syndrome or rhabdomyolysis from a major crush injury).

Prompt but non emergent Rx indications:

Prompt but not emergent intervention for asymptomatic children with acute hyperkalemia with potassium levels below 7 mEq/L (mmol/L) and who are not at-risk for rapid increase in potassium. Treatment is focused on lowering potassium levels over 6 to 12 hours.

Not only level of potassium, the rapidity of rise in potassium is important. Child with chronic hyperkalemia of 7 may be asymptomatic while child with tumor lysis syndrome and potassium of 6.5 may be symptomatic with ECG changes.

Question to panelist

- What are the emergent management steps in a case of hyperkalemia?

Dr Prasanna

1. **Stabilize Cardiac Membranes**

IV Calcium Gluconate (10%)

- Dose: 0.5 mL/kg IV over 5 minutes (max 20 mL or 2 g)
- Onset: Immediate
- Repeat if ECG abnormalities persist

Alternative (if cardiac arrest): Calcium Chloride

- Dose: 20 mg/kg IV (max 1000 mg) over 5–10 minutes
- Use central line if possible

Do not mix calcium with bicarbonate in the same IV line (precipitation risk)

2. **Shift Potassium Into Cells**

IV Insulin + Glucose

- Regular insulin: 0.1 units/kg IV (max 10 units)
- Dextrose:
  - <5 years: 10% Dextrose 5 mL/kg
  - ≥5 years: 25% Dextrose 2 mL/kg
- Onset: 10–20 minutes, peak at 30–60 minutes
- Monitor blood glucose hourly for 6 hours (risk of hypoglycemia)

- **Inhaled Salbutamol** (Albuterol)
- <25 kg: 2.5 mg via nebulizer
- Onset: ~30 minutes
- Can be combined with insulin/glucose
- Avoid if history of arrhythmias
- Side effects: tachycardia, tremor (usually mild)

Sodium Bicarbonate (Adjunct Only)

- Indication: suspected or confirmed metabolic acidosis
- Dose: 1 mEq/kg IV over 10–15 minutes
  - Use 8.4% solution (1 mL/kg) or
  - 4.2% solution (2 mL/kg for infants <6 months)
- Onset: ~15 minutes
- Risk: hypernatremia with repeated doses

3. **Monitoring & Reassessment**

- Continuous ECG monitoring
- Check serum potassium 1–2 hours after treatment
- Repeat therapy if:
  - Potassium remains ≥7 mmol/L
  - ECG changes persist
  - Muscular symptoms continue
- Monitor glucose hourly for 6 hours if insulin was given

Question to panelist

- Can you throw us light on non-emergent management of hyperkalemia in this child?

Dr Lakshmi

Indications

- After initial **emergent stabilization** for severe/symptomatic hyperkalemia
- For **asymptomatic children** with K^+ <7.0 mmol/L
- As **adjunctive therapy** to prevent recurrence

Treat Underlying Reversible Causes

- **Rehydrate** hypovolemic children to restore renal perfusion
- **Hormone replacement** in adrenal insufficiency (e.g., CAH)
- **Discontinue medications** that impair K^+ excretion (e.g., ACE inhibitors, spironolactone)
- Stop **K^+ containing IV fluids or high-K^+ medications**
- **Correct metabolic acidosis**, if present

Enhance Potassium Elimination from the Body

A. Loop Diuretics (e.g., Furosemide)

- Requires intact renal function and adequate volume status

B. Sodium Polystyrene Sulfonate (Kayexalate)

- Dose: **1 g/kg orally or rectally every 4 hours** (max 30 g/dose)
- Binds K^+ in the gut; excreted in feces
- Onset: 1–2 hours
- **Avoid** in: Post-op patients/Ileus or bowel obstruction/Neonates (especially if mixed with sorbitol)
- **Avoid mixing with sorbitol** (risk of colonic necrosis)
- Consider giving **lactulose or PEG** to counter constipation

C. Dialysis (Last Resort)

Indications:

- Persistent hyperkalemia >6.5 mmol/L unresponsive to meds
- Severe renal dysfunction or oliguria/anuria

Hemodialysis preferred (rapid, controlled)

CRRT or peritoneal dialysis as alternatives (slower, may be center-dependent)

Summary

- Let's summarise the evaluation and management of a child with hyperkalemia.

Definition and Significance of Hyperkalemia

- **Hyperkalemia**: Serum or plasma potassium >5.5 mmol/L
- **Infants** may have a normal upper limit as high as **6.5 mmol/L**
- **Severe hyperkalemia** (≥7.0 mmol/L) is **life-threatening** and requires **immediate treatment**
- **Primary danger**: Cardiac conduction abnormalities and arrhythmias

Urgency of Therapy

- Therapy is guided by:
  - **Potassium level**
  - **Rate of rise**
  - **Presence of symptoms**
  - **ECG findings**
- ECG changes and neuromuscular symptoms increase urgency
- **K^+ ≥7.0 mmol/L or symptomatic → emergent therapy is required**

Emergency Management (Before Diagnostics)

- **Immediate therapy takes priority** over diagnostic workup
- Obtain an **ECG** in any child with **K^+ >6.0 mmol/L**
- Confirm hyperkalemia quickly if clinical suspicion is low

Recommended Emergency Interventions

- **IV Calcium Gluconate 10%**
  - Dose: **0.5 mL/kg IV over 5 minutes** (max 20 mL or 2 g)
  - Purpose: Stabilize cardiac membranes
- **Insulin + Glucose**
  - Shifts potassium intracellularly
  - IV insulin (0.1 units/kg) + dextrose (0.5 g/kg based on age-appropriate solution)
- **Inhaled Beta-2 Agonists (e.g., Albuterol/Salbutamol)**
  - Also shifts K^+ into cells
  - Use in conjunction with or as an alternative to insulin/glucose
- **Sodium Bicarbonate** *(Not for monotherapy)*:
  - Causes K^+ to move intracellularly
  - Effectiveness is uncertain—**do not use as sole agent**

Non-Emergency Management (Post-Stabilization or Mild Cases)

- **Indications**:
  - K^+ <7.0 mmol/L and asymptomatic
  - As adjunctive therapy post-emergency stabilization
- **Therapies include**:
  - **Treating reversible causes** (e.g., dehydration, adrenal insufficiency, medications)
  - **Loop diuretics (e.g., furosemide)** to enhance renal K^+ excretion
  - **Cation exchange resins (e.g., sodium polystyrene sulfonate)** to bind and remove K^+ via gut
  - **Dialysis** (especially **hemodialysis**) if refractory hyperkalemia or renal

Quiz questions

1.1 yr old child, fever altered sensorium, seizures. No loose stools or vomiting, has serum Na 123 mEq/L. What is the most probable cause of hyponatremia and what type is it?

2. Same child was given 3%NS for raised ICT for 48 hours. Repeat Na 161 mEq/L.What is the type of hypernatremia?

3. What is figge formula ?

4. What does delta ratio more than 2 suggest?

5. Which inherited tubulopathy is characterized by hypokalemia, metabolic alkalosis, hypomagnesemia, and hypocalciuria?

6. Which hormone excess is commonly associated with hypokalemia due to increased renal potassium excretion?

7. A 10-month-old infant presents with vomiting, poor feeding, and lethargy. Blood tests reveal a serum potassium of **7.5 mmol/L**. Which of the following is the **most serious potential consequence** of this electrolyte abnormality?

8. A 3-year-old child is brought to the emergency department with a serum potassium of **7.2 mmol/L** and ECG showing peaked T waves. The child is hemodynamically stable. Which of the following is the **most appropriate initial management step**?

Basics and Principles of Hemodialysis in children

Valentine Lobo

Nephrology Unit,

King Edward Memorial Hospital, Pune

Outline & Disclosures

- Principles of Dialysis
- Equipment and disposables
- Guidelines and practical aspects
- Special considerations for pediatric patients

- Conflicts of Interest – None
- Financial disclosures - None
- I am not a Pediatric Nephrologist.
- Our unit dialyzes both adult and pediatric patients in the same areas.

Uremic Toxin Classification -EUTox

- **Low molecular weight** - Urea the commonest marker solute.
- Others – Creatinine, Uric acid, Phosphates, Potassium, guanidines, ADMA.
- Dose of dialysis expressed as LMW water soluble toxin clearance.

- **Middle molecules -** Mol wt > 500 daltons. β2 microglobulin is the prototype.
- Others – PTH, Endothelin, Ghrelin, some cytokines.

- Low molecular weight **protein bound** – p-cresol sulfate & Indoxyl sulfate, IAA, homocysteine.

- **Na^+ & Water**.

- *- Vanholder et al (2009)*

Basic Principles of dialysis

- **Dialysis** = diffusion = passive movement of solutes across a semi-permeable membrane down concentration gradient
- Hemodialysis = solute passively diffuses down concentration gradient
- Good for small molecules
  - Dialysate flows countercurrent to blood flow.
  - Urea, creatinine, K move from blood to dialysate
  - Ca and bicarb move from dialysate to blood.

- **(Ultra)filtration** = convection = solute + fluid removal across semi-permeable membrane down a pressure gradient (solvent drag)
- Hemofiltration: uses hydrostatic pressure gradient to induce filtration / convection plasma water + solutes across membrane.
  - Better for removal of fluid and medium-size molecules
  - Hemodiafiltration: combination of dialysis and filtration.

NEJM 336:1303-1309

Diffusion	Solute from higher concentration to lower concentration **Diffusive Flux J_d = DATdc/dx …….Ficks law**
Ultra-filtration	Fluid through semi-permeable membrane driven by pressure gradient
Convection	Solute and fluid (Depending on molecular weight and size) by ultra-filtration Hydraulic Permeability Jc= Qf (Cb*S) = Qf[Cb(1-σ)]
Adsorption	Molecular adhesion to inner surface of semi-membrane

Where D= diffusibility, A = surface area, T = absolute temperature, Qf = ultrafiltration, Cb = blood solute conc, S = sieving coeff, σ = Stavermans reflection coeff
Sieving coefficient S= Cf/Cb

Intermittent HD and SLEDD

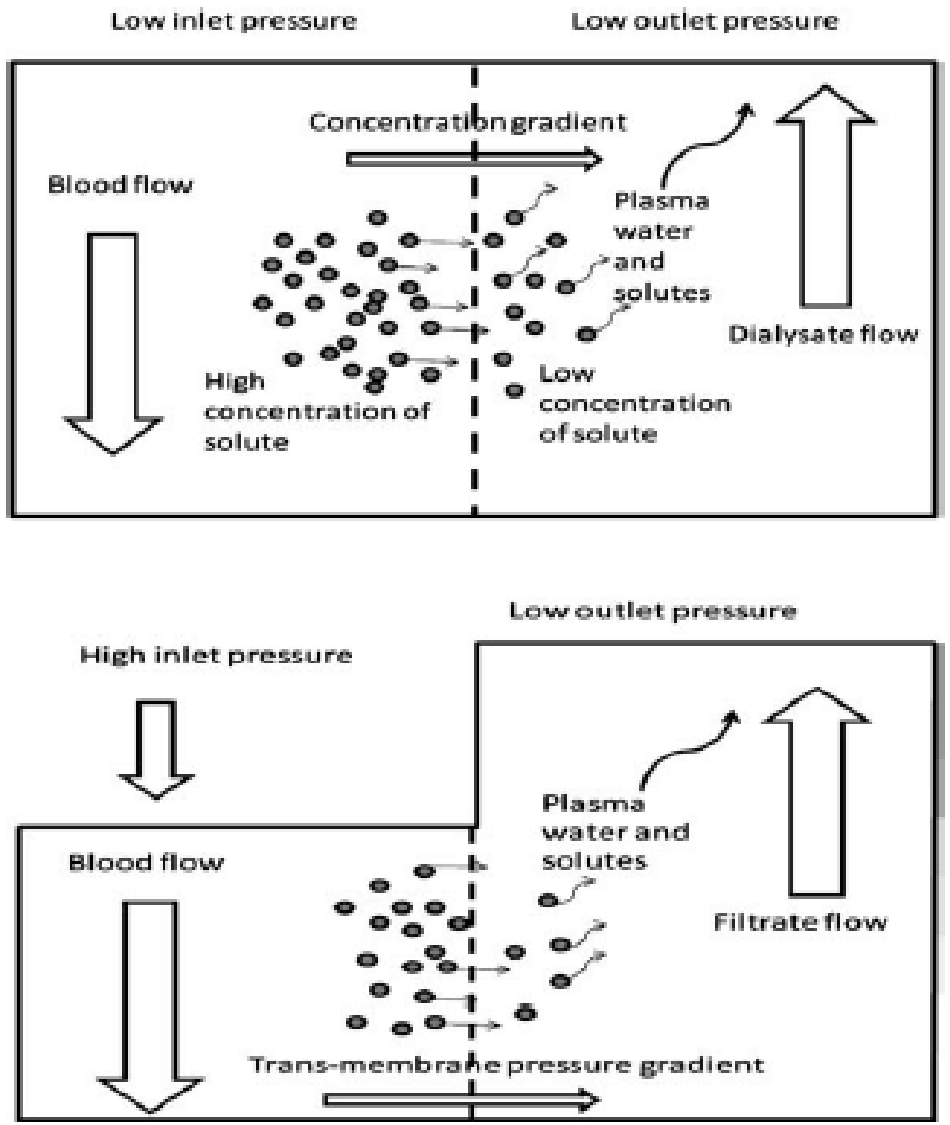
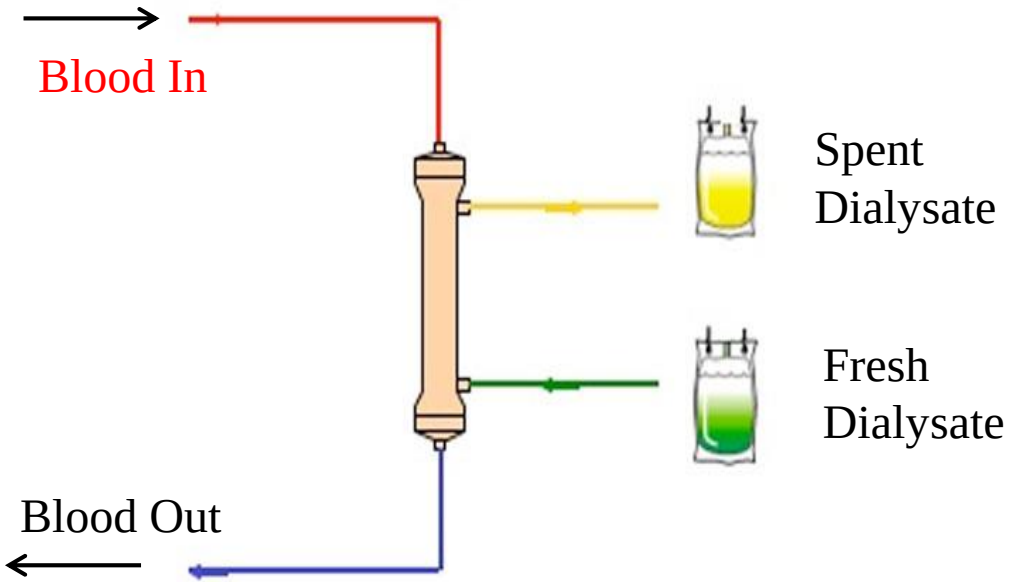
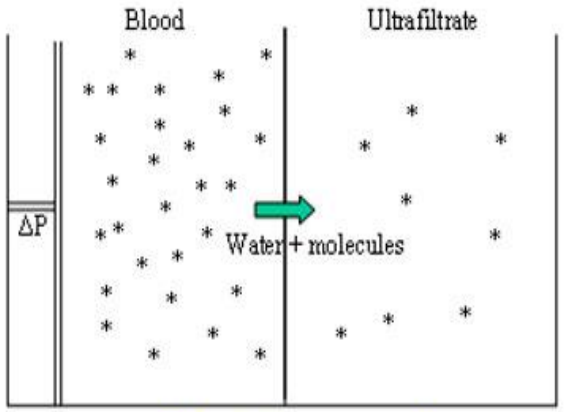


Figure 1 Principles of dialysis (top panel) and filtration (lower panel).



Convection



Hydrostatic pressure gradient

Concept of Clearance/Reduction Ratios

- Total Clearance $K_T = (K_D + K_c)$ X DF

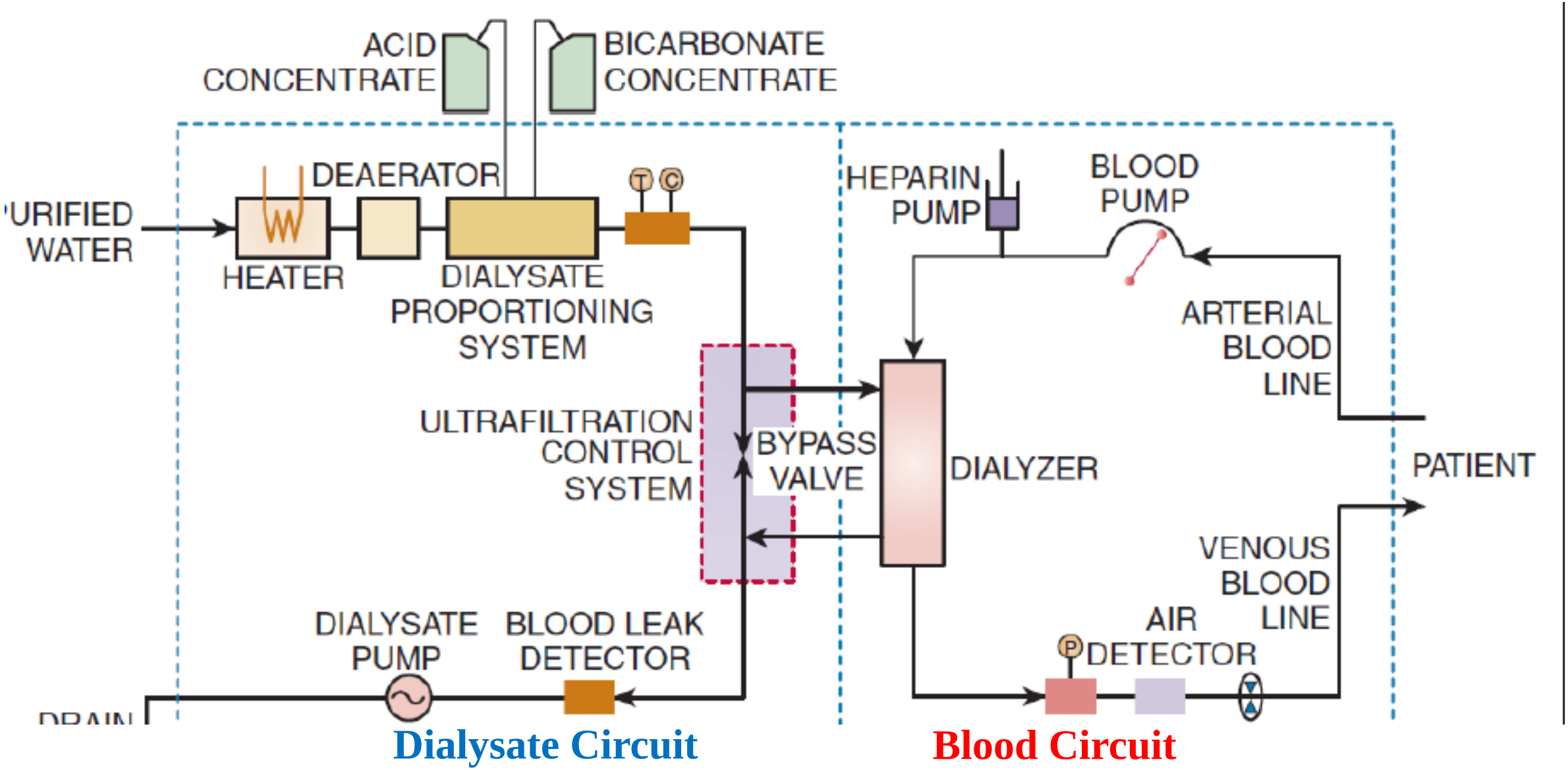
- Diffusive $K_d = \dfrac{1 - e^{KoA\ X\ [(Qb - Qd)/(QbXQd)]}}{(1/Q_b) - (1/Q_b\ X\ e^{KoA\ X\ [(Qb - Qd)/(QbXQd)]})}$

- Convective $K_c = Q_b - K_d\ X\ Q_f\ X\ S$

- *Hemodiafiltration/Hemofiltration - Percentage of effective convective transport greater than 20% of the total processed blood.*

- Extraction ratio of a dialyzer = (Cbi – Cbo)/Cbi.
- For a dialyzer doing no ultrafiltration Clearance K = Extraction ratio X blood flow.
- If UF is taking place K = Qb(Cbi – Cbo)/Cbi + Qf[Cbo/Cbi]
- The relationship between clearance and mass transfer coeff is
- $K = Qb\ X\ \dfrac{\exp [KoA/Qb(1-Qb/Qd)] - 1}{\exp[KoA/Qb(1-Qb/Qd)] - Qb/Qd}$
- Where exp is the base of the Naperian logarithm.

Dialysis Process



(C = conductivity monitor, P = pressure monitor, T = temperature monitor)

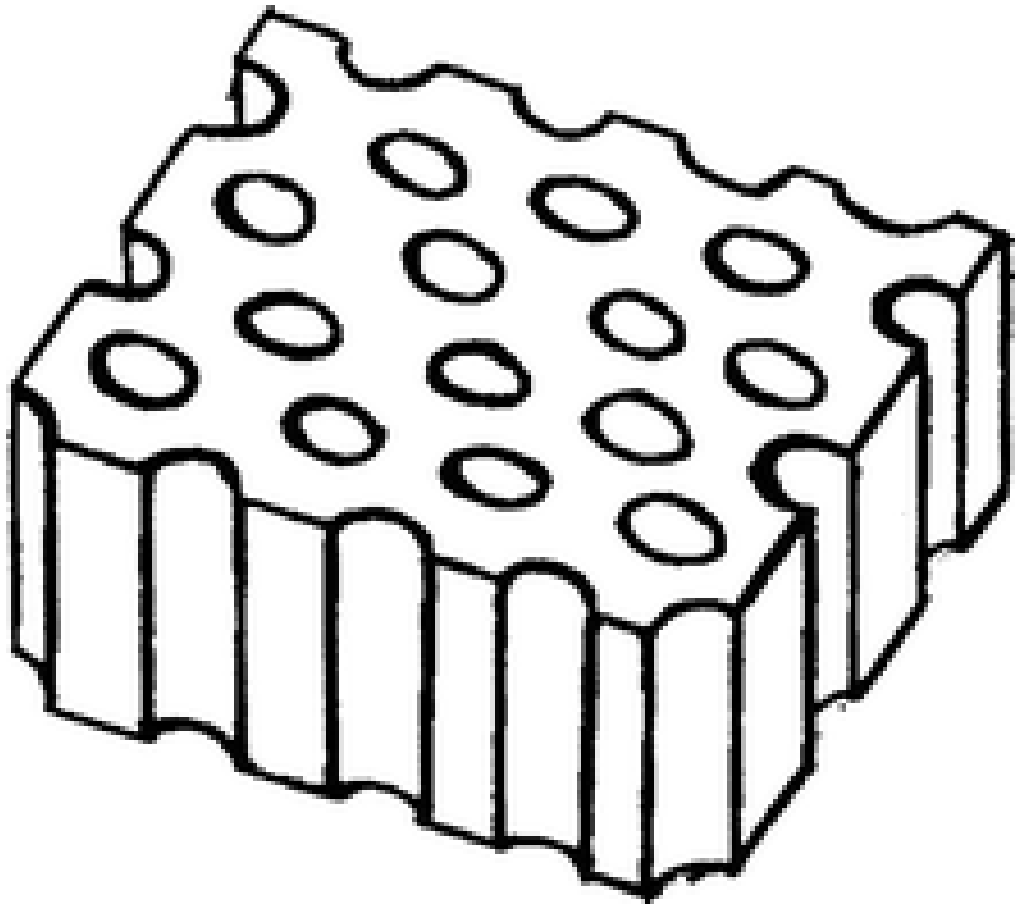
ISN on Hemodialyzers

- Made of biocompatible, synthetic (e.g., polysulfone, polyacrilonitrile, polymethylmethacrylate) or modified cellulose membrane (e.g., cellulose acetate).
- We recommend that either low flux or high flux biocompatible membrane may be used for regular HD.
- We recommend that use of high flux dialyzers be restricted to units that can ensure European standard of quality of water.
- Surface area of the dialyzers should be chosen based on the required dialysis dose and the body size of the patient.
- *Large surface area dialyzers should be avoided in pediatric patients and adult patients with small body size.*
- A large array of dialyzers based on biocompatibility, flux and surface area is available for clinical use.
- Most often a single type of dialyzer may be sufficient in most patients in a dialysis unit.
- *Some patients may have specific needs and may require change in the dialyzer specifications.*
- *Hence, dialyzers with specifications other than that generally used in the dialysis unit may also be stocked or should accessible at a short notice.*

Dialyzer Performance

- Physical Characters determining Membrane Performance
- Transport Parameters
  - Pore size
  - Surface Area
  - Membrane Thickness
  - Pore Density
  - Protein Adsorption

- Fibre Geometry
- Blood & Dialysate flow patterns
- Shear rates at the fluid membrane interface



Defining Efficiency

- Diffusive Flux J_d = -DATdc/dx …….Ficks law
- Where D= diffusibility
- A = surface area
- T = absolute temperature
- ***Efficiency – Capacity of a dialyzer to remove low molecular weight solutes.***
- Efficiency is defined as the effect of lowering solute concentration achieved for a given level of dialysis dose. ……K-DOQI (2007)
- Urea is the most extensively studied solute
- The mass transfer area coefficient KoA of a dialyzer is the clearance at infinite blood and dialysate flow rates.
- In clinical terms it is the maximum solute removal capacity of a dialyzer.
- Intrinsic Property of the dialyzer membrane.
- Larger dialyzers have a greater diffusive flux.
- Too tightly packed fibre bundles cause channeling of dialysate peripherally
- Compromise between a larger surface area and an optimum dialysate flow
- KoA < 450…….low efficiency
- KoA > 600…….high efficiency.

Variation in Dialyzer Sizes

Dialyzer	F3	Sureflux N5	F4	F5	F6	F7	F8
Blood Flow ml/min	50 - 200	50 - 100	50 - 200	100 - 200	200 - 300	300 – 400	300 -400
Urea clearance	125	130	155	170	222	236	240
Creatinine	95	109	128	149	194	210	216
Phosphate	50	62	78	103	145	155	165
Sterilization	Ethylene Oxide						
UF co efficient (Kuf)	1.7	2.7	2.8	4.0	5.5	6.4	7.5
Priming volume	28	34	42	63	82	98	110
Maximum TMP	500 mm of Hg						
Surface area	**0.4**	**0.5**	**0.7**	**1.0**	**1.3**	**1.6**	**1.8**
Fibre wall thickness (mic)	200	200	200	200	200	200	200
Fibre inner diameter (mic)	40	15	40	40	40	40	40
Membrane material	**Polysulfone**						

Potting compound - Polyurethane
Sterile plugs - Polycarbonate
Housing and caps - Polycarbonate
O ring - Silicone rubber

Variability in Body Size and Dialyzer requirement

Clearance & KoA of a Dialyzer

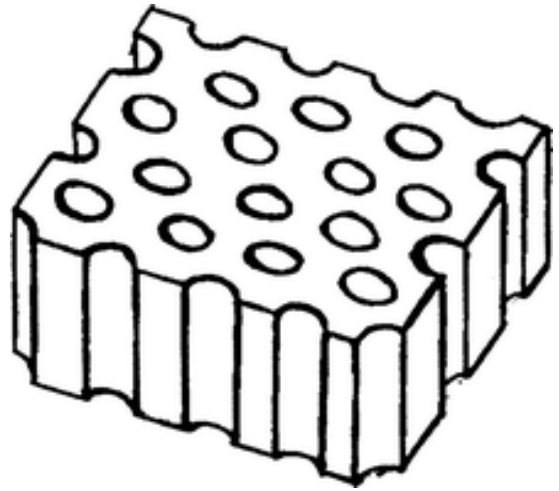
Dialyzer	Polyflux 14L		Polyflux 17L		Polyflux 21L	
Blood Flow ml/min	200	300	200	300	300	400
Urea clearance	190	252	194	264	275	328
Creatinine	171	214	179	230	246	283
Phosphate	152	183	163	200	218	247
Sterilization	Steam					
KoA (Urea)	**850**		**1027**		**1265**	
UF co efficient (Kuf)	10		12.5		15	
Priming volume	81		104		123	
Maximum TMP	600		600		600	
Surface area	**1.4**		**1.7**		**2.1**	
Fibre wall thickness	50		50		50	
Fibre inner diameter	215		215		215	
Membrane material	Polyamix		Polyamix		Polyamix	

Potting compound Polyurethane
Sterile plugs - Polypropylene

Housing and caps - Polycarbonate
O ring - Silicone rubber

Pore size, Flux, and Dialyzer Efficiency

- Hydraulic Permeability/Convective flux Jc = Qf (Cb*S) = Qf [Cb(1-σ)]
- Qf = ultrafiltration
- Cb = blood solute conc
- S = sieving coeff
- σ = Stavermans reflection coeff



- Sieving coefficient S= Cf/Cb
- Depends on mean pore size, molecular weight and configuration .
- Close to 1 for urea and K^+, decreases with increase in molecular weight
- Assuming the cylindrical shape of pores
- UF = TMP/R and substituting R from Poiseulles equation $R = 8l\,\eta / \pi\, r^4$
- All membranes actually have a distribution of pore radii and tortuous structures.

Dissociation of Flux and Efficiency

- More selective dialyzers have a narrow pore distribution
- No of pores = pore density = porosity = K X N X r^2
- Diffusive permeability dependant on pore size by an area factor (r^2) and flux by r^4 factor.
- 2 properties are independent of each other.
- High efficiency dialyzers have high diffusive permeability for small solutes , but low water permeability
- High flux dialyzers have significantly lower small solute diffusive permeability.
- Water flux and middle molecule permeability are directly related to each other.

Dialyzer characteristic	Conventional	High Efficiency	High Flux
KoA (Urea)	< 450	>600	Variable
K urea	<200	>200	Variable
Kuf	<12	Variable	> 12
K (beta2M)	< 10 ml/min	Variable	> 20 ml/min

All values from HEMO study

Assumes Qb = 300 – 450 ml/min, Qd = 500 - 800 ml/min

Dissociation of Flux and Efficiency

Dialyzer	F5	F5HPS	F50S	FX50	F6	F6HPS	F60S	FX 60
Blood Flow ml/min	200	200	200	200 - 300	300	300	300	300
Urea clearance	170	179	178	189	222		235	261
Creatinine	149	163	160	170	194		192	230
Phosphate	103	139	158	165	145		170	221
Sterilization	**ETO**		**Inline Steam**		**ETO**		**Inline Steam**	
UF co efficient (Kuf)	4.0	10	30	33	5.5	13	40	46
Priming volume	63	53	63	53	82	75	82	74
Maximum TMP	**500 mm of Hg**							
Surface area	1.0	1.0	1.0	1.0	1.3	1.3	1.3	1.4
Fibre inner diameter (mic)	200	200	200	185	200	200	200	185
Fibre wall thickness (mic)	40	40	40	35	40	40	40	35
Membrane material	**Polysulfone**			**Helixone**	**Polysufone**			**Helixone**

Recommendation for requirements of the HD machine: ISN (2020)

- **Mandatory:**
- Blood pump to achieve a unidirectional flow of up to 400 ml/min.
- *Low blood flow rate (3–5 mL/kg/min down to 50 mL/min), guided by the child's weight.*
- Heparin pump
- Arterial line and venous line pressure monitors
- Functional air bubble detector with *sensitivity adaptable for paediatric tubing use.*
- Safety devices: functioning alarms, venous blood clamp
- **Smaller blood volume in young children necessitates both low-volume tubing systems and dialyzers, and**
- **Dialysis machines with a high precision of ultrafiltration control.**
- The safe and tolerable extracorporeal blood volume in an individual is less than 8 ml/kg body weight, corresponding to 10% of the total blood volume

Recommendation for requirements of the HD machine: ISN (2020)

- Mixing proportion unit with bicarbonate dialysis facility, rate of dialysate delivery from 300 to 500 ml/min or more.
- *Flexibility of the dialysate flow rates should be as low as 100 mL/min.*
- Dialysate temperature regulator that has a range of temperature 35 to 39^{o} C.
- Conductivity meter.
- Functional blood leak detector
- Precisely controlled ultrafiltration with volumetric balancing chambers or electromagnetic flow sensor controlled dialysate pumps
- *Accuracy of ultrafiltration for children < 15 kg body weight not validated by the manufacturer.*
- *Machines with dedicated paediatric modules such as Fresenius 5008 and Gambro AK200S discontinued by manufacturer*
- *Fresenius Medical Care (July 2017) recommended that the 5008 machine not be used in children < 17 kg*
- *Reports of balancing system errors leading to excessive ultrafiltration in smaller children.*
- Disinfection, decalcification and Rinse Cycles

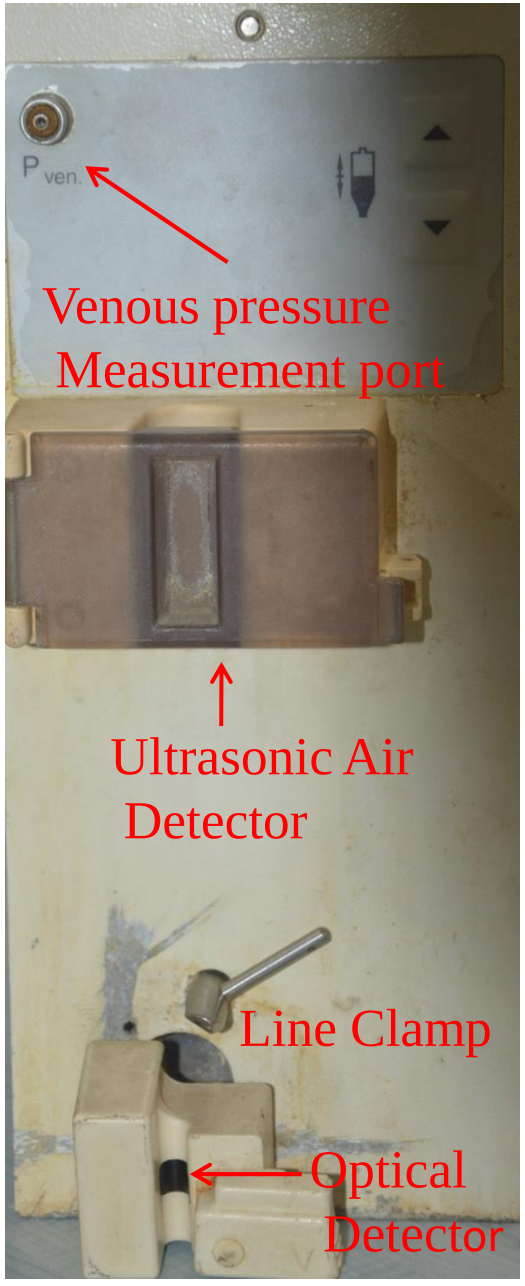
Availability of Dialysis Machines specifically for Pediatric Patients

Countries	Weight (kilograms)					
	<10	10-<15	15-<20	20-<25	25-<30	30-<40
Australia	none	one	one	one	two	two
Canada	none	none	one	two	four	five
USA	none	none	one	two	three	five
European Community	none	one	one	two	four	six
Japan	none	none	none	one	one	one

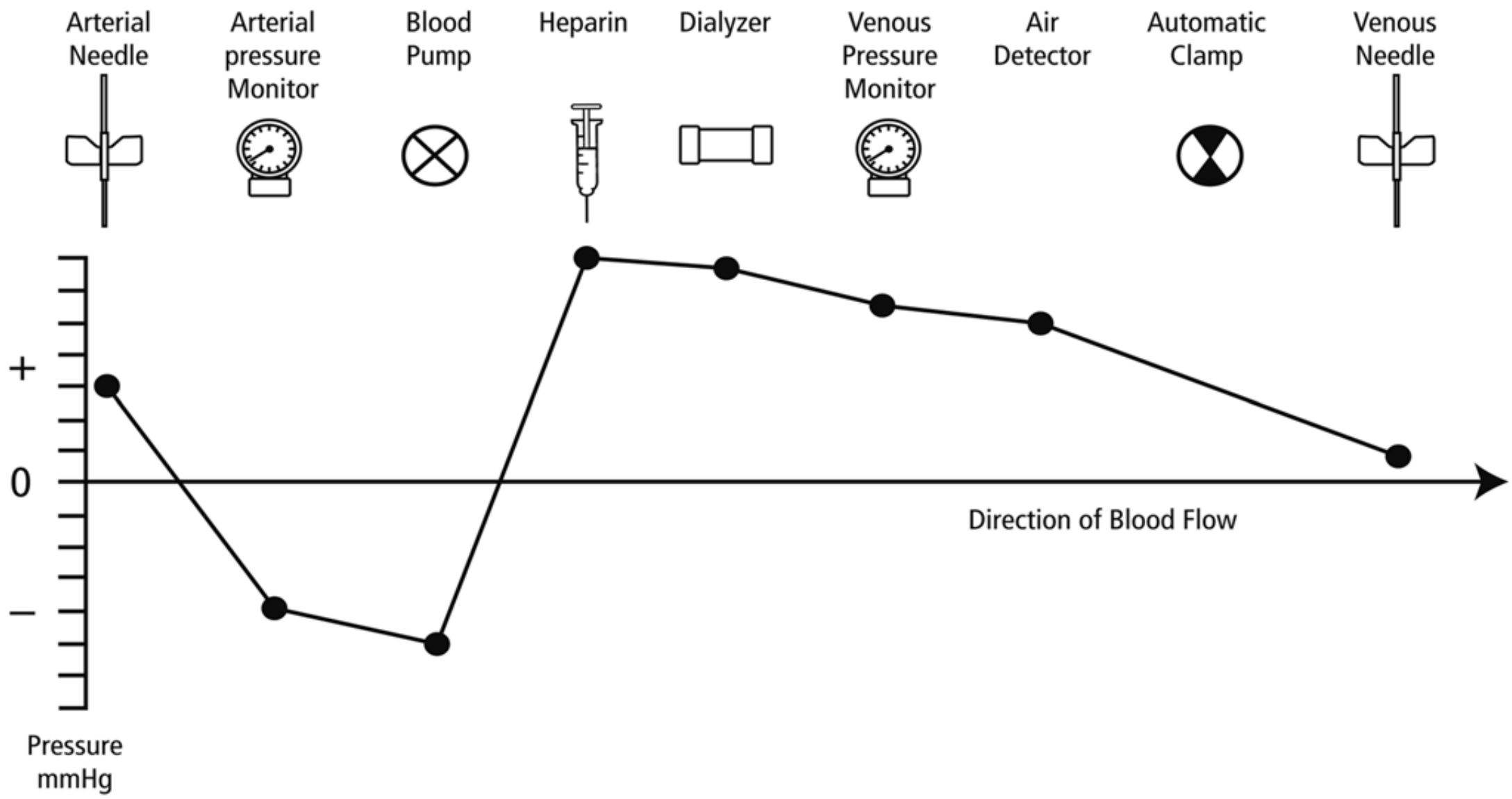
Kidney Int, 103:1038–1040; (2023)

Blood Circuit Operation in Hemodialysis

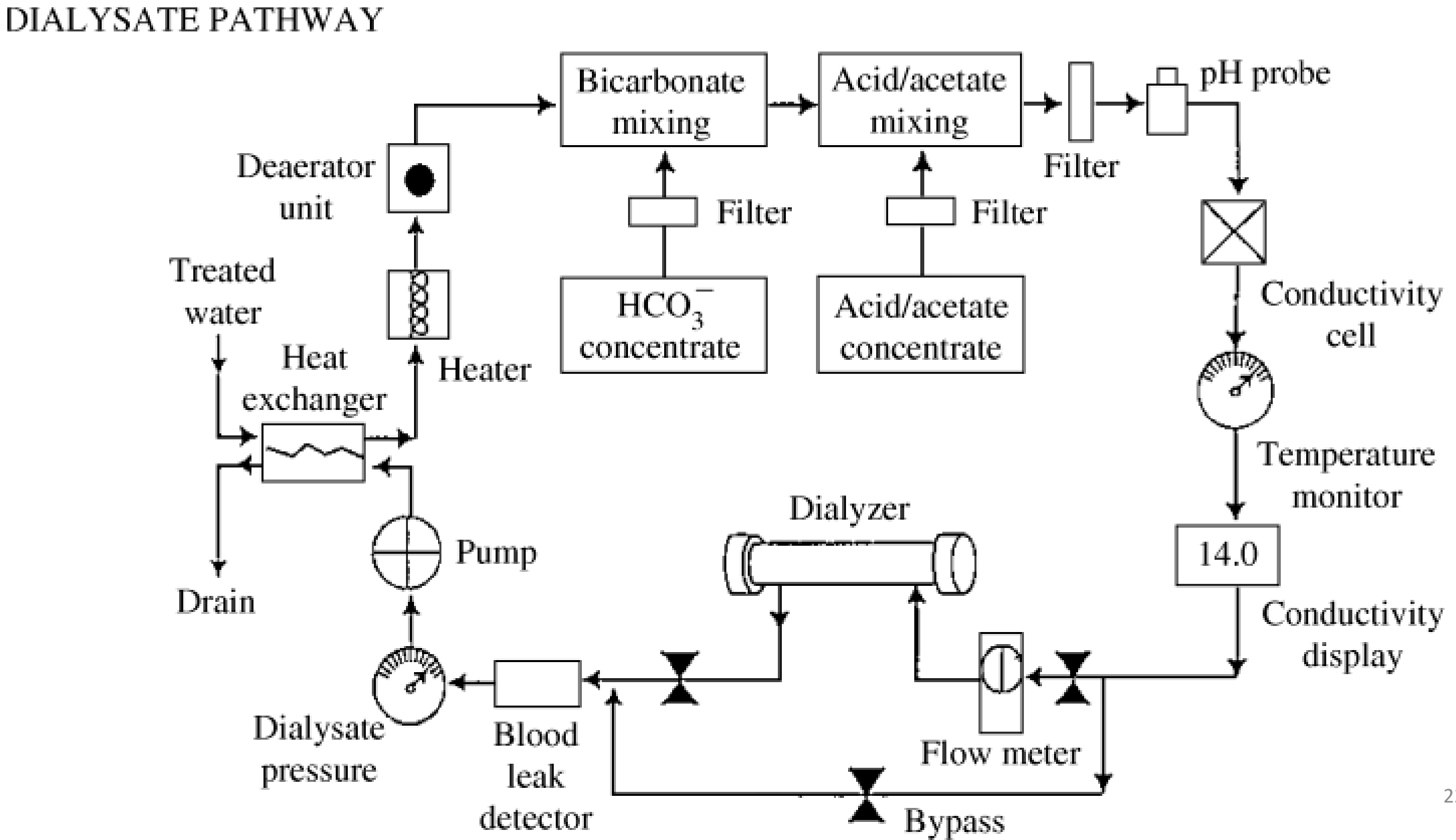
“Safe Mode" of operation would mean disabling the Arterial blood pump, clamping the venous line, and stopping UF, thus isolating the patient by all blood alarms (air detector, arterial, venous, blood leak, transmembrane pressure, blood pump torque).



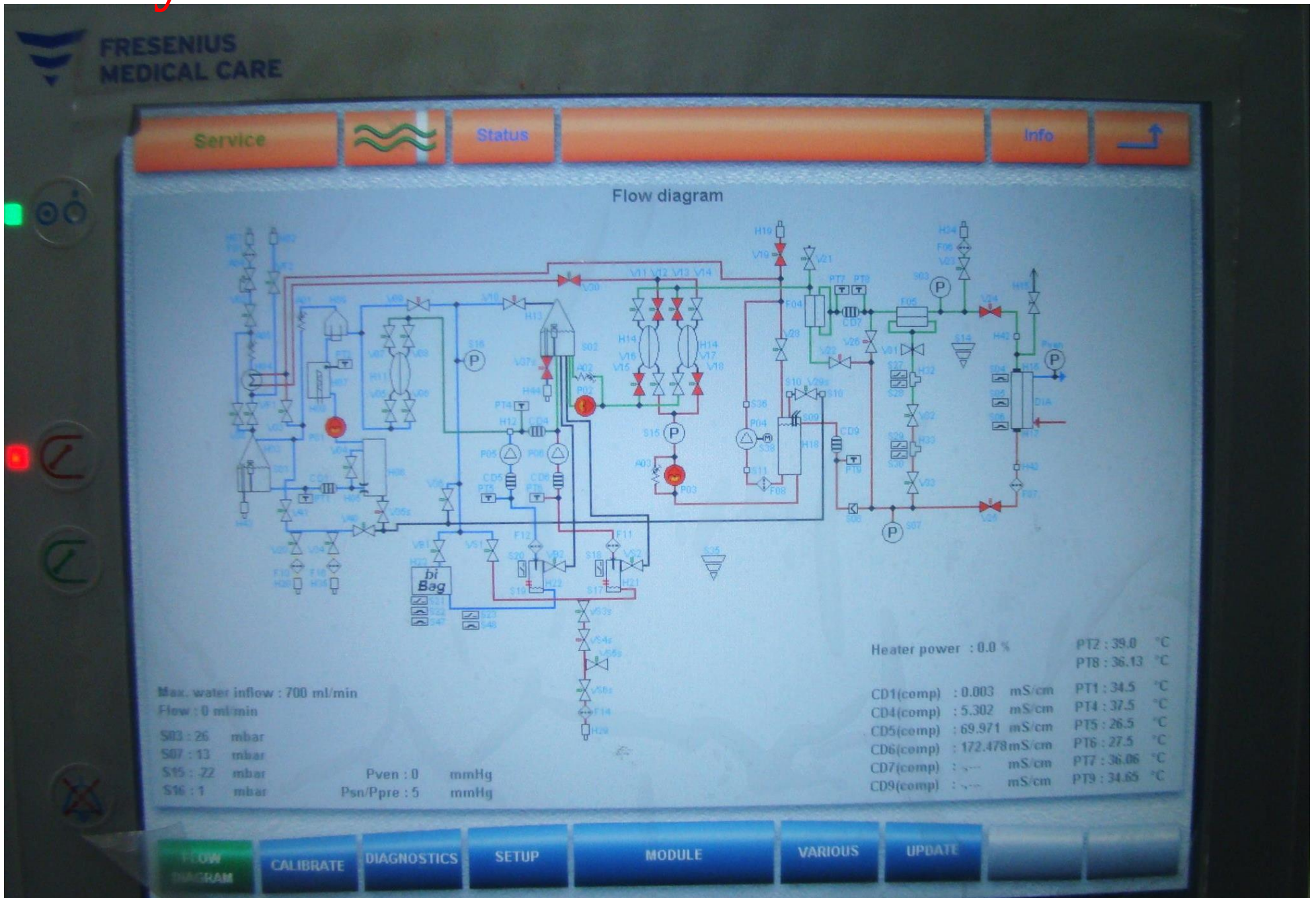
Blood Path Pressures



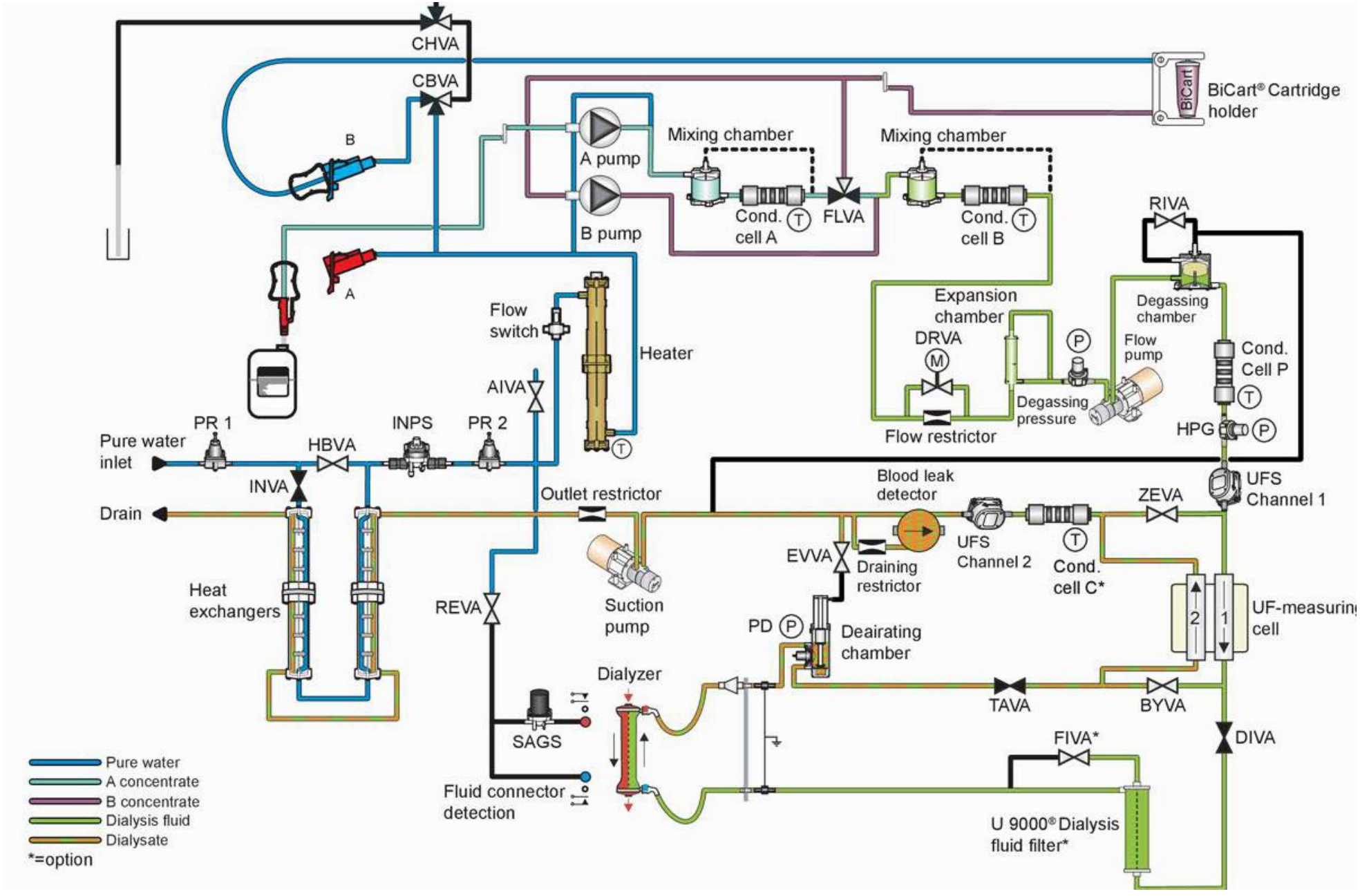
Hydraulic Schematics of a Dialysis Machine



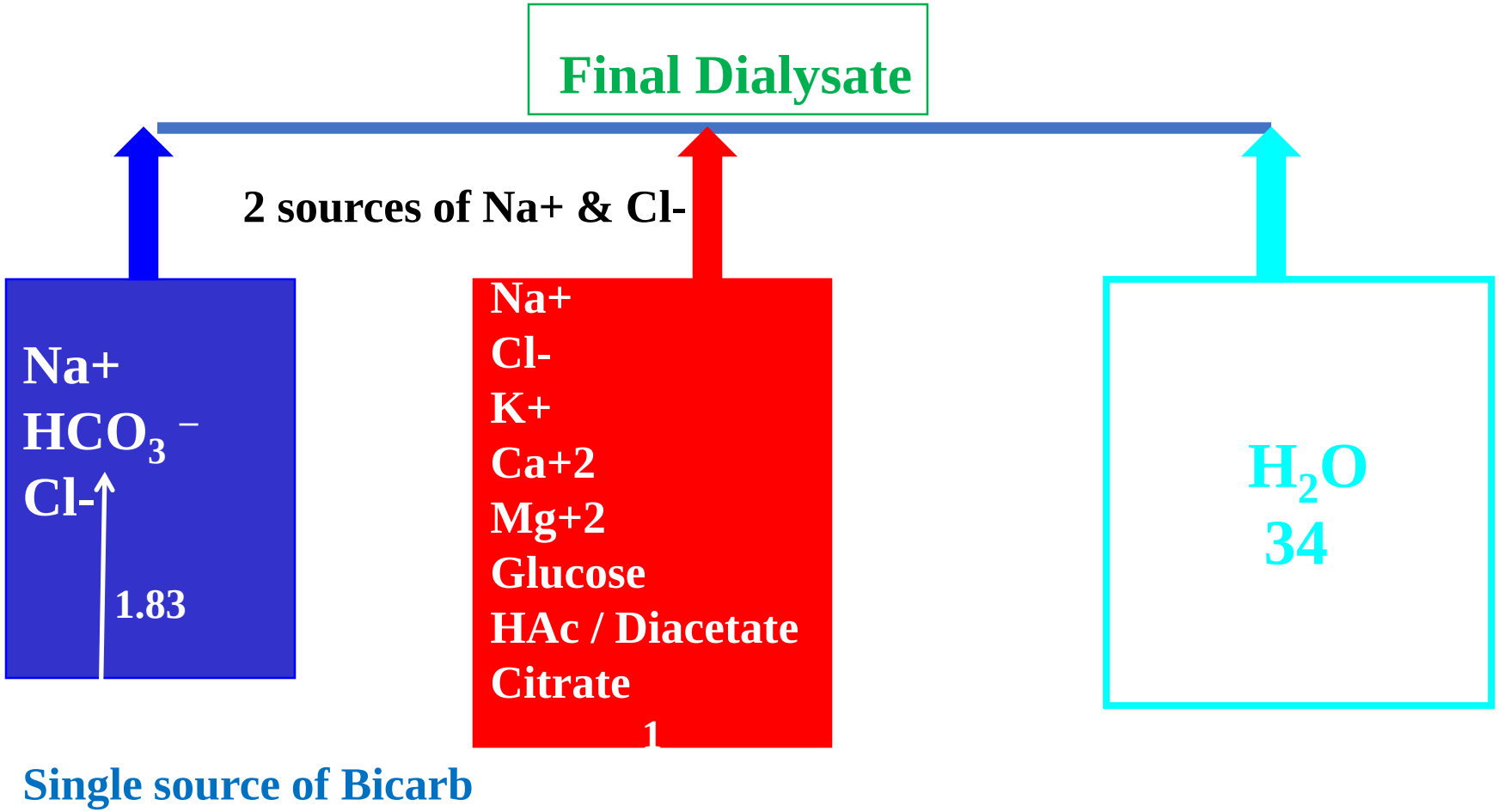
Hydraulic Schematics of 5008 Machine



Hydraulic Schematics of AK 98 Machine



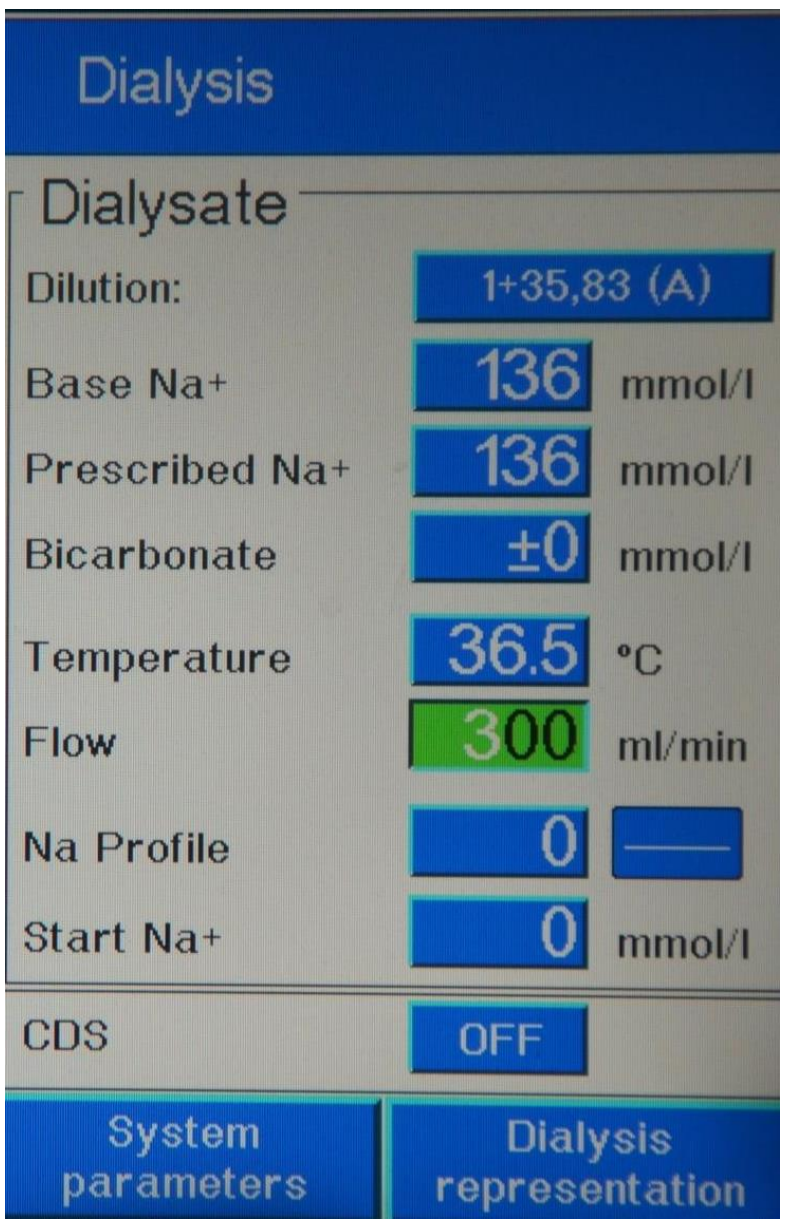
Three stream proportioning

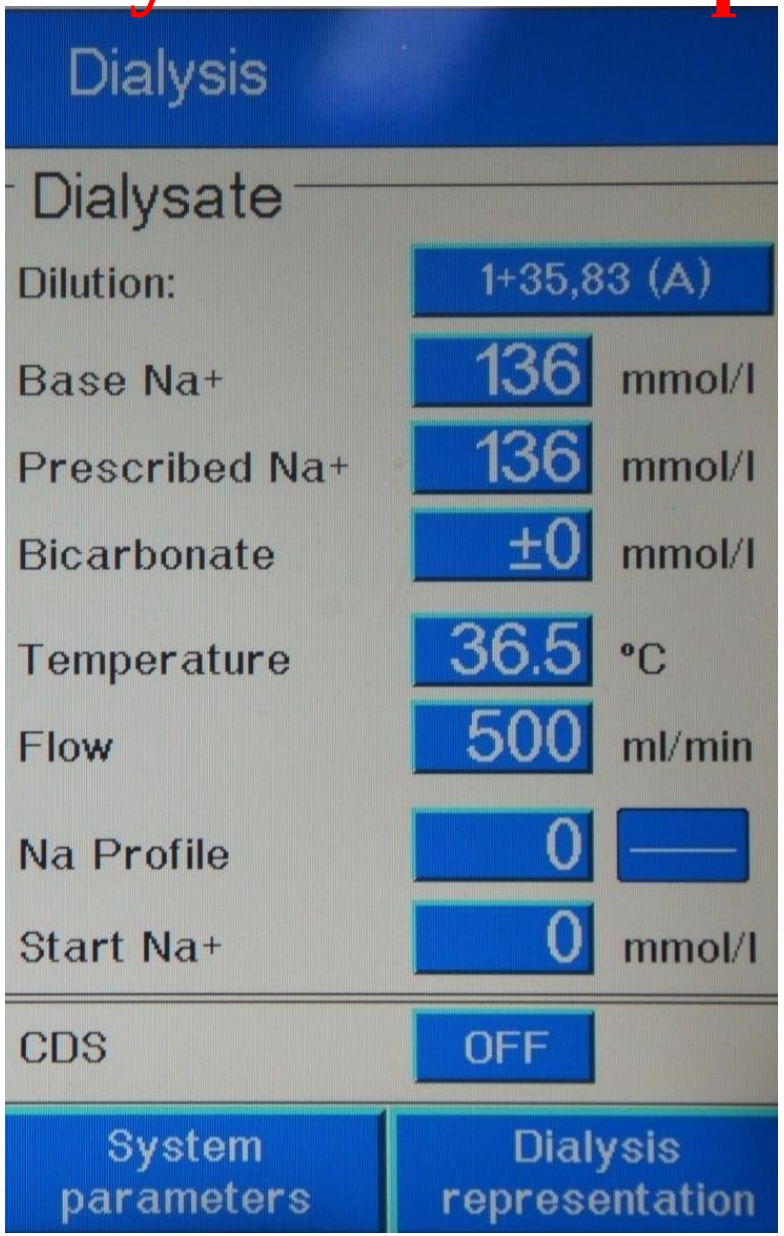


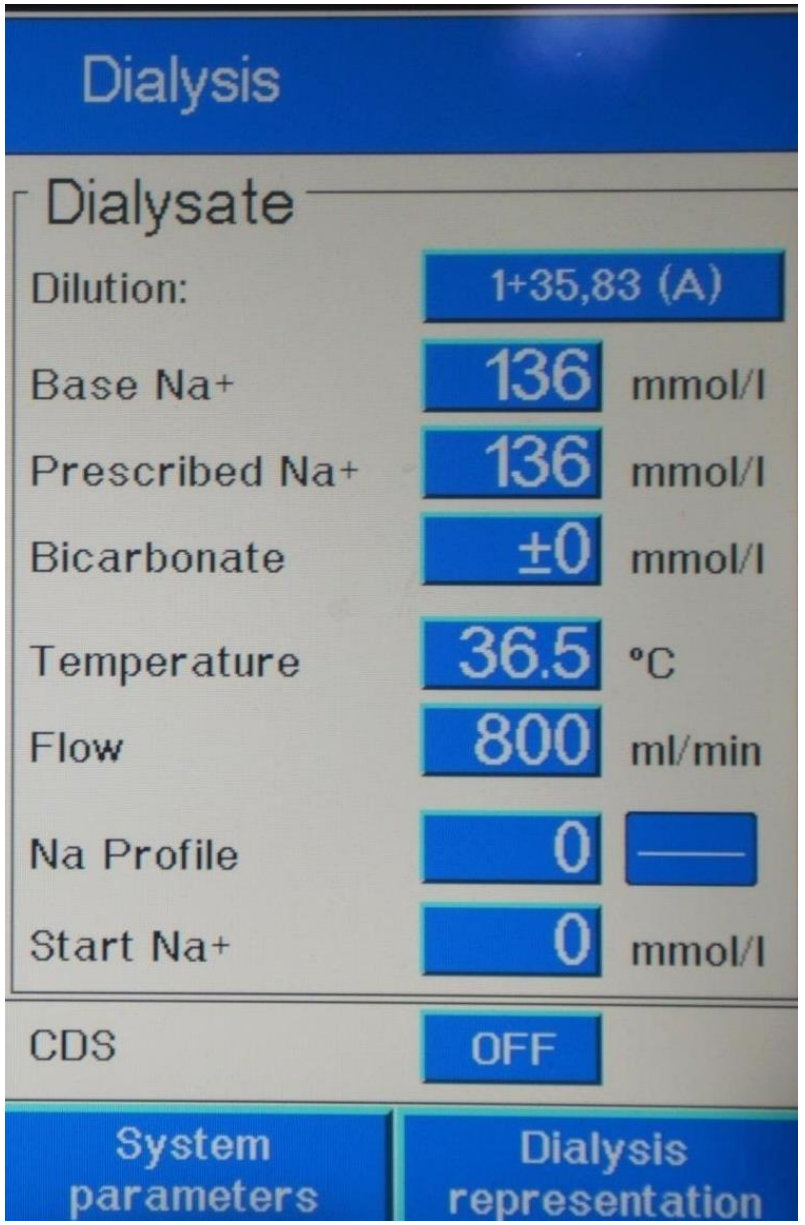
Na^+	82 from acid, 57. 8 from bicarb
Cl^-	82 from acid, 21 from B concentrate

Dialysate Flow Options

Dialysate Flow Options

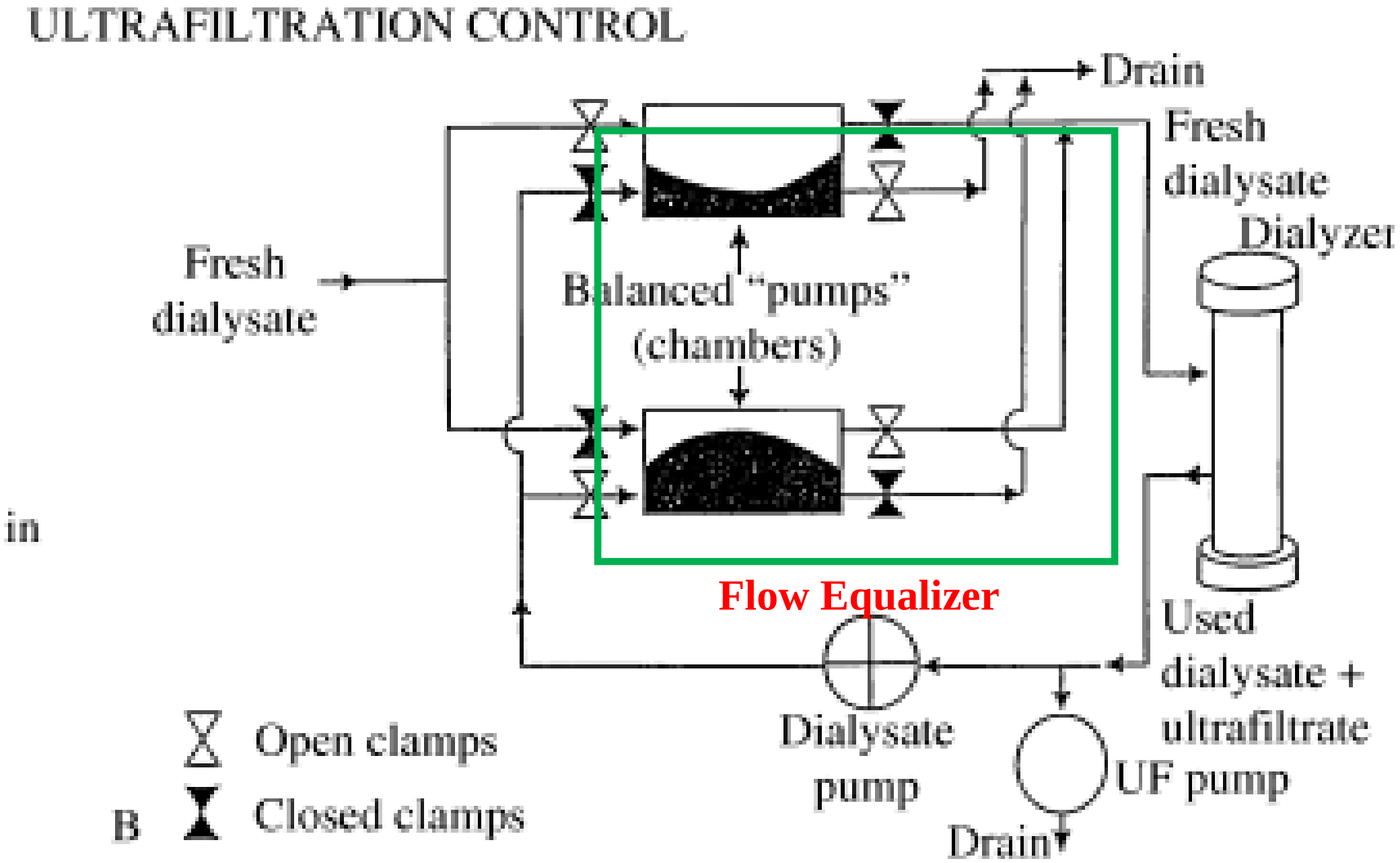




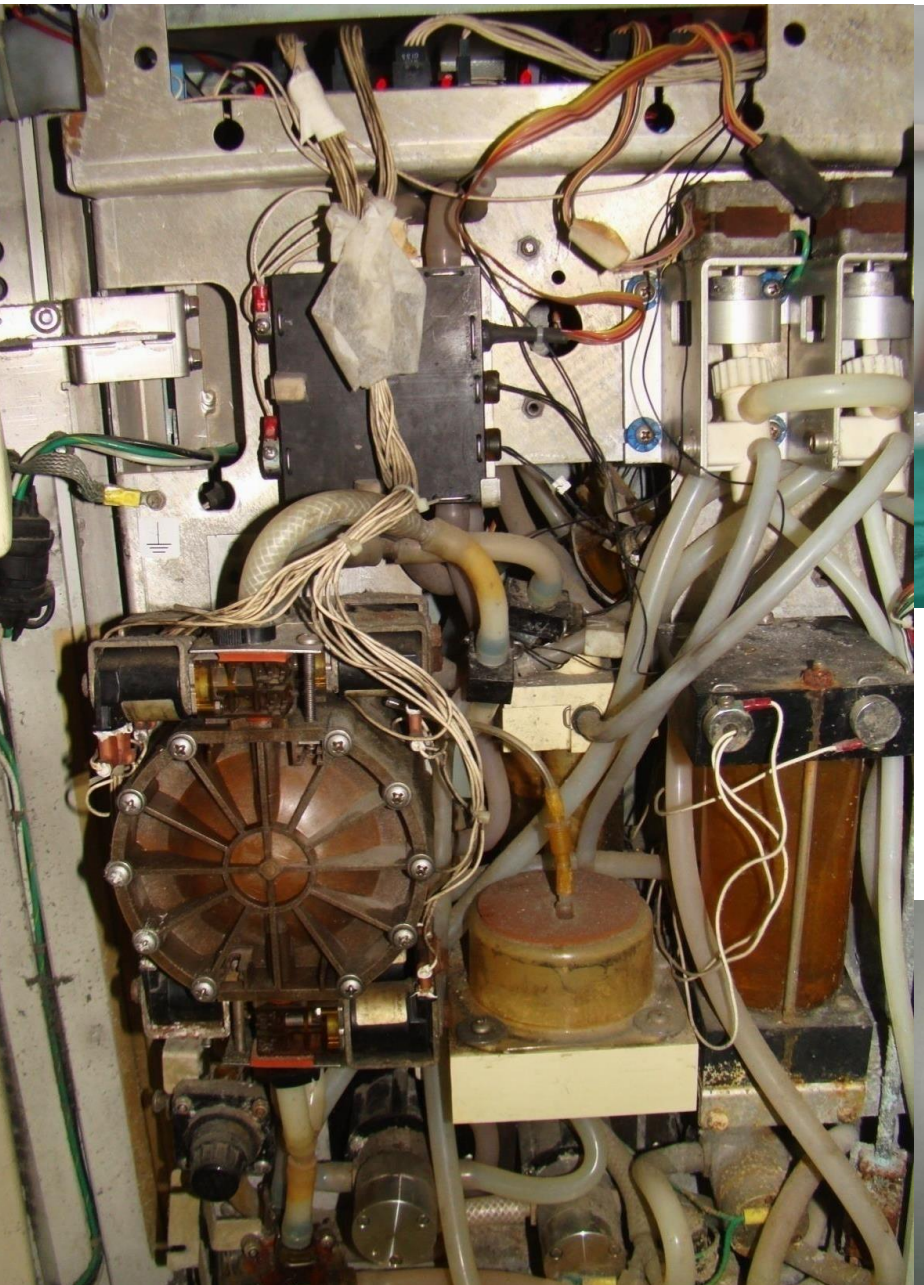


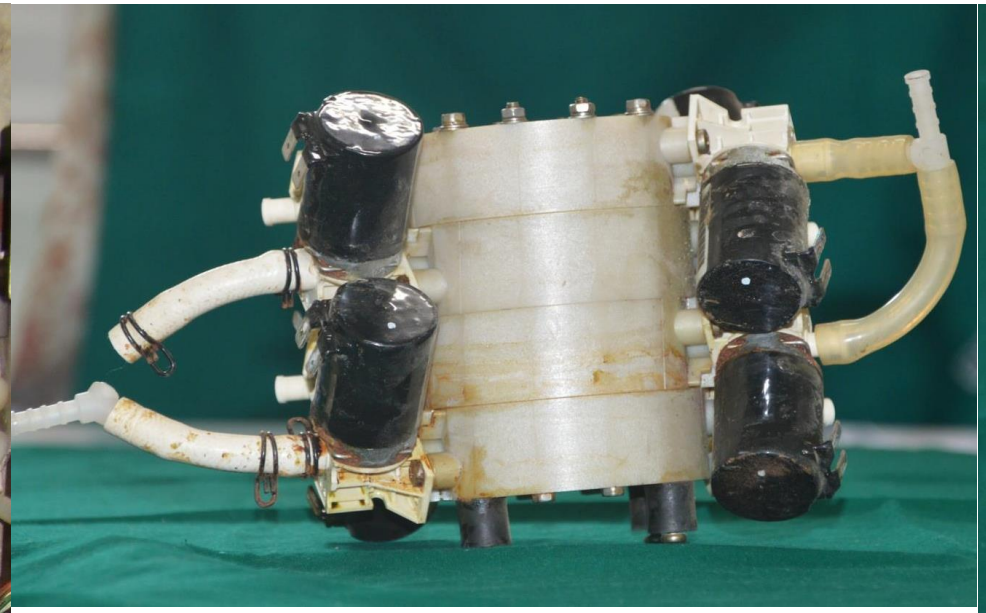
Flow is a function of Dialysate flow motor RPM and gear ratio

Volumetric Controlled Ultrafiltration – Theory of Balancing Chamber



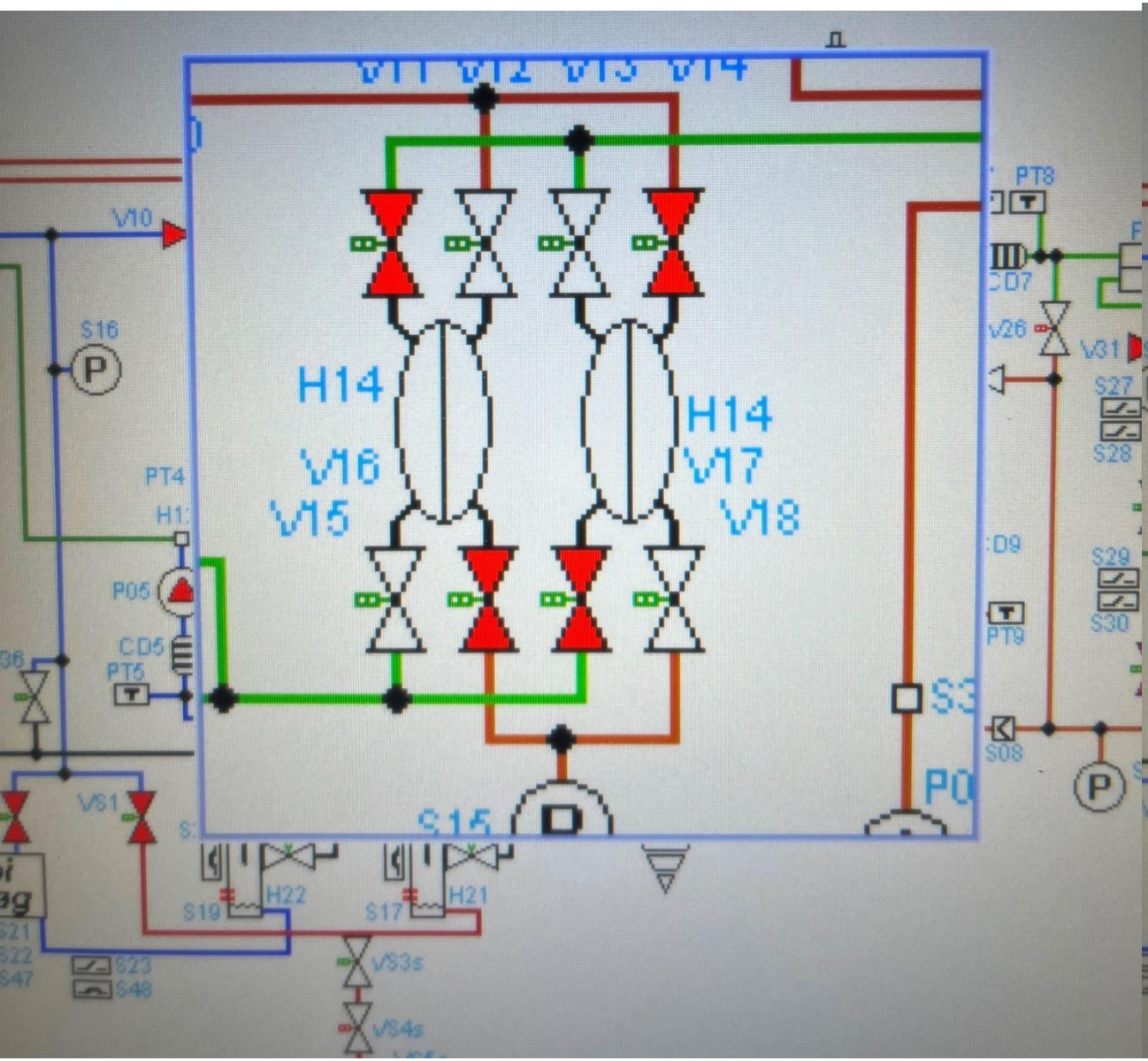
Volumetric Controlled Ultrafiltration



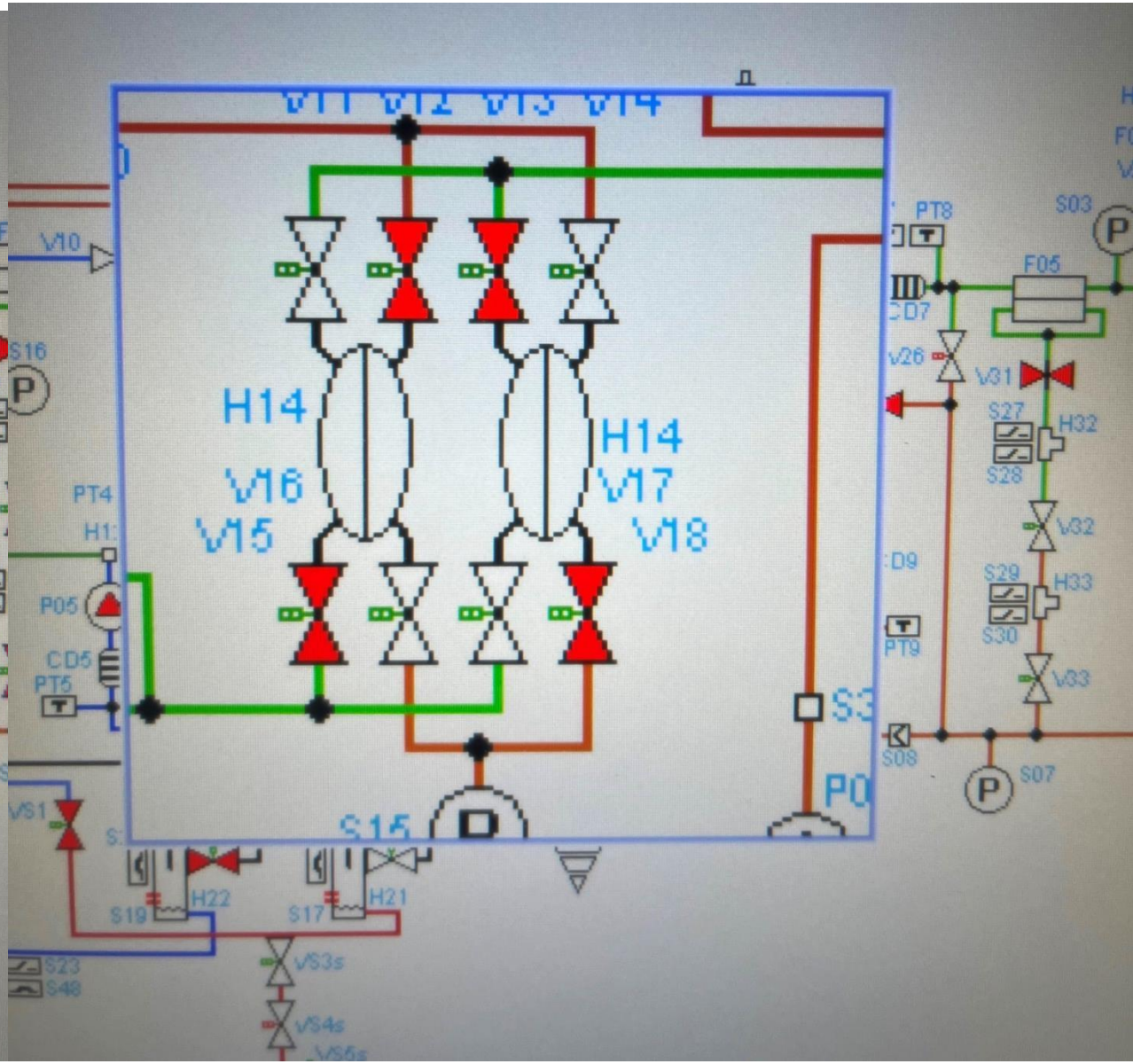


- Balancing Chamber operation is controlled by a movable diaphragm and solenoid valves.

Balancing Chamber Operation – Dialysate Flow & UF



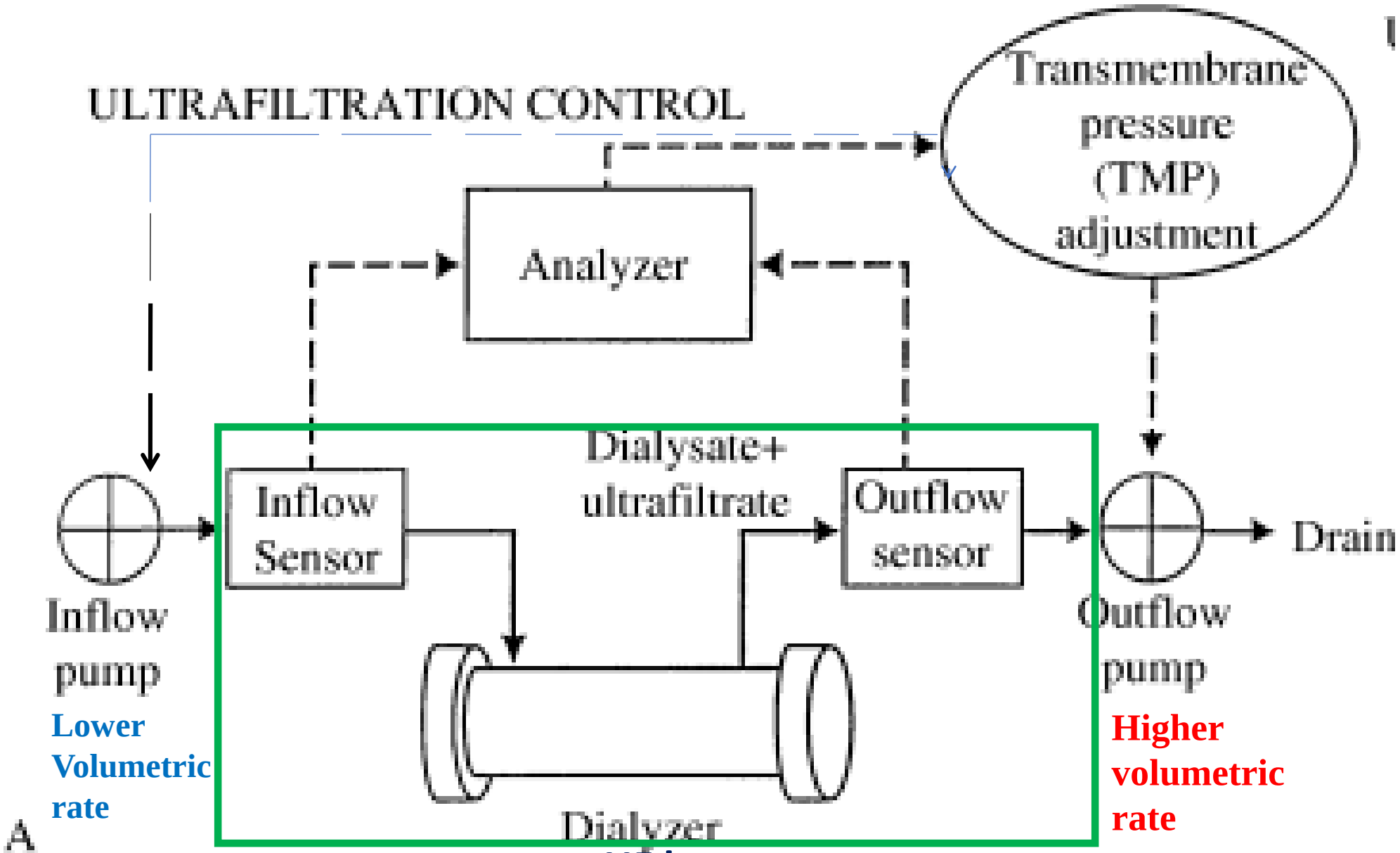
1st Cycle operation



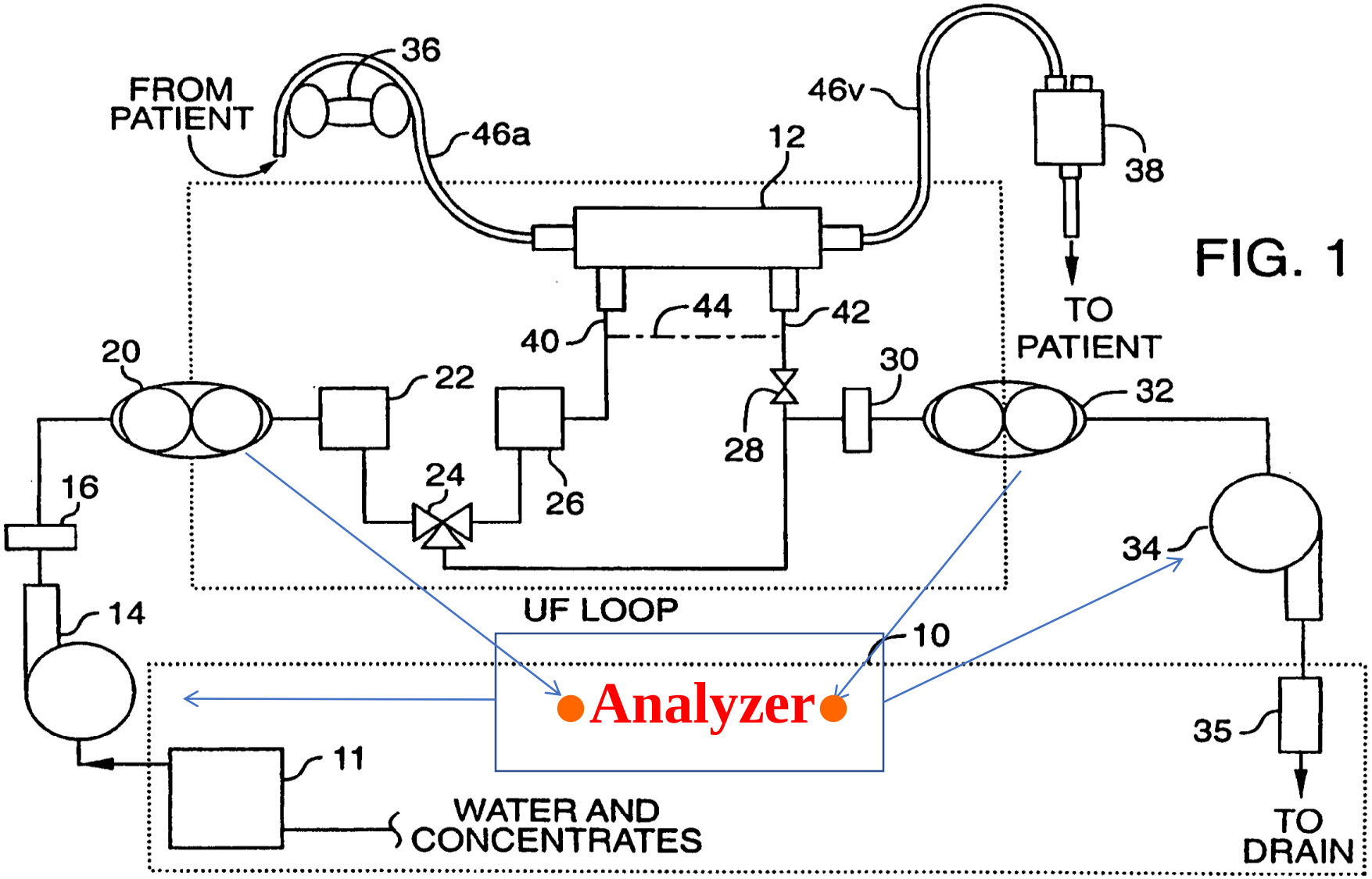
2nd Cycle operation


Fresenius Medical Care
REF 670706
CW 50/07
SN 389605

Flow Controlled Ultrafiltration



Flow Controlled Ultrafiltration EP 1100559 A1



Recommendation for requirements of the HD machine:

- **Optional/Desirable:**
- *On-line blood volume monitor*
- Blood temperature monitor
- *On-line solute clearance monitor.*
- *Sodium profiling of dialysate.*
- Isolated Ultrafitration & UF profiling
- Single needle dialysis facility.
- **Hemodiafiltration** *to provide the highest standard in terms of tolerance and efficiency*
- Facility for ultrapure dialysate preparation from dry powder concentrates
- Optical detector

Cardiovascular risk, growth and patient-related outcome measures in children: an observational comparison of hemodiafiltration to conventional hemodialysis – the HDF, Heart and Height (3H) study

190 children recruited
(28 centres, 10 countries)

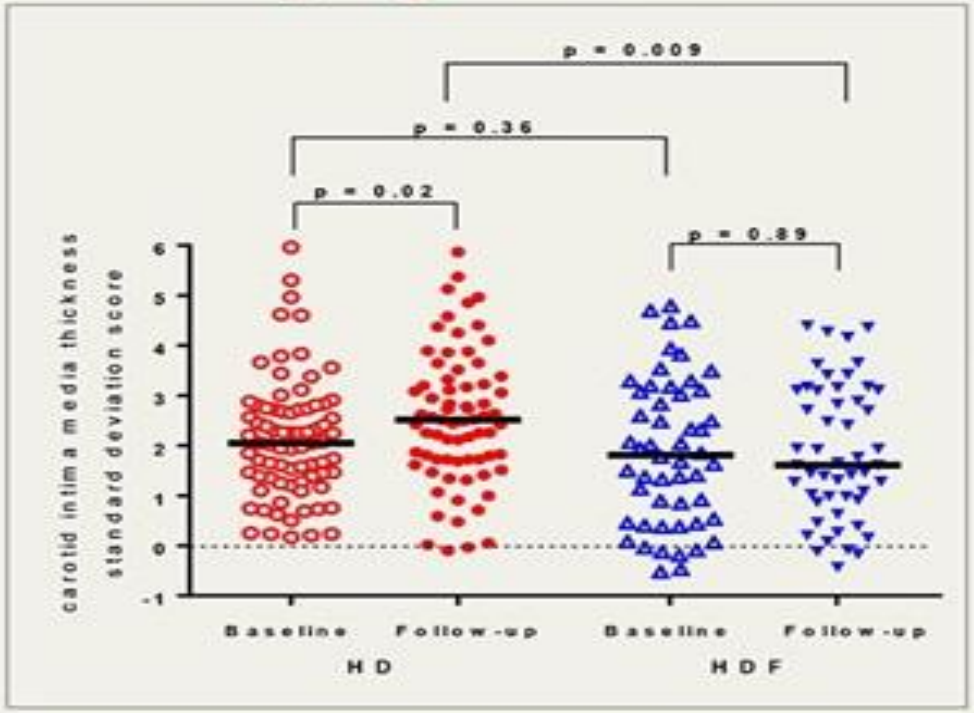
177 entered study

106 HD | **71 HDF**

1 year follow-up

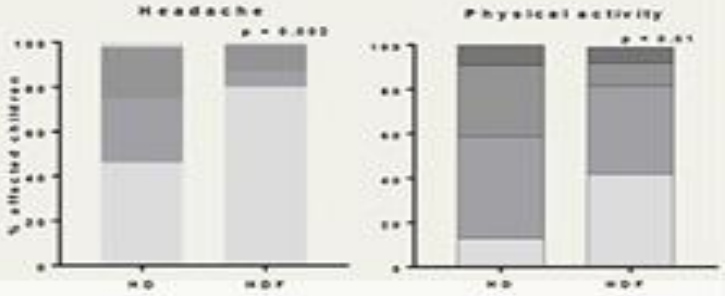
78 HD (74%) | **55 HDF** (77%)

No progression of vascular changes in HDF



In HDF vs HD cohort:
- ↑ Height SDS
- ↓ 24-hour BP
- ↓ β2-microglobulin
- ↓ PTH
- ↓ hs-CRP
- ↑ Hemoglobin

Improved PROMs on HDF



Methods

1. Vascular measures –carotid intima-media thickness, pulse wave velocity, 24-hour BP, ECHO
2. Height SDS
3. Biochemistry
4. Patient related outcome measures (PROMs)

CONCLUSION 3H suggests an association between HDF modality with lack of progression in vascular measures, increase in height and improved patient-related outcomes compared to HD. This correlated with improved BP control and clearances on HDF. Confirmation through randomised trials is required.

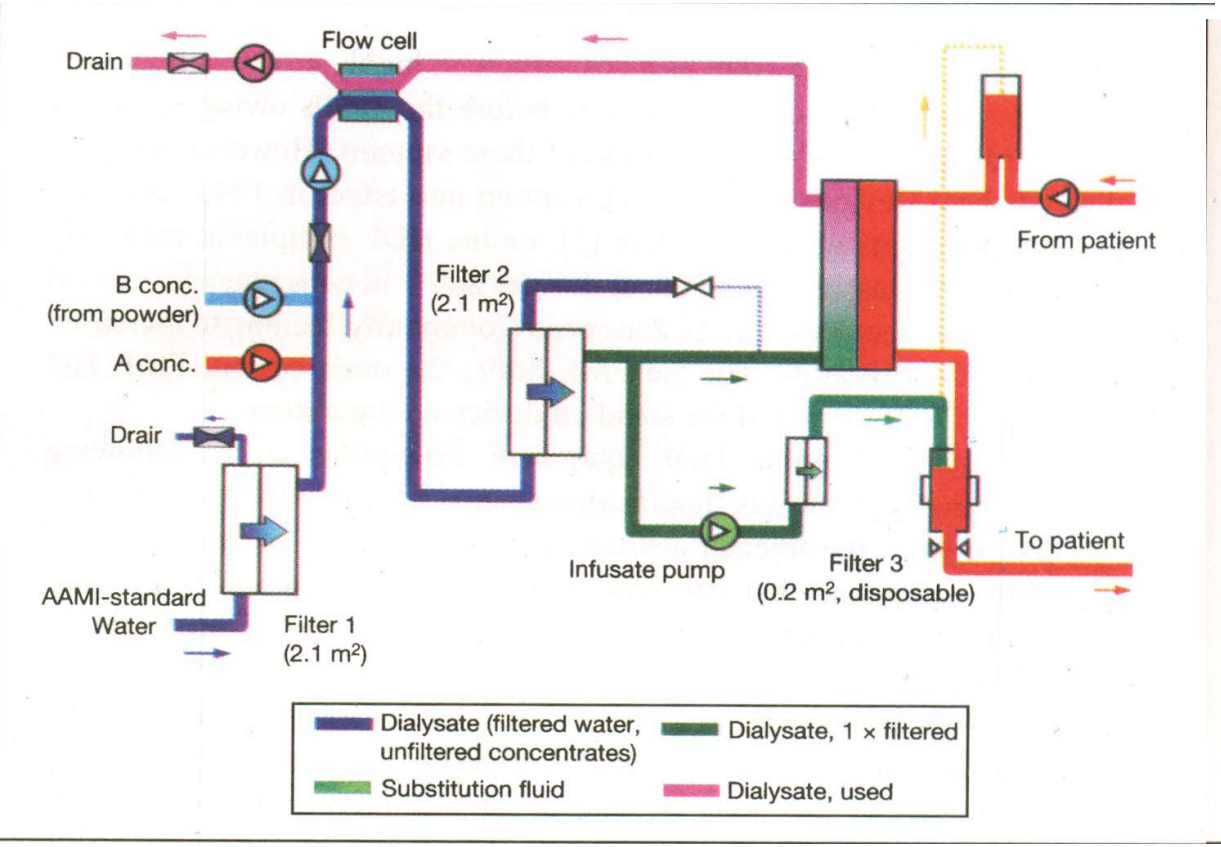
doi: 10.1681/ASN.2018100990

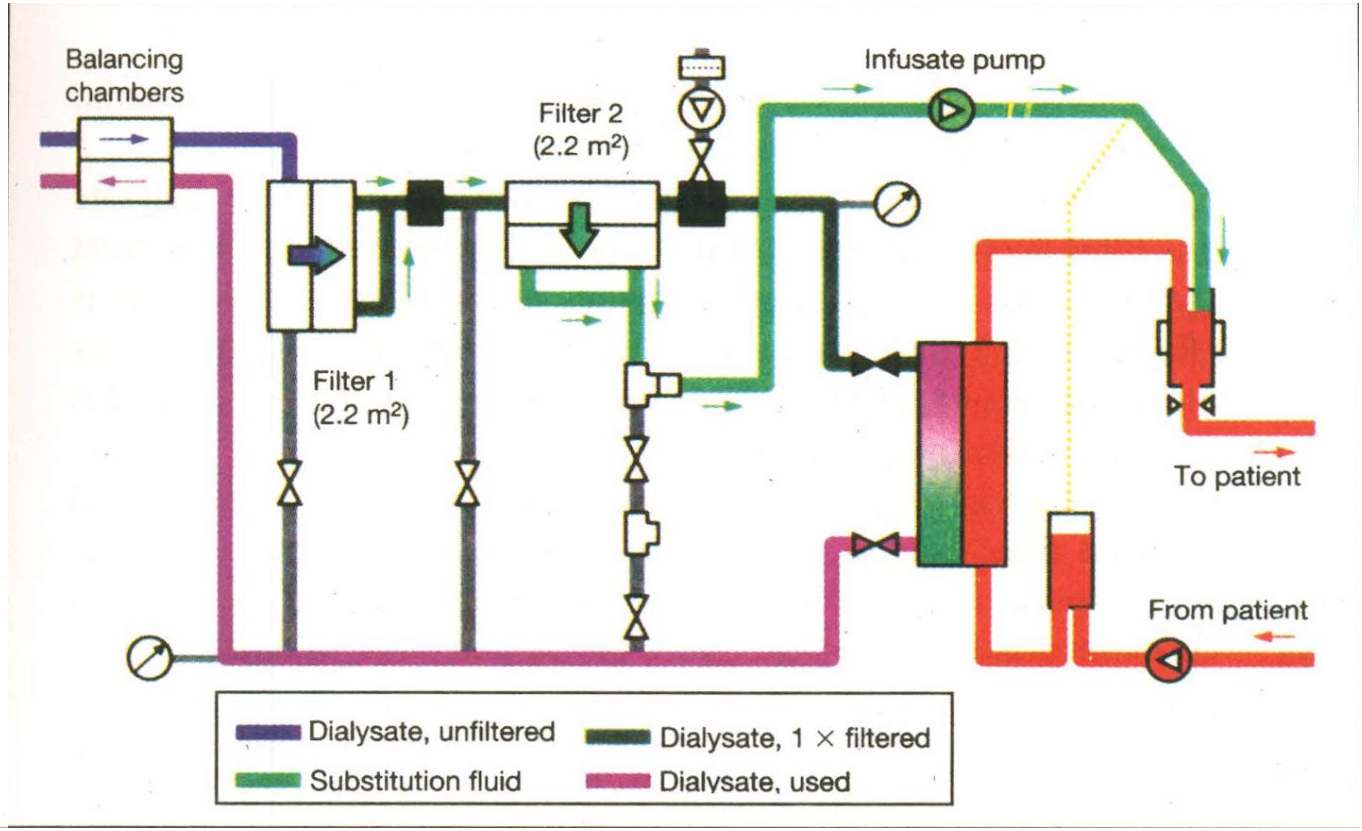
JASN

Microbiological Purity Standards for Water, Dialysate & Infusate

	AAMI	ESBP - EDTA	Renal UK	CARI	JSDT
Water for Dialysis					
Bacteria CFU/ml	100	100	100	100	-
Endotoxin EU/ml	0.25	0.25	0.25	0.25	0.05
Standard Dialysate					
Bacteria CFU/ml	200	100	100	100	-
Endotoxin EU/ml	2	0.25	0.25	0.25	0.05
Ultrapure Dialysate					
Bacteria CFU/ml	**0.1**	**0.1**	**0**	**0.1**	**-**
Endotoxin EU/ml	**0.03**	**0.03**	**0.015**	**0.03**	**0.01**
HDF Infusate					
Bacteria CFU/ml	**10^{-6}**	**10^{-6}**	**0**	**10^{-6}**	**-**
Endotoxin EU/ml	**0.03**	**0.03**	**0.015**	**0.03**	**.01**

Hydraulics for Online Hemodiafiltration

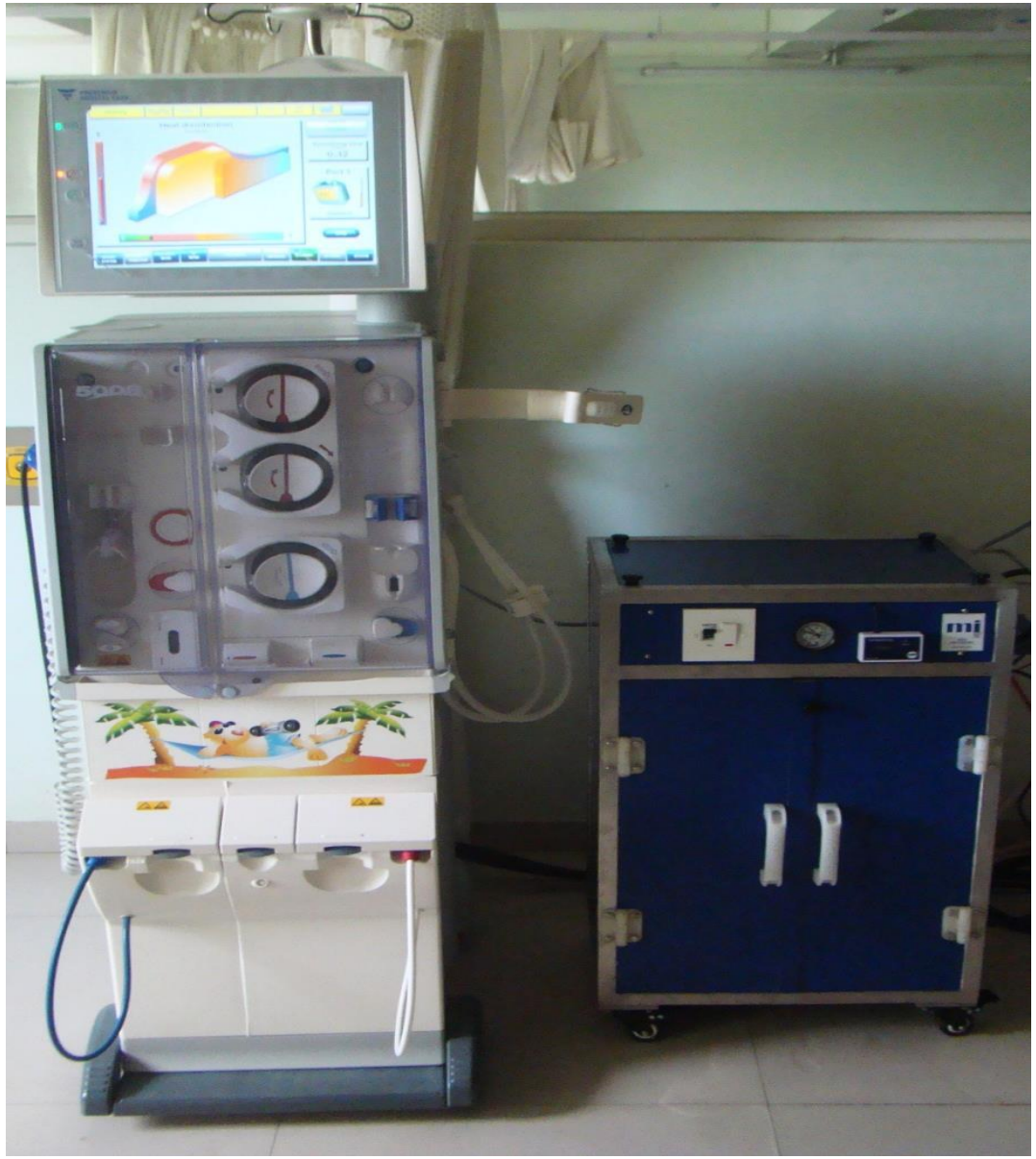




Gambro AK Series

Fresenius 5008/ArrT plus

Portable reverse Osmosis Systems



Can be used to “polish” water already treated by a regular system

Indications for HD for pediatric CKD patients

- (1) peritoneal dialysis is impossible due to abdominal conditions
- omphalocele or gastroschisis,
- bladder exstrophy,
- diaphragmatic hernia,
- peritoneal membrane failure,
- previous abdominal surgery;
- (2) presence of diseases requiring HD, such as primary hyperoxaluria and inborn error of metabolism;
- (3) a short waiting period for a kidney transplant; and
- (4) lack of an appropriate caregiver.

Issues with Pediatric Hemodialysis

- 11 to 37% of children initiating maintenance hemodialysis (HD) weigh < 20kg, 4 to 14% between 10 and 15 kg and 2 to 9% < 10kg.
- Dialysis units with pediatric designation < 0.1% of the total number of dialysis facilities in the United States.
- Approximately 11 children per pediatric dialysis unit, only about half the American children receive care at a pediatric center.
- Rest receiving dialysis services at an adult facility.
- In some regions, more children (upto 80%) are dialyzed in adult facilities than in pediatric facilities.
- Dialysis units where team members lack specific pediatric training but nonetheless must care for children with ESRD,
- Ready access to consultative colleagues in their disciplines both trained to care for children and intimately aware of current standards of pediatric dialysis care is imperative.
- Most children accompanied by a parent or other adult caregiver who may remain with the child throughout the dialysis treatment,
- Involvement in care maneuvers and procedures also increases nursing responsibilities.

Special Considerations in Pediatric Hemodialysis

- Expertise in the growth and developmental abnormalities associated CKD, and formal consultation should be considered in addressing treatment adequacy or proposing alternate therapies.
- Interdisciplinary dialysis team must involve the family as an integral component of care planning
- *Unlike adults on dialysis therapy, most children have little autonomy to implement prescribed care routines that occur outside the dialysis unit.*
- Small fluctuations in volume status and weight may be clinically more significant in children, and expected growth rates in any child with ESRD on dialysis therapy must be taken into account when setting dry weight targets or assessing interval anthropometric data.
- Frequency of feeding difficulties and failure to thrive in children with ESRD necessitating the use of nasogastric or gastrostomy tubes
- Effect of ESRD on acid-base balance, bone and mineral metabolism, and normal growth

Technical requirements for Pediatric Dialysis

- Guidelines establish minimal physical space requirements for dialysis stations, based on equipment needs
- 100 to110 square feet) per machine to enable convenient movement of equipment and personnel
- For children, the necessary physical space often must be larger as many children are accompanied to dialysis by an adult.
- Waiting areas need to be configured and designed to take into consideration, accompanying siblings.
- Water supply meeting all regulatory specifications is critical for any HD unit. (Ultrapure required for HDF)
- Relative cost of technical services in proportion to the number of stations is higher in pediatric units than in the typical adult dialysis unit.
- Wider variety of supplies must be readily available to create a safe extracorporeal dialysis circuit, although items may be used infrequently.

Given high manufacturing costs and limited demand, not uncommon for manufacturers to discontinue products, forcing dialysis units to stock a larger inventory of supplies, some of which may never be used before expiry.

Technical requirements for Pediatric Dialysis

Machine	Approved Use
None	< 10 kg body weight
Fresenius 6008 for HDF	> 10 kg
Fresenius 4008, Baxter Phoenix X 36	> 15 kg
Nikkiso–DBB-EXA	> 20 kg
Gambro's Artis Physio	> 25 kg
B. Braun Dialogue Q & Nipro Surdial X	> 30 kg

- Ultrafiltration accuracy of many dialysis machines, varies from 20 to 50 ml per hour depending on the machine and dialysis modality (±1% of ultrafiltration ± 0.1% of dialysate flow).
- Smaller blood volume in young children necessitates both low-volume tubing systems and dialyzers,
- Safe and tolerable extracorporeal blood volume in an individual <8 ml/kg body weight, corresponding to 10% of the total blood Volume
- Dedicated paediatric sets with low blood volumes not easily available.
- Children often treated "off-label" using medical devices and consumables that lack data on pediatric safety and efficacy.
- Most currently available blood tubing sets contain relatively large extracorporeal volume due to the larger tubing pump segment of the machine.

Nursing Staff for Pediatric Hemodialysis

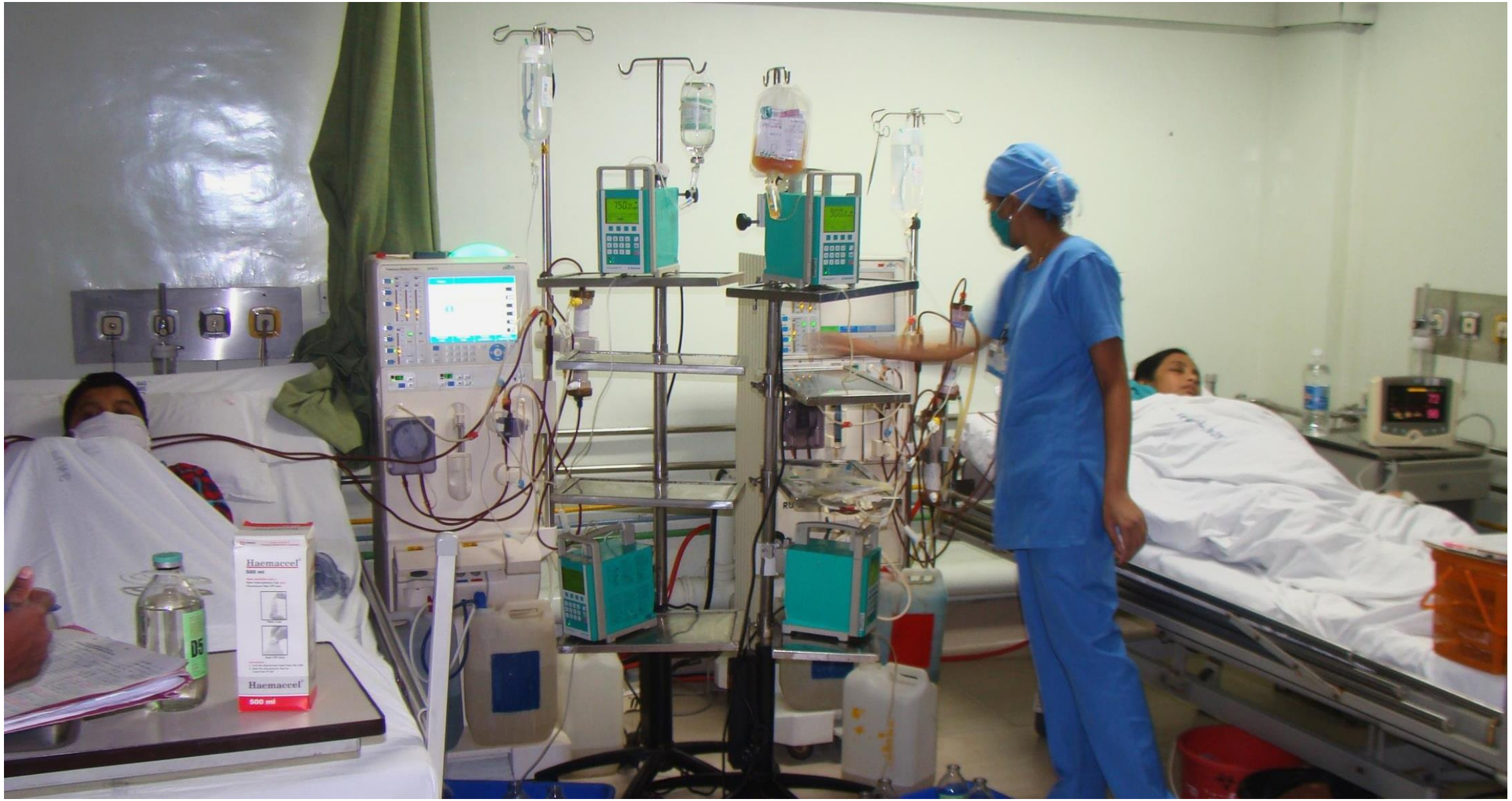
- In a facility dialyzing children, all dialysis nurses must have appropriate training for pediatric dialysis care.
- Even experienced adult dialysis nurses, require a substantial initial period of training and supervision to deliver pediatric dialysis care independently.
- Facilities that only occasionally dialyze children, coordinating visits at a pediatric unit useful to refresh local practices, policies, and procedures when a child is to be dialyzed.
- Infants and toddlers may require more frequent dialysis than thrice weekly, often with shorter treatment times.
- Hemodynamic differences with HD of infants and small children need a higher nurse to patient ratio.
- Provision of HD for young children or those with significant neurocognitive deficits often requires 1:1 care and, in the case of infants, even 2:1 care.
- Older children and adolescents who are developmentally intact and clinically stable, nurse to patient ratios of 1:2.
- All children in isolation receiving HD must be assigned 1:1 nursing.
- Children may not be able to recognize or verbalize symptoms associated with adverse dialysis-related events, such as excessive ultrafiltration.
- Hence, pediatric dialysis nursing care includes increased frequency of vital sign measurements coupled with careful visual observations and repeated clinical assessment

Personnel – Nursing and Technicians

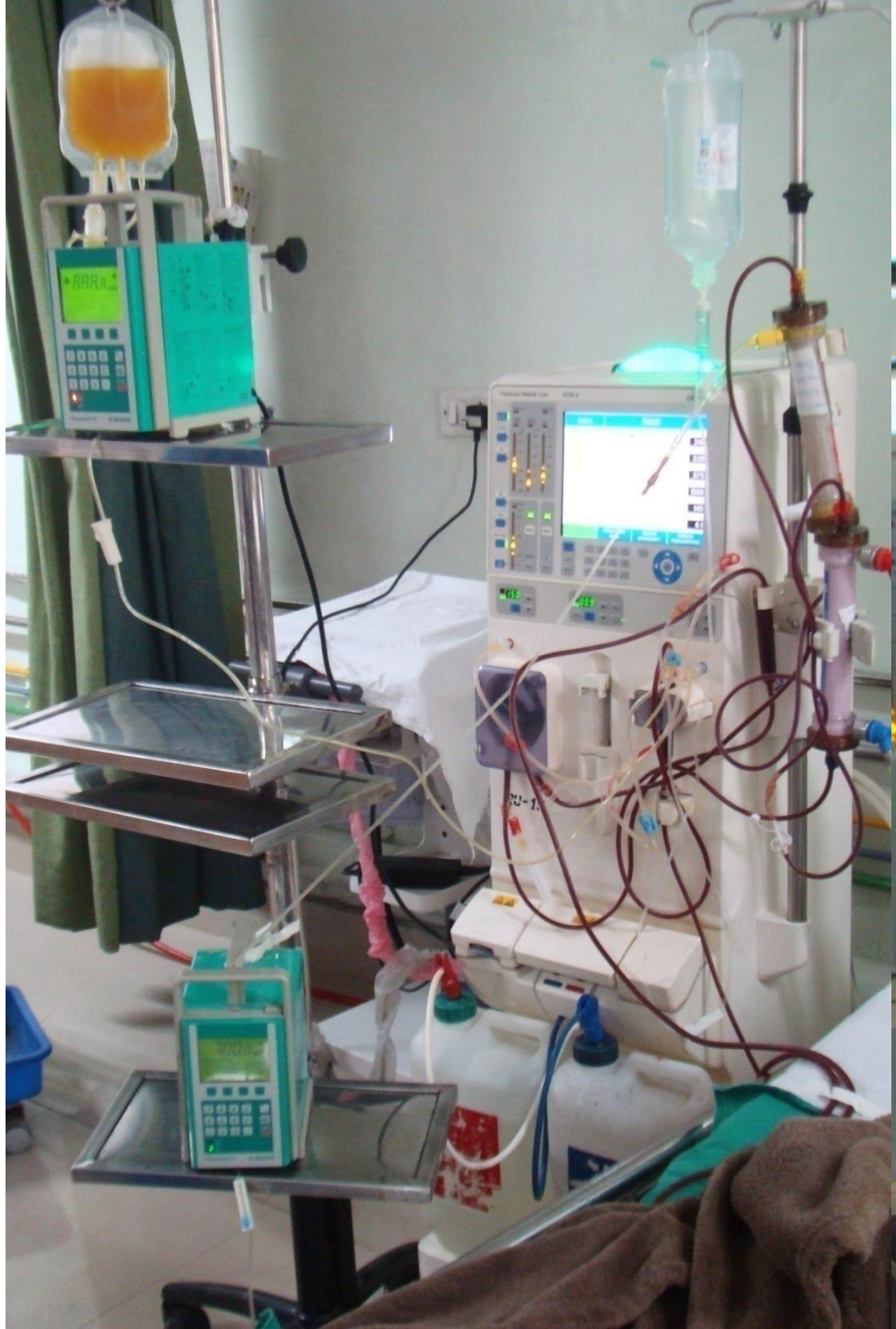
- Hospital-based pediatric dialysis units not only provide urgent and maintenance HD and PD , but also continuous renal replacement therapy and apheresis services.
- Nurse staffing models must consider these additional demands, their fluctuating frequency, and train a nurse to be independent in providing these services to children of all ages without compromising staffing needs in the long-term outpatient dialysis unit.
- In an inpatient setting, cross training with other skilled nurses may help with the provision of certain dialysis-related nursing services.

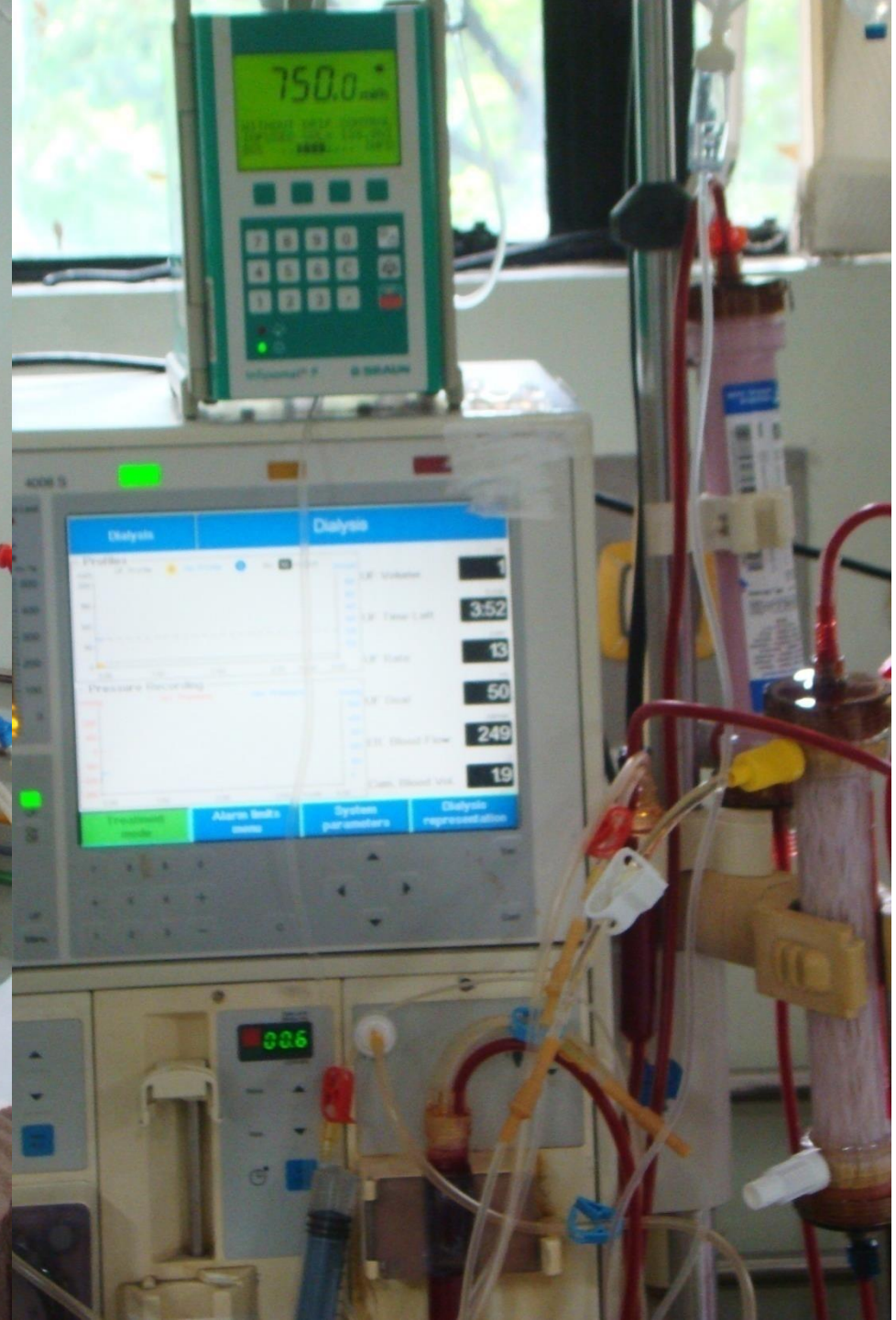
- Role of the dialysis technician much more restricted because children receiving dialysis through central venous catheters (CVCs) require locking with heparin for dialysis access patency,.
- In some pediatric units, under the direct supervision of a dialysis nurse, technicians may access fistulas in older children.
- Within the pediatric dialysis unit, technicians often assist with setting up and taking down machines, obtaining vital signs, and s as skilled adjuncts to nursing staff.
- Assist with equipment maintenance and documentation of water quality and safety.

Plasma Exchange using Conventional HD Machines



Multiple treatments can be run simultaneously without increased staffing




750.0
Dialysis
Dialysis
3:52
13
50
249
19

Role of the Social Worker

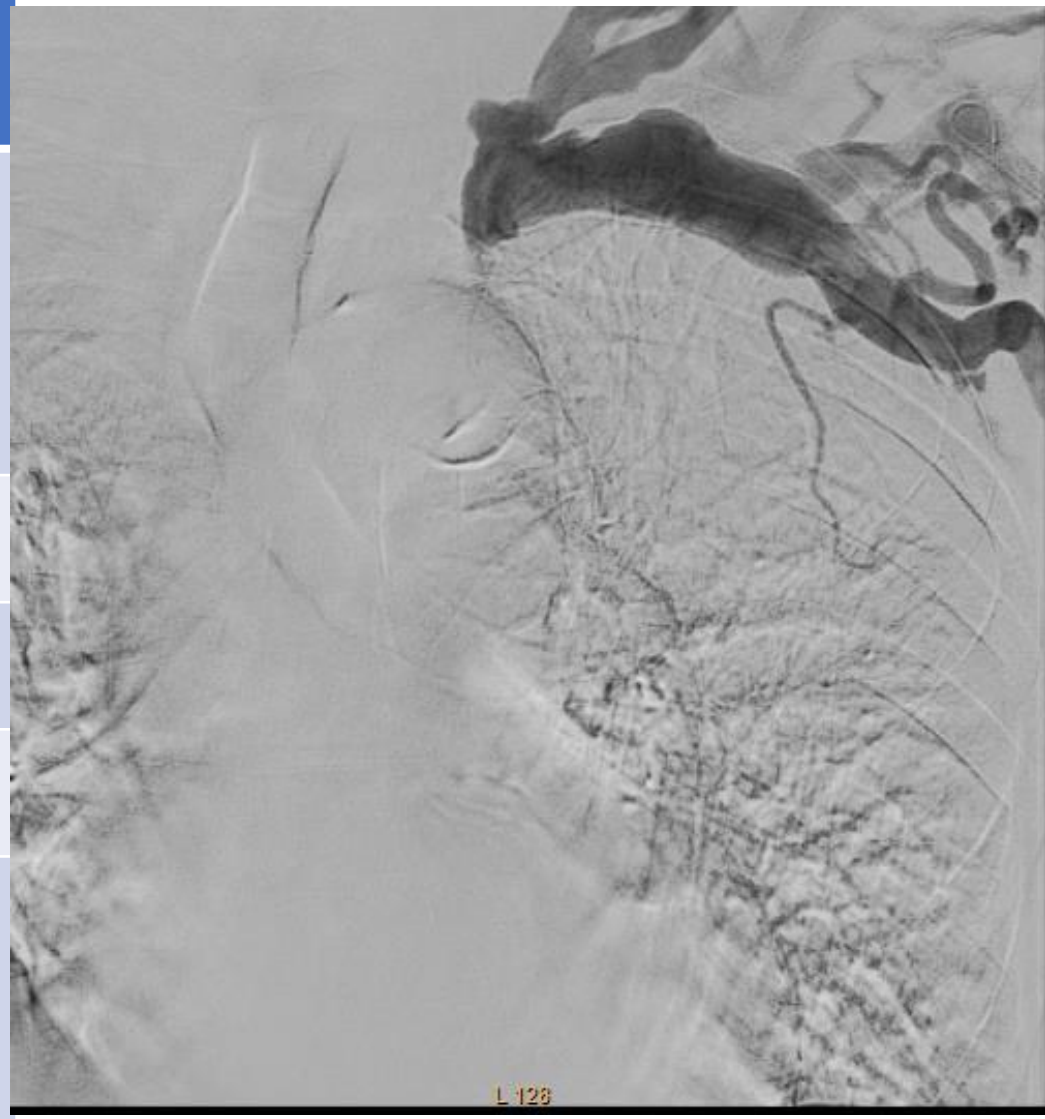
- Needs to possess in-depth knowledge of available local, regional, state, and national resources for the child and family
- Liaises for educational resources with the local school system to implement an individualized educational program
- Offers effective counseling to both adult caregivers and the child.
- Child life specialists assume an important role in devising strategies to help children on dialysis therapy cope with the challenges of treatments and their chronic illness.
- Focus on the needs of the child and the family without the need to attend to technical or logistical concerns of the dialysis treatment

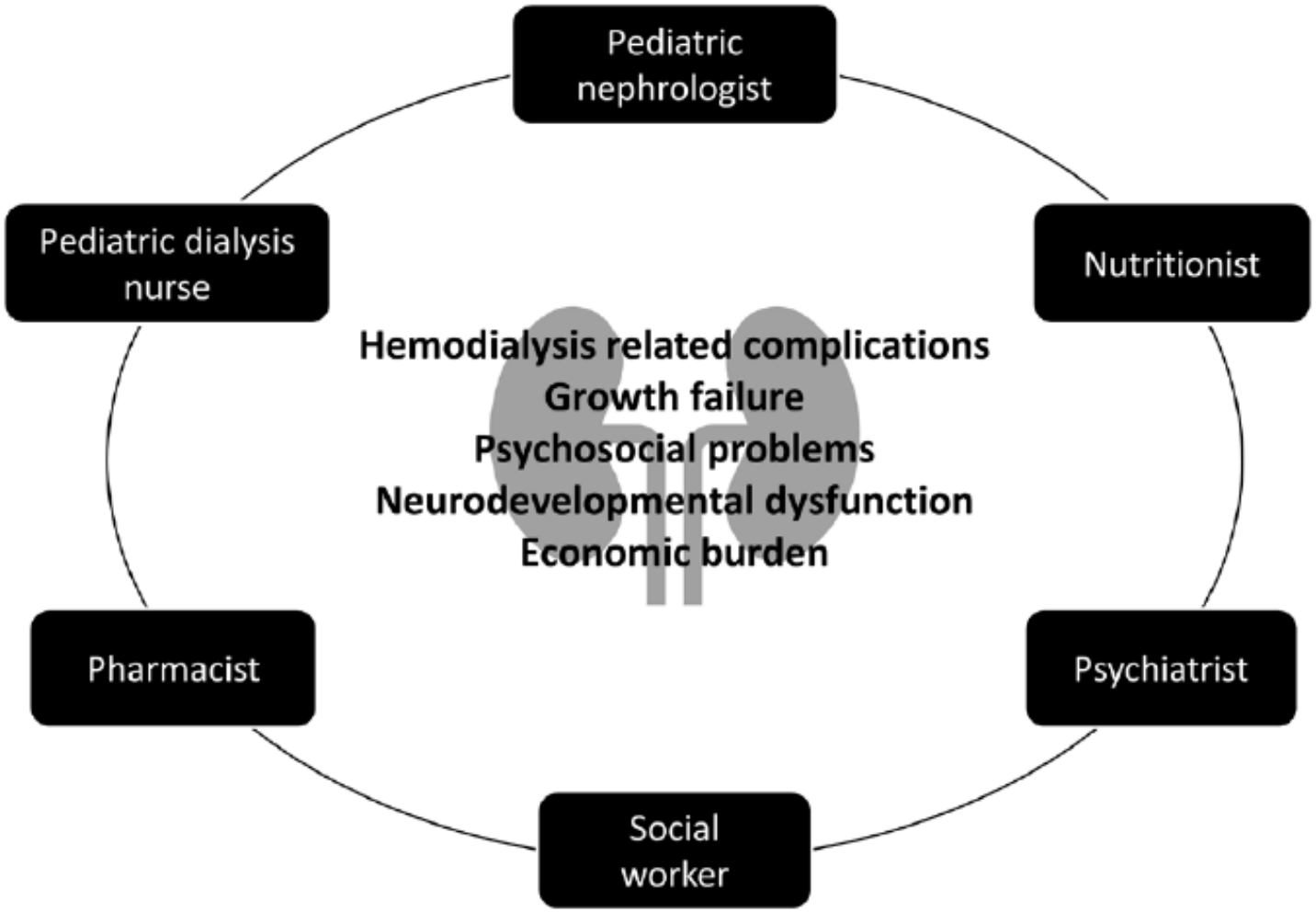
Vascular Access in Children

- Minimizing catheter use with a “catheter last” philosophy should be a priority.
- Should include discussion about preemptive transplantation, PD in suitable candidates, or placement of permanent HD access at CKD stage 4 with a goal of catheter avoidance.
- Catheter avoidance strategy mitigates the risk for vascular injury.
- Preservation of forearm and upper-arm vessels by minimizing venipuncture and avoidance of peripherally inserted central catheters should be implemented in early CKD.
- Access reassessment should occur frequently in patients with a CVC, and a permanent access should be created as soon as medically possible.
- Expertise in the creation of internal access in children may come from vascular surgeons, pediatric transplantation surgeons, pediatric general surgeons, or even plastic surgeons,
- Use of the operating microscope useful in children with small blood vessels.
- In small children, if a CVC may be necessary; should always be replaced by a permanent access at the earliest.
- For children older than 10 years weighing > 20 kg, arteriovenous fistulas or arteriovenous grafts are preferred for HD therapy beyond a few months
- Permanent vascular access use results in fewer access related infections, fewer episodes of vascular stenosis, fewer access-related procedures, more normalized parathyroid hormone values, improved electrolyte control, and better anemia management compared with children using a CVC

Vascular Access in Children – Availability & Complications

Childs Weight	Length for IJV	Diameter
< 10 kg	No tunnelled catheters available and limited temporary options, usually 8 cm.	6.5 to 7 F,
11 – 20 kg	15 cm	8 F
21 – 30 kg	15 cm	10F
>30 kg	15 cm	11.5 – 12 F
> 40 kg	19 cm	Adult size (14.5 F) Confirm diameter of vein





Pediatric Dialysis Interdisciplinary Team Members

Required

- Nephrologist
- Dialysis nurse
- Renal social worker
- Dietitian
- Patient
- Parent/guardian

Essential

- Child life specialist
- Schoolteacher
- Psychologist


RU-35
KEMH PUNE

Case 2

- 10 year old boy diagnosed with IgA nephropathy in 2021 on renal biopsy was lost to follow up for 2 years .
- Creatinine was 1.4 mg/dl
- Came to ER in 2023 with decreased urine output, swelling of feet for 1 month and laboured breathing since 2 days.
- Ht = 124 cm, Wt = 23 kg, BSA = 0.94m^2, BP = 146/70, P = 102/min, RR = 27/min.
- Edema 4+ and pallor present
- Systemic examination:- Pericardial rub faintly heard on sitting up, few rales in chest, no organomegaly or free fluid on abdominal examination.
- Initial investigations:- Hb = 5.4 g/dl, TLC= 4800/mm^3, platelets 1.56 lacs.
- BUL = 278 mg/dl, creatinine = 13.2 mg/dl, Electrolytes – 129/5.5/108
- Venous bicarbonate = 9.3 mmol/L
- 2 D Echo screening- Concentric LVH, thin non tappable rim of pericardial effusion.
- Few B lines on lung fields.

- *What should be his dialysis prescription when initiating RRT ?*

Selecting A Dialyzer for HD

Parameter	Sureflux 5N (Nipro)	FX40 (Fresenius)	F4 (Fresenius)	Polyflux 6H (Gambro)	F4HPS	F40S
Surface Area (m^2)	0.5	0.6	0.7	0.6	0.8	0.7
Priming Volume (ml)	34	32	32	52	51	42
Ultra filtration Coefficient	2.7	20	2.8	33	8	20
Urea Clearance	130*	170#	155	50§	170	165
Creatinine Clearance	109*	144#	128	50§	149	140
Phosphate Clearance	62*	138#	78	49§	123	138
Material	Cellulose triacetate	Helixone	Polysufone	Polyflux^	Polysulfone	Polysulfone
Blood flow (ml/min)	50 - 100	50 - 200	40 - 200	50 - 200	50 - 200	50 - 200
Sterilization	Gamma ray	Inline Steam	Inline Steam	Inline Steam	Inline Steam	Inline Steam
Fibre inner diameter (mic)	200	185	200		200	200
Fibre wall thickness (mic)	15	35	40		40	40

* At Qb = 200 ml/min # At Qb = 200 ml/min ! At Qb = 100 ml/min § At Qb = 50 ml/min ^ Polyflux is a blend of

Selecting A Dialyzer for HD

Parameter	FX 50	F 50S	F5 (Fresenius)	F5HPS
Surface Area (m^2)	1.0	1.0	1.0	1.0
Priming Volume (ml)	53	63	63	63
Ultra filtration Coefficient	33	30	4.0	10
Urea Clearance	189	178	170	179
Creatinine Clearance	170	160	149	162
Phosphate Clearance	165	158	103	155
Material	Helixone	Polysufone	Polysufone	Polysulfone
Blood flow (ml/min)	200 - 300	200 - 300	200 - 300	200 - 300
Sterilization	Inline Steam	Inline Steam	ETO	Inline Steam
Fibre inner diameter (mic)	185	200	200	200
Fibre wall thickness (mic)	35	40	40	40

* At Qb = 200 ml/min. # At Qb = 200 ml/min. ! At Qb = 100 ml/min § At Qb = 50 ml/min,

Case 2 cont'd

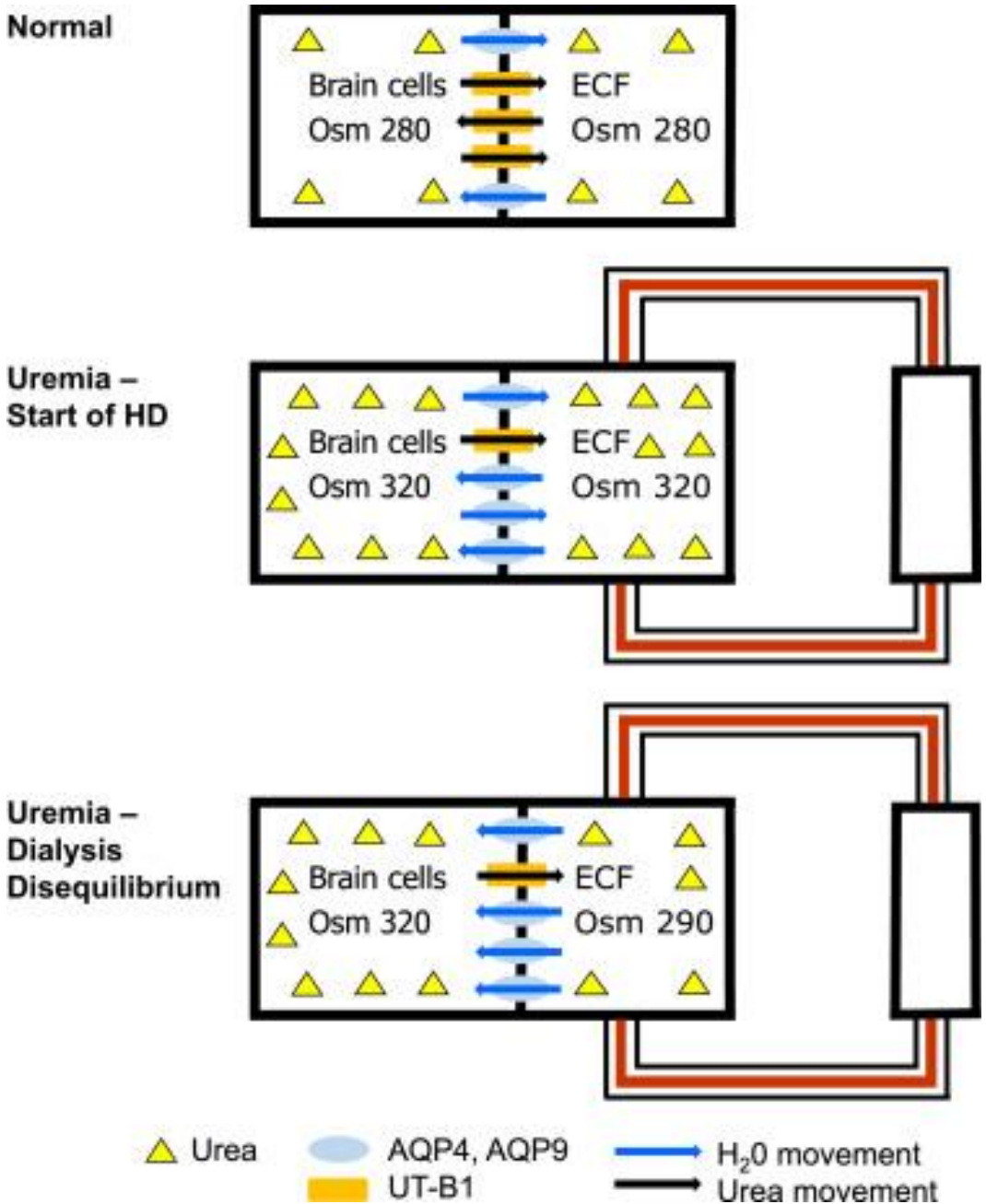
- Was taken for a 2 hours HD session from a left femoral 10F 2-lumened catheter. Blood flow = 150ml/min, Dialysate flow = 300 ml/min
- F4HPS dialyser used.
- No heparin used. No UF done
- Started feeling uneasy 15 minutes after HD was completed.
- Appeared restless and did not want to eat.
- Lab reports sent:- BUL = 124, creatinine = 7.1 mg/dl, Elec – 135/4.3/103 mmol/L, bicarb = 17.8 mmol/L
- Patient had a sudden seizure.

- *What is the possible cause?*
- *What is the treatment?*
- *How can such events be avoided?*

Dialysis Disequilibrium Syndrome

- Clinical manifestations include headache, nausea/vomiting, confusion, agitation, seizures, encephalopathy coma, and death.
- Spectrum ranges from headache and restlessness in mild forms to nausea, vomiting, and hypertension in patients with moderate cases to seizures and coma in patients with severe cases
- Typically seen in patients with significantly elevated blood urea nitrogen (BUN) undergoing their first dialysis treatment.
- No set BUN value above which patients predictably develop DDS.
- Both a high BUN level (>175 mg/dl) and its rapid decline are risk factors for DDS
- Other risk factors include extremes of age, metabolic acidosis, hypernatremia, liver disease, and pre-existing neurologic conditions.
- Incidence believed to have declined in recent decades
- Now very rare, although possibly underrecognized among patients who exhibit milder symptoms.

Dialysis Disequilibrium Syndrome



- **Reverse urea effect.**
- Water movement into brain cells leads to cerebral edema in dialysis disequilibrium syndrome.

- Decrease in brain urea transporters and an increase in aquaporins (AQPs; AQP4 and AQP9), providing a potential molecular mechanism for the reverse urea effect

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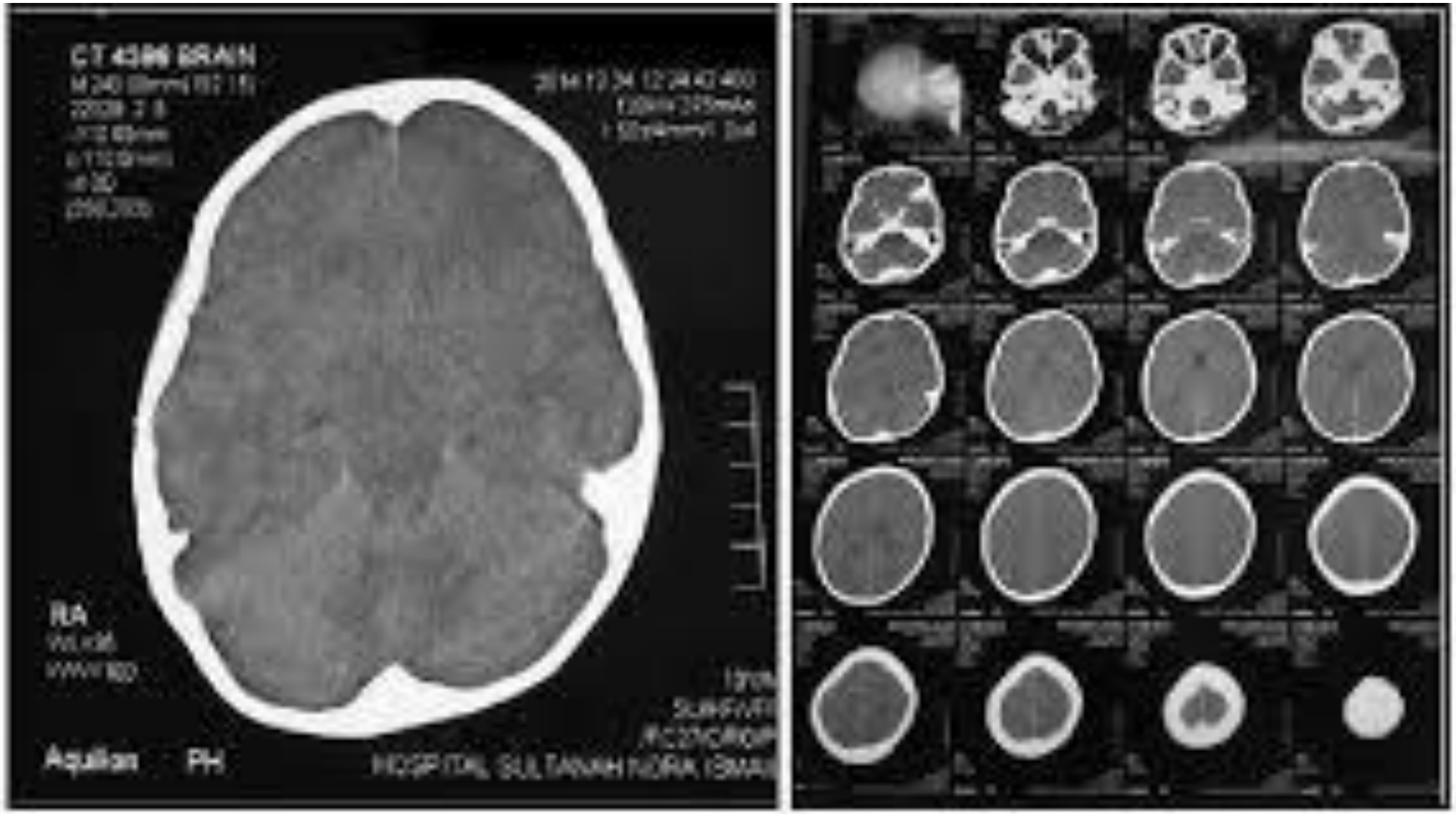
Dialysis Disequilibrium Syndrome

- Water movement into brain cells leads to cerebral edema in dialysis disequilibrium syndrome.
- Idiogenic osmoles (myoinosotol, glutamine, and taurine) and intracerebral acidosis also proposed as possible mechanisms.
- Paradoxical CNS acidosis
- Hydrogen ions may displace bound sodium and potassium ions, increasing osmolality.
- Rapid correction of acidosis may increase CNS uptake of opioids, causing changes in mental status in severely acidemic patients initiating HD
- Despite slower rate of urea reduction during CRRT, DDS can develop if the decreases in BUN and serum Osmolality are of sufficient magnitude to induce fluid shifts in the brain.
- Can occur even in severe acute kidney injury (AKI).
- **DDS can occur even when the reduction in BUN is modest if there is another electrolyte (e.g. sodium) contributing to the hyperosmolar state.**

- Clin J Am Soc Nephrol. 2017 Feb 7; 12(2): 357–369.

Dialysis Disequilibrium Syndrome



ebral oedema with obliterated basal cisterns, loss of grey-white differentiation and glob

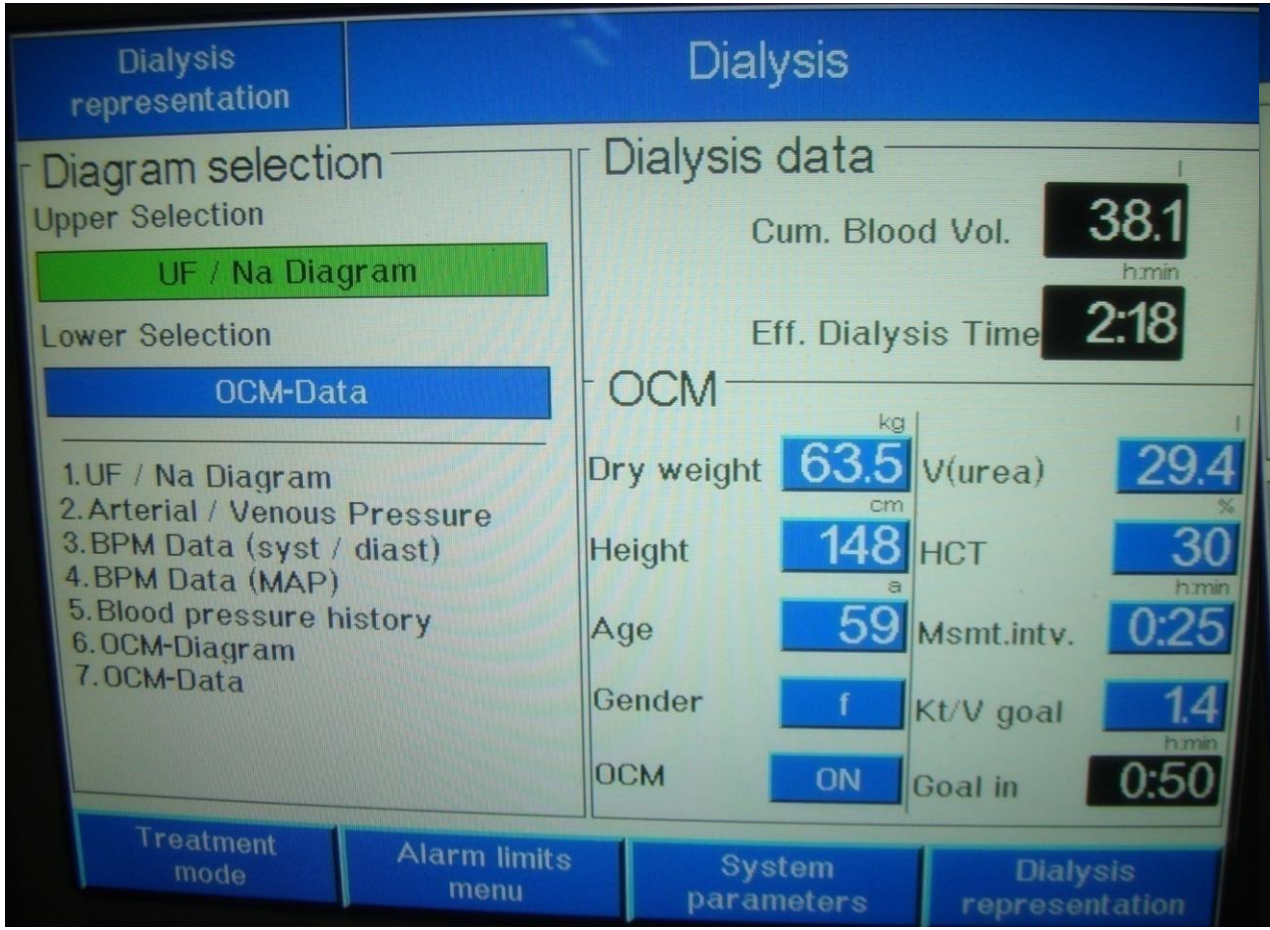
Cerebral edema seen on computed tomography (CT) and magnetic resonance imaging (MRI).

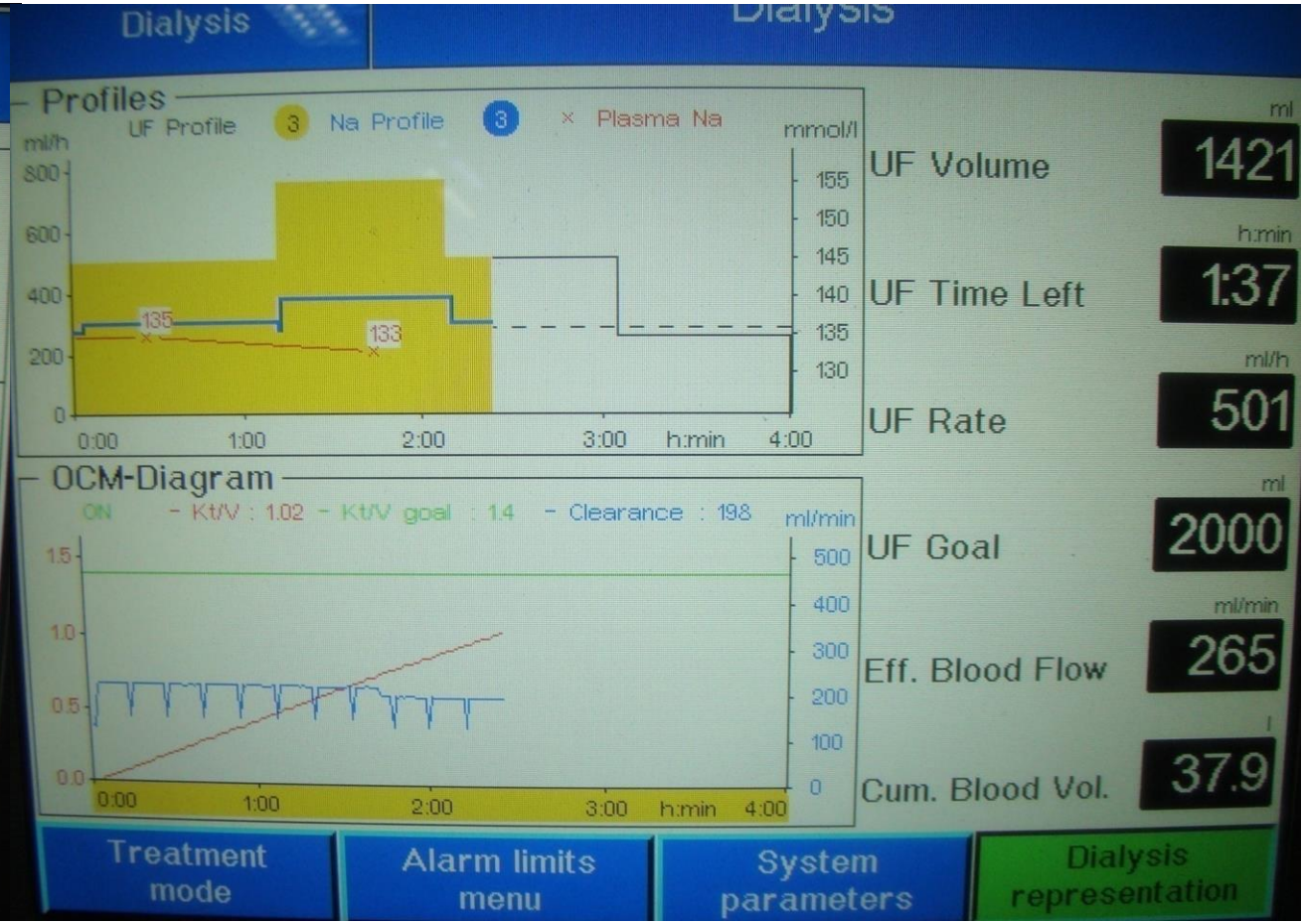
Treatment of DDS

- If symptoms of DDS develop during dialysis, the treatment should be stopped.
- Mild symptoms managed supportively.
- For severe cases measures to reduce intracranial pressure .
- Administration of hypertonic saline or mannitol and hyperventilation have been used.
- Initiating HD using a low blood flow of 200 mL/min over 2 hours or even less is recommended.

- **Use of formal UKM.**
- $Ct = Coe^{-Kt/V}$
- For a 30% reduction $Ct = 0.7*Co$ Or $Ct/Co = 0.7 = e^{-Kt/V}$
- So $Ln\ 0.7 = -Kt/V*Ln\ e$ and as $Lne = 1$
- $-0.356 = -kt/V$ Or $Kt/V = 0.356$.
- For this 24 kg patient V = 16L, using a F4HPS dialyzer at Qb = 150 ml/min and Qd = 300 ml/min, K = 100 ml/min
- Substituting in the equation above t = 0.356 X V/K = 59.96 minutes
- If we reduce Qb to 100 ml/min and Qd to 300 ml/min K = 75 ml/min and t increases to 76 minutes.

Use of the Online Clearance Monitor





Setting a Target URR and Kt/V

Monitoring

Prevention of DDS

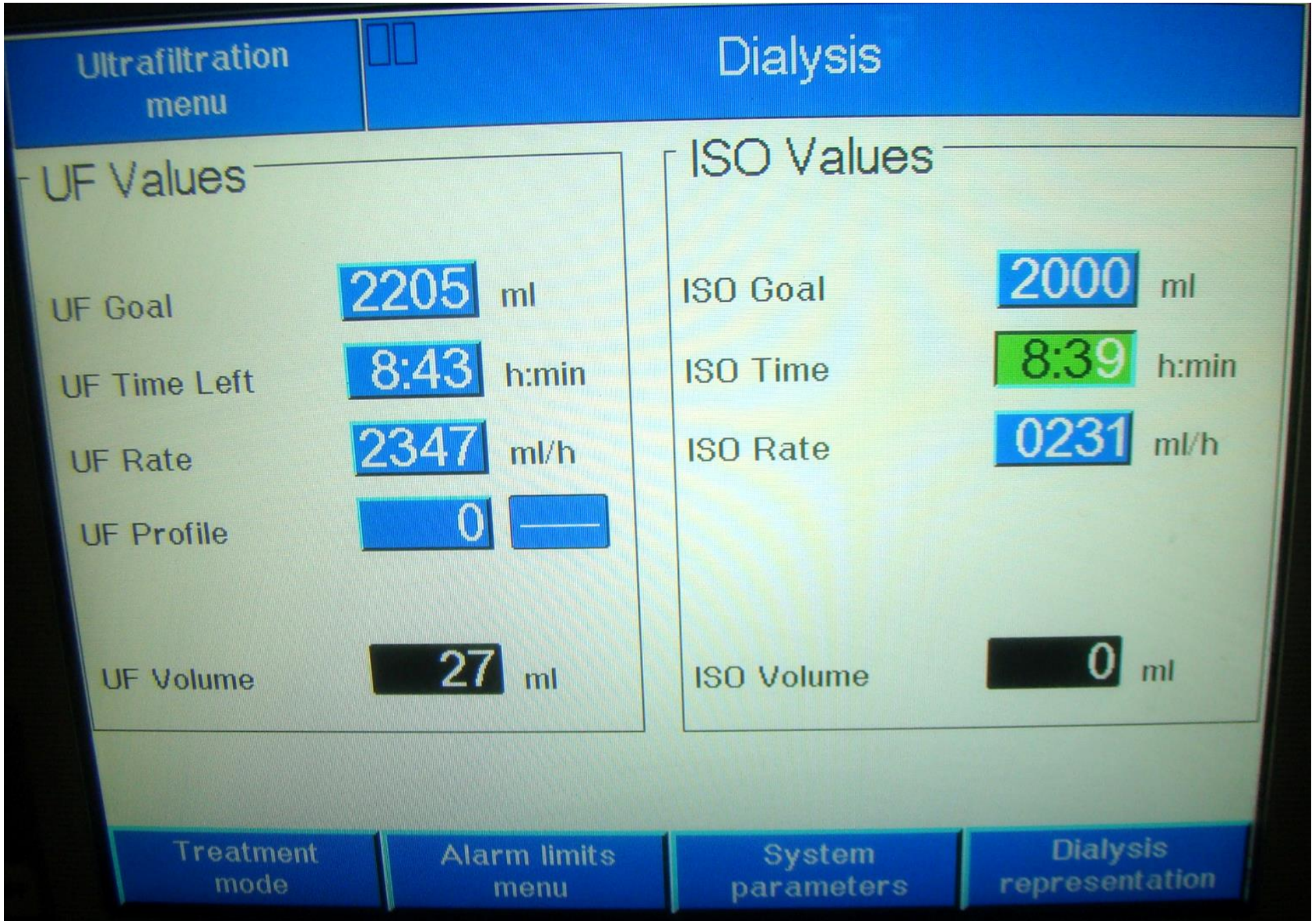
- Using a lower blood flow in patients with very elevated SUN is recommended.
- In patients with very high BUN, slower reduction using CKRT should be considered.
- KDIGO recommends CRRT over intermittent dialysis for AKI in patients with brain injury/edema or elevated intracranial pressure
- In a patient with coexisting hypernatremia, correction of BUN and serum sodium must be more gradual, limiting reduction in serum osmolality to <24 mmol/kg (24 mOsm/kg) in 24 h.
- In a patient with normal serum sodium, BUN should, therefore, not be decreased by >24 mmol/L (67 mg/dL) in 24 h.
- This equates to a URR of 30% in 24 h.
- Higher the BUN, the lower the goal URR should be, to limit the absolute drop in osmolality to <24 mmol/kg (24 mOsm/kg) in 24 h.
- Another approach is to increase the osmolality in the blood or dialysate to reduce the degree of change in osmolality with dialysis.
- Use of a higher sodium dialysate (144–154 mmol/L) has been reported to prevent symptoms of DDS.
- Each 1-mmol/L increase in serum sodium offset the osmotic effect of 12 mg/dl BUN.
- Thus, sodium modeling may be useful in preventing DDS during the initial HD sessions in patients at risk
- Other agents that have been used include mannitol, glucose, glycerol, and urea.
- Increasing the dialysate glucose concentration to 450 mg/dl contributed 2–3 mosM/kg H_2O, whereas intravenous mannitol (1 g/kg) added 8.5–10 mosM/kg H_2O

Case 2 cont'd

- The patients formal UKM suggests that one hour of HD should have been enough as initial RRT.
- He was given a mannitol infusion and a single dose of Levaricetam and gradually improved over 24 hours.
- His second dialysis session was 1 ½ hours long, the third 2 ½ hours and were tolerated well.

- *What if the patient had Pulmonary edema at admission and needed either high flow oxygen or NIV?*
- *How would the prescription for the first dialysis differ ?*
- *What would be changed?*

ISO - UF on a conventional Dialysis Machine (4008S)



Case 3

- An 8 year old boy CKD -5D secondary to P-U valves initiated CAPD in 2019,
- 6months later had to switch to HD following a non resolving peritonitis.
- Rt temporary IJV 2LC initially used, converted to TCC in September 2019.
- In Feb 2020 had CRBSI with suspicion of IE and MRSA on blood culture, so catheter was removed and 2 weeks of dialysis done through Lt femoral temporary catheter .
- Received Vancomycin and gentamicin,
- After 2 negative cultures Lt TCC was inserted, 8F 19 cm long catheter.
- A-V fistula not possible as artery and vein in both UL were too small
- (Patients height was 118 cm , weight = 19.5 kg)
- Catheter gave a blood flow of 200 ml/min, Kt/V was > 1.4 always.
- Fathers donor workup put on hold because of Covid – 19.

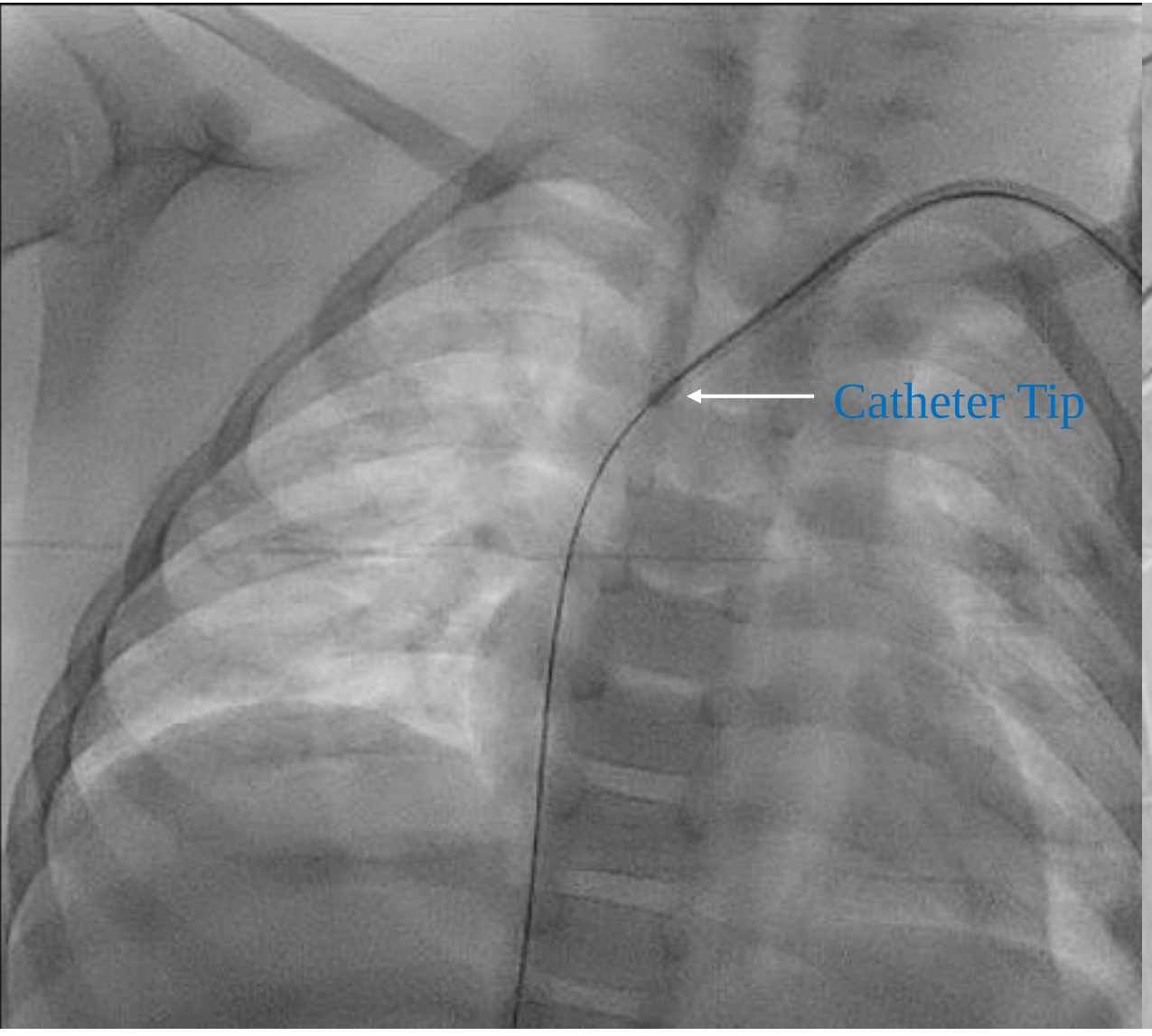
Case 3 cont'd

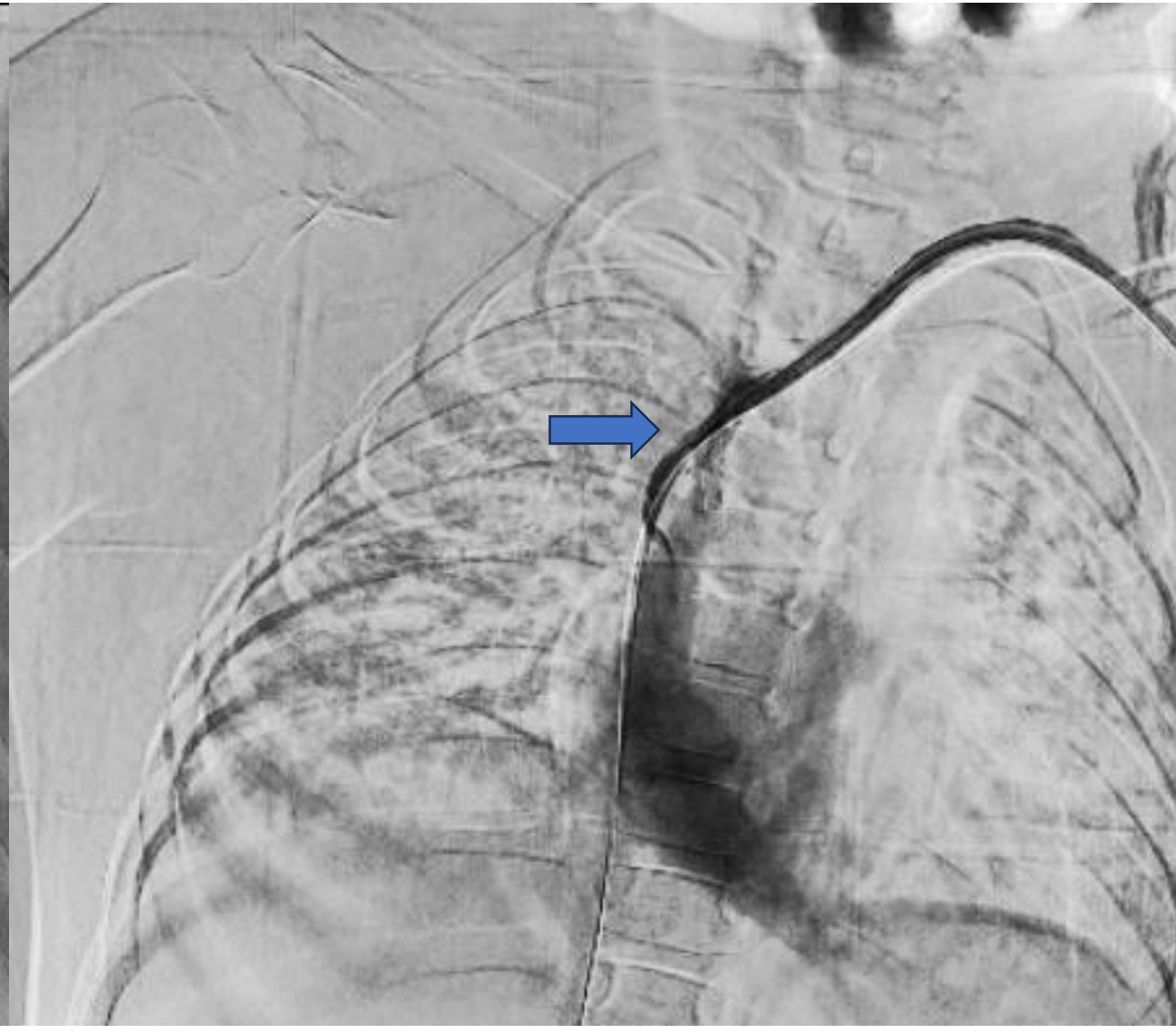
- In March 2021, had another episode of CRBSI, resolved with systemic antibiotics and antibiotic catheter lock.
- Following this episode had decreased blood flow between 130 to 160 ml/min. (Nurses frequently interchanged bloodlines and lumens)
- In April 2021, no flow from the catheter – Urokinase 5000 units instilled in each lumen flow obtained from blue port so dialysis started at 120 to 125 ml/min.
- One more such episode so catheter was locked with Urokinase.
- On 18th May 2021, no flow from both catheter lumens, no improvement with Urokinase.
- Easy passage of saline if injected, but no blood could be aspirated.

- *What is the likely cause?*
- *What are the treatment options?*

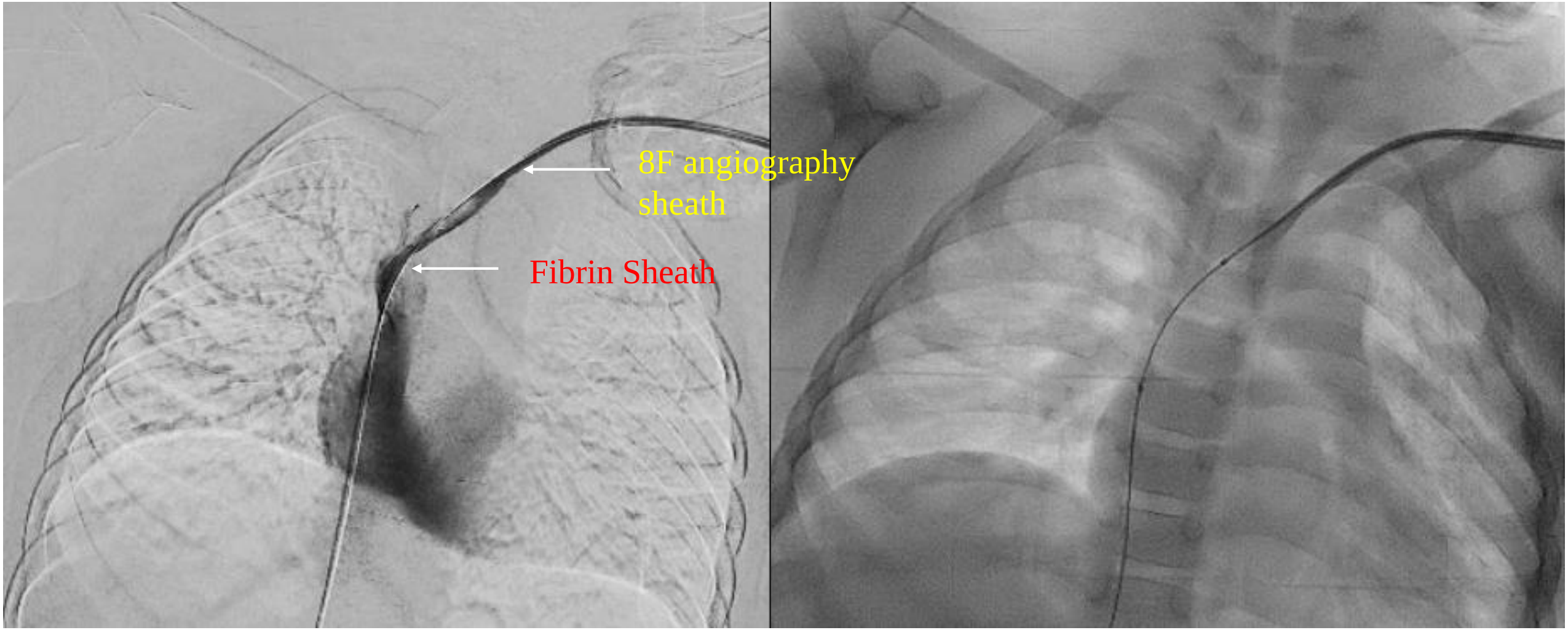
Lt IJV TCC

Catheterogram



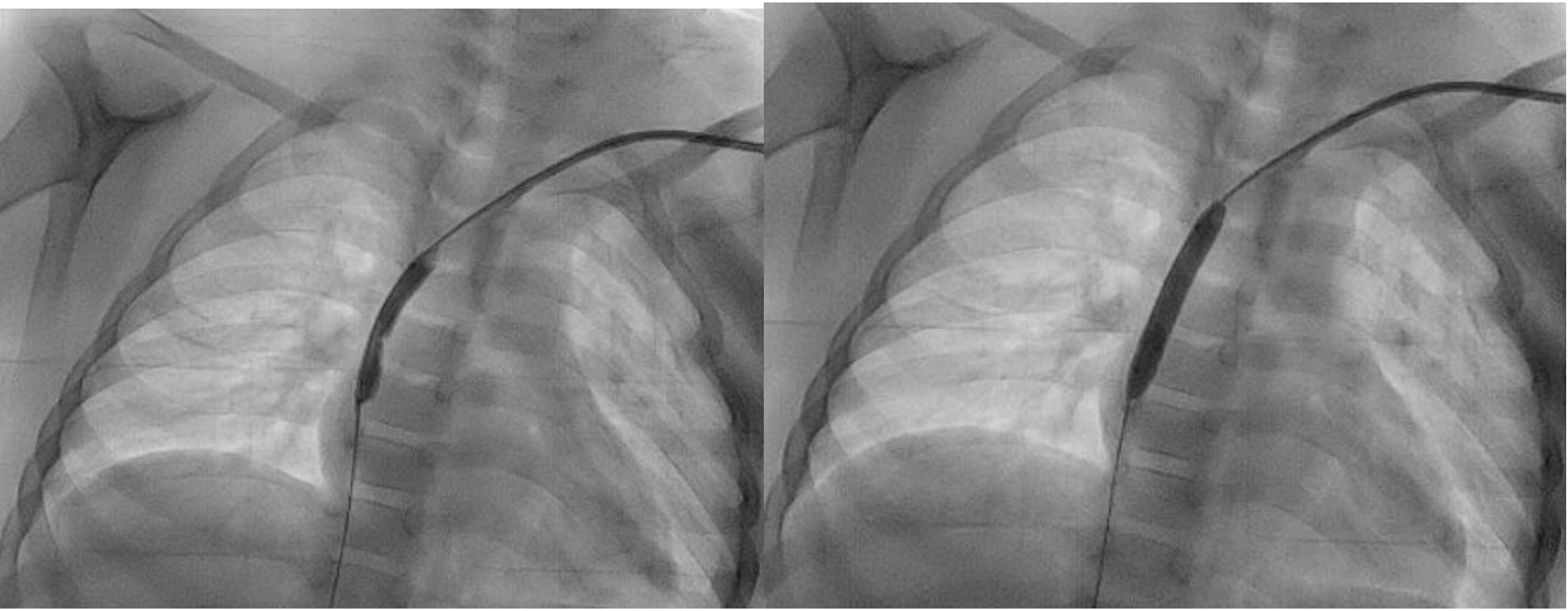


Fibrin Sheath with Ball Valve like Effect

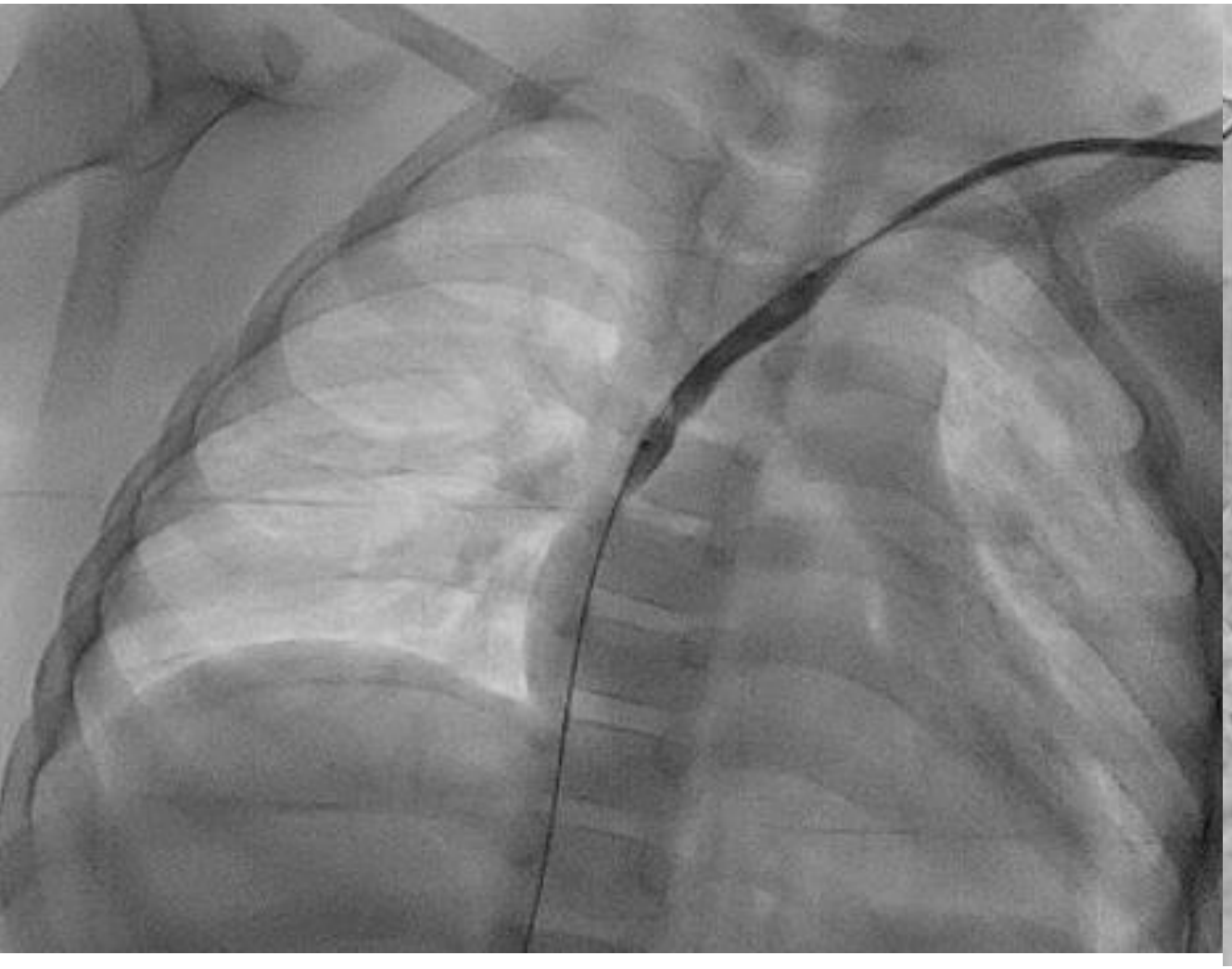


What is the treatment?

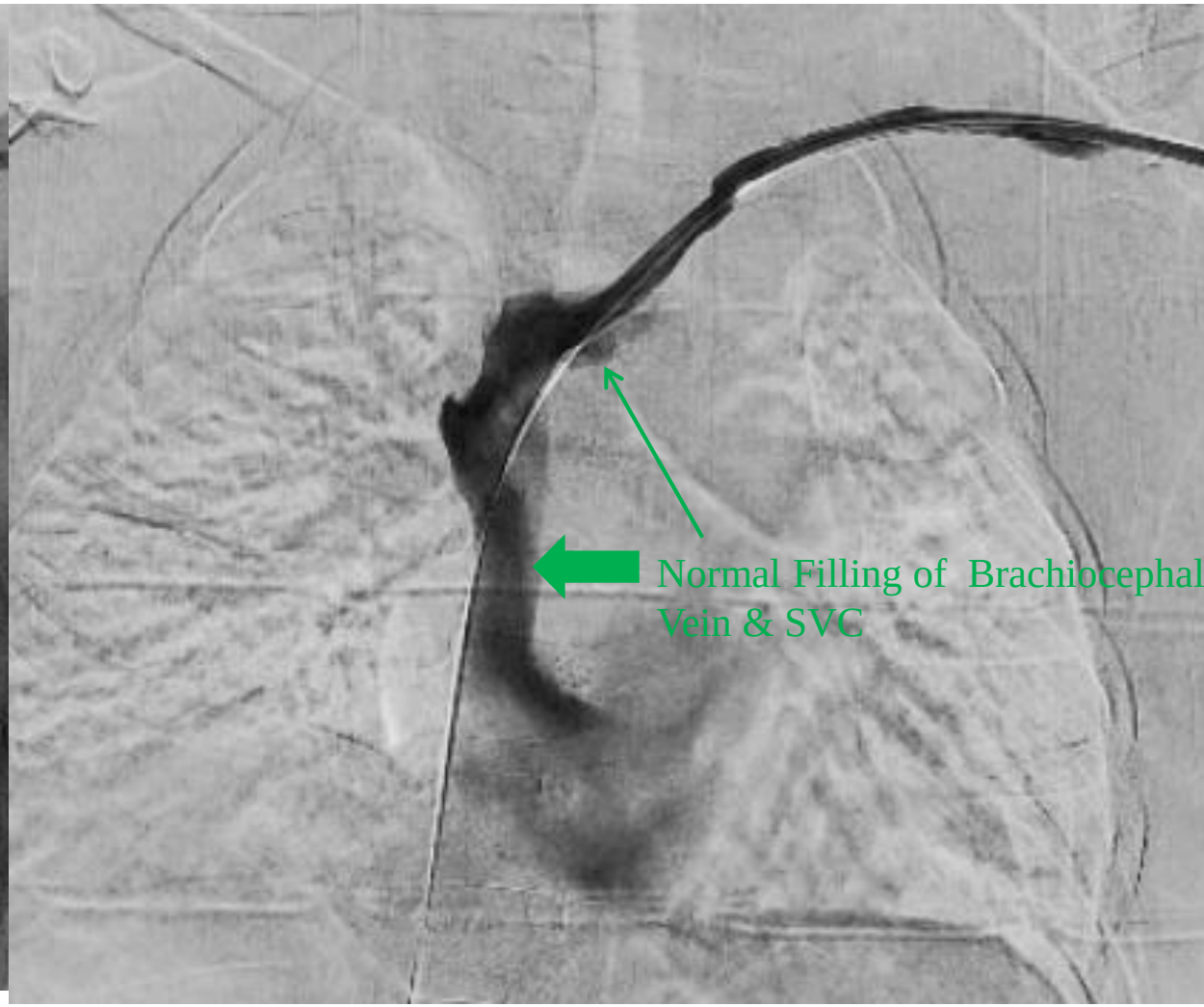
Angioplasty Balloon Rupture of Fibrin Sheath



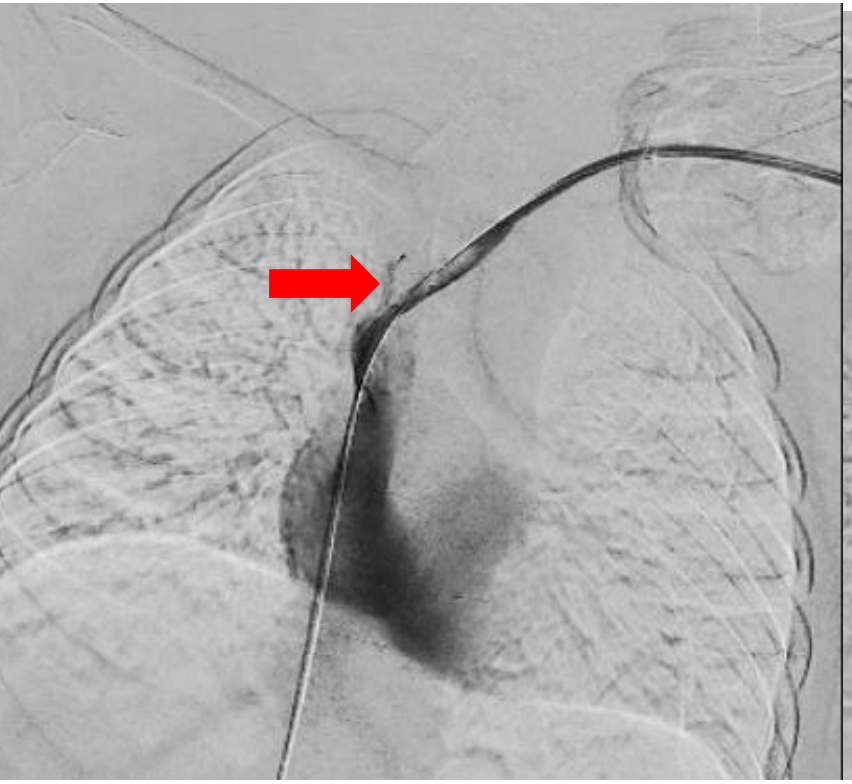
Balloon Rupture of Fibrin Sheath

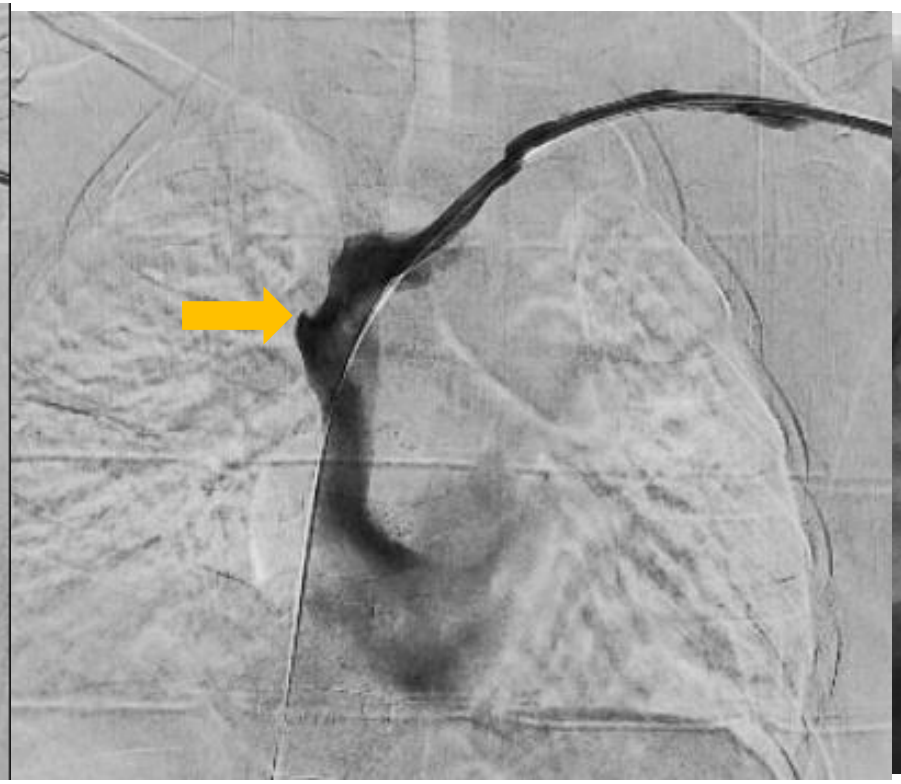


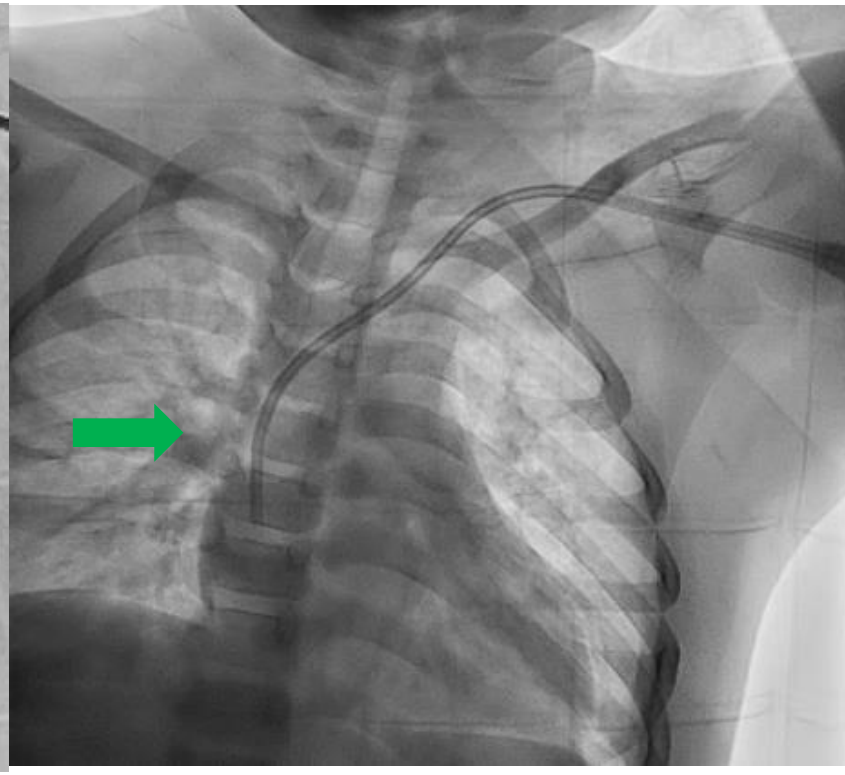
Post Fibrin Sheath Rupture



Management of Catheter Dysfunction due to Fibrin Sheath





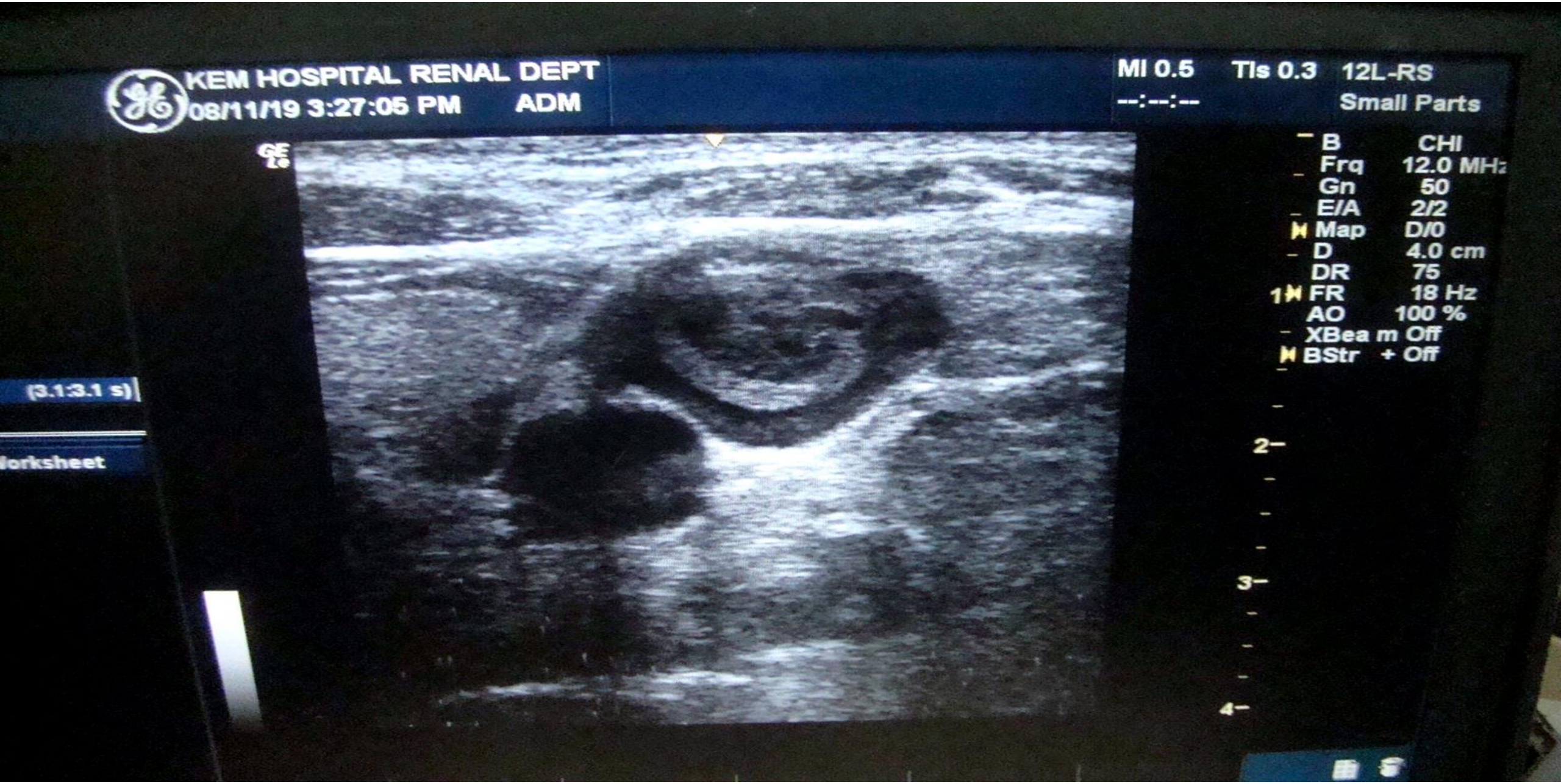


Fibrin Sheath after catheter withdrawl

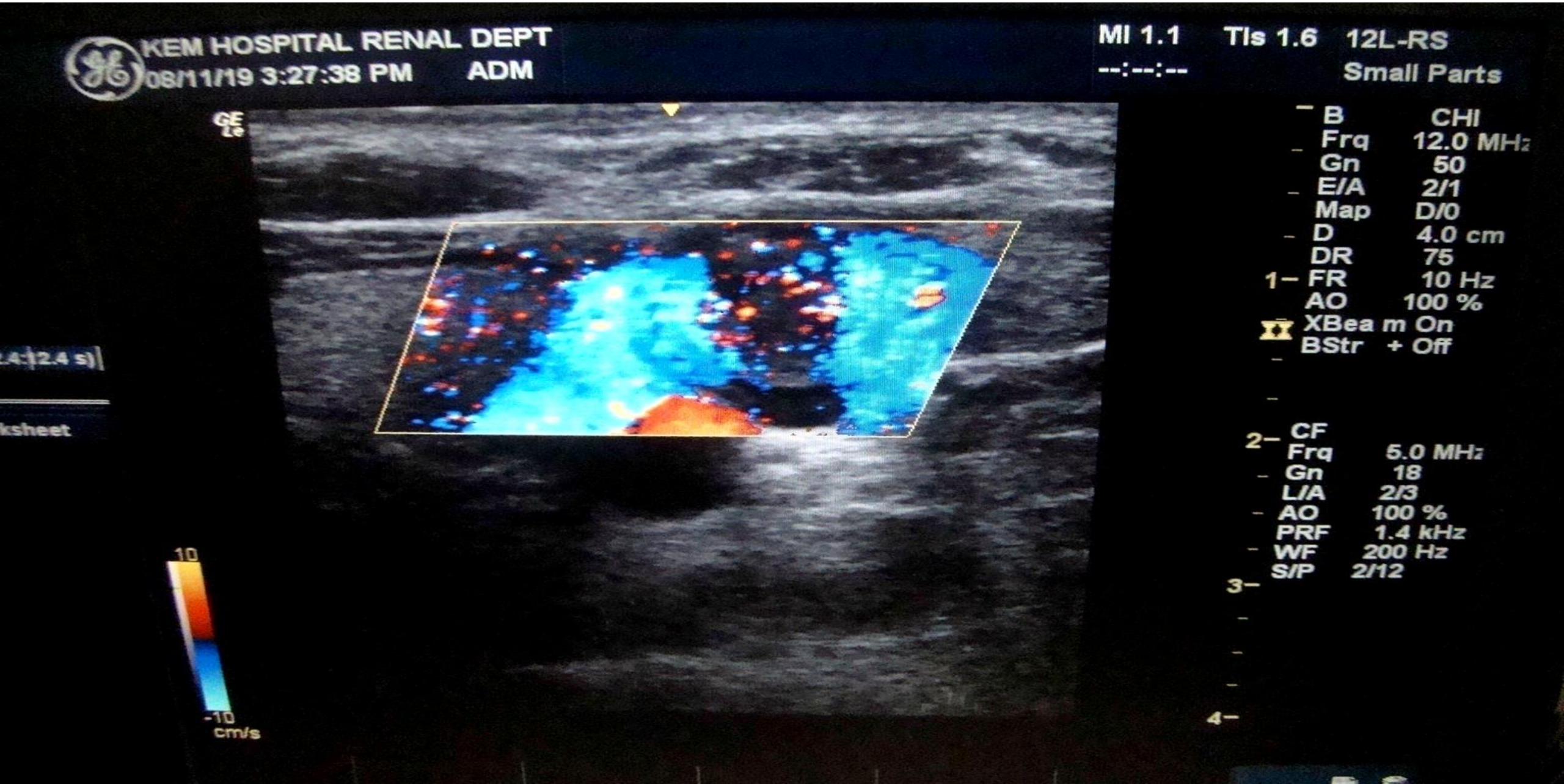
Sheath disrupted by Balloon angioplasty

Fresh TCC inserted over Wire

Prior Catheter Malfunction



Central Flow Void

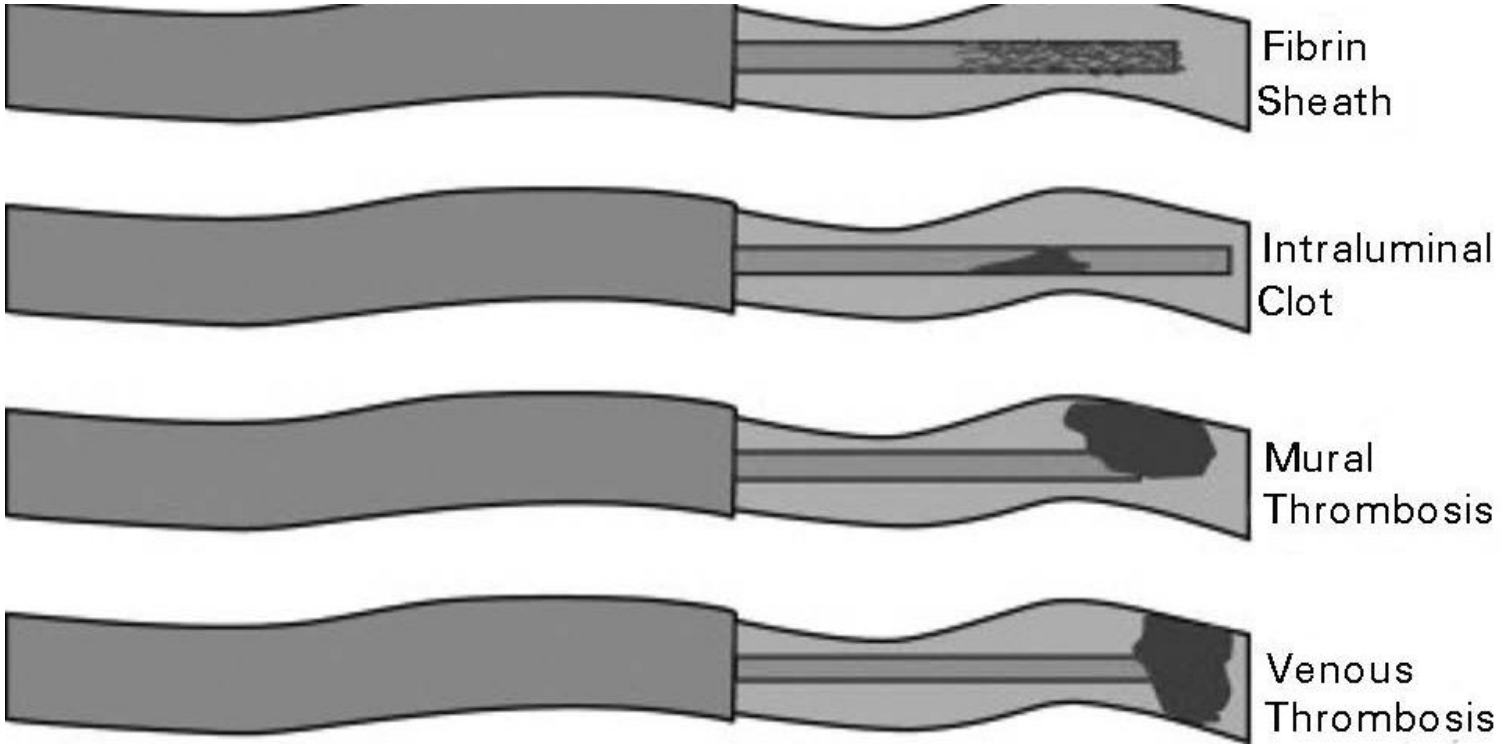


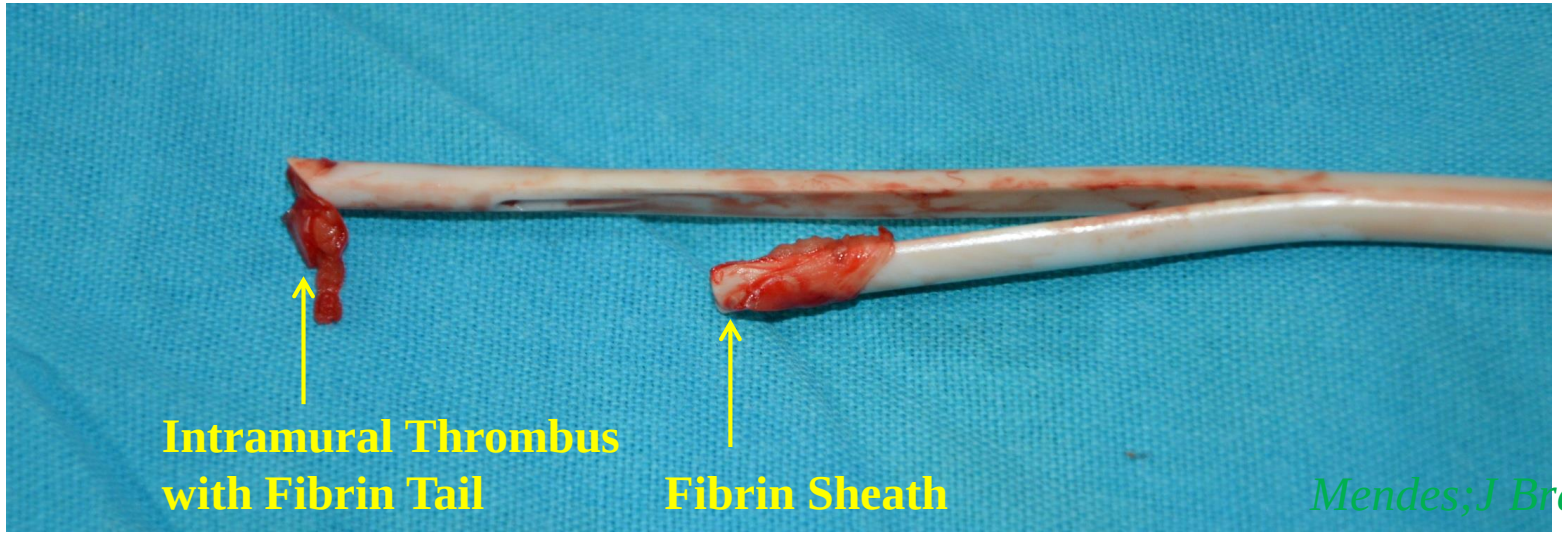
TCC & Access Dysfunction

Type	Features	Symptoms
Fibrin tail or flap	Fibrin extends from the end of the catheter causing partial occlusion (fibrin tail acts as one-way valve)	Ability to infuse but not withdraw blood
Fibrin sheath	Fibrin adheres to the external surface encasing the catheter, possibly extending the length of the catheter; thrombi trapped between sheath and catheter tip	Inability to infuse and/or withdraw blood
Mural thrombus	Fibrin from vessel wall injury binds to fibrin-covered catheter; increased risk of venous thrombosis	Leakage of infusate from the insertion site, swelling, pain, tenderness, engorged vessels
Intraluminal thrombus	Fibrin forms inside catheter lumen causing partial or complete occlusion	Inability to infuse and/or withdraw blood

Besarb, cjasn.org Vol 6 January, 2011

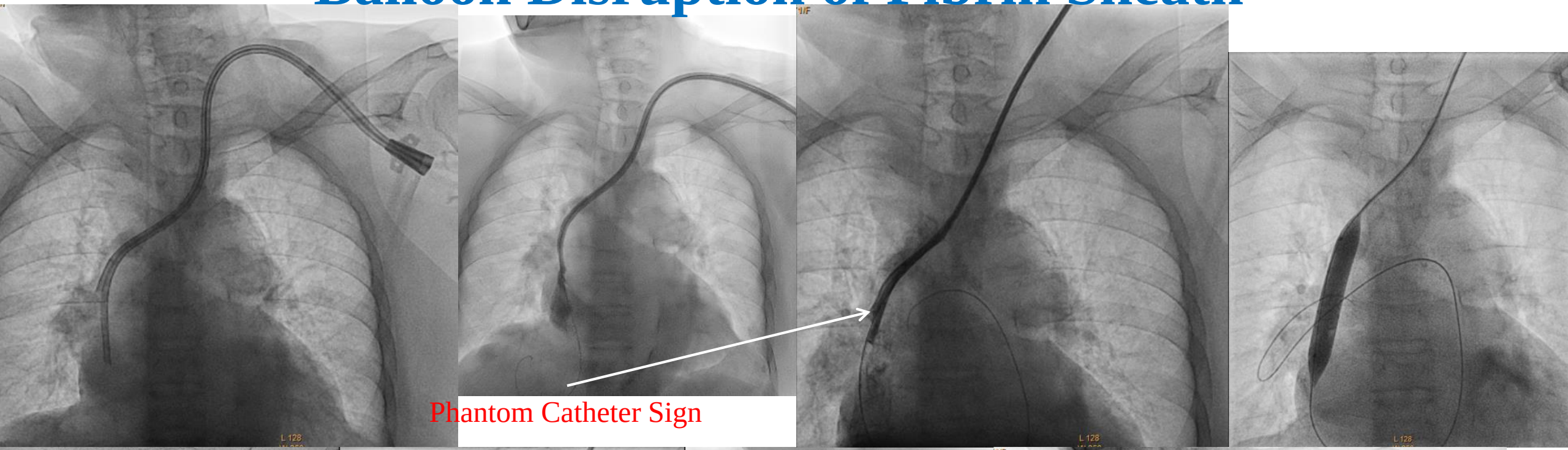
Approach to Catheter Dysfunction



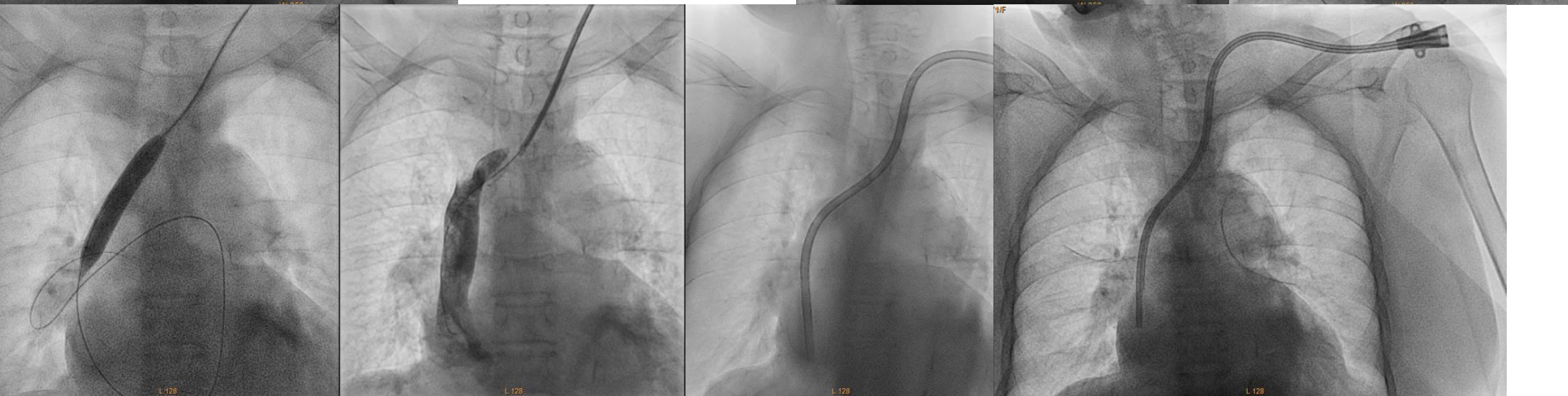


Mendes;J Bras Nefrol 2015;37(2):221-227

Balloon Disruption of Fibrin Sheath



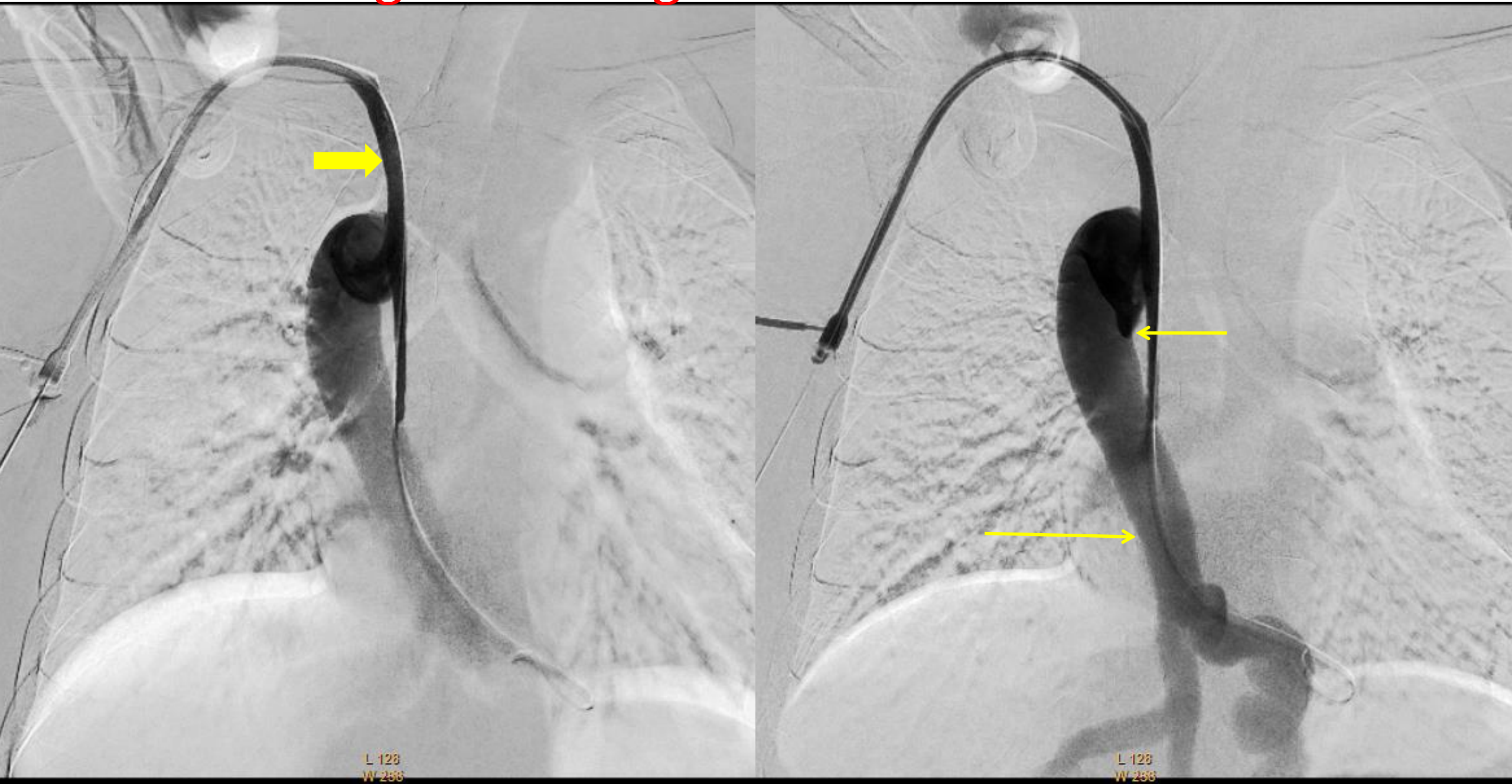
Phantom Catheter Sign

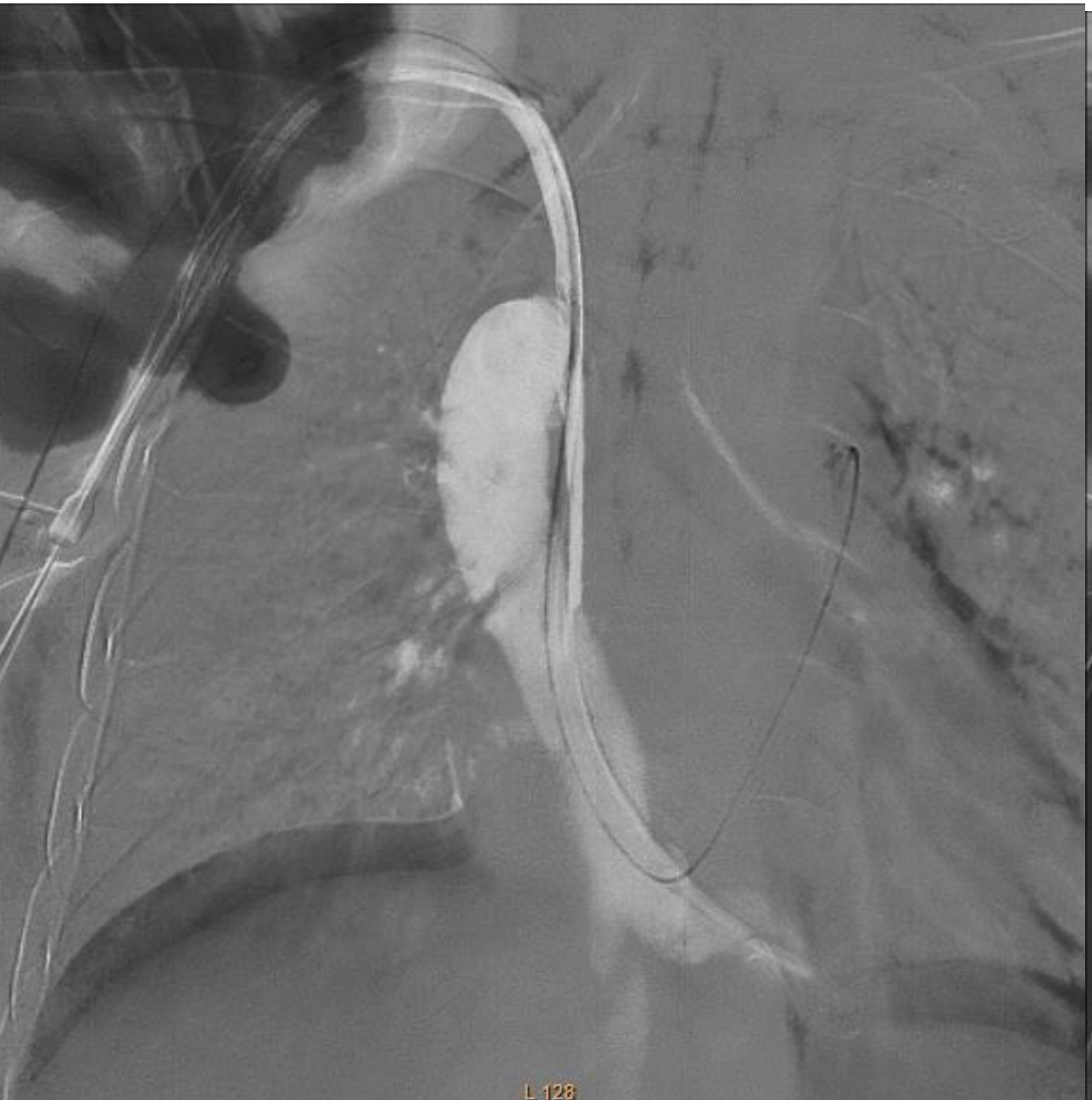


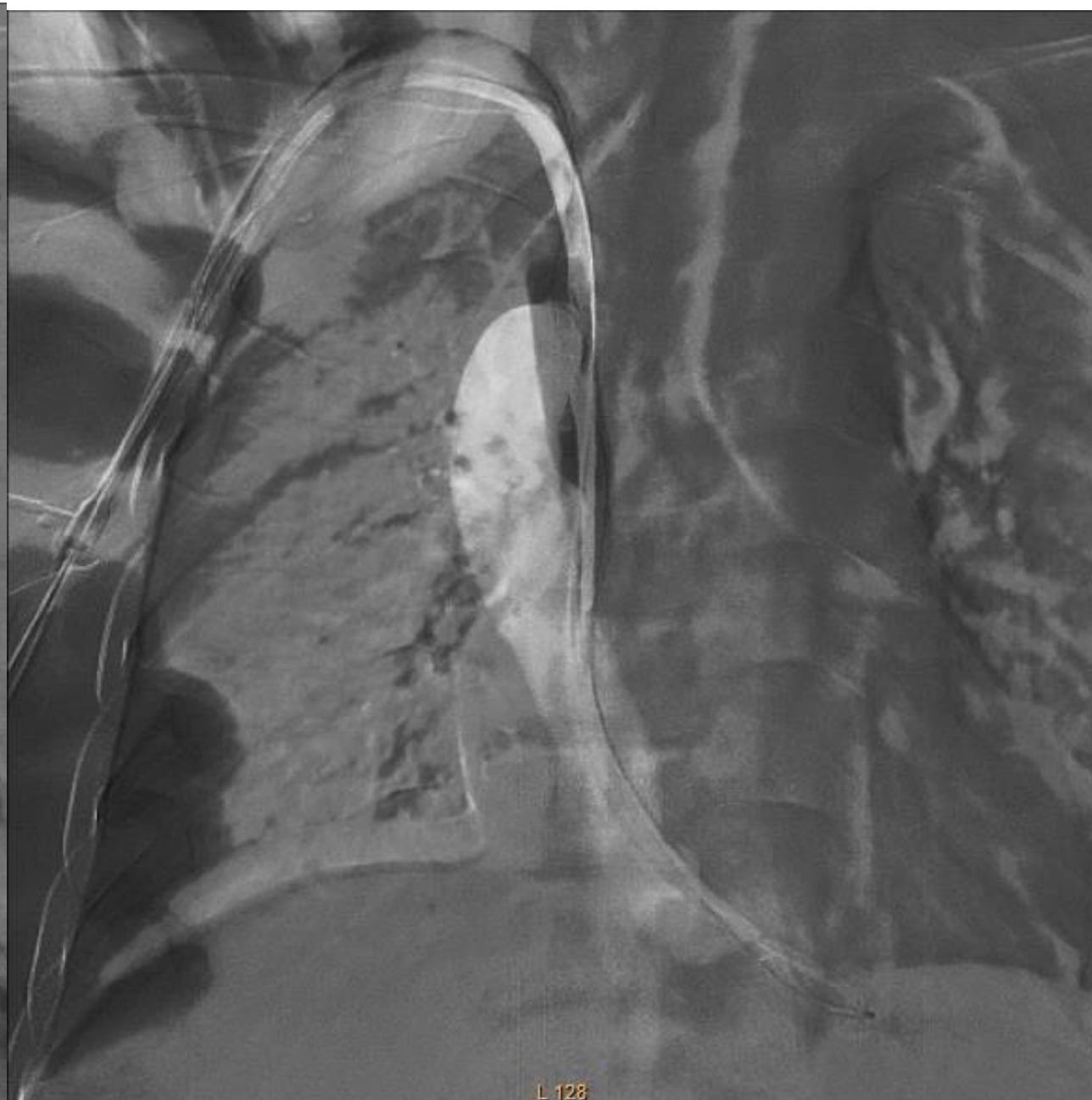
Case 4

- A 13 year old boy CKD – 5D initiated HD in 2014 through Rt IJV – 2LC.
- CAPD not possible owing to prior multiple abdominal surgeries in ealy childhood & functioning Lt ureterostomy.
- Lt radiocephalic AVF constructed in 2013 – Primary failure.
- Lt brachiocephalic A-V fistula constructed in June 2014. Bruit and faint thrill.
- Fistula thrombosed after 1 week. Could not be salvaged by thrombectomy.
- Lt IJV TCC inserted in June 2014 and 3/week MHD done.
- In September 2019, CRBSI due to Pseudomonas led to catheter removal and use of Lt femoral temporary catheter.
- Evaluated for Rt radiocephalic AVF- Radial artery calibre too poor.
- Offered loop graft in Rt forearm – declined by patient.
- Rt IJV TCC inserted- 19 cm 14.5F hemosplit.
- Had 2 additional episodes of endotoxic shock, suspected catheter biofilm. (All cultures negative)
- In Jan 2025, declining flow from TCC, underwent thrombolyis with transient improvement.
- Jan 2025 – CRBSI with Enterococcus fecalis and no flow from arterial lumen.
- Venous lumen – good inflow but poor outflow, 100 ml/min on bllod pump with arterial pressure of – 160 mm of Hg.
- 2D- Echo – No vegetations
- Treated with Vancomycin and gentamicin and taken for catheterogram

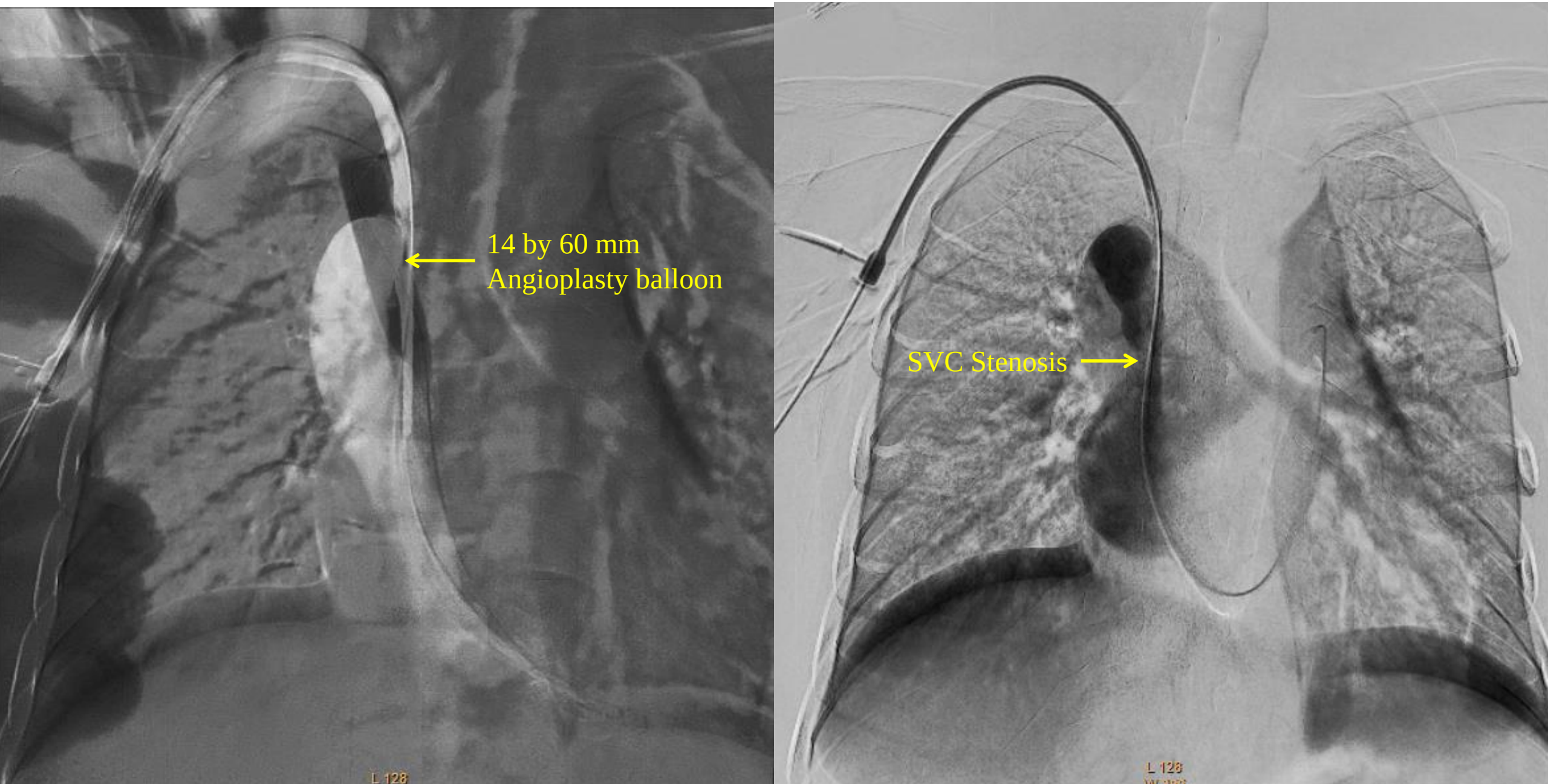
Venogram through 8F sheath in IJV

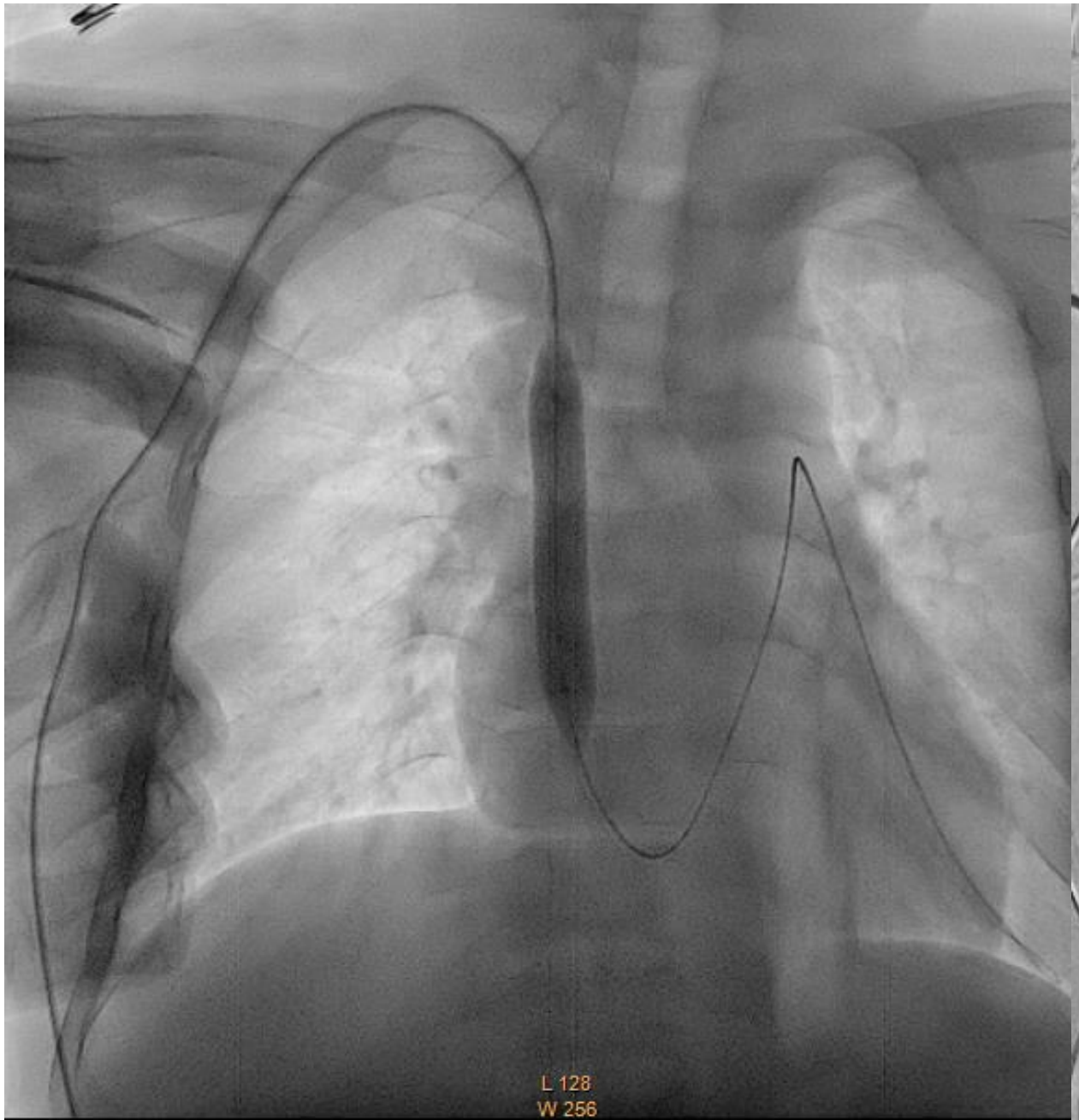



L 128


L 128

Angioplasty of SVC




L 128
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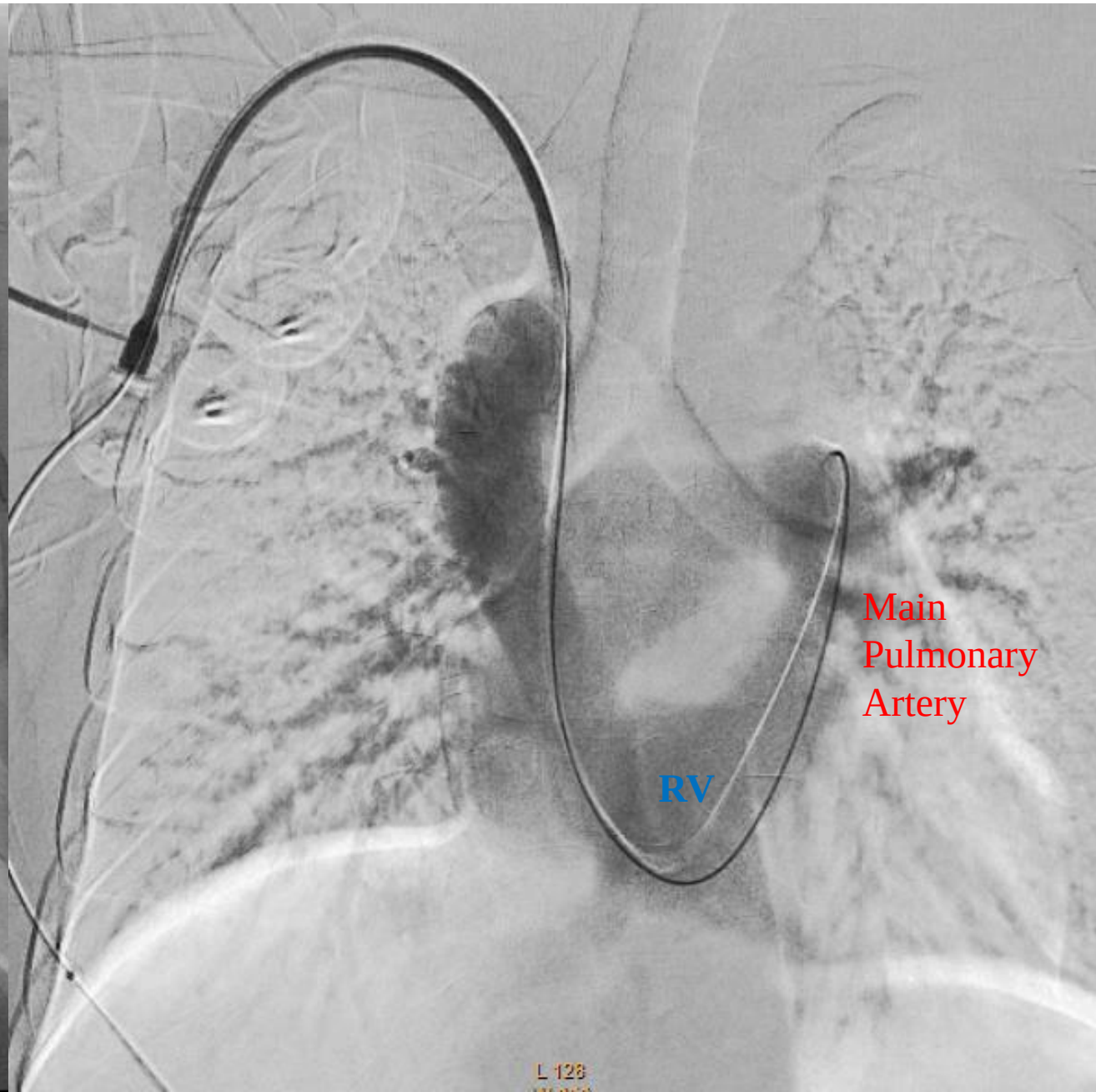
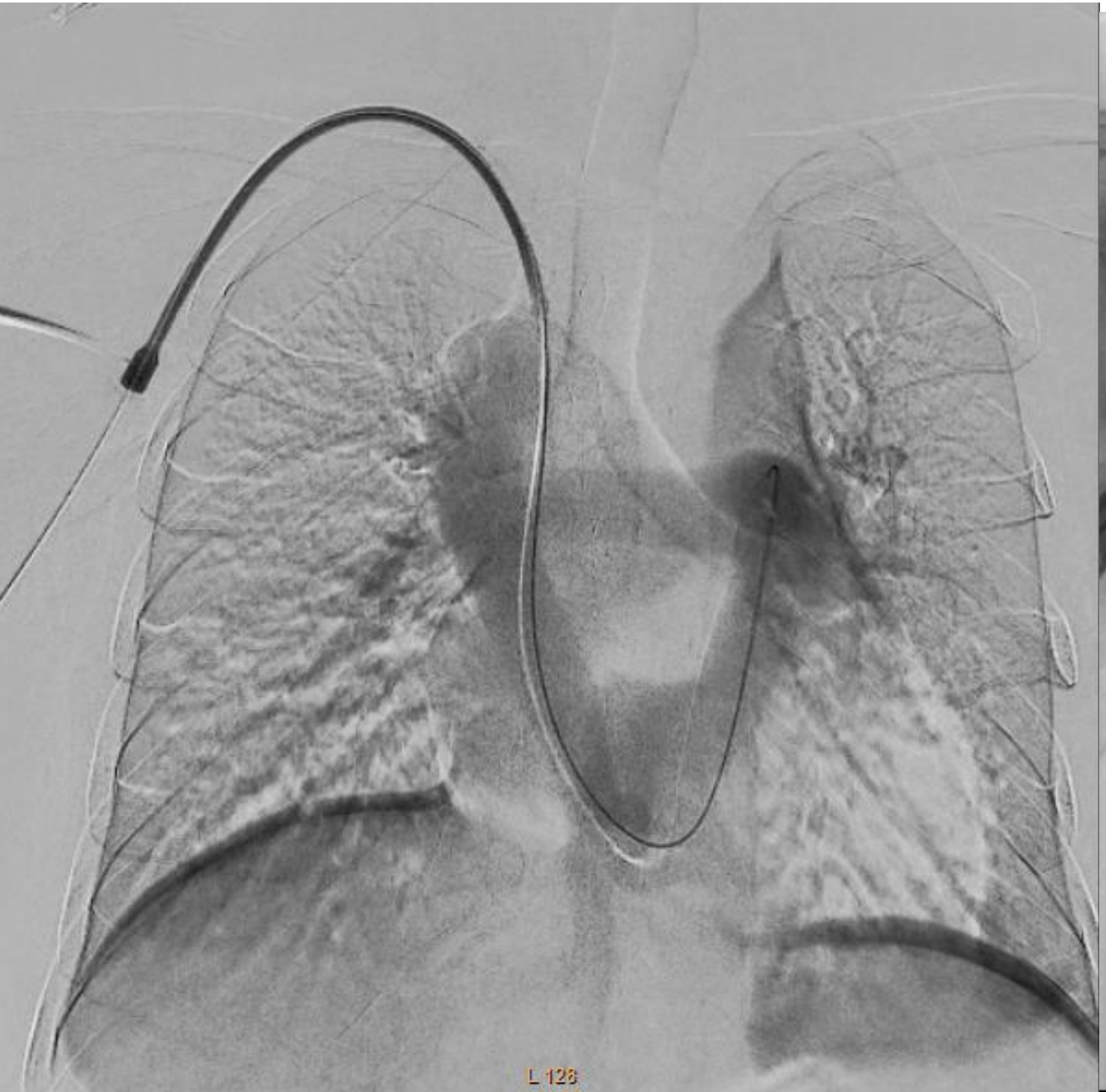
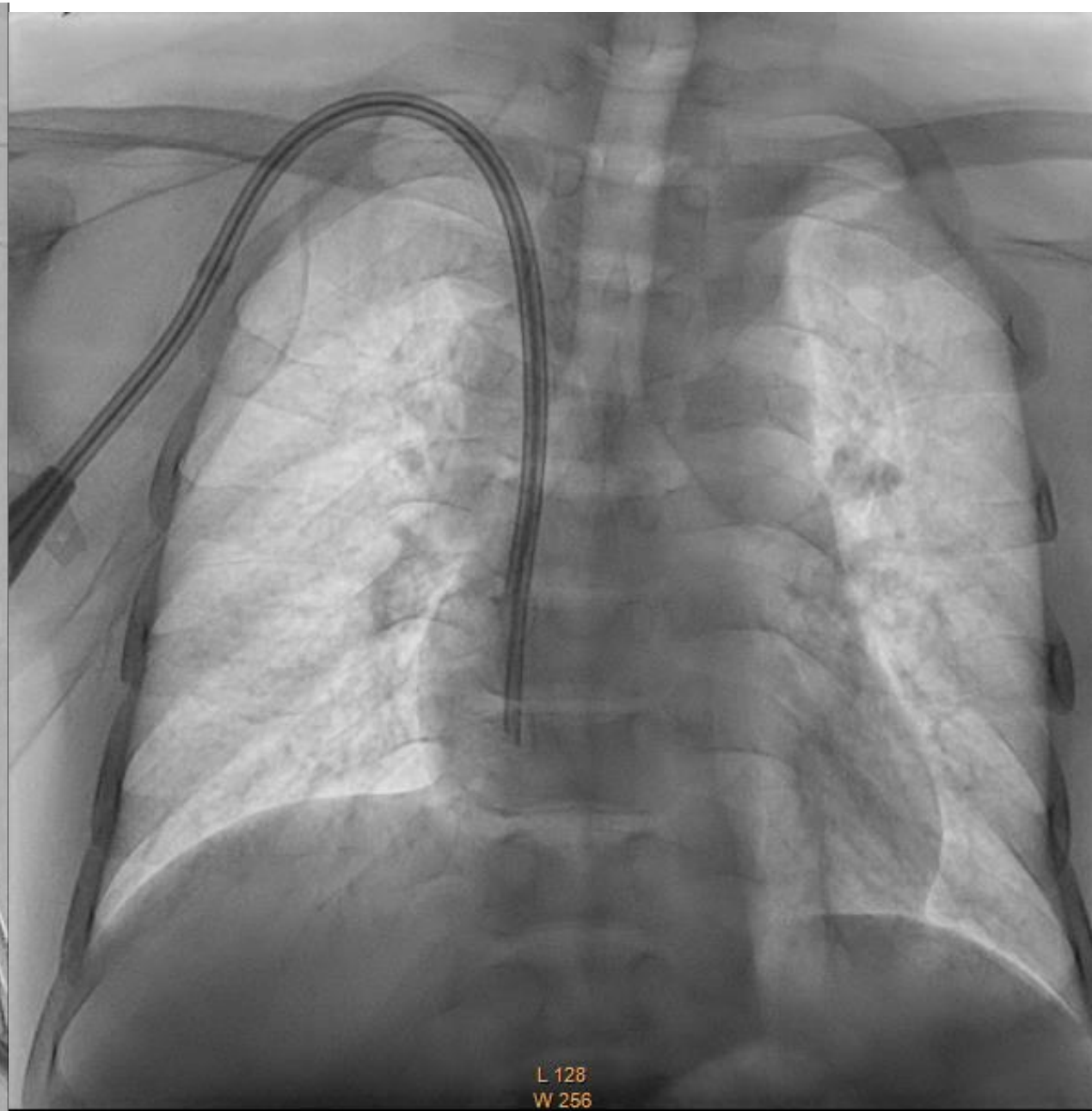
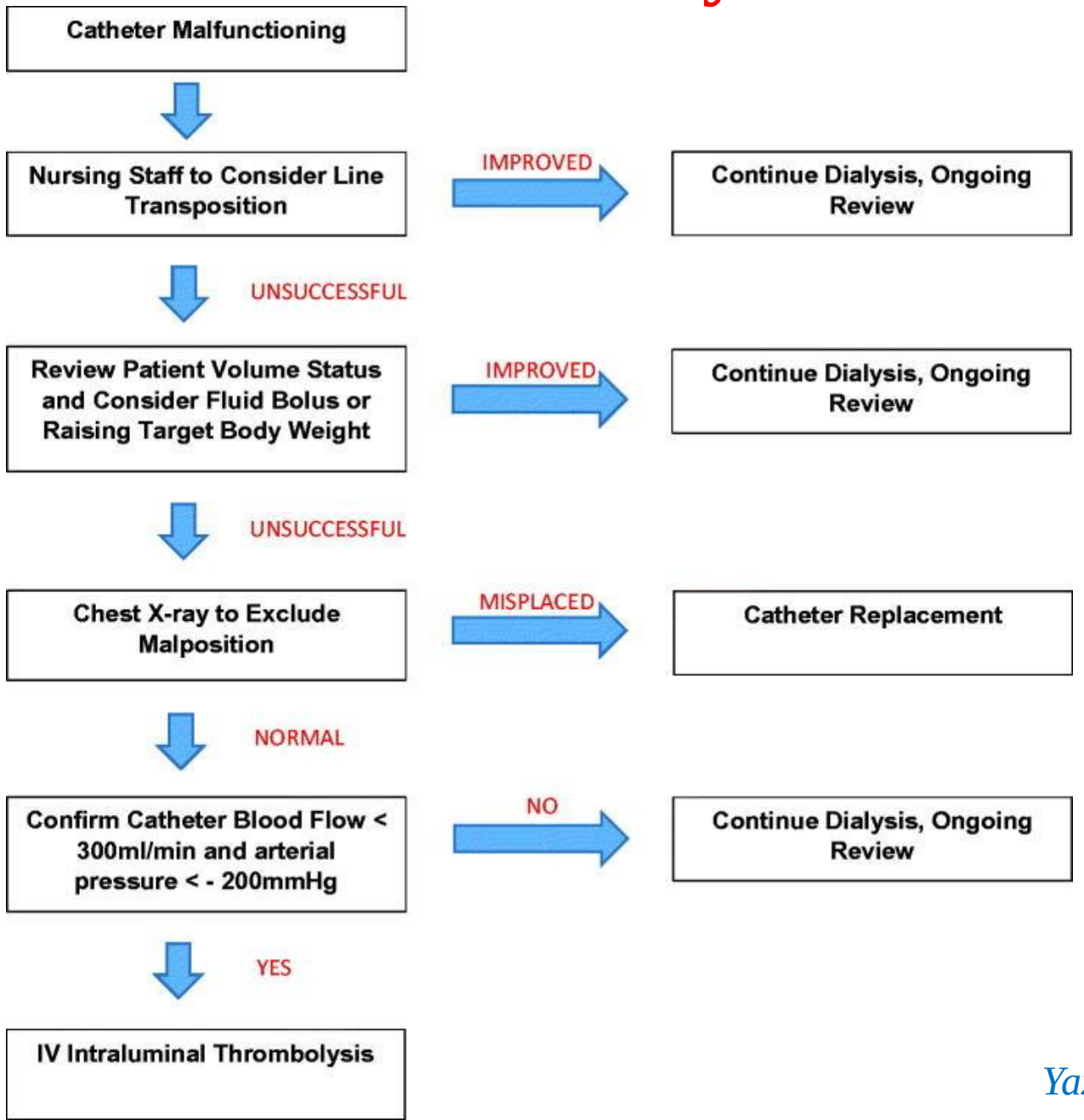

Main
Pulmonary
Artery
RV
L 128

Post Angioplasty TCC Replacement





Approach to Catheter Dysfunction



Yaxley , Ren Fail. 2020; 42(1): 622–623.

Case 5

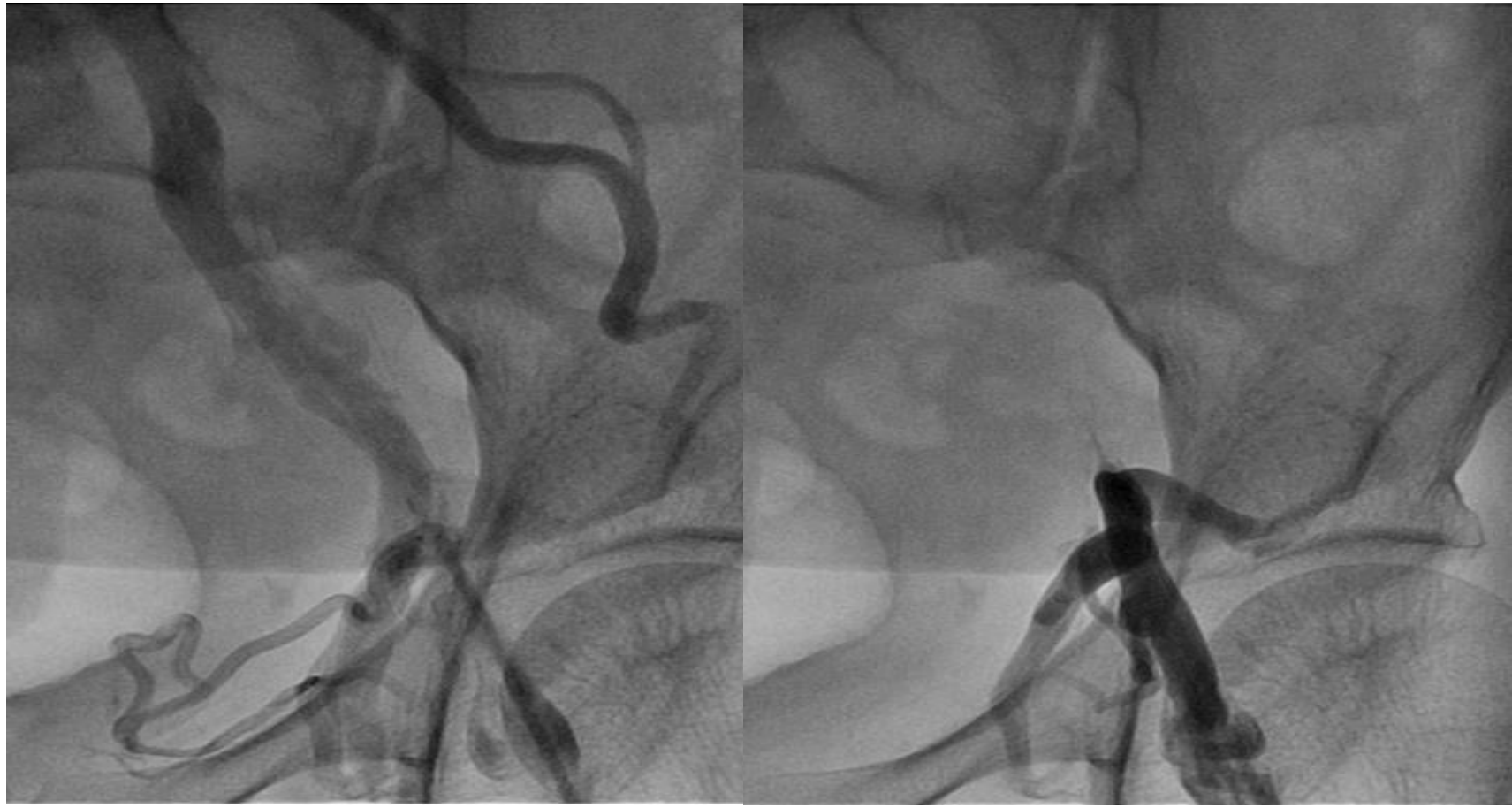
- A 12 year old boy with ESRD secondary to FSGS started MHD in 2014,
- Initially left femoral temporary, then right internal jugular temporary catheter for 6 months
- Left radiocephalic A-V fistula used from November 2014.
- April 2015 - came to KEM hospital with severe pain, redness and swelling of the left upper limb
- Diagnosed cellulitis and severe thrombophlebitis of the fistula veins.
- Blood culture - Enterococcus.
- Treated with Vancomycin weekly, and post HD gentamicin.
- Cuffed tunnelled catheter inserted in the Left internal Jugular vein
- Used for a period of 3 month till cellulitis and thrombophlebitis resolved
- Resumed HD through the AVF.
- 2 further episodes of swelling and pain, treated at dialysis center with antibiotics and dialyzed from temporary catheters.

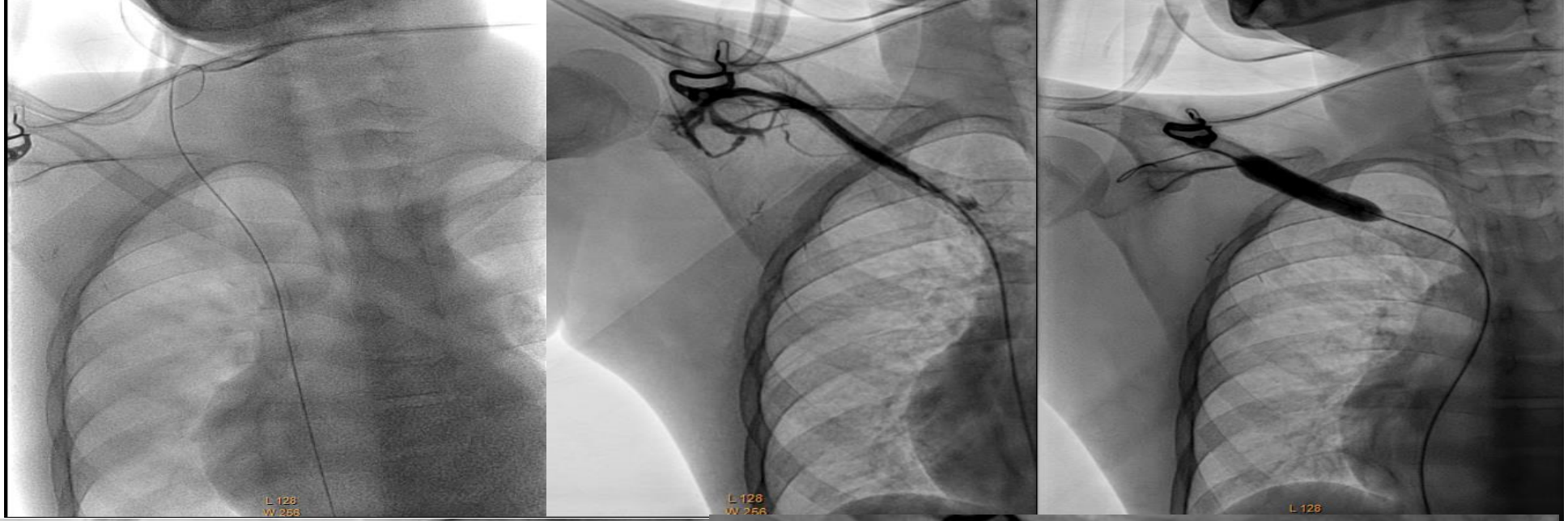
Case 5

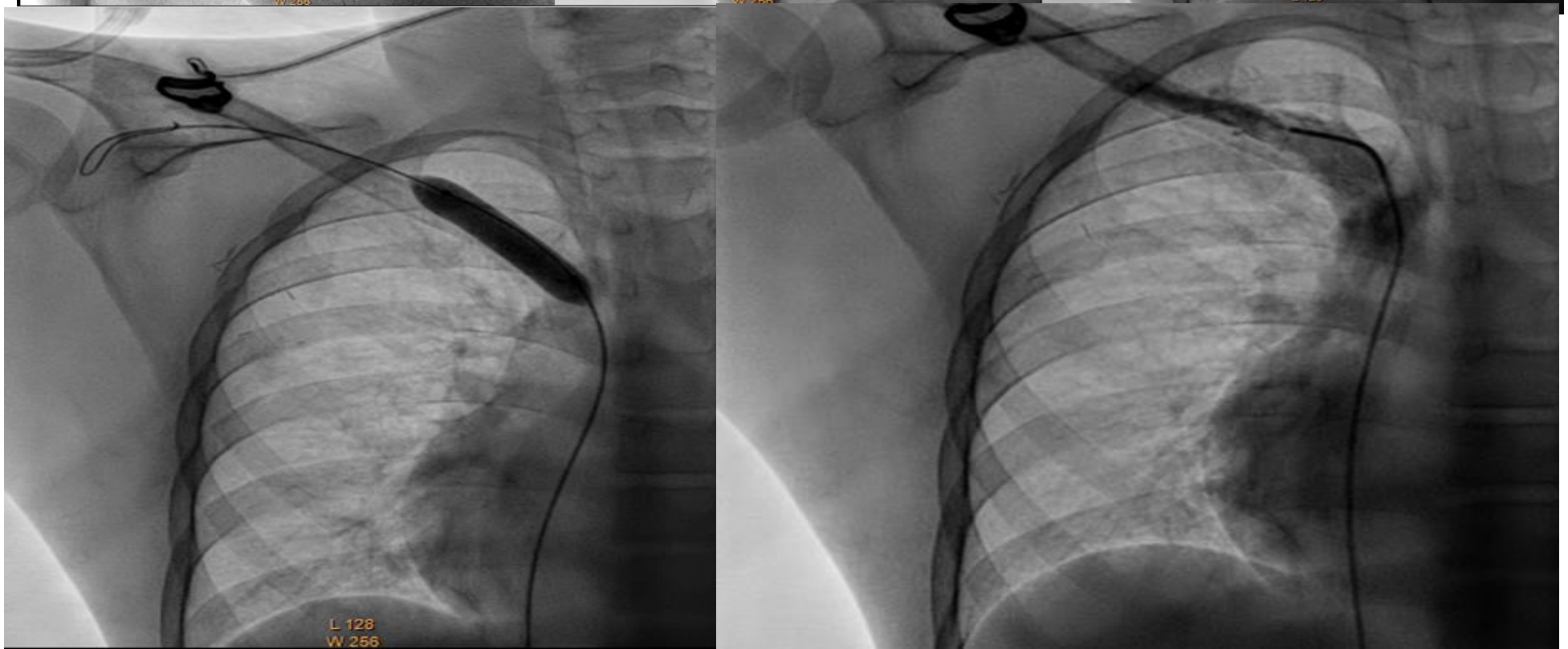
- August 2015 - swelling of the fistula arm with prolonged bleeding after needle removal
- Inability to completely extend his elbow.
- Angiography - normal anastomosis and cephalic vein in the forearm and arm
- Complete thrombotic occlusion of the left brachiocephalic vein at origin. Angioplasty attempted – failed.
- Reinforced corrugated necklace PTFE graft placed between the right and left axillary veins.
- Venous hypertension resolved within 48 hours and the fistula used for HD.
- March 2017, - recurrence of swelling in both upper limbs left > right
- Increased bleeding from needle punctures , elbow contracture
- Inability to use the AVF for dialysis.
- Facial swelling and dyspnoea.
- No improvement with aggressive ultrafiltration

Case 5 – cont’d

- Doppler studies - Normal graft flow
- CT venogram - Stenosis of the right brachiocephalic and subclavian veins
- Both Internal Jugular and Lt Brachiocephalic veins thrombosed with absence of flow.







- Rt femoral vein cannulated.
- Brachiocephalic and right subclavian vein plasty done.
- Cuffed Tunnelled catheter inserted in RT femoral vein for HD
- Venous hypertension resolved after 16 days.
- Fistula HD resumed April 2017.

Pediatric Urinary Tract Infection In Children

Dr.G.Sangeetha MD; MRCPCH; FPN; FISN
Paediatric Nephrologist
Kauvery Hospital
Chennai

Outline of the talk

- UTI - definition
- Simple and complicated febrile urinary tract infection
- Recurrent urinary tract infection
- Urinary tract infection with vesicoureteric reflux
- Urinary tract infection with bowel bladder dysfunction

CASE 1

- 5 yrs old girl brought with h/o fever for 5 days
- H/o pain during urination
- No h/o hematuria, cloudy urine or passage of crystals/mud in urine
- No h/o vomiting/loose stools
- O/E febrile, hydration good
- No vulval synechiae
- Systems - normal

CASE 1

- Urine routine
- Turbid in appearance
- Plenty of pus cells & pus clumps
- 1 + proteinuria

- Urine culture grew E.coli 10^5 CFU/mL
- Sensitive to cefixime, amikacin, ofloxacin and cefoperazone+sulbactam
- TC- 18000cumm, P80 L20, CRP- 12mg/dL, blood culture - sterile

Diagnosis

- Simple febrile UTI

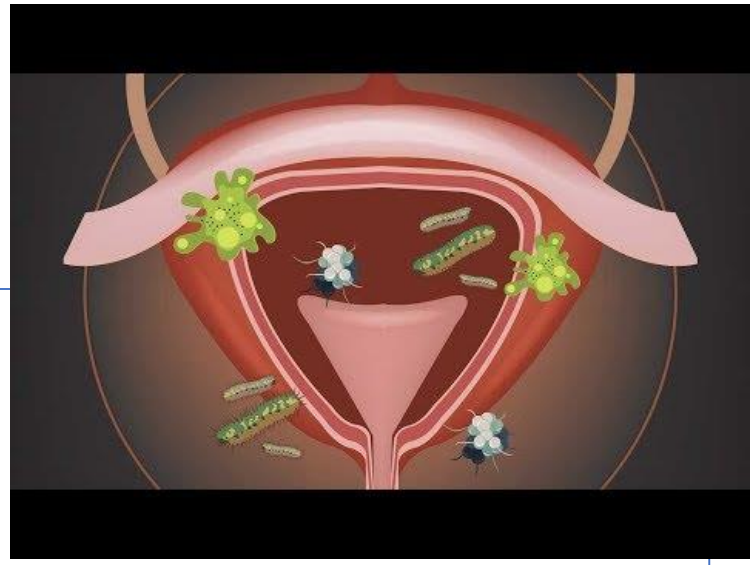
CASE 2

- 3years old boy with high grade fever of 4 days with chills & rigors. He also had vomiting & cry during urination
- On examination he was febrile, toxic, dehydrated. Right loin tenderness+
- Investigations
- CBC – 20200/cumm; P76 L24
- CRP – 86mg/dL; RFT: BUN: 25mg/dL, S.Cr- 1.3mg/dL
- Urine microscopy – plenty of pus cells/HPF; 2+ proteinuria Occ RBCs/HPF
- Urine C/S : E.Coli 10^5CFU/mL, S: Ceftriaxone, Amikacin
- USG Abd: Right renomegaly with pelvic wall thickening

Diagnosis

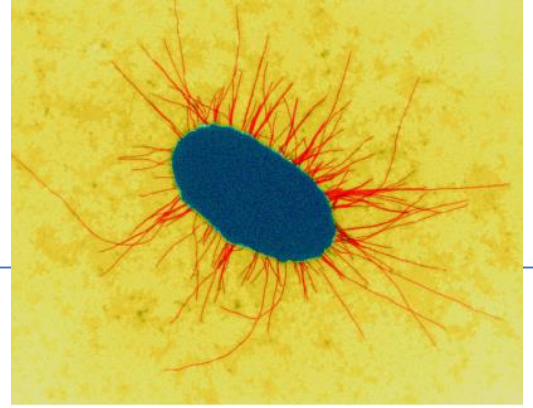
- **Complicated UTI**

UTI



- It is identified by presence of symptoms with significant growth of a single species of bacteria in urine culture
- Boys are affected more during infancy with the ration of 2.8-5.4 : 1
- Beyond infancy - more common in girls with F:M - 10:1
- Approximately 8 to 30% of children with UTI get recurrence of symptoms

Etiology



- Escherichia coli is the most common bacterial cause of UTI (80%)
- Other gram-negative bacterial pathogens - klebsiella, proteus, enterobacter and citrobacter
- Gram-positive bacterial pathogens - staphylococcus saprophyticus, enterococcus & rarely staphylococcus aureus

UTI by ESBL

- They have inherent resistant to the usual antibiotics such as penicillin and cephalosporin
- Prevalence ranges from 1% to 11%
- Known risk factors for ESBL UTI

  renal anomaly, recent hospitalization, instrumentation, recurrent UTI, and use of inappropriate antibiotics

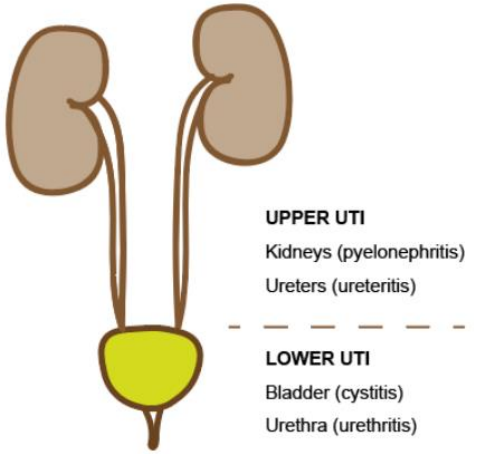
Clinical Significance of ESBL-producing Bacteria in First Pediatric Febrile UTI and Differences between Age Groups. Child Kidney Dis 2017; 21(2): 128-135.

Etiology

- Viral UTI are generally limited to the lower urinary tract (eg, adenovirus, enteroviruses, coxsackieviruses and echoviruses) & uncommon in children
- Fungal UTI (eg, Candida, Aspergillus, Cryptococcus neoformans)
- Risk factors for fungal UTI

  Immune suppression, long-term use of broad-spectrum antibiotic therapy and indwelling urinary catheter

Pathogenesis



- Ascending infections - the most common mode of spread in children
- Organisms which colonize the perineum - the main source of infection

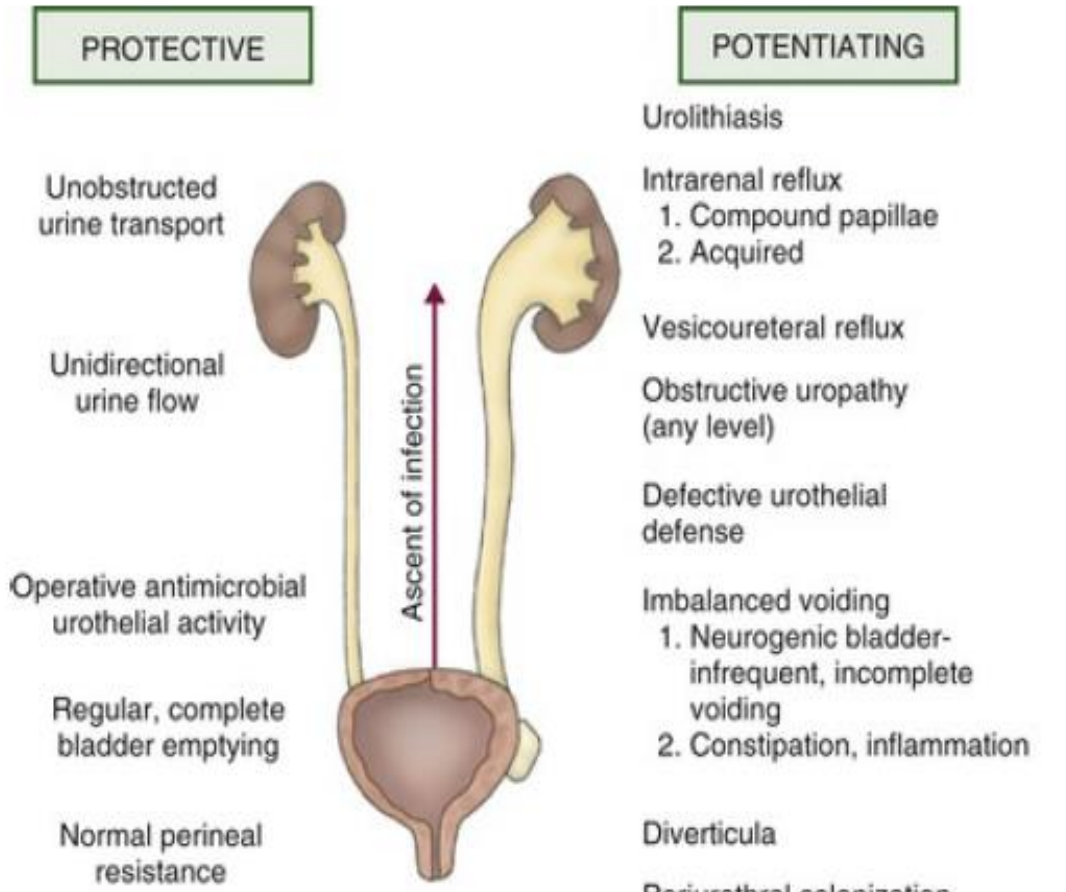
- Compound papillae situated at the upper and lower poles of the kidney allow intra renal reflux
- The infected urine triggers immunologic and inflammatory response
- Repeated infection in an anatomically disturbed system can cause renal parenchymal injury and subsequent scarring

Kaufman J, et al. BMJ Paediatrics Open 2019;3:e000487. doi:10.1136/bmjpo-2019-000487

Protective & risk factors for UTI in children

Identifiable risk factors

- Young age
- High-grade vesicoureteric reflux
- Posterior urethral valve
- Neurogenic bladder
- Bowel bladder dysfunction
- Phimosis
- Vulval synechiae
- Worm infestations



Holcomb III GW, Murphy JP, Ostlie DJ [eds]: Ashcraft's pediatric surgery, 6th ed, Philadelphia, 2014, Elsevier; Fig. 55-3, p. 735.

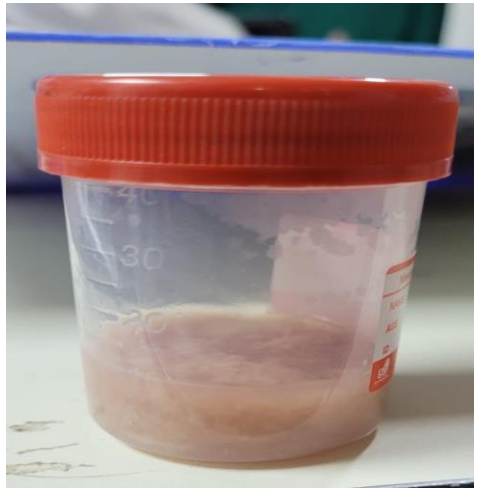
Case 3

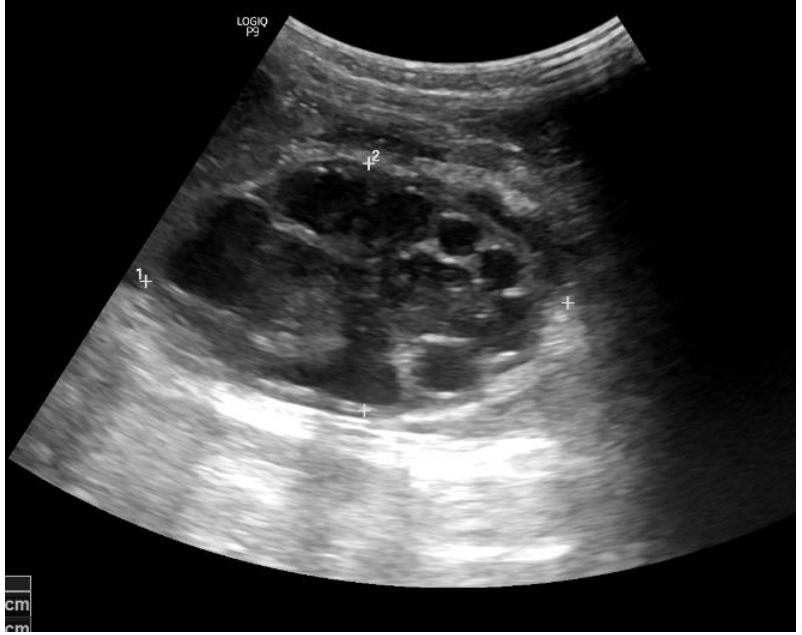
- A 6 months old boy baby presented with fever for 2 days, and vomiting.
- No weight gain for a month; Reduced urine output and activity
- Child was lethargic and dehydrated

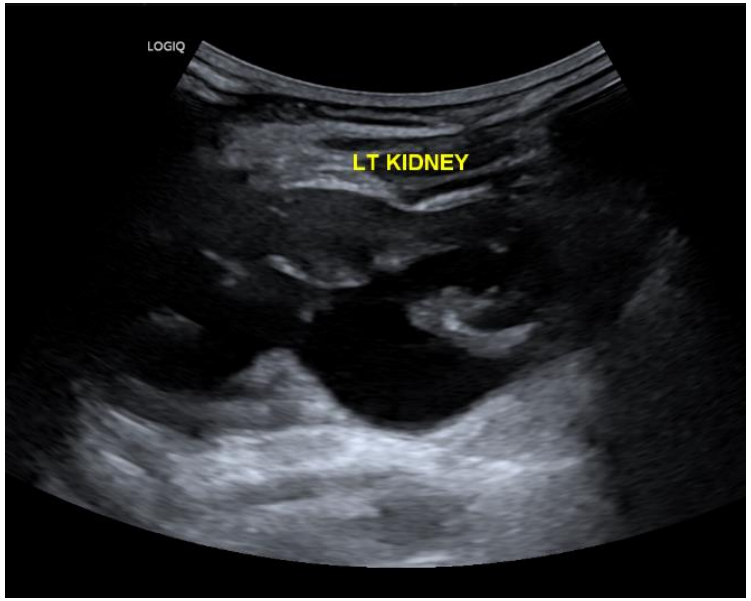
- Underwent Lt pyeloplasty 5 weeks ago and stent removal a week ago.

- USG Abdomen: LK: Dilated renal pelvis with solid echogenic floating echoes s/o fungal ball

UTI – following pyeloplasty





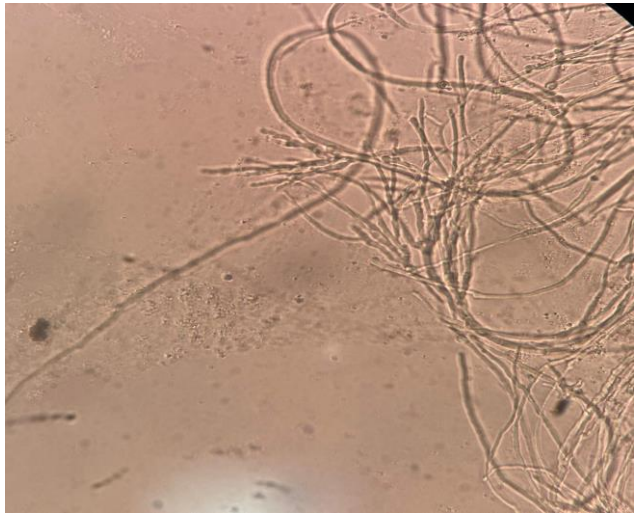


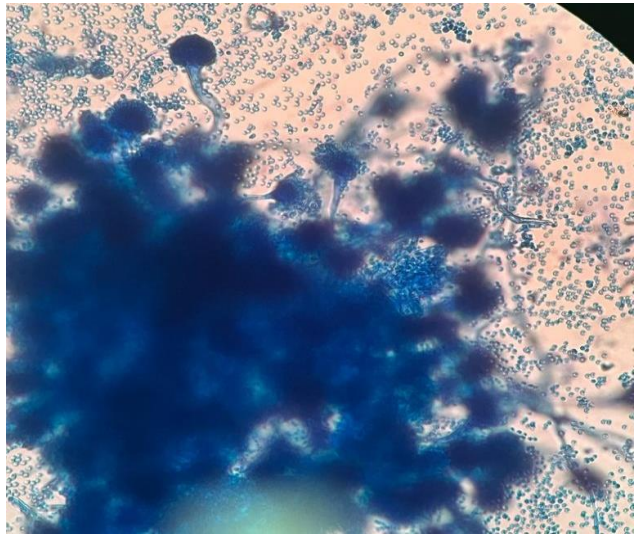
ASPERGILLUS FLAVUS

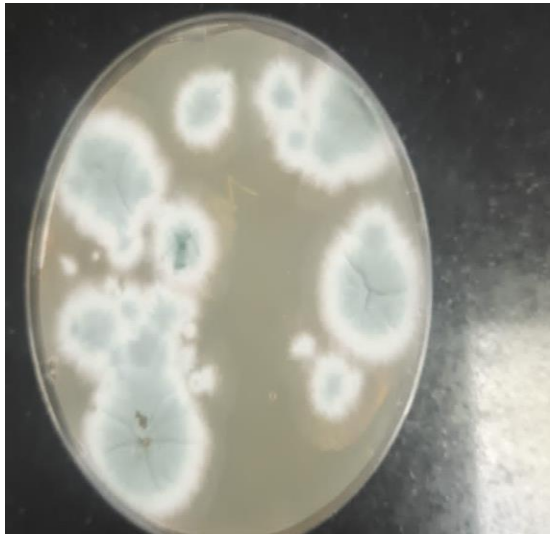
Potassium hydroxide mount showing fungal growth

Fungal growth in Lactophenol cotton blue stain

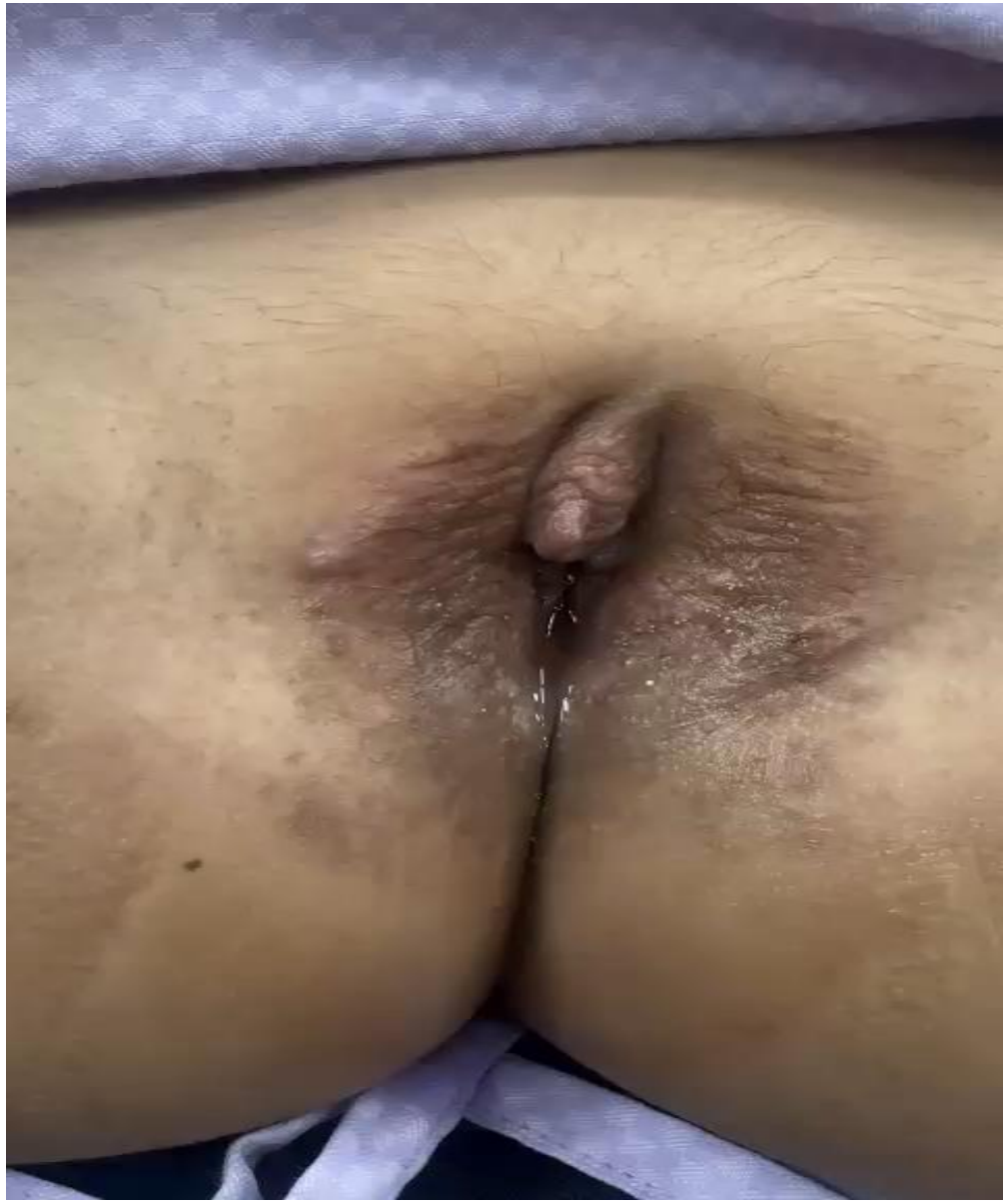
Growth on Sabourauds dextrose agar



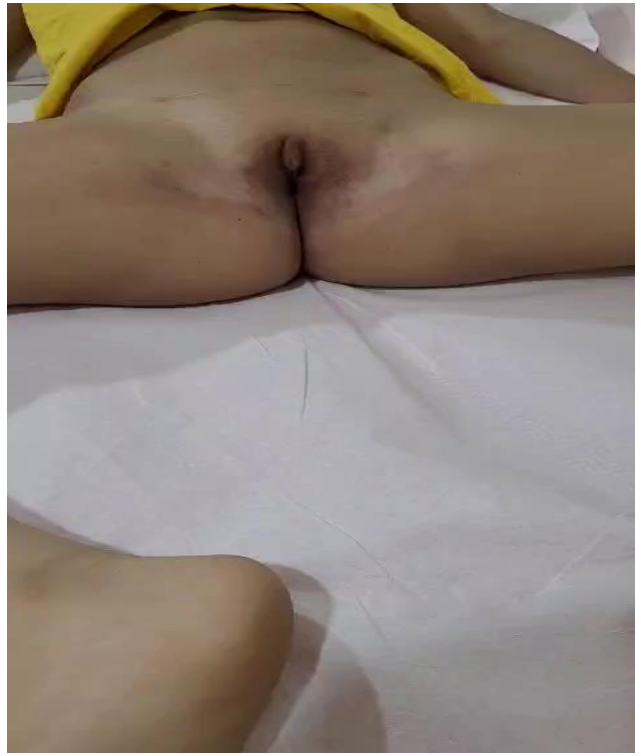




Amphotericin / voriconazole oral for 4 weeks



- Case 4 : 8 yr 9months old girl – continuous dribbling on diaper
- Treated multiple times for UTI and vulvovaginitis
- Cystoscopy- b/l ectopic ureter, right at the bladder neck and left –below sphincter
- Underwent **ureteric reimplantation**



Clinical features

- Sepsis with poor feeding
- Vomiting
- Jaundice
- Temperature instability

- Low grade fever
- Dysuria,
- Frequency
- Urgency
- Hematuria & foul-smelling urine

Older children

uncomplicated /

- High grade fever with chills & rigors
- Persistent vomiting
- Loin pain
- Dehydration

Complicated / upper
UTI

Clinical features

- Recurrent fever, diarrhoea, abdominal pain and failure to gain weight may be the presentation in toddlers

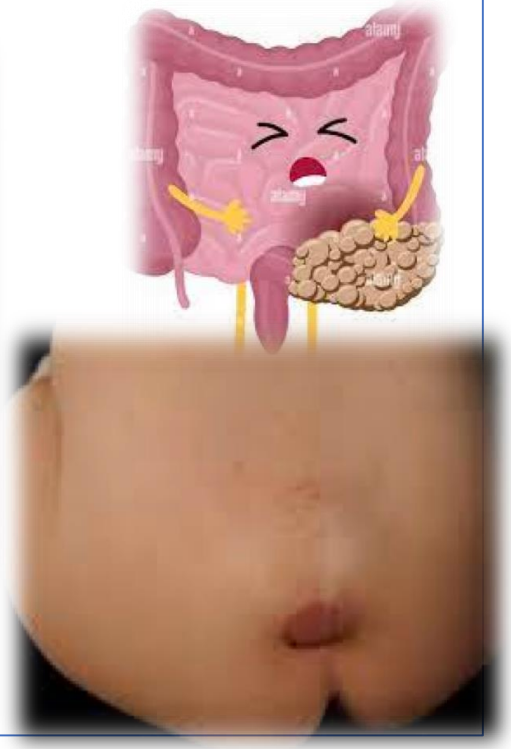
- Urinary incontinence, straining during urination, poor urinary stream, anorectal malformation and spinal abnormalities are seen in children with underlying structural abnormality

Clinical examination

- Growth parameters, blood pressure and systemic toxicity signs

Look for

- Palpable distended bladder, enlarged kidneys, supra pubic and renal angle tenderness
- Palpable faecal mass in the colon
- Vulval synechiae/phimosis
- Spinal examination



Investigations

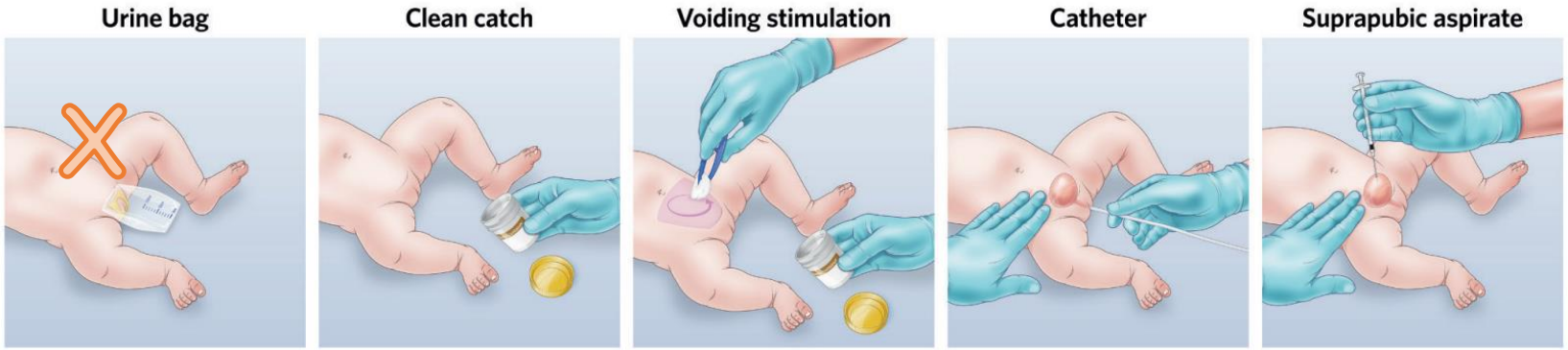
- **Urine microscopy**: Pyuria in a centrifuged sample (>5WBCs/HPF) favors UTI
- **Rapid dipstick-based tests** are useful for screening
- A positive **Leucocyte esterase test** is suggestive of UTI
- **Nitrate reduction test** is highly specific, but false-negative tests are common

Screening tests for UTI

Test	Sensitivity (%)	Specificity (%)
Microscopy WBCs	73	81(45-98)
Leucocyte esterase (LE)	83 (67-94)	78(64-92)
Nitrite reduction (NR)	53(15-82)	98(90-100)
LE and NR +	93(90-100)	72(58-91)
LE, NT and microscopy	99.8(99-100)	70(60-92)
Enhanced urinalysis (Pyuria + Bacteria/oil immersion field by Gram stain)	85%	99.9%

American Academy of Pediatrics, sub comittee on UTI Pediatrics. 2011; 128(3):595-610

Methods of urine collection



- Urine culture – **gold standard investigation**
- In neonates and infants, urine sample is obtained by either suprapubic aspiration or transurethral bladder catheterization
- In toilet trained children – **midstream sample** is adequate

Methods of urine collection

Method of urine collection	Colony forming unit /mL of urine
Suprapubic aspiration	1000
Urethral catheterization	10000
Midstream clean catch	> 10^4 to 10^5

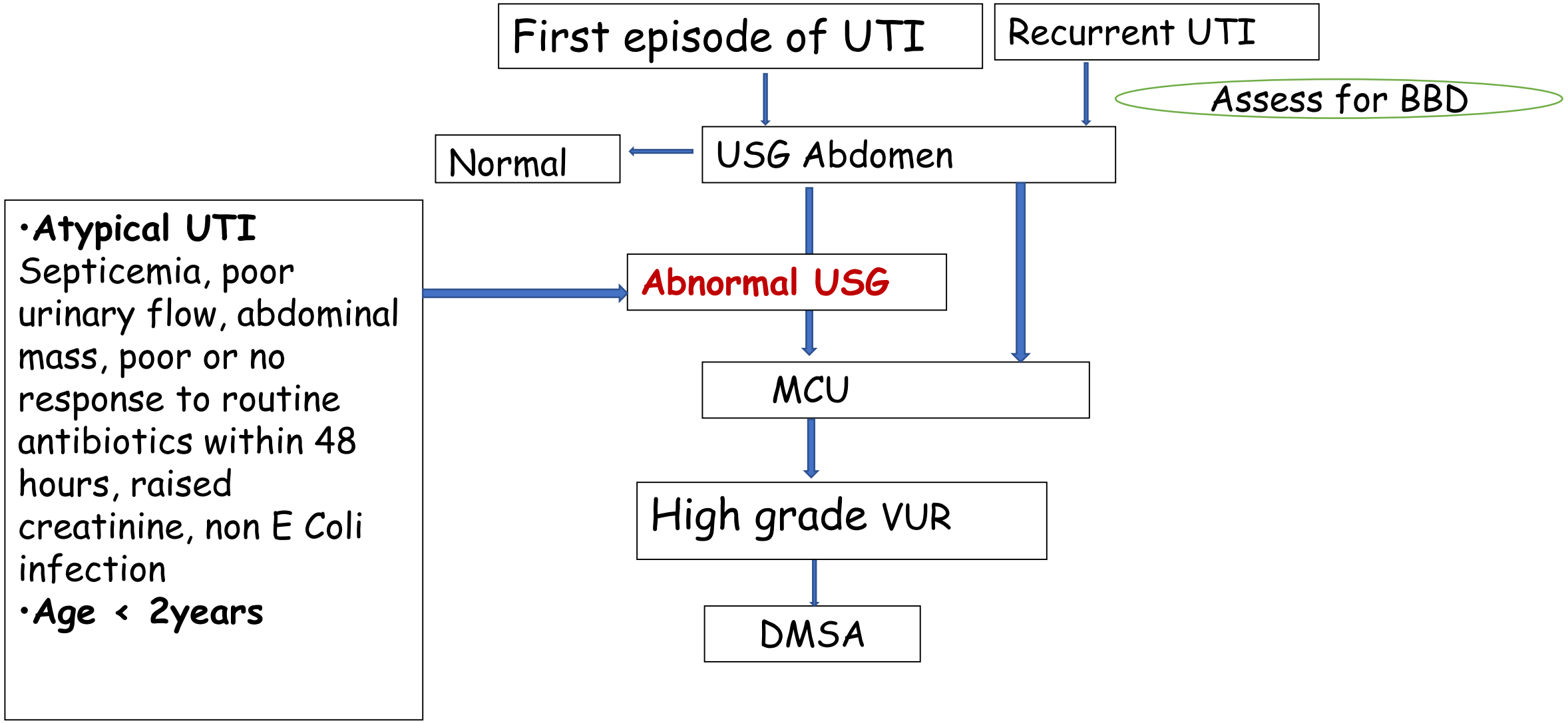
Practical difficulties in colleting urine sample

- Simple, and clear instructions should be given to the patient for correct urine collection
- Wash the hands and urethral meatus
- Collect the sample after spreading the vulvar labia (female) or withdrawing the foreskin of the glans (male)
- Midstream collection
- Transport urine sample to lab with in 2 to 3hours/store in 2 to 8°C
- False-positive results: Contamination from genital secretions or bacterial overgrowth upon standing
- False-negative results: Misinterpretation of bacteria or lysis of leukocytes, favored by alkaline pH and/or low specific gravity, or delayed urine sediment examination

Evaluation of the child

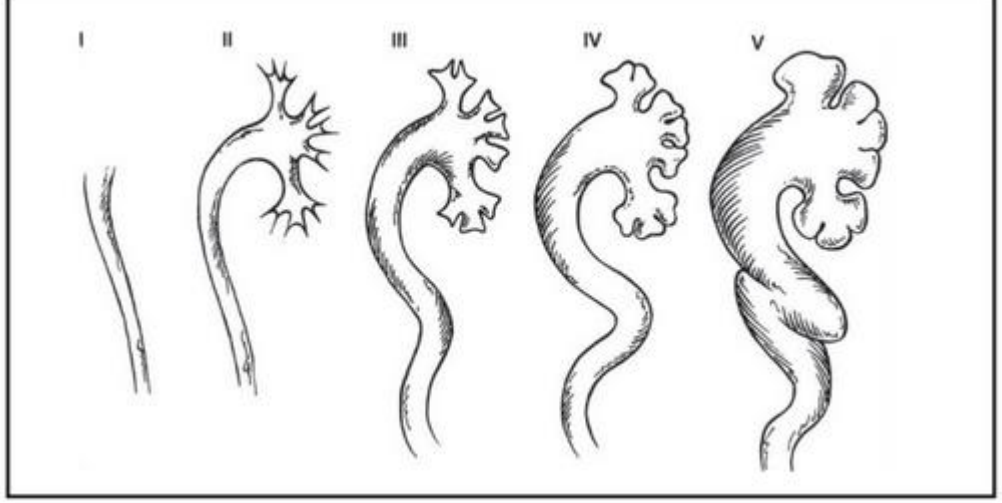
- Urine routine
- Urine culture
- CBC, CRP, procalcitonin, blood culture and RFT
- USG abdomen

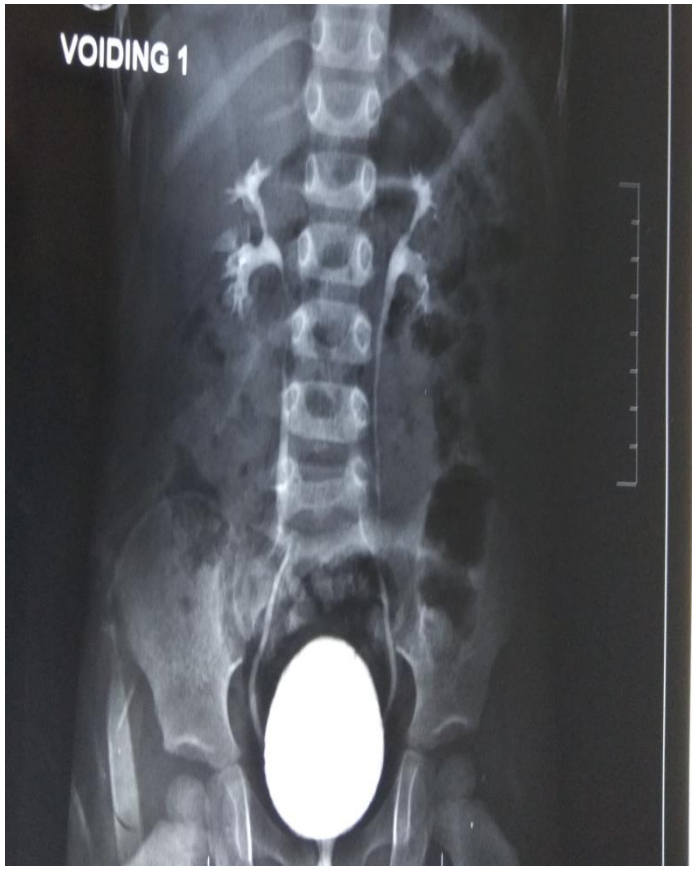
Role of various imaging in febrile UTI

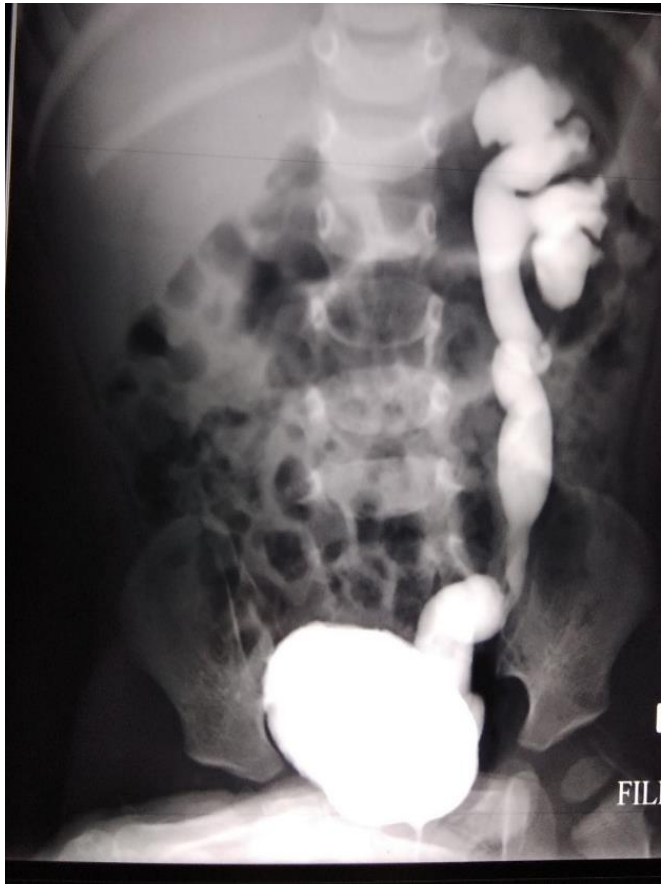


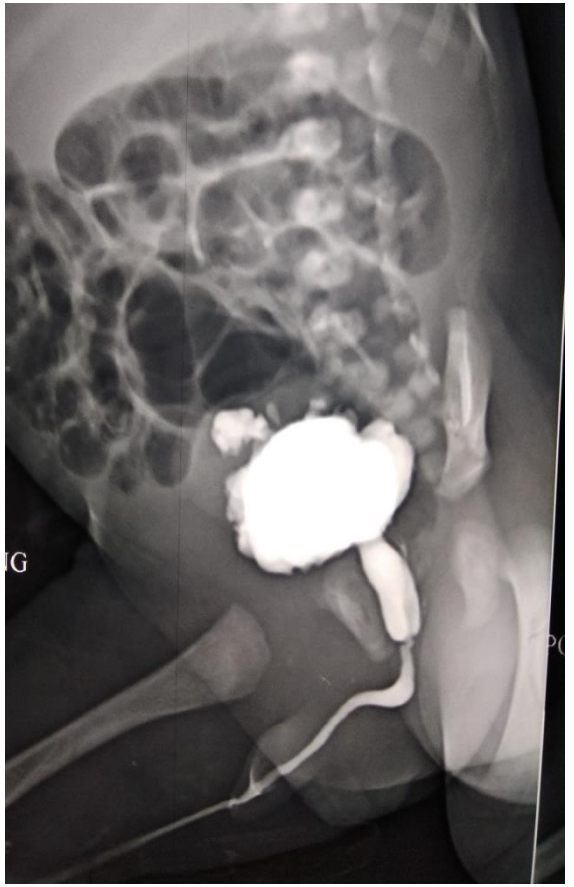
Pankaj H. UTI ISPN guidelines 2022

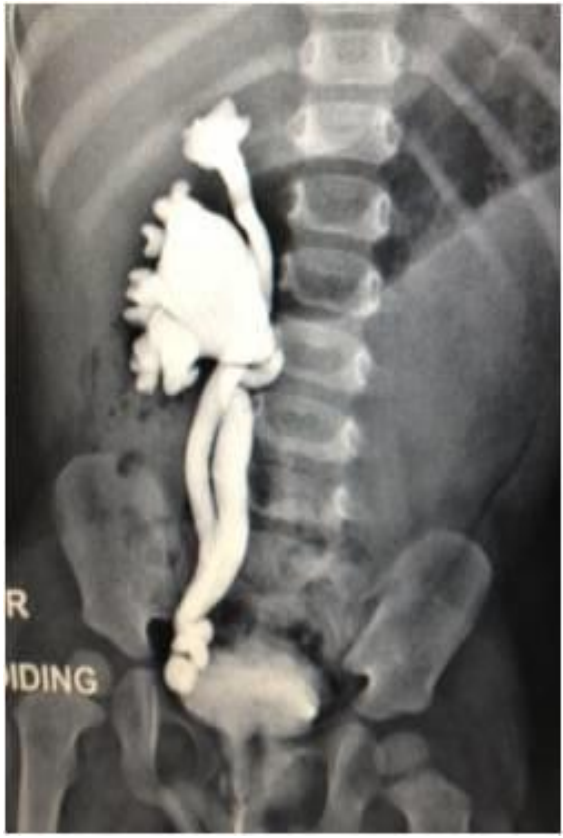
VCUG



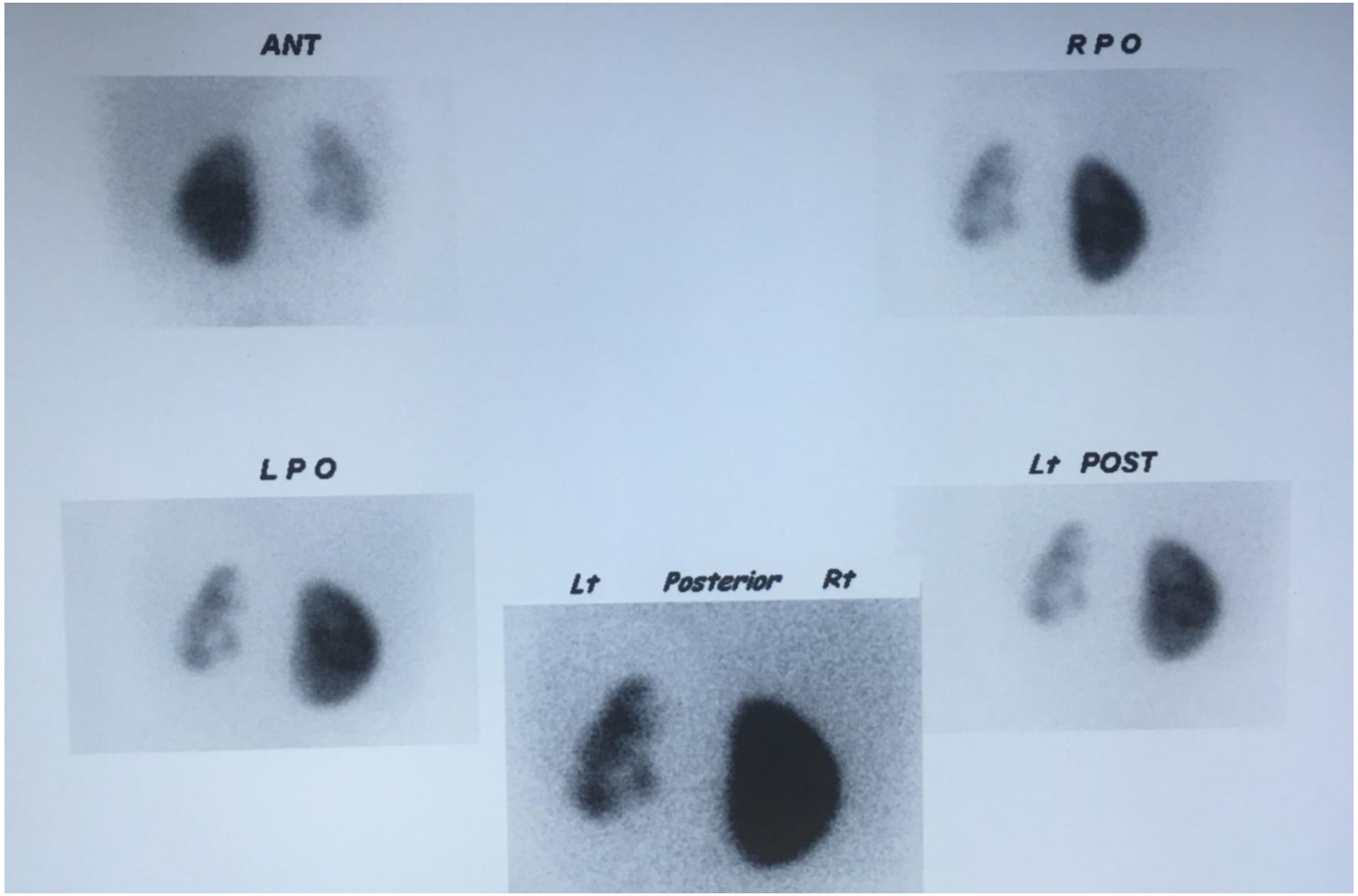


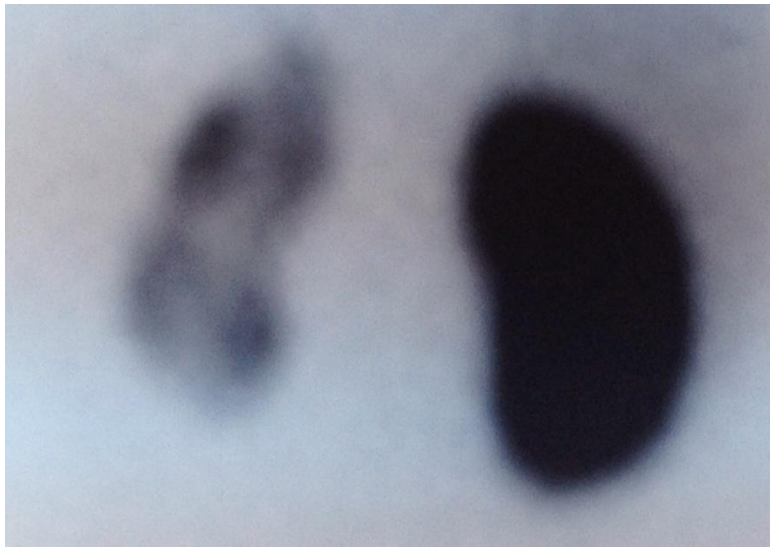






DMSA in UTI





Antimicrobials for treatment of UTI

ORAL

Medication	Dose, mg/kg/day
• Cefixime	8-10, in 2 divided doses
• Coamoxiclav	30-35 of amox., in 2 divided doses
• Ciprofloxacin	10-20, in 2 divided doses
• Ofloxacin	15-20, in 2 divided doses
• Cephalexin	50-70, in 2-3 divided doses

Antimicrobials for treatment of UTI

Parenteral

Medication	Dose, mg/kg/day
• Ceftriaxone	75-100, in 1-2 divided doses IV
• Cefotaxime	100-150, in 2-3 divided doses IV
• Amikacin	10-15, single dose IV or IM
• Gentamicin	5-6, single dose IV or IM
• Coamoxiclav	30-35 of amoxicillin, in 2 divided doses IV

Treatment of ESBL producing organism causing UTI

- Meropenam20 mg/kg/dose 8 hourly (max dose: 3g/day)
- Ertapenam15 mg/kg/dose twice daily (max dose 1g/day)

- Imipenam 60 to 100 mg/kg/day divided every 6 hours (max dose: 4g/day)

Carbapenem sparing agents can be used in non-severe ESBL infections

- Piperacillin tazobactam 200-300 mg/kg/day piperacillin in 3-4 divided doses IV (max. dose 12g piperacillin/day)

Repeat the urine culture in a child with UTI?

- Persistent fever and toxicity despite 72 hours of adequate antibiotic therapy
- Suspected contamination

Few definitions

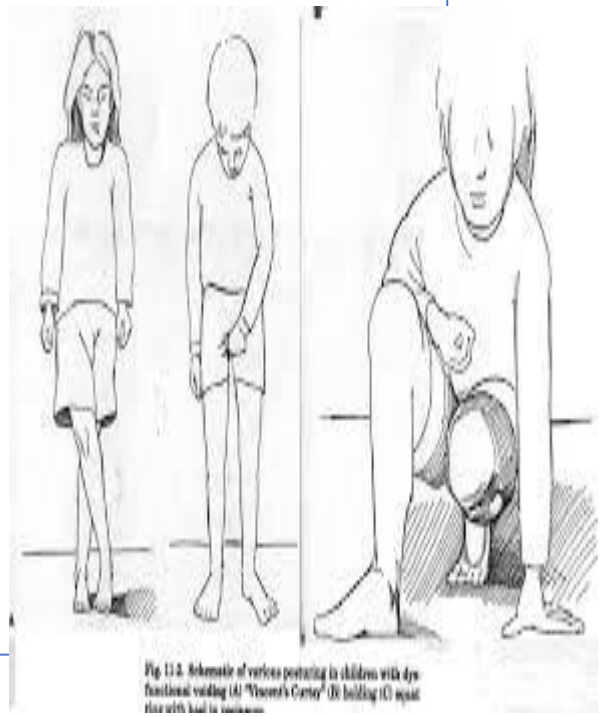
- **Recurrent infection:** second episode of UTI
- **Asymptomatic bacteriuria:** Significant bacteriuria in the absence of symptoms of UTI

Case 5

- 6 year old female child presented with
- H/o fever for 5 days
- H/o pain during urination
- No h/o cloudy urine or hematuria
- No h/o vomiting
- Oral intake good
- H/o febrile UTI thrice in the past, evaluated and found to have right acute pyelonephritis, Gr. IV VUR B/L

Further history

- Voiding diary – in frequent voiding <3 times a day
- Day and night time wetting+
- H/o standing while passing urine/stools
- Constipation +



Case 3

- O/E febrile, hydration adequate
- Abdomen – Soft, UB- palpable, no loin or suprapubic tenderness, loaded sigmoid, no vulval synechiae
- Other system examination – Normal
- Urine routine showed pyuria
- Urine culture grew E.Coli
- USG Abdomen – B/L renomegaly, UB wall thickening and PVR 30ml

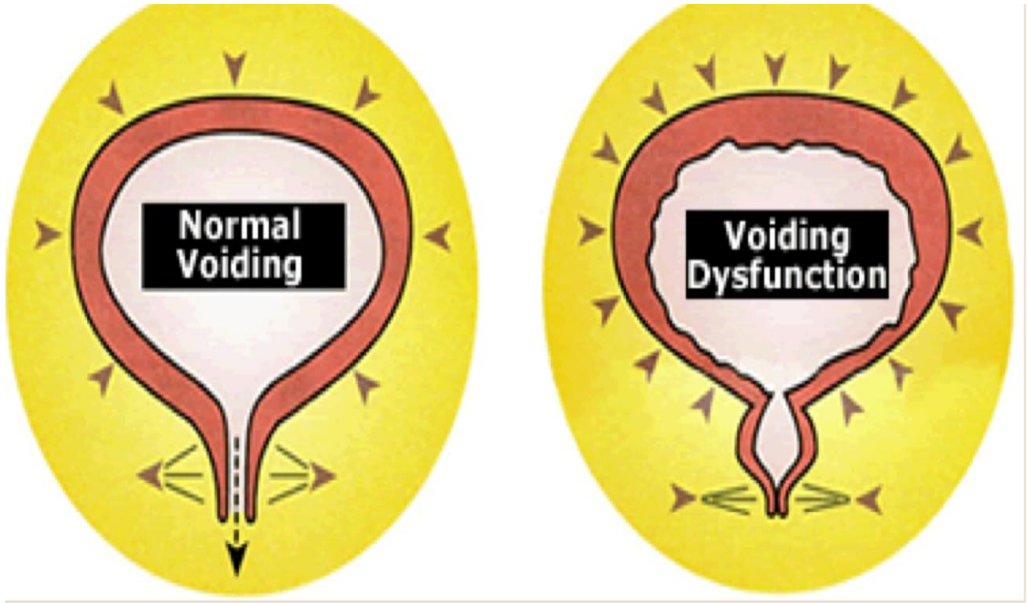
- Recurrent UTI with BBD

Bladder Bowel Dysfunction

- Abnormal patterns of micturition in the presence of intact neuronal pathways without congenital or anatomical abnormalities
- Abnormality - filling phase (overactive bladder) or evacuation phase (dysfunctional voiding)

- H/O constipation, manoeuvres to postpone voiding, voiding <3 or >8/day - suspect BBD

- Thickened UB wall
- PVR >20 ml
- Persistent high grade VUR
- Spinning top configuration of bladder on MCU



Management

- Adequate fluid intake and balanced diet with whole grains, fruits and vegetables

- Treatment of irregular bowels with stool softeners

  PEG 3350, mineral oil, lactulose, lactitol, magnesium hydroxide, sorbitol

  and senna

- Timed voiding, double voiding and squat to void

Prevention of UTI

Cranberry

Large pro-anthocyanidin polymer that inhibits bacterial adherence

No better than antibiotic prophylaxis in preventing UTI

Large quantity of active ingredient required (36-72 g/day)

Non-uniform availability

ISPN 2022

Recommendation

Suggest using cranberry products to prevent UTI in children with recurrent UTI and normal urinary tract (2⊕⊕◯◯)

Circumcision

ISPN 2022

Recommendation

Suggest circumcision be offered to prevent UTI in boys at risk of recurrence (2⊕⊕⊕◯)

Asymptomatic Bacteriuria

- It is a benign condition
- Doesn't cause renal injury and requires no treatment
- The organism isolated in most instances is E. coli (low virulence)
- Eradication often follows symptomatic infection with virulent strains

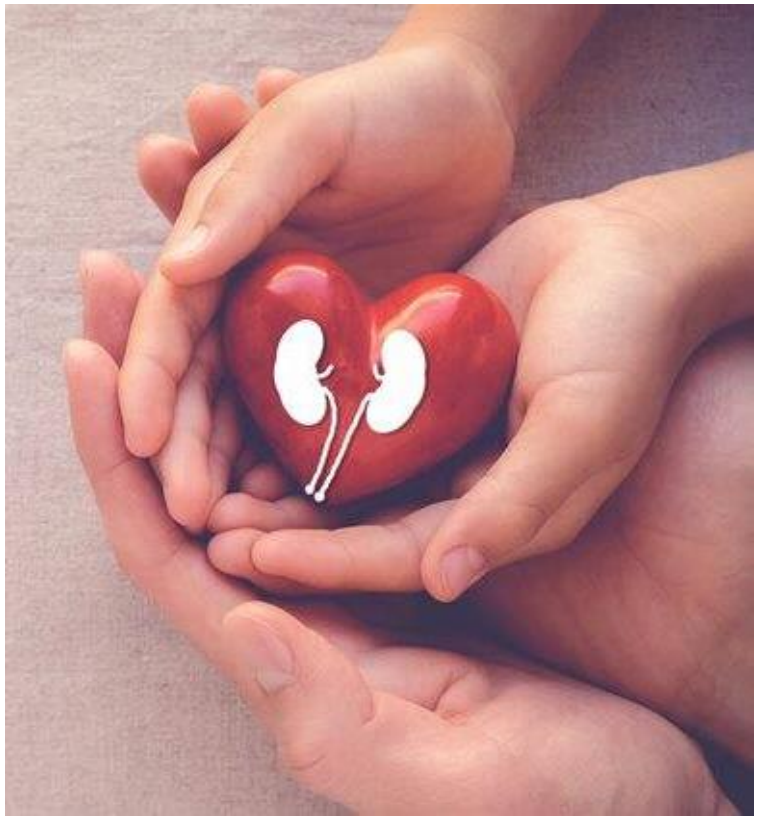
The presence of ABU in a child previously treated for UTI should not be considered as recurrent UTI

Referral to a Pediatric Nephrologist

- Recurrent urinary tract infections
- UTI in association with bowel bladder dysfunction
- Children with VUR
- Underlying urologic or renal abnormalities
- Children with
    - Renal scar
    - Deranged renal functions
    - Hypertension

Take home messages

- Rapid dipstick based tests are useful in screening for UTI
- Culture & sensitivity – Gold standard for diagnosing UTI
- Bladder bowel dysfunction - an important cause for recurrent UTI
- Radio imaging in a stepwise manner - to r/o underlying abnormality
- Children with recurrent UTI, BBD and VUR need regular follow up



Thank you

SLED for AKI in children

Valentine Lobo

Nephrology Unit,

King Edward Memorial Hospital, Pune

Introduction

- Previously healthy 8 year old child, weighing 19 kg,
- Climbed a stone wall which collapsed on him on 5/10/2020.
- Distended, tender abdomen with guarding
- Complete anuria for 8 hours after the event.
- Received around 1000 ml of crystalloid at the time of evacuation.
- Admitted in the PICU at KEM Hospital
- BP = 76/40 mm of Hg, RR 26/min, heart rate 170/min, GCS 15/15.
- Right internal jugular cannula inserted - CVP of 4 cm.
- Other Systems – Unremarkable.
- Further fluid resuscitation and Noradrenaline infusion did not improve urine output
- Hb = 14.8g%, TLC = 16400/mm^3, Plt = 1.64 lacs
- BUN = 92, Creat = 2.7 S. Bil = 0.7, LDH = 1174, SGPT = 734, GOT = 342, Amylase 2371 I U
- CXR – Bilateral small effusions
- USG:- Minimum hemoperitoneum. Mild perisplenic collection.
- Distended bowel loops. Liver normal
- Lt kidney – Normal appearing with 2X 2 cm collection at lower pole, Rt kidney not visualized.

Case 1 contd…

- **CECT abdomen:**
  - solitary left kidney, a non visualized renal artery,
  - splenic lacerations,
  - multiple lacerations in the body and tail of pancreas
  - numerous large & small intraperitoneal collections.

- **Exploratory laporotomy** showed
  - hemoperitoneum
  - widespread intra & retroperitoneal fat necrosis,
  - liquefaction of the jejunal wall, edematous pancreas with slough collection,
  - a thrombosed left renal artery with cyanotic kidney
  - Splenic laceration

- Desloughing, necrosectomy, drain insertion for pancreas
- Splenectomy , nephrectomy & feeding jejunostomy done.
- Post operatively received antibiotics, noradrenaline infusion, intravenous fluids @ 20 ml/hour,
- Elective ventilation.

Case 1 contd…

- **POD-2**: sudden bleeding from the abdominal drain
- Hb: 2.6g%, Platelets- 47000/mm^3, PT & aPTT - prolonged.

- Despite transfusions, developed shock with a systolic BP of 60, hypoxia, bradycardia, & a cardiac arrest.
- Resuscitated

- Circulation was stabilized with
  - Noradrenaline at 0.5 mcg/kg/min
  - Vasopressin at 2.4 U/hr.
  - TPN , RBC & platelet concentrates and fresh frozen plasma given
  - Patient was anuric

  - **What will you do?**
- Restrict fluids
- Start Frusemide
- Initiate CRRT
- Start SLED
- Need more information

Case 1 contd…

- Hb = 5.6g%, TLC = 31,200,Plt =64000/mm3, PT =18/13, aPTT = 54/34
- Blood urea= 167mg%, Creatinine= 7.3mg%,
- Sr. Potassium= 6.5mmol/L. Sodium = 132, Chloride 110mmol/L
- pH= 7.00, pCO2 = 29 mm of Hg, pO2 = 61 mm of Hg, Bicarbonate= 7.3mmol/L,

- CXR – Pulmonary Edema

- BP = 96/52 on Noradrenaline & vasopressin
- Daily Intake (TPN, blood products, drugs & vasopressor infusions) = 1300 ml

- **What are the indications for RRT**
- Hyperkalemia
- Metabolic Acidosis
- Pulmonary Edema
- Uremia
- Anuria with requirement for nutrition, blood products, antibiotics and pressors.

- **What abnormalities will be corrected by RRT?**
- **All of the above**

Planning RRT

- **What difficulties are posed by RRT in this patient?**
- **Multiple pressors with risk of hypotension.**
- **Pulmonary edema needing negative fluid balance.**
- **Coagulopathy and risk of bleeding if anticoagulated**

- **Aims of RRT**
- Achieving a negative balance - Difficulty in ultrafiltration as patient is on 2 pressor agents
- How much fluid should an anuric patient be given keeping in mind pulmonary edema and How should he be monitored?
- Managing lactic (metabolic) acidosis
- How does one ensure that all essential medications and nutrition are given without compromising circulation and ventilation

Planning RRT

- **What information will we require when planning our prescription of RRT ?**
- **Daily obligatory intake**
- **Cumulative fluid balance**
- **Timings of antibiotics**
- **Catabolic state – Rise of BUL**

- **What modality of RRT should such a patient receive?**
  - **Peritoneal Dialysis**
  - **Intermittent Hemodialysis**
  - **CRRT**
  - **Sustained Low Efficiency Dialysis**

  - **What modality of RRT will you choose?**

Prescription for SLEDD

- **Goals**
- The volume of blood products, TPN, antibiotic and pressor infusions, and intravenous fluids amount to 54 ml/hour.
- Within 36 hours he will gain 10% of his dry weight.
- He also has Pulmonary edema and is on Noradrenaline and Vasopressin infusions.
- Needs daily negative balance, correction of acidosis & hyperkalemia.

- **Components**
- *Vascular Access*
- *Dialyzer:-* His body surface area is 0.8m^2,
- *Blood Flow*
- *Dialysate Composition and Flow*
- *Ultrafitration rate and Duration*
- *Anticoagulation*
- *Convection (Optional)*

Prescription for SLEDD

- **What vascular access is ideal in this situation?**
- Central line in Rt IJV being used for antibiotics TPN, Noradrenaline and Vasopressin.
- Femoral line – dedicated
- Catheter should be at least 15 to19 cm long.

- **KDIGO**
- Right internal jugular -first option,
- Femoral site - second option,
- Left internal jugular (LIJ) - third option,
- Avoid subclavian insertions

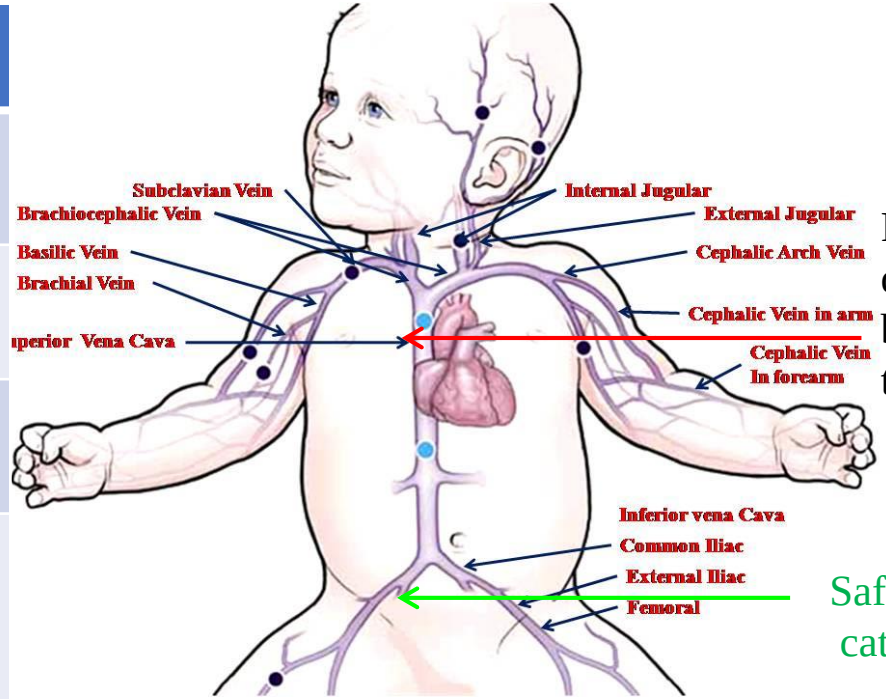
Are Inotropes and Vasopressors Dialyzable

Drug	Vd L/Kg	T1/2 min	Protein Binding	Route of Elimination
Epinephrine	Negligible	short	Absent	Metabolized at site
Norepinephrine	Negligible	2	Absent	Metabolized at site
Dobutamine	0.2	2-3	Absent	Metabolized at site
Dopamine	0.8 to 1.6	2-20	Absent	Metabolized at site
Milrinone	0.45	120	70	Renal
Isoprenaline	0.5	2	35	Metabolized at site

- **Current KDIGO guidelines recommend:**
- Use of a non-tunneled temporary dialysis catheter;
- Diameter according to patient size
- Location of the catheter tip in the mid-atrium with arterial lumen facing the mediastinum but not allowing the catheter tip to touch the atrium floor
- Double lumened catheters preferred to triple lumened catheters for renal replacement therapy in critically ill patients.

-See and Bellomo Crit Care (2021) 25:1

Patient size	Catheter size	Site of insertion
< 10 kg	double lumen 6.5, OR 7F	Femoral / Jugular vein
10 to 20 Kg	Double lumen 8F	Femoral / Jugular vein
20 to 30 Kg	Double lumen 10F	Femoral / Jugular vein
> 30 Kg	Double lumen 11.5F	Femoral / Jugular. Avoid subclavian unless no other site available



RRT access will interfere w drugs, inotropes & nutritio being administered through a central line

Safe site for a dedicated RRT catheter

Cardiac arrest in intensive care unit: Case report and future recommendations

A. Mohammad,
N. Zafar,
A. Feerick[1]

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www.saudija.org

A B S T R A C T

Initiation of hemofiltration in a patient in septic shock can cause hemodynamic compromise potentially leading to cardiac arrest. We propose that the standard '4Hs and 4Ts' approach to the differential diagnosis of a cardiac arrest should be supplemented in critically ill patients with anaphylaxis and human and technical errors involving drug administration (the 5th H and T). To illustrate the point, we report a case where norepinephrine infused through a central venous catheter (CVC) was being removed by the central venovenous hemofiltration (CVVH) catheter causing the hemodynamic instability. CVVH has this potential of interfering with the systemic availability of drugs infused via a closely located CVC.

Key words: *CVVH, cardiac arrest, errors*

DOI: 10.4103/1658-354X.62613

Case Report

When Drugs Disappear from the Patient: Elimination of Intravenous Medication by Hemodiafiltration

Kay H. Stricker, MD*†
Jukka Takala, MD, PhD*
Roger Hullin, MD, PhD‡
Christoph C. Ganter, MD*

Twenty-three hours after heart transplantation, life-threatening acute right heart failure was diagnosed in a patient requiring continuous venovenous hemodiafiltration (CVVHDF). Increasing doses of catecholamines, sedatives, and muscle relaxants administered through a central venous catheter were ineffective. However, a bolus of epinephrine injected through an alternative catheter provoked a hypertensive crisis. Thus, interference with the central venous infusion by the dialysis catheter was suspected. The catheters were changed, and hemodynamics stabilized at lower catecholamine doses. When the effects of IV drugs are inadequate in patients receiving CVVHDF, interference with adjacent catheters resulting in elimination of the drug by CVVHDF should be suspected.

(Anesth Analg 2009;109:1640–3)

Selecting A Dialyzer for SLED/SLED-f

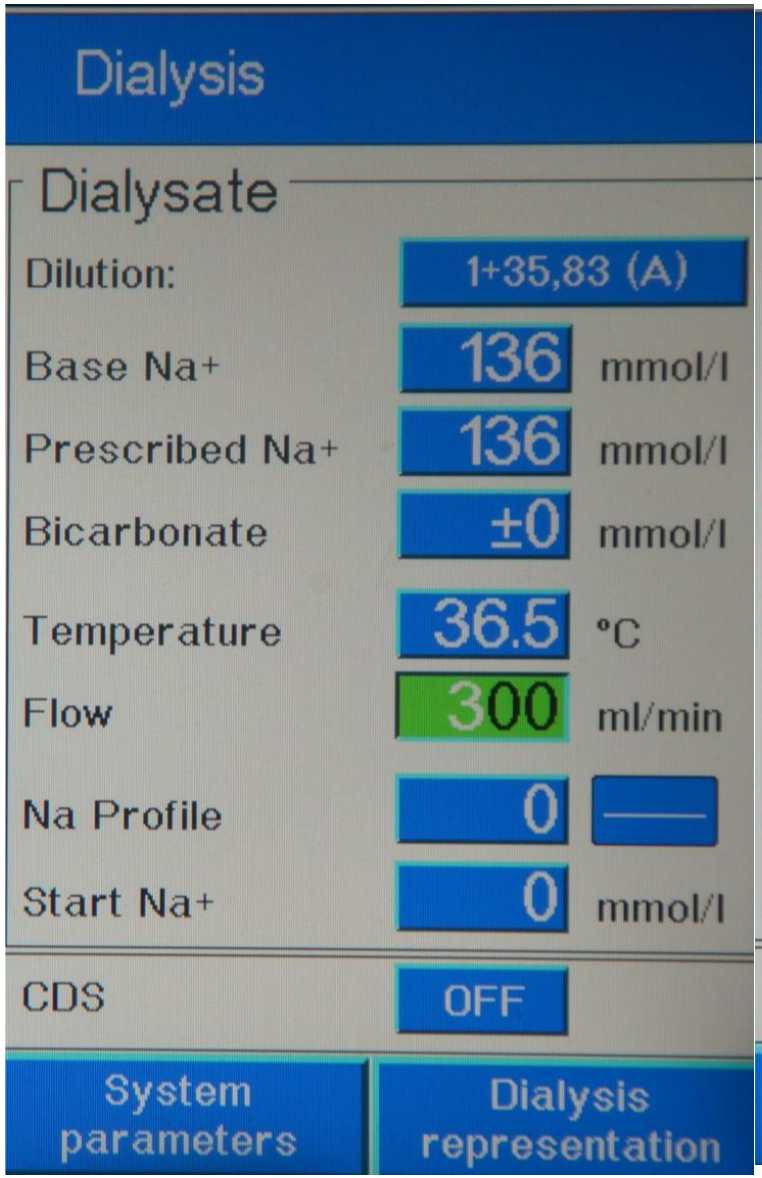
Parameter	Sureflux 5N (Nipro)	FX40 (Fresenius)	FX ped (Fresenius)	Polyflux 6H (Gambro)	F4HPS	F3
Surface Area (m^2)	0.5	0.6	0.2	0.6	0.8	0.4
Priming Volume (ml)	34	53	18	52	51	28
Ultra filtration Coefficient	2.7	20	7	33	8	1.7
Urea Clearance	130*	170#	76!	50§	170	125
Creatinine Clearance	109*	144#	64!	50§	143	95
Phosphate Clearance	62*	138#	57!	49§	123	50
Material	Cellulose triacetate	Helixone	Helixone	Polyflux^	Polysulfone	Polysulfone
Blood flow (ml/min)	50 - 100	50 - 200	30 - 100	50 - 200	50 - 200	40 - 100
Sterilization	Gamma ray	Inline Steam	Inline Steam	Inline Steam	Inline Steam	ETO

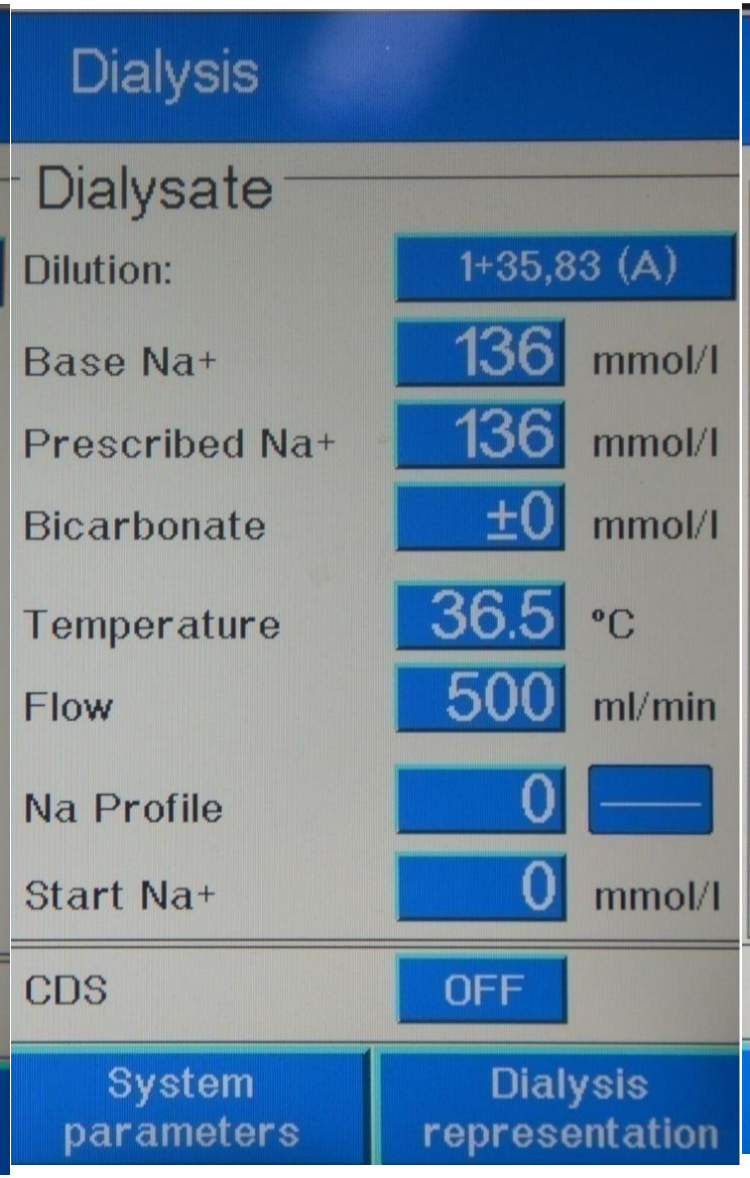
* At Qb = 200 ml/min. # At Qb = 200 ml/min. ! At Qb = 100 ml/min § At Qb = 50 ml/min, ^ Polyflux is a blend of Polyarylethersulfone, Polyvinylpyrrolidone, Polyamide.

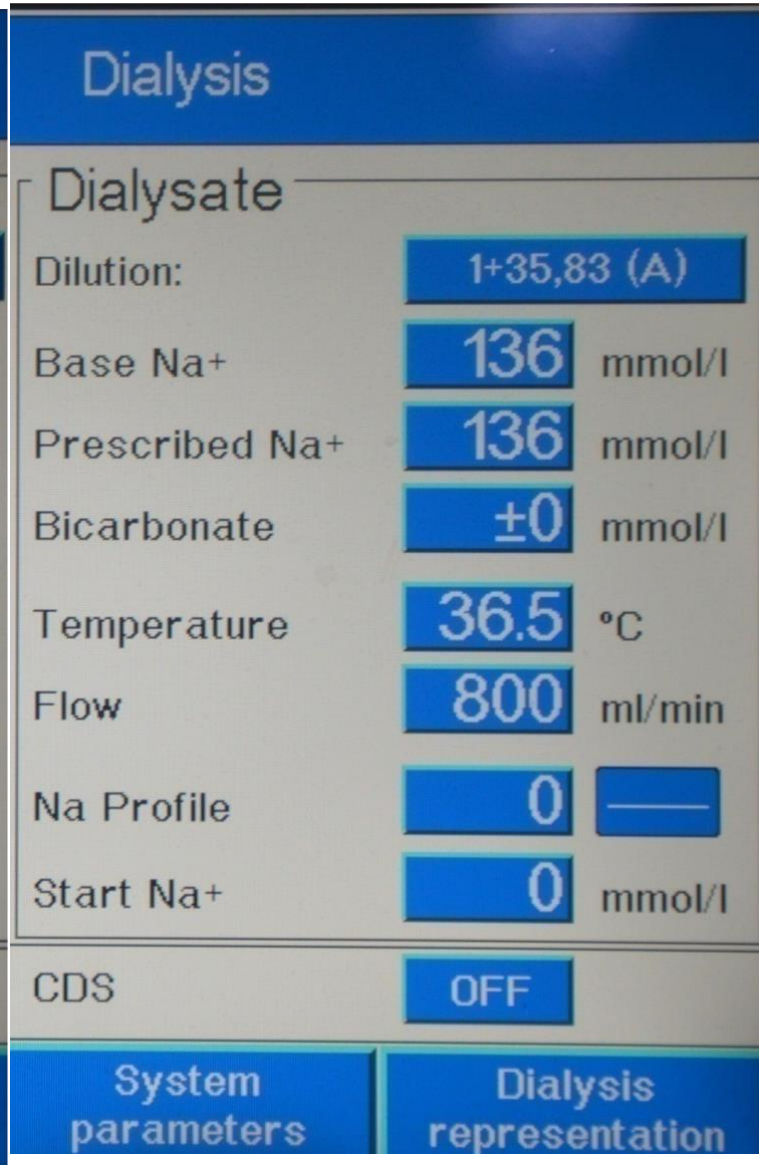
Blood &Dialysate Flow rate & Composition

- Blood flow rate (Qb) usually between 200-300 mL/min,
- Limited by temporary access in AKI patients.
- Higher blood flows allow lower anticoagulation or anticoagulation free sessions
- Higher blood flows in SLED-f to enhance convection without increasing filtration fraction and compromising circuit life.
- Prevent DDS by using smaller dialysers and by reducing Qb , Qd & dialysis time.
- Dialysate flow rate (Qd) ranges from 100 to 300 mL/min, usually lowest possible on the machines, which avoids wastage of the dialysate.
- Session length and dialysate flow usually inversely related.
- Sessions longer than 8 hours, a dialysate potassium concentration of 4 mmol/L and bicarbonate of 24 to 28 mmol/L
- Shorter sessions performed with a potassium of 3-4 mmol/L and bicarbonate of 28-32 mmol/L.
- Calcium in the dialysate may vary between 1.5 to 2.5 mmol/L, a higher value may improve cardiac contractility in selected cases.
- The dialysate composition may be tailored for individual patients according to intra-dialytic or postdialysis plasma values.

Dialysate Flow Options







Flow is a function of Dialysate flow motor RPM and gear ratio


T1 test
Status
Info
Info
100
ml/min
ART
mmHg
0
300
-300
Flow
ml/min
100
AutoFlow
Yes
HDF factor
1.2
Flow
I/O
Temperature
°C
36.5
BTM
--
Blood flow
Ø 8.0mm
I/O
Bld. press.
- / -
0
1
0
0
1000
900
800
700
600
500
400
300
200
100
C
OK
VEN
mmHg
0
500
-100
HEPARIN
ONLINE
BLOOD SYSTEM
PARATION
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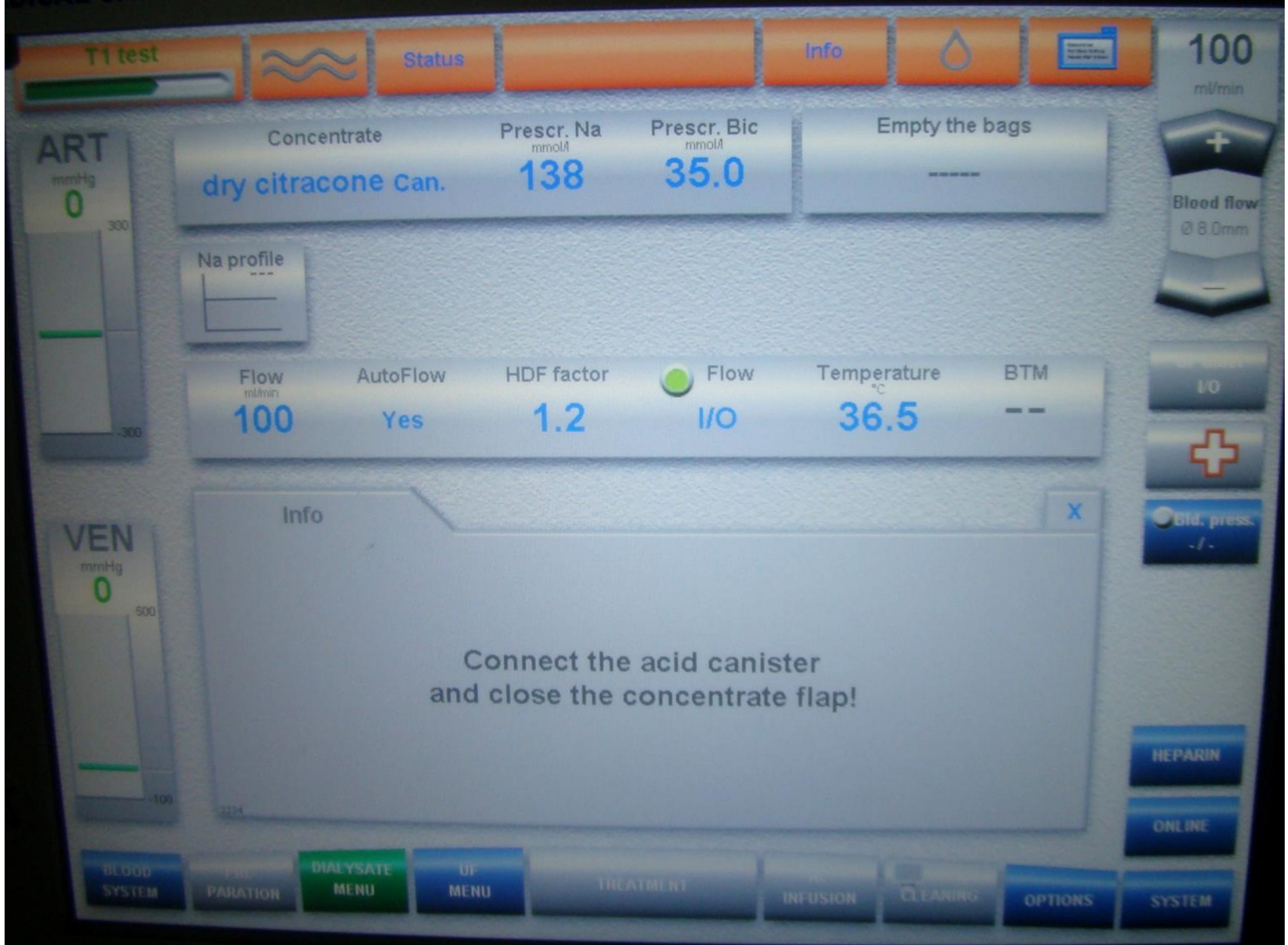
UF MENU
TREATMENT
INFUSION
CLEANING
OPTIONS
SYSTEM


T1 test
Status
Info
100
ml/min
ART
mmHg
0
300
-300
Concentrate
dry citracone Can.
Prescr. Na
mmol/l
138
Prescr. Bic
mmol/l
35.0
Empty the bags

Blood flow
Ø 8.0mm
Na profile

Flow
ml/min
100
AutoFlow
Yes
HDF factor
1.2
Flow
I/O
Temperature
°C
36.5
BTM
--
I/O
Bld. press.
-/-
VEN
mmHg
0
500
-100
Info
X
Connect the acid canister
and close the concentrate flap!
HEPARIN
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TREATMENT
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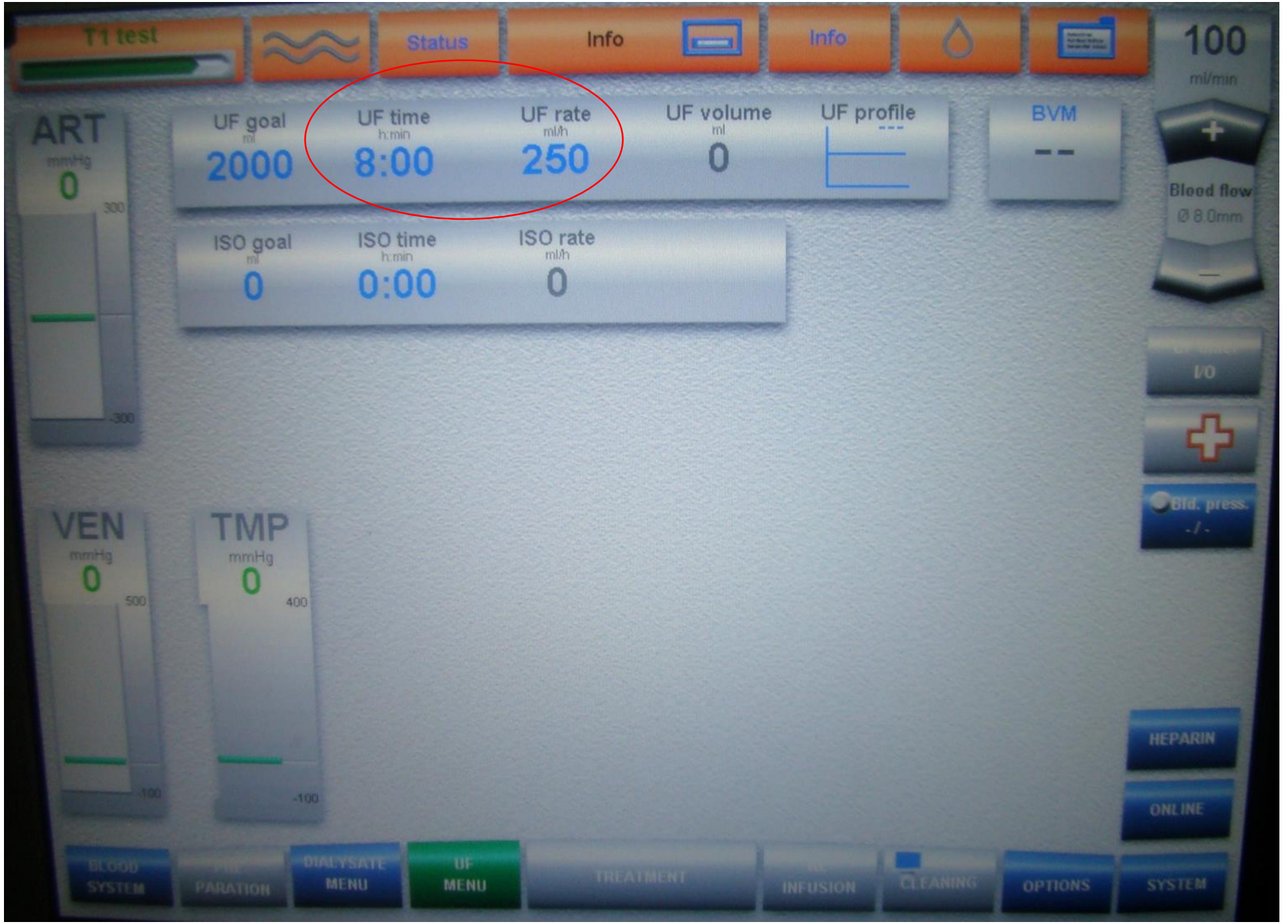
T1 test
Status
Info
Info
100
ml/min
ART
mmHg
0
300
-300
UF goal
ml
2000
UF time
h:min
8:00
UF rate
ml/h
250
UF volume
ml
0
UF profile
BVM
--
Blood flow
Ø 8.0mm
ISO goal
ml
0
ISO time
h:min
0:00
ISO rate
ml/h
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I/O
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-/-
VEN
mmHg
0
500
100
TMP
mmHg
0
400
-100
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TREATMENT
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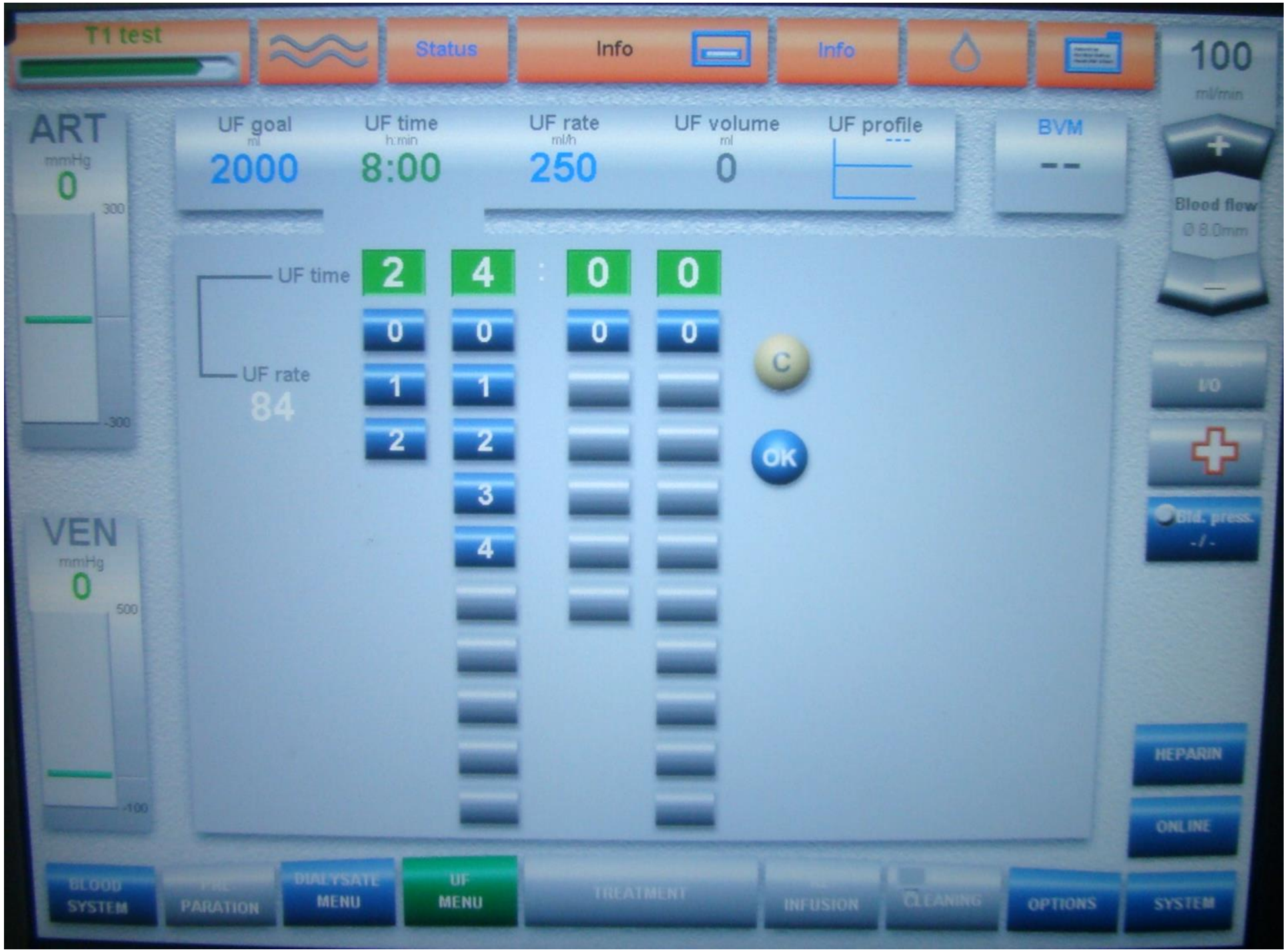
CLEANING
OPTIONS
SYSTEM


T1 test
Status
Info
Info
100
ml/min
ART
mmHg
0
300
-300
UF goal
ml
2000
UF time
h:min
8:00
UF rate
ml/h
250
UF volume
ml
0
UF profile
BVM
--
Blood flow
Ø 8.0mm
UF time
2 4 : 0 0
UF rate
84
C
OK
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OPTIONS
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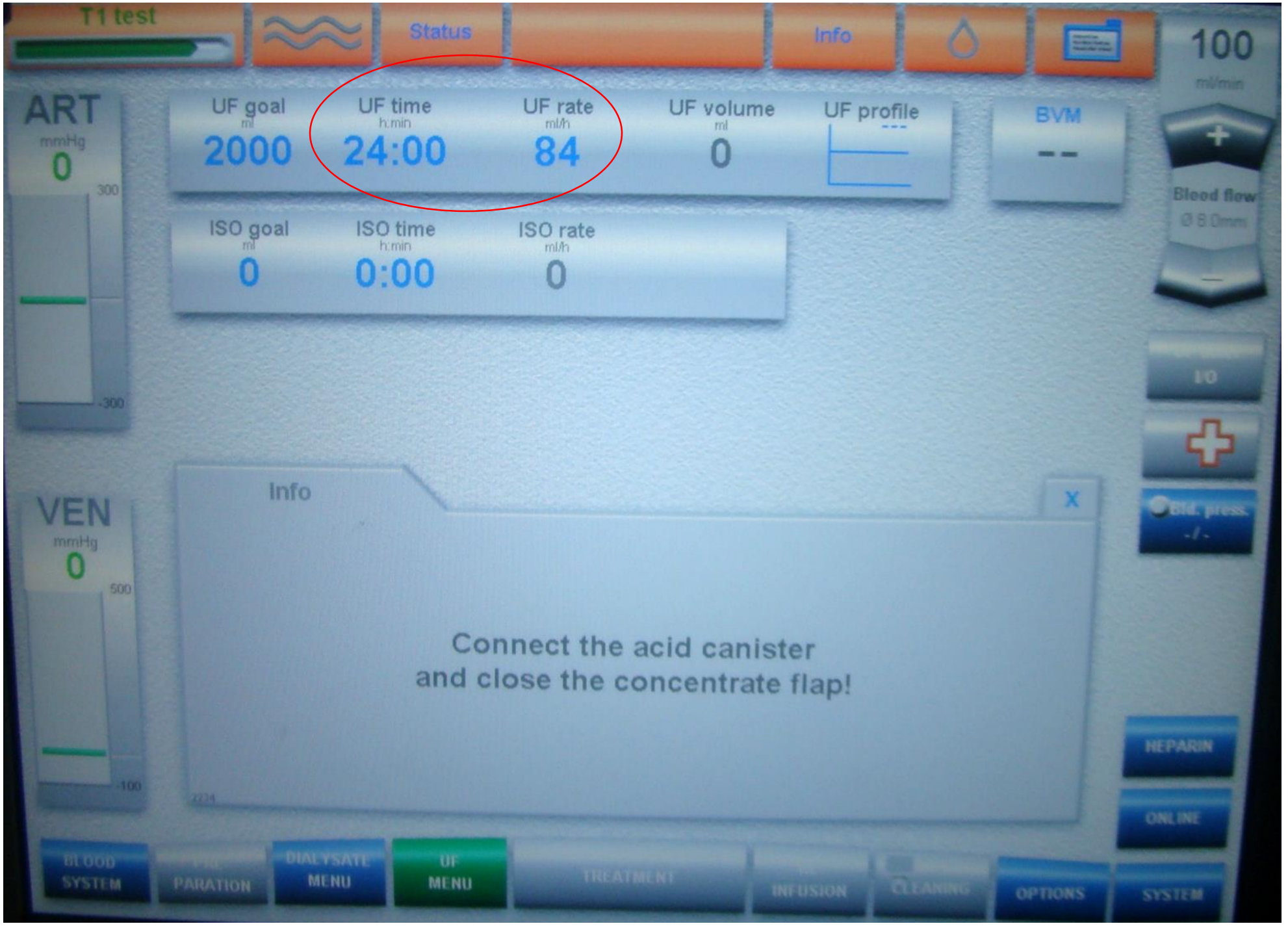
T1 test
Status
Info
100
ml/min
ART
mmHg
0
300
-300
UF goal
ml
2000
UF time
h:min
24:00
UF rate
ml/h
84
UF volume
ml
0
UF profile
BVM
--
ISO goal
ml
0
ISO time
h:min
0:00
ISO rate
ml/h
0
Blood flow
Ø 8.0mm
VEN
mmHg
0
500
-100
Info
X
Connect the acid canister
and close the concentrate flap!
2234
HEPARIN
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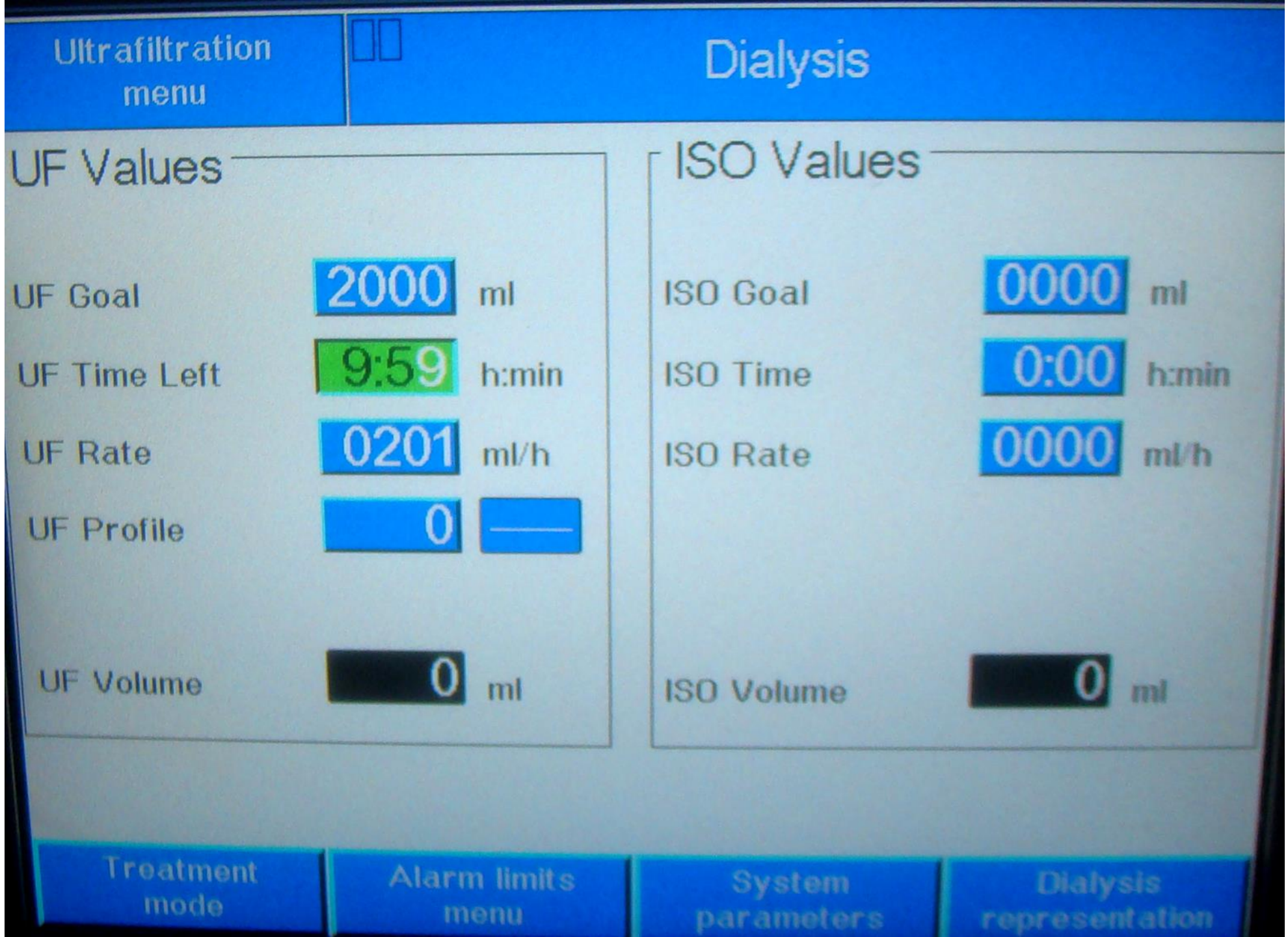
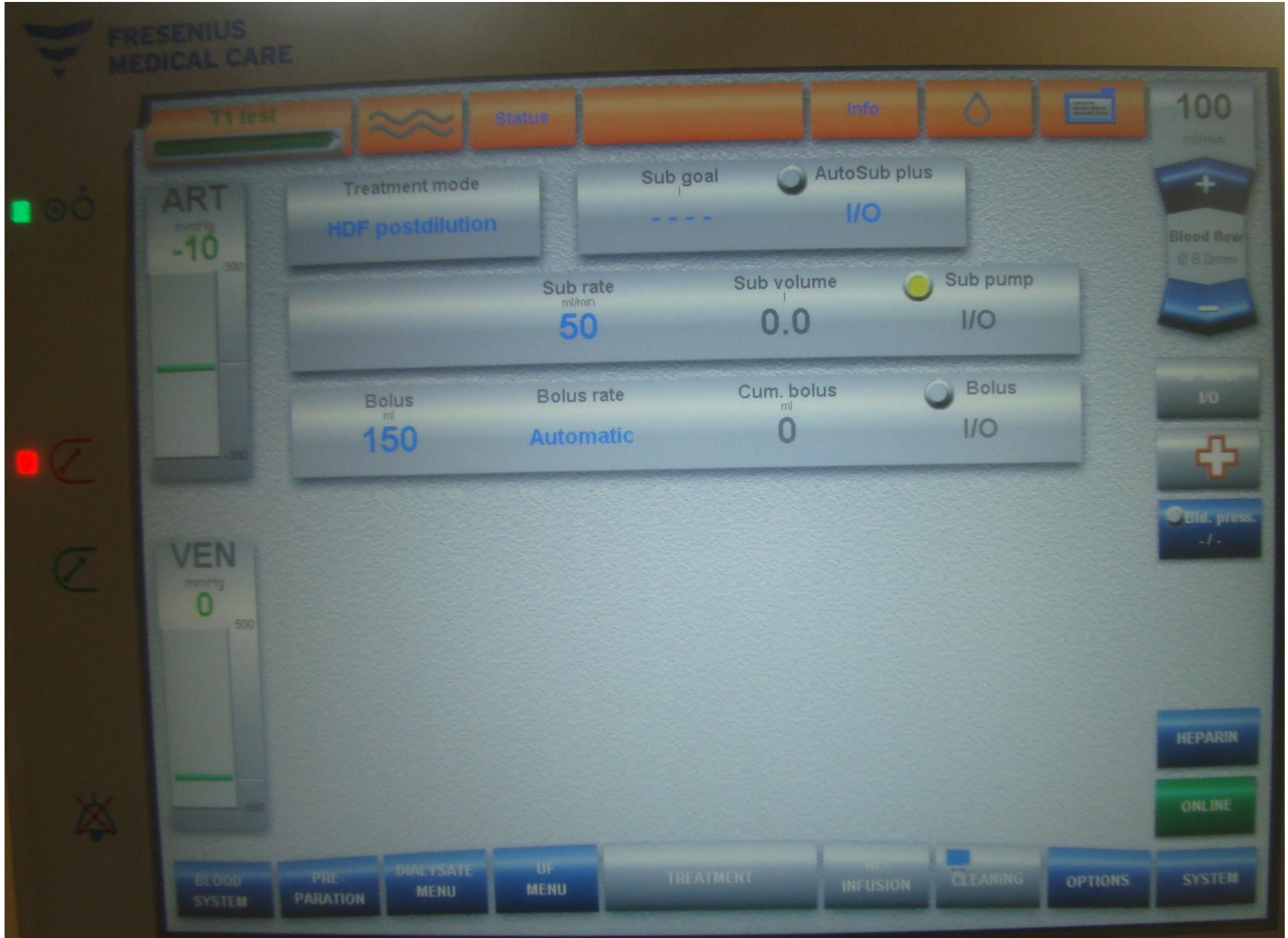
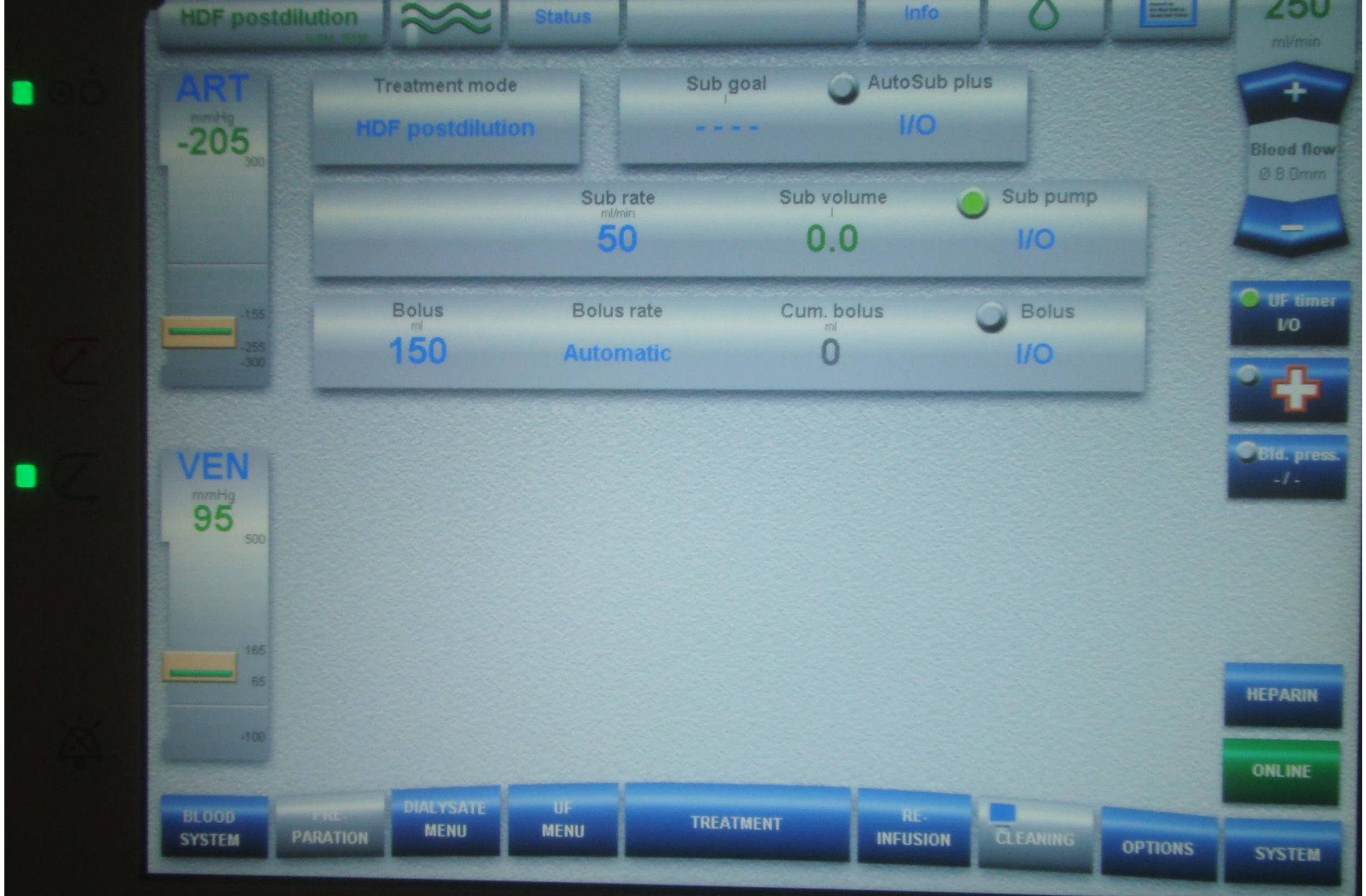
UF MENU
TREATMENT
INFUSION
CLEANING
OPTIONS
SYSTEM


Ultrafiltration menu
Dialysis
UF Values
UF Goal
2000
ml
UF Time Left
9:59
h:min
UF Rate
0201
ml/h
UF Profile
0
UF Volume
0
ml
ISO Values
ISO Goal
0000
ml
ISO Time
0:00
h:min
ISO Rate
0000
ml/h
ISO Volume
0
ml
Treatment mode
Alarm limits menu
System parameters
Dialysis representation

Infusion flow rate – in SLED-F

- Relatively little information on the optimal SLED-F prescription.
- Substitution flow rates vary between 33 and 100
- May use higher rates in septic multiorgan failure (> 200ml/min)
- One third of the blood flow in a post-dilution modality and half the blood flow in pre-dilution, to minimize the filtration fraction, and fouling/ risk of clotting.
- Auto-substitution systems optimise infusion flows, based on TMP and Kuf measurement,
- Preferred substitution modality when SLED-F is used.


FRESENIUS
MEDICAL CARE
TI test
Status
Info
100
ml/min
ART
mmHg
-10
300
-300
Treatment mode
HDF postdilution
Sub goal
- - - -
AutoSub plus
I/O
Blood flow
@ 8.0mm
Sub rate
ml/min
50
Sub volume
0.0
Sub pump
I/O
I/O
Bolus
ml
150
Bolus rate
Automatic
Cum. bolus
ml
0
Bolus
I/O
Bld. press.
- / -
VEN
mmHg
0
500
-100
HEPARIN
ONLINE
BLOOD SYSTEM
PRE-PARATION
DIALYSATE MENU
UF MENU
TREATMENT
INFUSION
CLEANING
OPTIONS
SYSTEM


HDF postdilution
Status
Info
250
ml/min
ART
mmHg
-205
300
-155
-255
-300
Treatment mode
HDF postdilution
Sub goal
- - - -
AutoSub plus
I/O
Sub rate
ml/min
50
Sub volume
l
0.0
Sub pump
I/O
Bolus
ml
150
Bolus rate
Automatic
Cum. bolus
ml
0
Bolus
I/O
Blood flow
Ø 8.0mm
UF timer
I/O
Bld. press.
- / -
VEN
mmHg
95
500
165
65
-100
HEPARIN
ONLINE
BLOOD SYSTEM
PRE-PARATION
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UF MENU
TREATMENT
RE-INFUSION
CLEANING
OPTIONS
SYSTEM


TT test
Status
Info
100
ml/min
ART
mmHg
-10
300
-300
Treatment mode
HDF postdilution
Sub goal
l
71.7
AutoSub plus
I/O
Blood flow
Ø 8.0mm
Sub rate
ml/min
49
Sub volume
l
0.0
Sub pump
I/O
I/O
Bolus
ml
150
Bolus rate
Automatic
Cum. bolus
ml
0
Bolus
I/O
Bld. press.
- / -
VEN
mmHg
0
500
-100
HEPARIN
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PRE-PARATION
DIALYSATE MENU
UF MENU
TREATMENT
INFUSION
CLEANING
OPTIONS
SYSTEM


FRESENIUS
MEDICAL CARE
T1 test
Status
Info
100
ml/min
ART
mmHg
-10
300
-300
Treatment mode
HDF postdilution
Estimated sub goal
0.0
AutoSub plus
I/O
Blood flow
Ø 8.0mm
Sub rate
ml/min
0
Sub volume
0.0
Sub pump
I/O
I/O
Bolus
ml
150
Bolus rate
Automatic
Cum. bolus
ml
0
Bolus
I/O
Bld. press.
- / -
VEN
mmHg
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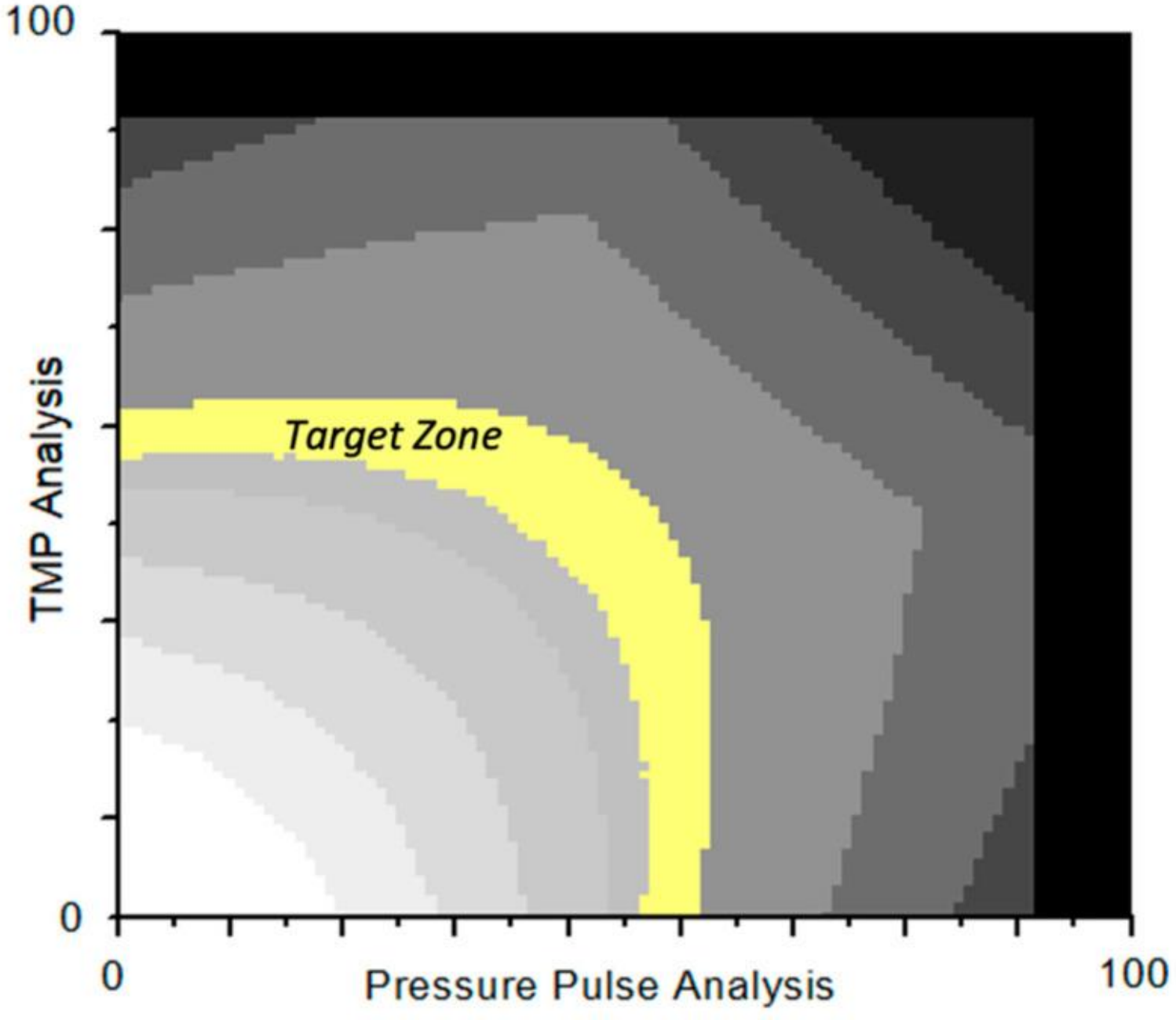
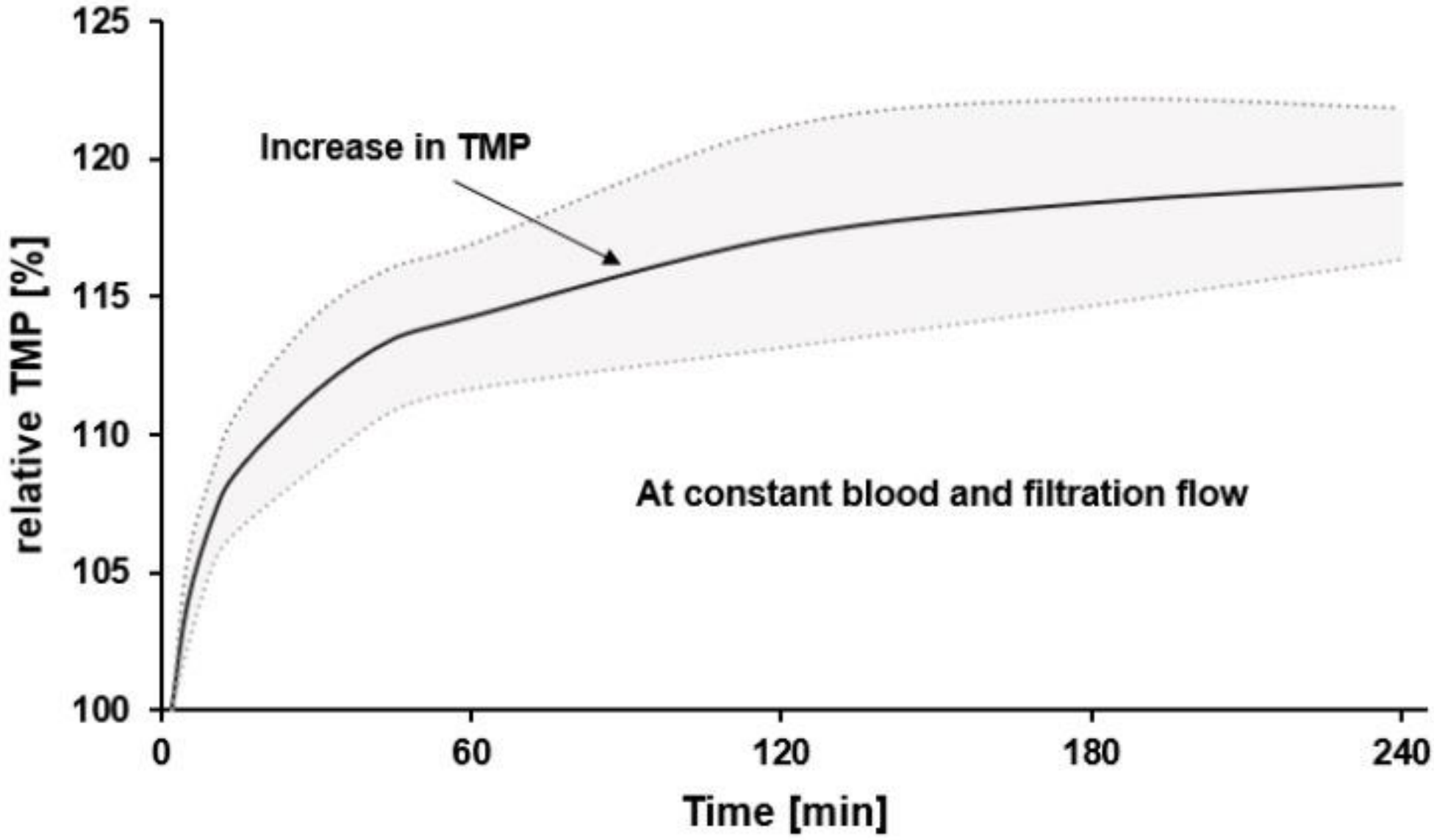
CLEANING
OPTIONS
SYSTEM

Auto Subplus™ - Substitution target matrix



AutoSub plus™



(B)

Artificial Organs (2019)


HDF postdilution
Status
Info
200
ml/min
ART
mmHg
-200
300
-155
-255
-300
Treatment mode
HDF postdilution
Estimated sub goal
l
118.8
AutoSub plus
I/O
Blood flow
Ø 8.0mm
Sub rate
ml/min
84
Sub volume
l
4.1
Sub pump
I/O
UF timer
I/O
Bolus
ml
150
Bolus rate
Automatic
Cum. bolus
ml
0
Bolus
I/O
Bld. press.
- / -
VEN
mmHg
140
500
210
110
-100
HEPARIN
ONLINE
BLOOD SYSTEM
PRE-PARATION
DIALYSATE MENU
UF MENU
TREATMENT
RE-INFUSION
CLEANING
OPTIONS
SYSTEM


HDF postdilution
Status
Info
270
ART
-120
Treatment mode
HDF postdilution
Estimated sub goal
123.4
AutoSub plus
I/O
Sub rate
ml/min
87
Sub volume
23.6
Sub pump
I/O
Bolus
ml
150
Bolus rate
Automatic
Cum. bolus
ml
0
Bolus
I/O
VEN
mmHg
235
500
295
195
-100
UF timer
I/O
Bld. press.
-/-
BTM
HEPARIN
ONLINE
BLOOD SYSTEM
PREPARATION
DIALYSATE MENU
UF MENU
TREATMENT
RE-INFUSION
CLEANING
OPTIONS
SYSTEM


FRESENIUS
MEDICAL CARE
HDF postdilution
Status
Info
270
ml/min
ART
-110
Treatment mode
HDF postdilution
Sub goal
71.7
AutoSub plus
I/O
Sub rate
ml/min
42
Sub volume
l
23.6
Sub pump
I/O
Blood flow
Ø 6.0mm
Bolus
ml
150
Bolus rate
Automatic
Cum. bolus
ml
0
Bolus
I/O
UF timer
I/O
Bld. press.
- / -
VEN
310
BTM
HEPARIN
ONLINE
BLOOD SYSTEM
PREPARATION
DIALYSATE MENU
UF MENU
TREATMENT
RE-INFUSION
CLEANING
OPTIONS
SYSTEM


HDF postdilution
Status
Info
270
ml/min
ART
mmHg
-125
Concentrate
SK-F 311 Can.
Prescr. Na
mmol/l
138
Prescr. Bic
mmol/l
35.0
Empty the bags
Na profile
Blood flow
@ 8.0mm
Flow
ml/min
324
AutoFlow
Yes
HDF factor
1.2
Flow
I/O
Temperature
°C
36.0
BTM
UF timer
I/O
Bld. press.
- / -
VEN
mmHg
240
500
295
195
-100
CD
mS/cm
13.7
15.7
14.5
13.1
12.8
BTM
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ONLINE
BLOOD SYSTEM
PREPARATION
DIALYSATE MENU
UF MENU
TREATMENT
RE-INFUSION
CLEANING
OPTIONS
SYSTEM

Prescription for SLEDD

- *Vascular Access:*- 8F double lumened canula in left femoral vein.
- The canula length needs to be increased from 9-11 cm for the internal jugular to around 15 cm in the femoral vein for this boy.

- *Dialyzer:*- His body surface area is 0.8m^2, :-
- His body surface area is 0.8m^2, so we choose a dialyzer of 0.6 to 0.8m^2. FX40, F4HPS, or Polyflux 6L are all appropriate and will give adequate small solute clearance.
- FX40, F40S or Polyflux 6H have ultrafiltration coefficients capable of use for HDF.

- *Blood Flow:*- at 5ml/kg/min this is 95ml/min, so we will start with 100ml/min.
- If HDF increase to 120ml/min, achievable easily with an 8F canula.

- *Dialysate Composition and Flow :*- Ideally 100ml/min or the lowest possible on the machine.
- Ensure a dialysate sodium of 140mmol/L or higher for the first session.
- As there is severe acidosis and hyperkalemia, choose a bicarbonate of $\geq$ 32mmol/L and potassium of 2.1mmol/L(default)

Prescription for SLEDD

- *Ultrafitration rate and Duration:*- We need to accommodate the intake of 1300ml/day and also fluid removal to correct pulmonary edema and make ventilation easier.
- Adding an additional 500 ml gives us a target UF of 1800 ml.
- If we target 80ml/hour (4ml/kg/hour), this gives us a 24 hour session, which would be well tolerated.
- This can be modified during the session depending on MAP, fluid intake and PaO2/FiO2 ratio.
- In fact we can start without UF and add it after MAP stabilizes with acidosis & Hyperkalemia correction.

- *Anticoagulation:*- None as the patient is coagulopathic, bleeding and has had recent major surgery.

- *Convection (Optional):*- We can add replacement fluid pre filter or post filter.
- The smallest permissible amount 25ml/min is around 75 ml/kg/hour for this child and would give a filtration fraction of 25% at 100ml/min of blood flow and 20% at 120 ml/min.

Final Solutions

- Taken for SLEDD-f on 4008 ArrT plus machine with FX-40 Polysulfone dialyzer
- 20 hour session done.
- UF of 1800 ml.
- Blood flow 135 ml/minute,
- Dry Bicarbonate dialysate at 200 ml/minute & replacement fluid at 33 ml/min (100 ml/kg/hr)
- No anticoagulant
- Amphotericin B given post SLEDD.
- No Hypotension so Noradrenaline decreased to 0.5 mcg/Kg/min and Vasopressin stopped.

- 7 further cycles of SLEDD done over 9 days using Dry Citrasate bicarbonate dialysate at 200 ml/min,
- Extubated after 3rd cycle.
- Noradrenaline requirement decreased to 0.02 mcg/kg/minute & Patient shifted to the ward.
- 1 cycle of SLEDD done from the ward.
- Oral feeding established

- Was discharged on the 29th post operative day, on a maintenance hemodialysis program.
- Cuffed tunneled catheter inserted in the left internal jugular vein
- Jejunostomy pull through and closure at follow up
- Planned for renal transplantation.

Primary Hypertension In Children: What pediatricians should know

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Professor & Head, Dept of Pediatric Nephrology
St John's Medical College, Bangalore

check-up in your OPD. He has no complaints but his mother is concerned that he is addicted to his mobile phone.

On examination, weight = 54kg, height = 152cm, BMI = 23.4 (90^{th} percentile).

BP = 128/82mmHg and 130/76mmHg

- You must document whether BP is normal is his school form
- How would you classify this child's BP?
- What is your approach?

Defining HTN in children

- AAP 2017

BP Category	Age < 13 years	Ages 13 years & older
Normal	<90th percentile for age, sex, and height	<120/<80 mm Hg
Elevated	90th–<95th percentile for age, sex, and height	120 129/<80 mmHg
Hypertension	≥95th percentile	SBP 130 or more
	≥95th percentile + 12 mm Hg	≥140/≥90 mm Hg

True or False?

- Routine BP measurement in children in not required in primary care settings
- Healthy (asymptomatic) children do not have HTN
- Hospital anxiety typically gives falsely elevated BP readings
- Secondary HTN is more common in children > 13yrs
- Avoiding anti-hypertensive medications for otherwise healthy children is ideal.
- If HTN is detected, pediatricians must refer child to pediatric nephrology centre

Common Misconceptions regarding pediatric HTN

Primary Hypertension is diagnosed when there no evidence of a secondary cause of HTN

1.3 billion adults estimated to have HTN. Only 42% are diagnosed / treated

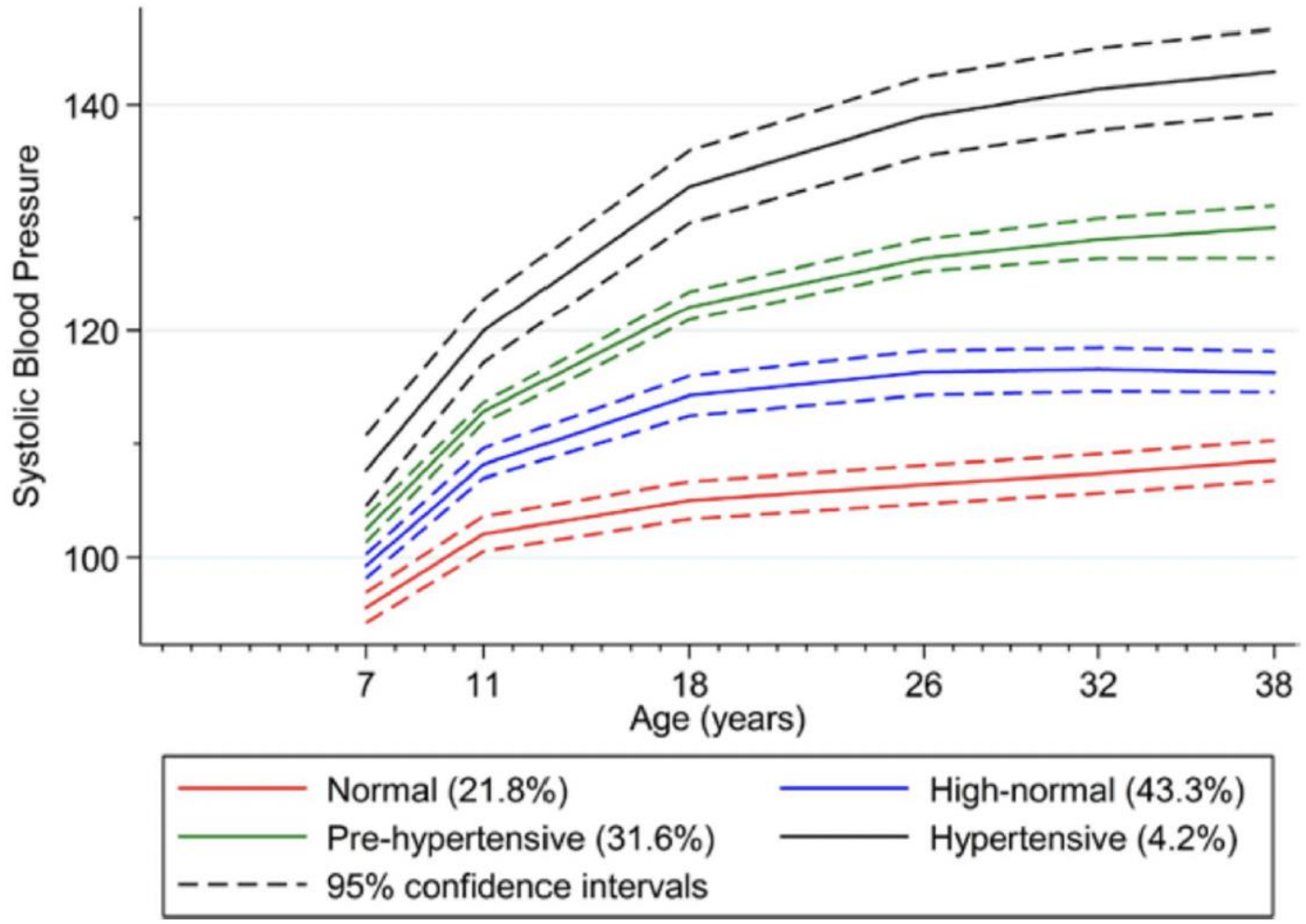
HTN is the greatest modifiable risk factor for cardiovascular death

How does this information apply to pediatricians?

World Health Organization

BP trajectory during life course:

Hypertensive child → hypertensive adult



Theodore RF,

What is the Prevalence of Childhood HTN?

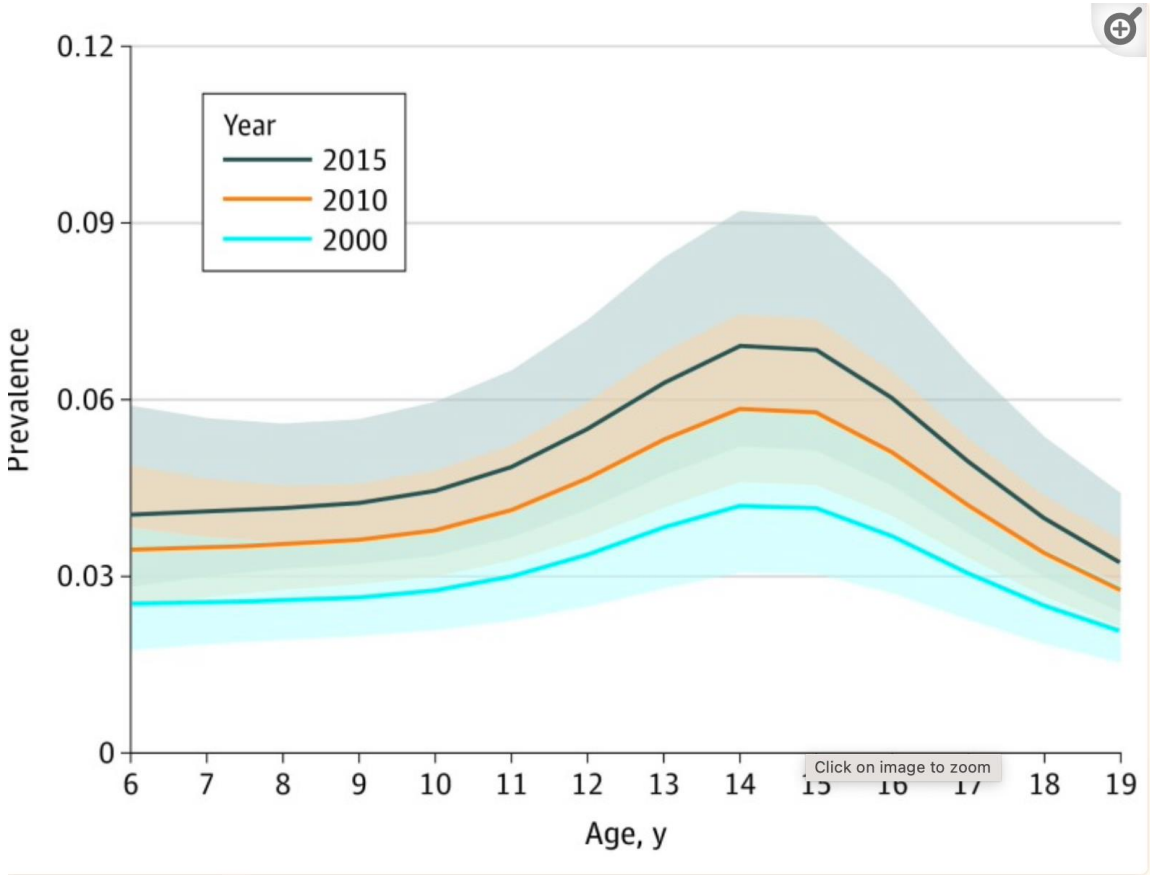
4% at 6 yrs
8% at 14 yrs
15% in obesity

JAMA Pediatrics
View Article

JAMA Pediatr. 2019 Dec; 173(12): 1154–1163.
Published online 2019 Oct 7. doi: 10.1001/jamapediatrics.2019.3310
PMCID: PMC6784751
PMID: 31589252

Global Prevalence of Hypertension in Children

A Systematic Review and Meta-analysis



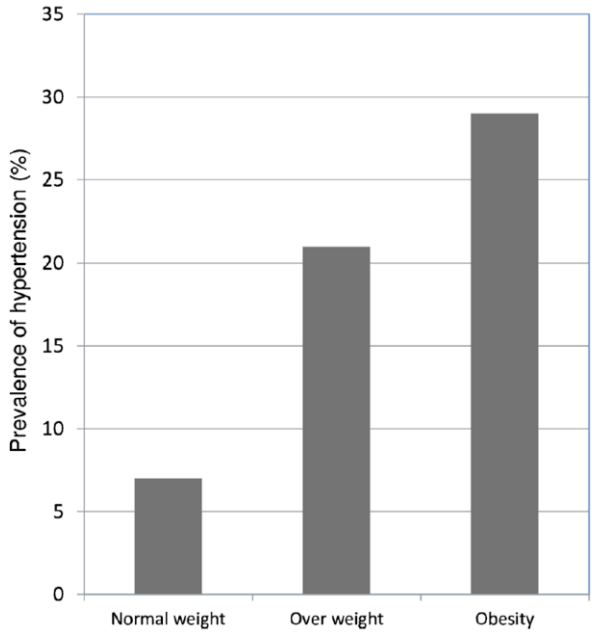
The Indian Journal of Pediatrics
https://doi.org/10.1007/s12098-021-03686-9

ORIGINAL ARTICLE

Prevalence of Hypertension among Children and Adolescents in India: A Systematic Review and Meta-Analysis

Jitendra Meena[1] · Meenu Singh[1] · Amit Agarwal[1] · Anil Chauh

- Based on screening of children in community
- ≥ 3 blood pressure measurements
- Overall pooled prevalence of HTN = 7%
- Higher than global prevalence estimates
- Higher in urban & obese children



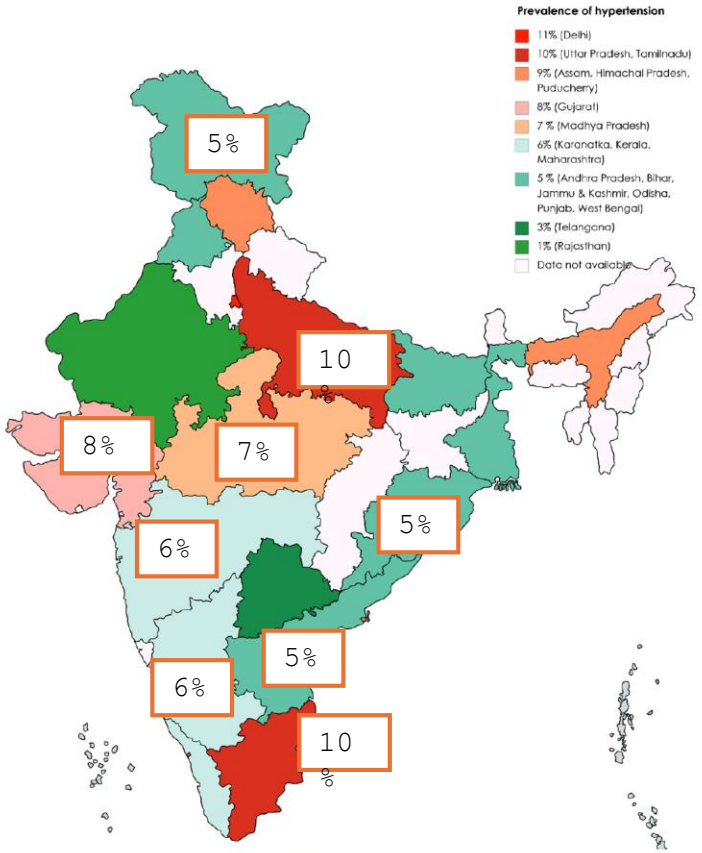


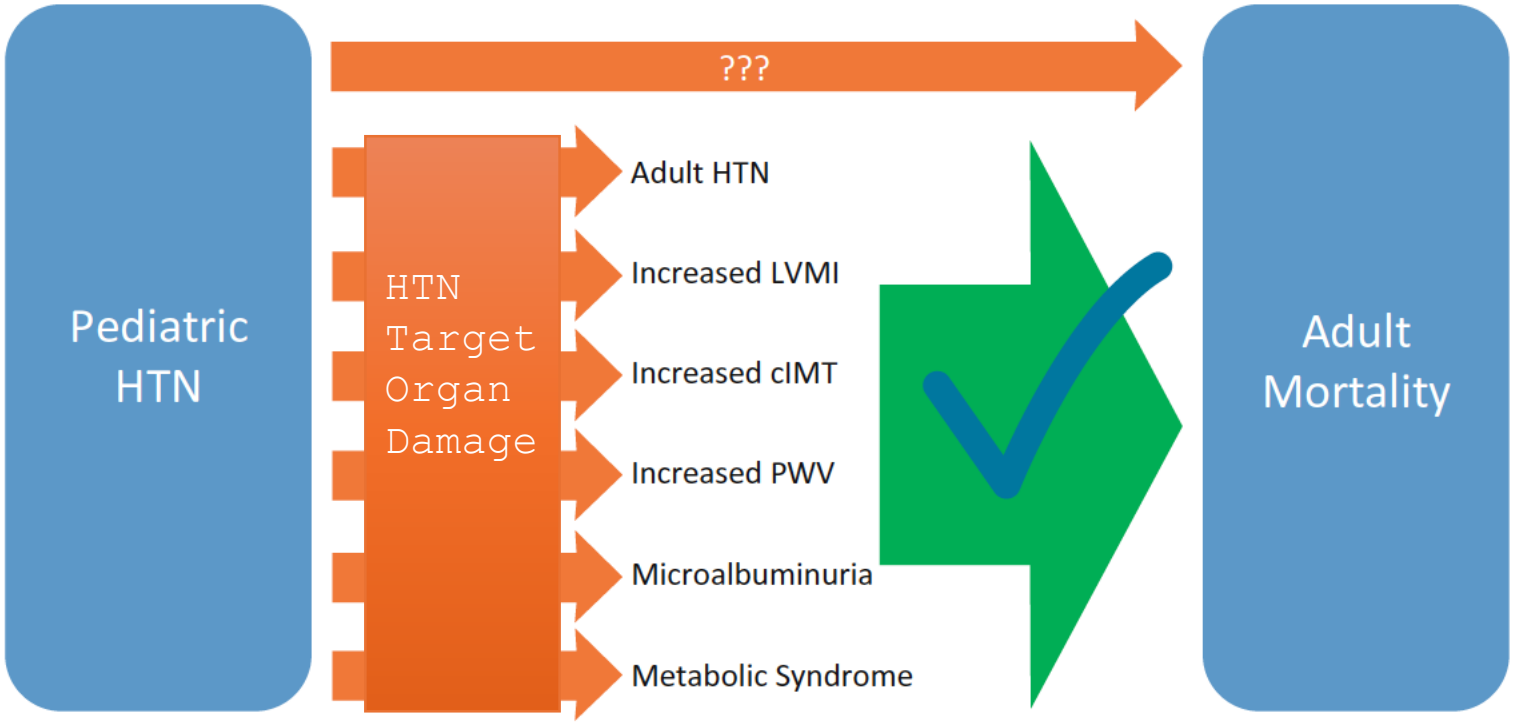
Fig. 3 Pooled prevalence of childhood hypertension across states of India

? Proportion of children with primary (vs secondary) HTN

- Data limited
- Referral clinics always have higher proportion of secondary HTN (>20%)
- In Primary care settings
  - 85% of hypertensive children had primary HTN
  - Only ~ 4% of otherwise healthy children who were evaluated for HTN had secondary cause
- ? Indian data

Yoon et al 2014 Arch of Pediatr & Adol, Nugent F 2022 J Pediatr

Relevance of Pediatric HTN --> Intermediate CV Outcomes → Adult CV Outcomes



Pediatric HTN 5th Ed

Does ***Primary*** HTN in children → Target Organ Damage?

Hypertension

CURRENT ISSUE

RESEARCH ARTICLE | Originally Published 21 February 2023 |

Check for updates

Risk of Target Organ Damage in Children With Primary Ambulatory Hypertension: A Systematic Review and Meta-Analysis

Jason Chung, Cal H. Robinson, Andrew Yu, Abdulaziz A. Bamhraz, Joycelyne E. Ewusie, Stephanie Sanger, Mark Mitsnefes, Rulan S. Parekh, Rupesh Raina, Lehana Thabane, Janis M. Dionne, and Rahul Chanchlani

AUTHOR INFO & AFFILIATIONS

- Compared with normal children, those with primary HTN had
  - More LVH and increased LV mass
  - Increased arterial stiffness
  - Thickening of arteries (early atherosclerosis)

Is Primary HTN under recognized?

- ~ 4% prevalence of HTN in general pediatric population
- But 13 – 18% prevalence of *elevated BP → HTN*
- Prevalence of primary HTN is 10 times > prevalence of secondary HTN
- ?? How many cases of primary HTN have you diagnosed??

If the prevalence of HTN in Indian children is > western children, primary HTN must be going unrecognized

Falkner B et al, AHA Scientific

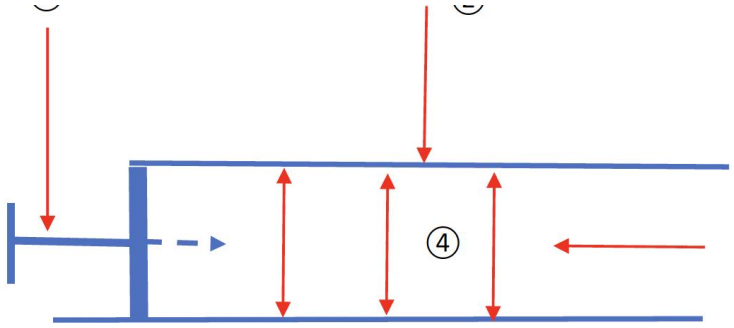
Understanding primary HTN in children: pathophysiology

Litwin M, Pediatric Nephrology 2024 https://doi.org/10.1007/s00467-023-06142-2 (free full text)

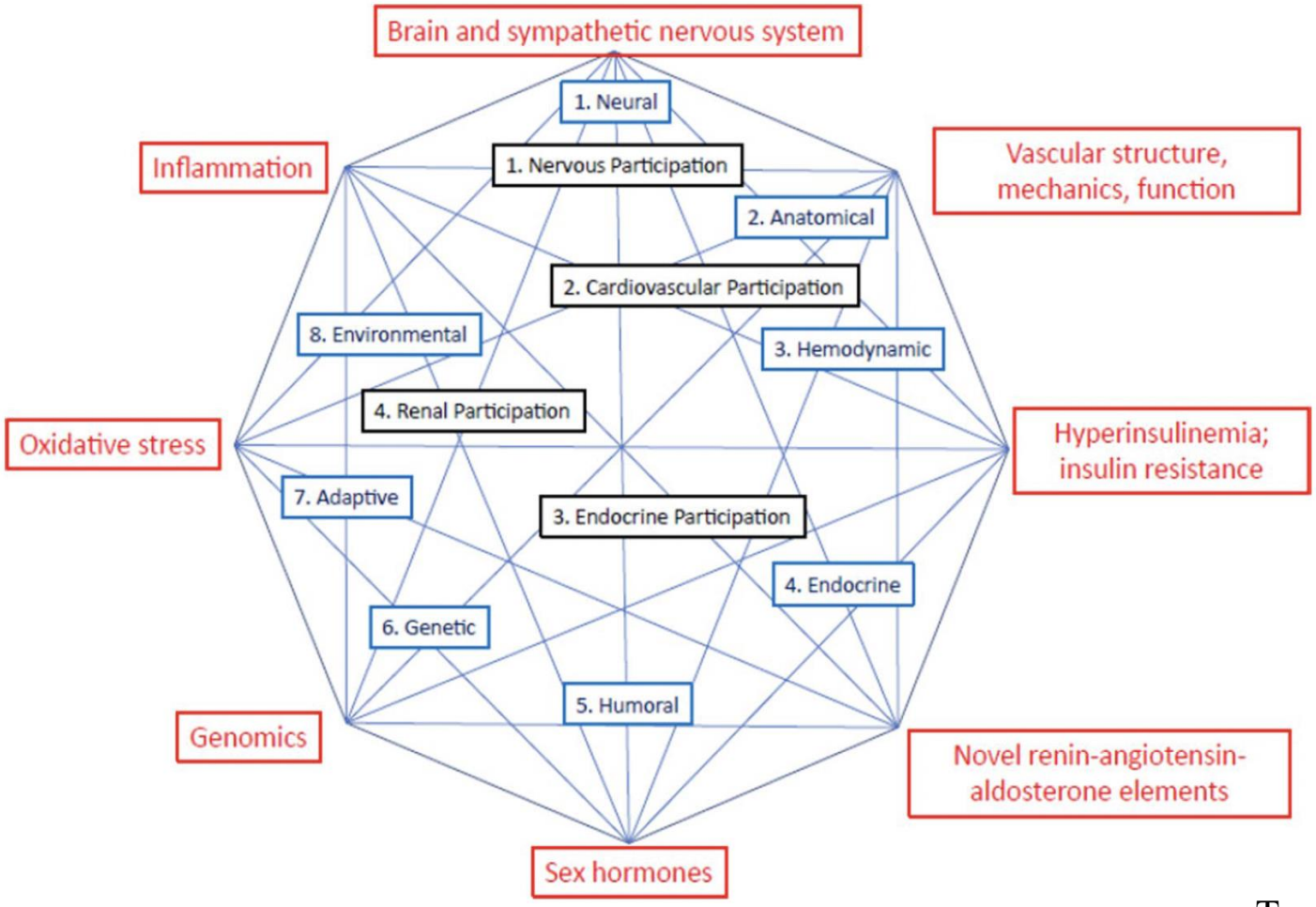
Basic BP Equation: Still the same!

- **BP = Cardiac output X Total peripheral resistance(TPR)**
- Mean arterial pressure = Stroke volume x Heart Rate x TPR
- **Volume** of circulating blood + Contraction force of LV → Stroke Volume
- Determinant of volume is **Salt** homeostasis

Determinants of flow through vessels:
Volume, elasticity of walls, pressure within the vessel

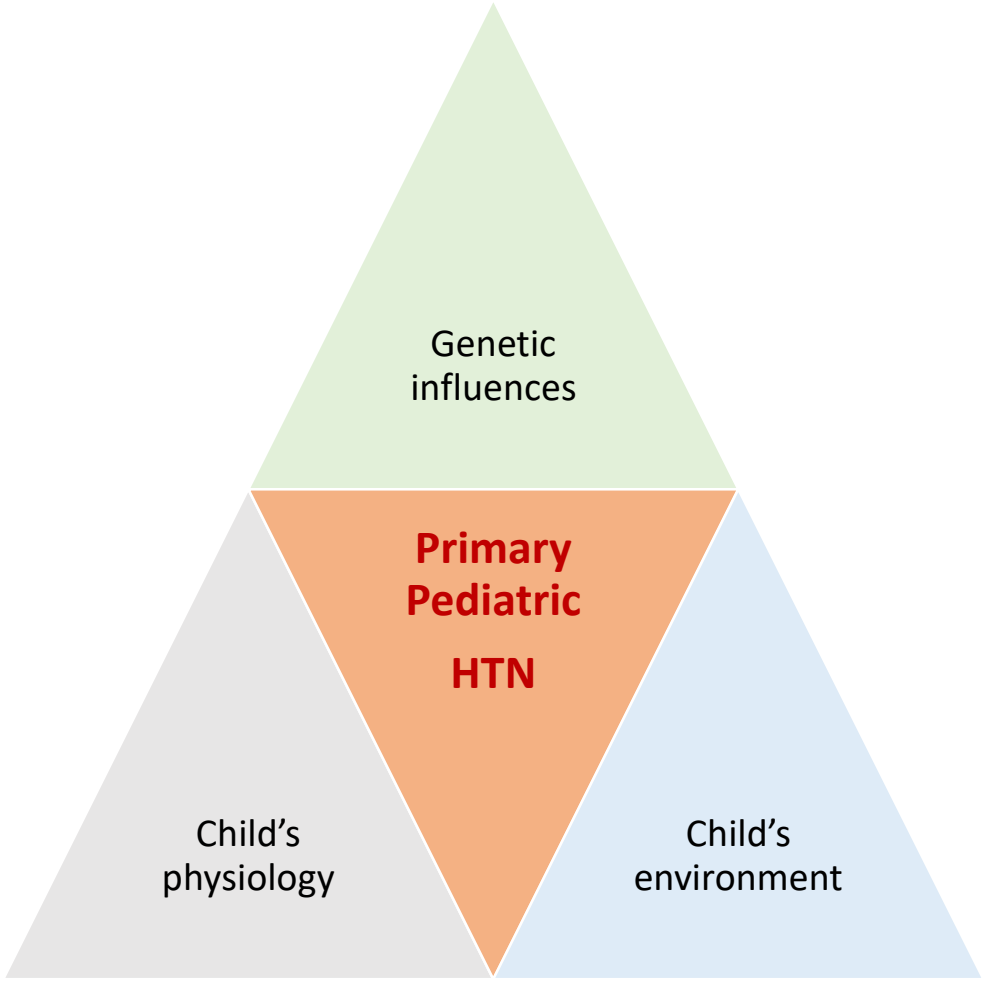


Page's Mosaic: Evolving awareness of Pathogenesis of hypertension



Touyz RM, (2020) Can J Cardiol

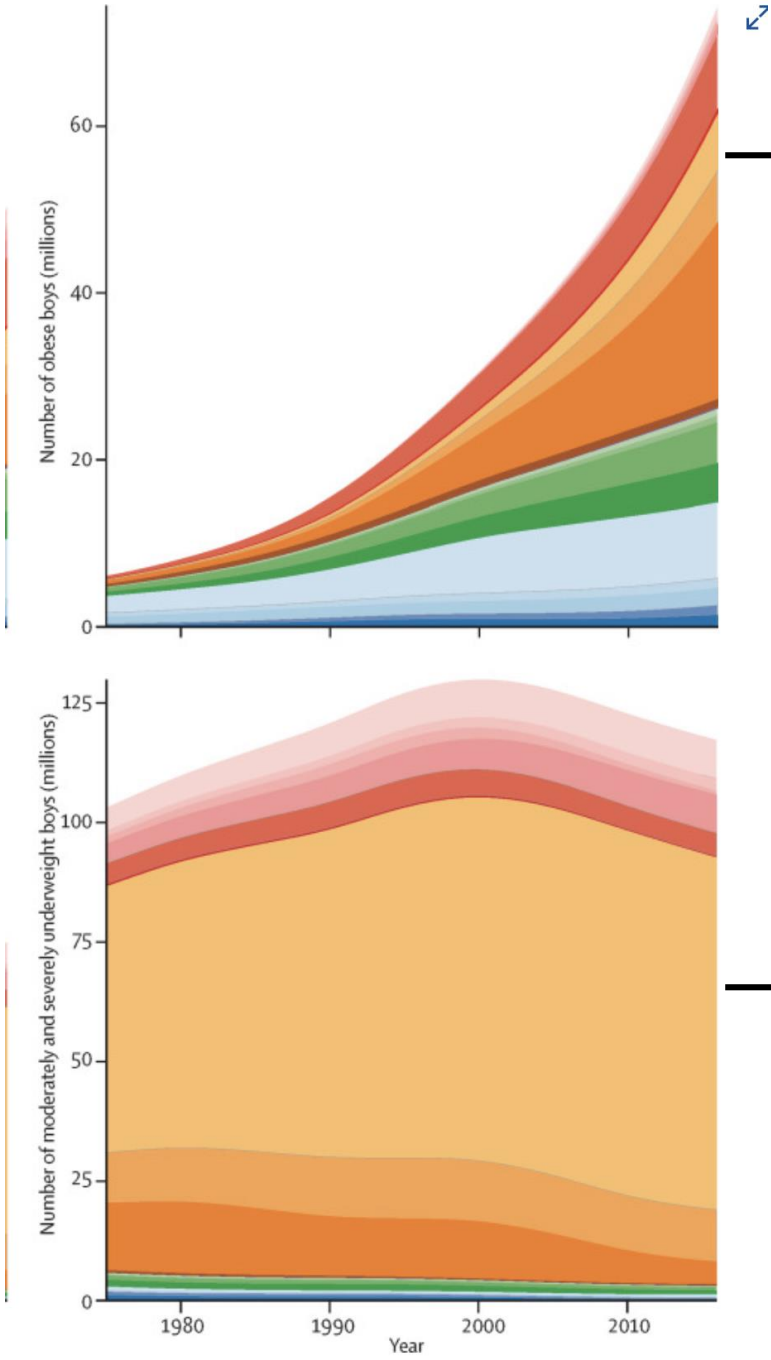
Primary HTN is multifactorial



Modulators of Primary HTN in Children

- **Obesity** = visceral adiposity (disturbed body composition)
- Salt sensitivity
- Others
  - Autonomic nervous system abnormalities
  - Metabolic abnormalities
  - Vascular remodeling

Face of ‘Malnutrition’ is changing

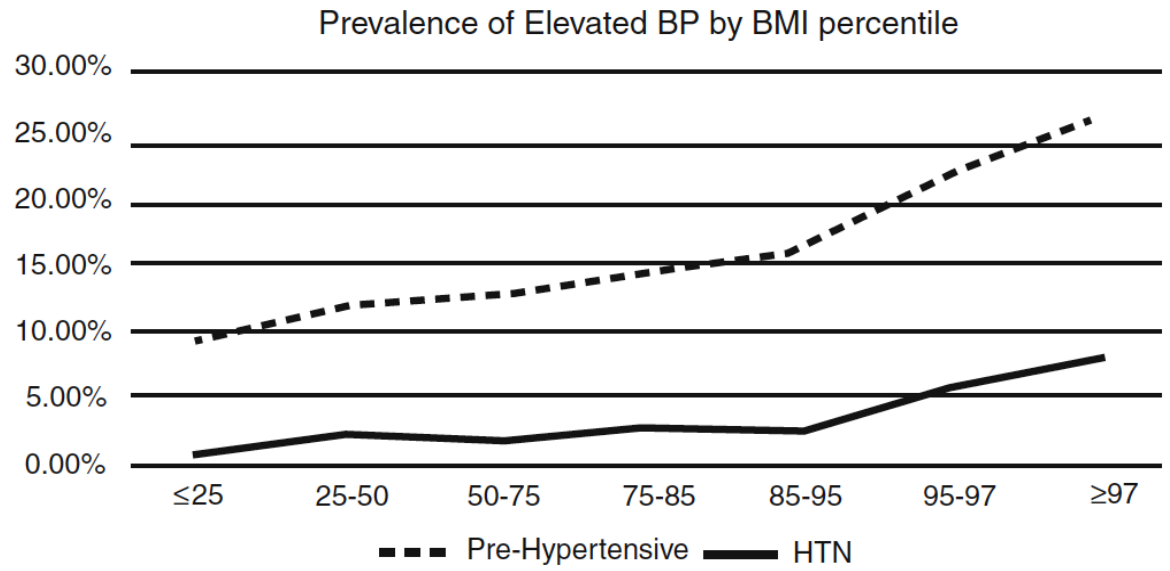


Prevalence of obesity in South Asians

Prevalence of underweight in South Asians

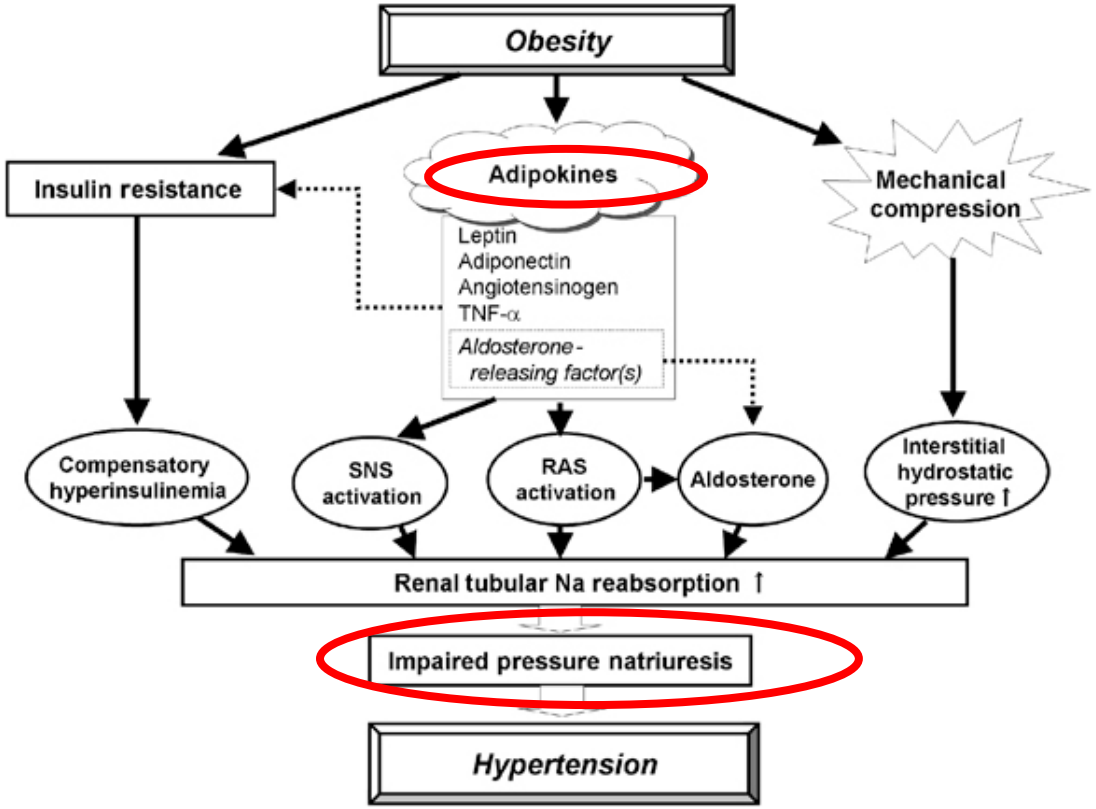
The Lancet, NCD Risk Factor Collaboration 2017

Obesity is the most important Risk Factor for Primary HTN



McNiece et al 2007 Ped HTN 5th Ed

HTN in Obesity – a complicated story!



Mechanisms of HTN in childhood obesity

Insulin resistance and hyperinsulinemia[a] leading to: 1. Sympathetic nervous system activation 2. Renal sodium reabsorption 3. Impaired vasodilatation 4. Vascular smooth muscle proliferation Hyperleptinemia leading to 1. Sympathetic nervous system activation 2. TGF-β synthesis and increased type 1V collagen leading to glomerulosclerosis [a]Unexplained insulin resistance in lean individuals with hypertension has been reported. Mechanisms for increased BP secondary insulin resistance and hyperinsulinemia are hypothesized to be similar to those in obese individuals
Activation of RAAS and elevation of plasma renin
Increased pro-inflammatory cytokines such as TNF-α, IL-6 contributing to insulin resistance
Increased oxidative stress
Direct renal damage 1. Renal compression by perirenal fat leading reduced medullary blood flow, tubular compression leading to increased sodium reabsorption 2. Hyperfiltration injury 3. Increased TGF-β1 expression synthesis
Poor sleep quality and sleep apnea leading to sympathetic nervous system activation
Low vitamin D level

Adapted from Bucher et al. (2013), Yamaguchi and Flynn (2009)

Salt sensitivity

- In a proportion of population changes in dietary sodium intake → exaggerated and parallel changes in BP
- Modulated by ENaC channels present in various organs and blood vessels
- Pathophysiology of SS:
  - Increased volume
  - Also increased stiffness of vessels
- Asians, blacks, obese and small for gestational age birth history = SS

Weinberger M Hypertension, Elliott P BMJ 1996 INTERSALT cooperative research group

> Ann Glob Health. 2016 Mar-Apr;82(2):234-42. doi: 10.1016/j.aogh.2016.02.001.

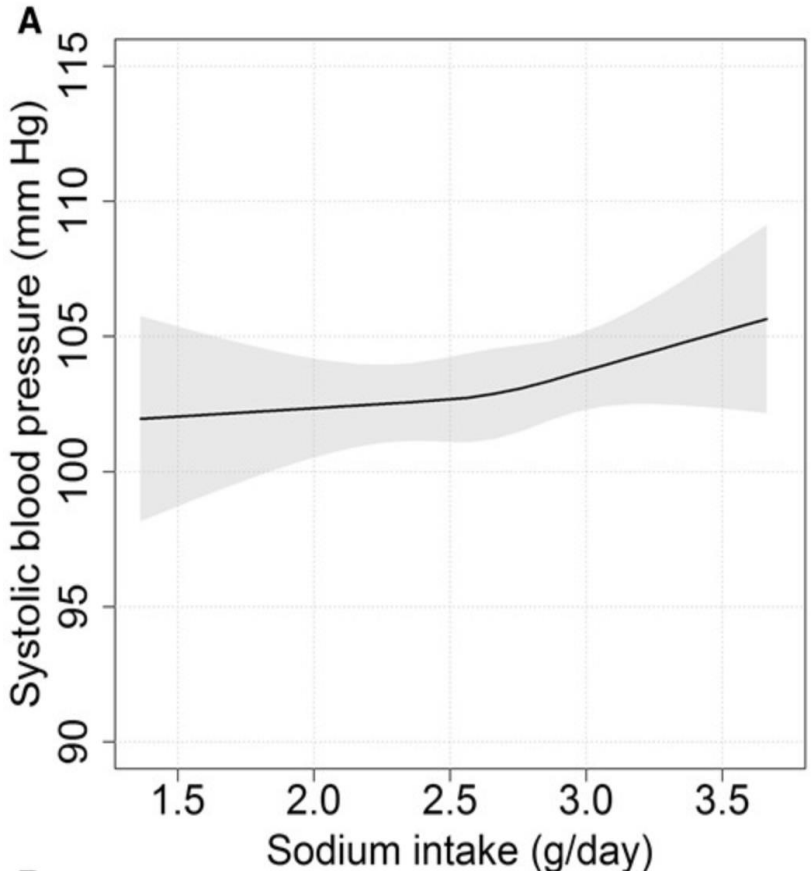
Sodium Intake, Blood Pressure, and Dietary Sources of Sodium in an Adult South Indian Population

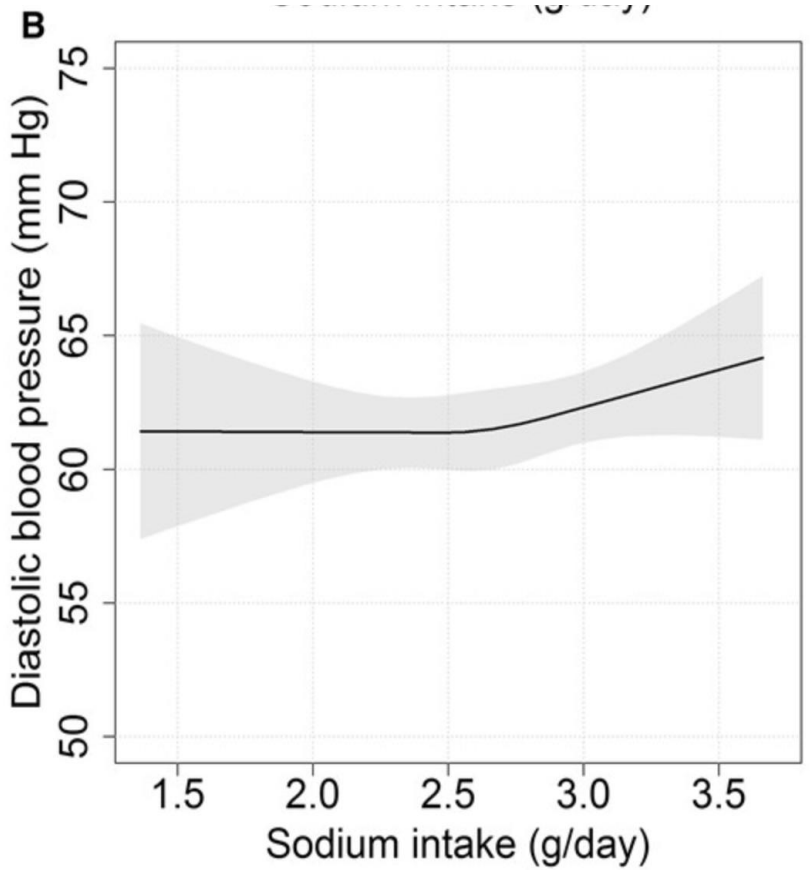
Sripriya Ravi [1], Odilia I Bermudez [2], Vijayakumar Harivanzan [3], Kwan Ho Kenneth Chui [2], Preethi Vasudevan [3], Aviva Must [2], Sadagopan Thanikachalam [3], Mohan Thanikachalam [4]

- 8000 Indians
- Dietary salt intake independently associated with SBP
- Dietary intake was higher than guidelines
- Source of salt homemade foods

Dose response relationship between sodium intake and BP in children

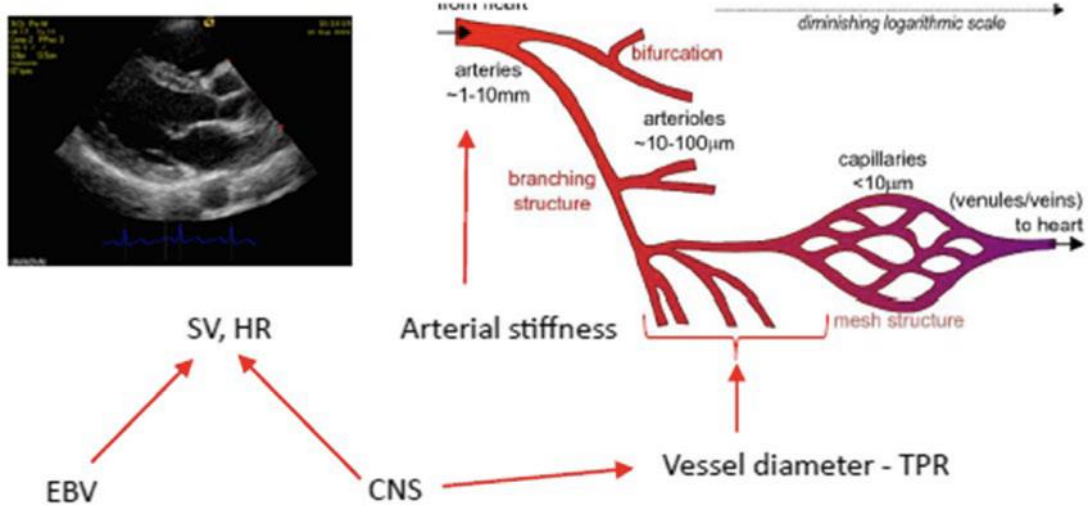
1 gram extra sodium intake = 1 mmHg increase in SBP/DBP





Int J Epidemiol, Volume 47, Issue 6, December 2018, Pages 1796–1810, https://doi.org/10.1093/ije/dyy121

Alteration of macro and microcirculation



- Children with PH have
- Macrocirculation
  - Increased vessel wall thickness & stiffness
  - [increased cIMT/ higher pulse wave velocity/ greater pulse pressure]
- Microcirculation
  - Vasoconstriction of retinal vessels
  - Reduction in perfusion

Autonomic activation & Metabolic abnormalities associated with Primary HTN

- Primordial factors: prematurity, SGA, lower nephron number (Brenner hypothesis

After birth:

- Higher insulin and insulin resistance
- High uric acid levels
- Sympathetic NS activation
- Adipocytokines dysregulation
- Dysregulation gut microbiome (salt intake)

Litwin M, Pediatr Nephrol 2024

Approach to Child with Hypertension

Recognizing Primary HTN

I-SCREAM – an approach for pediatricians

- **I** = pediatrician or primary care physician (no need for referral)
- **S** = screen for HTN
- **C** = confirm diagnosis of HTN
- **R** = Risk factor assessment by history [primary + secondary HTN]
- **E** = Evaluate with labs to rule out secondary and risk for primary
- **A** = Assessment for Target Organ Damage (LVH, Fundus examination)
- **M** = Manage with lifestyle modification +/- antihypertensive medications

Screening for HTN

- Healthy children > 3 yrs: Annually
- Children at risk for developing HTN: < 3 years, at every health encounter

TABLE 9 Conditions Under Which Children Younger Than 3 Years Should Have BP Measured

History of prematurity <32 week's gestation or small for gestational age, very low birth weight, other neonatal complications requiring intensive care, umbilical artery line
Congenital heart disease (repaired or unrepaired)
Recurrent urinary tract infections, hematuria, or proteinuria
Known renal disease or urologic malformations
Family history of congenital renal disease
Solid-organ transplant
Malignancy or bone marrow transplant
Treatment with drugs known to raise BP
Other systemic illnesses associated with HTN (neurofibromatosis, tuberous sclerosis, sickle cell disease,[114] etc)
Evidence of elevated intracranial pressure

Adapted from Table 3 in the Fourth Report.[1]

AAP 2017 and ESH

Checking BP – the only way to diagnose HTN!

- HTN defined as **mean (average)** of **replicate BPs** measured on **3 separate occasions**
- **Validity of Automated oscillometric BP measurements+/-**
  - **Good agreement (Araujo Moura 2021)**
  - **Only moderate agreement (Hanevold 2020)**
- **High Oscillometric BPs must be repeated by auscultation**

Role of ABPM in Investigating HTN

- Is ABPM superior to clinic BP in making an accurate diagnosis of HTN?
- AB[illegible]t mandatory

Indication	AHA/ ESH
For Diagnosis of HTN	
Confirm HTN in those with 'elevated BP' and Stage 1 HTN prior to evaluation	+
Confirm HTN before starting treatment (if TOD is present)	+
Detect masked HTN in high-risk patients – CKD, Tx, DM, Coarct of A, obesity, OSA	+
During Treatment of HTN	
Assess effectiveness of BP control	+
In CKD to intensify BP control	+
Repeat ABPM regularly to ensure BP control	+
In Clinical Research	

Primary vs Secondary HTN

- Secondary HTN: Specific Cause

- Age < 6 years
- Stage 2 HTN
- HTN urgencies & emergencies
- ABPM masked HTN, nocturnal HTN
- Potentially correctable

- Primary HTN

- Diagnosis of exclusion?
- Older children
- Milder HTN
- Overweight/ obese
- Family history of HTN in parents/ Grandparents

Causes of Secondary Hypertension

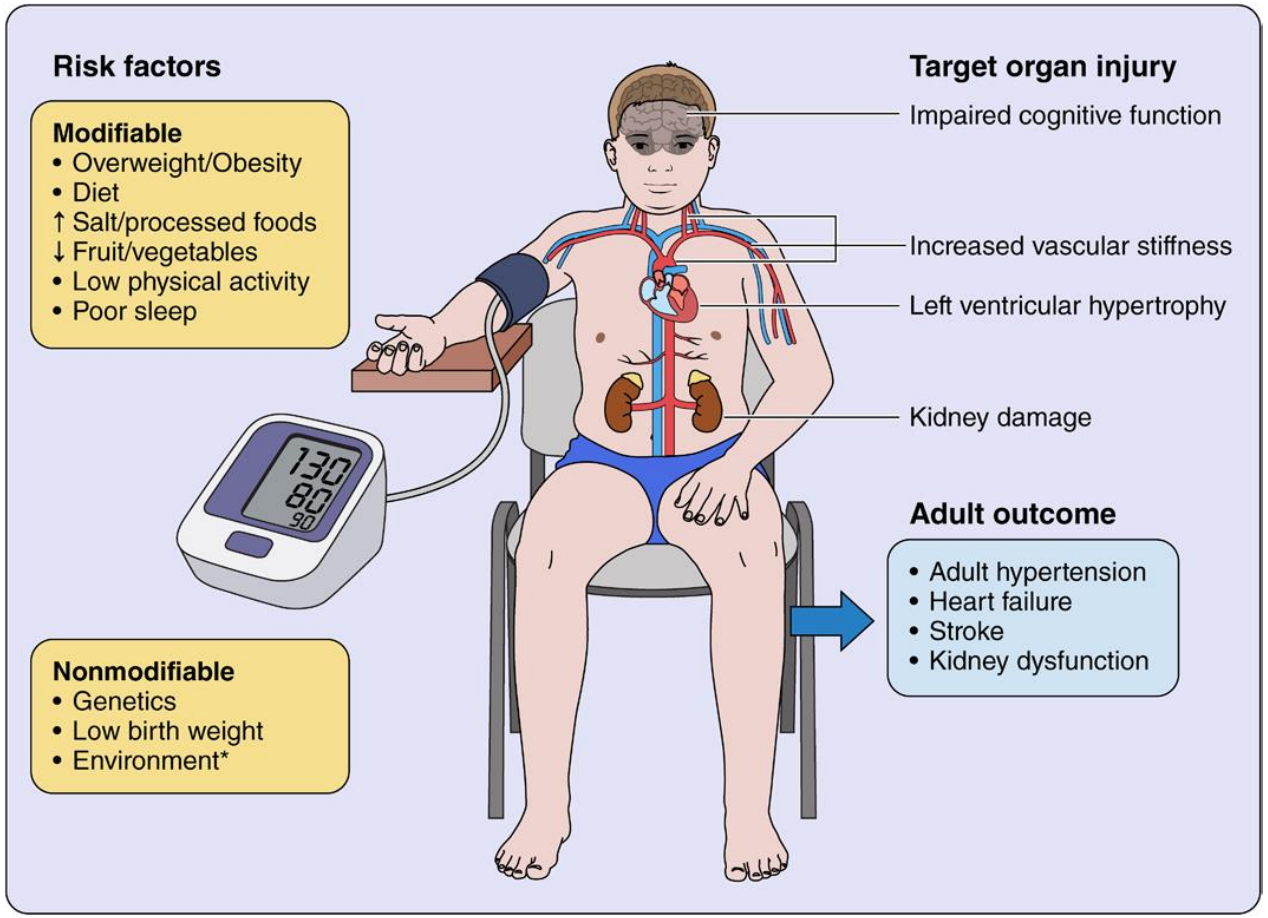
Age Group	Cause
Newborn	**Renal artery thrombosis (UAC)** **Renal vein thrombosis** Polycystic Kidney disease Coarctation of Aorta
1 – 5 years	**Renal Parenchymal** disease – Acute GN, HUS Renal Artery Stenosis Coarctation of Aorta
5 – 10 years	**Renal Parenchymal Disease** **Renal artery stenosis** Endocrine causes
Adolescence	Renal parenchymal disease Primary hypertension Renal artery stenosis

Prevalence of HTN in at risk pediatric populations

CKD 60 %- 70%
Post Kidney Transplant 60% - 90%
Other Solid Organ Transplants 30%(liver) - 70% (heart)
Coarctation of Aorta 45%
Type I DM 30%
Type II DM 30%
Syndromes with HTN 20% (Turners, NF1 etc)

Avner 8th Edition

Risk Factors to assess for Primary HTN

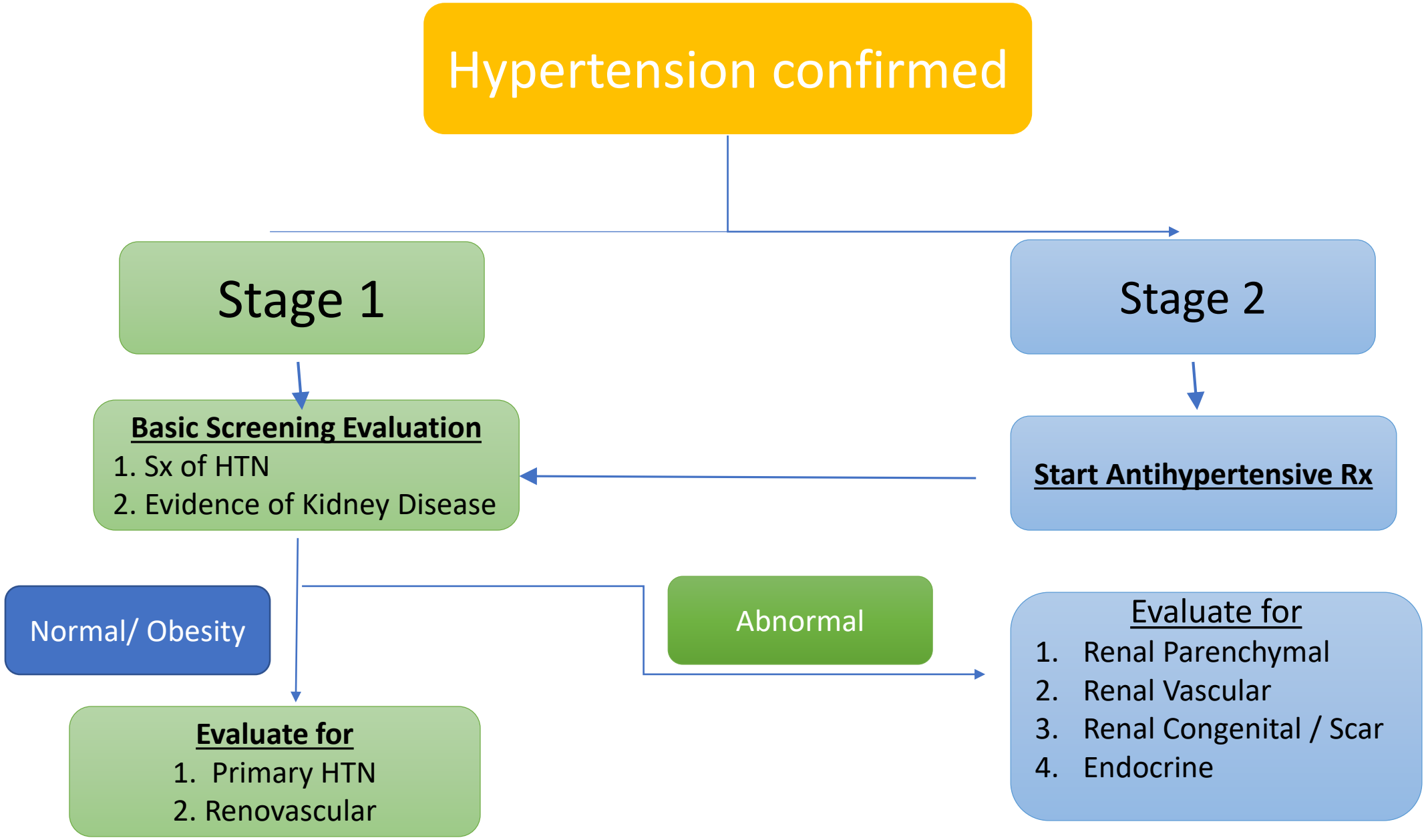


Examination	What to Look for	Significance
BP measurement	Upper & Lower Extremity BP discrepancy	Coarctation of Aorta/ Mid-Aortic Syndrome
Pulses	Distal Pulses poorly felt	Coarctation of Aorta
Height, Weight	Poor growth Obesity	CKD, chronic HTN Primary HTN
Facies	Cushingoid Elfin Short webbed neck	Steroid induced Williams syndrome Turner's syndrome
General Examination	Pallor Edema Ambiguous Genitalia	CKD, HUS Glomerular Disease, Severe CKD CAH
Severe HTN	Fundus, S/o CHF, Mental Status, Bell's Palsy, Fundus	HTN urgency, Emergency
Abdomen	Bruit	Renovascular Disease

Basic Screening Evaluation - Labs

Lab Test	What to Look for?	Significance
Urine first	RBCs, RBC casts, proteinuria	Presence of renal parenchymal Disease
CBC	Anemia	Chronic kidney disease
Creatinine	elevated	renal parenchymal disease
Electrolytes	Low or high K, acidosis	? Rare inherited renal tubular disorders→ HTN
Renal Ultrasound	Small kidney (one side) Two small kidneys Large but normal Large with Cysts Hydronephrosis	Scar, Renal artery stenosis Renal dysplasia, bilateral RAS Acute GN Polycystic Kidney Disease

If clinically indicated: fasting glucose, Lipids, Echo


Hypertension confirmed
Stage 1
Stage 2
Basic Screening Evaluation
1. Sx of HTN
2. Evidence of Kidney Disease
Start Antihypertensive Rx
Normal/ Obesity
Abnormal
Evaluate for
1. Primary HTN
2. Renovascular
Evaluate for
1. Renal Parenchymal
2. Renal Vascular
3. Renal Congenital / Scar
4. Endocrine

LVH Prevalence in Youth with Primary HTN at diagnosis

- Risk of LVH increases with BP values > 90 percentile.
- **Pooled Prevalence of LVH in Primary HTN 31%**
- (Prevalence of LVH in secondary HTN is higher)
- Effective antihypertensive treatment AND weight loss leads to LVH regression

Sinha MD Frontiers in CV med 2022, Litwin M Ped Nephrol 2010

Managing HTN : Prevention

- Address primordial risk factors (**ask** maternal/ birth history)
- Prevent Obesity: **ask** about diet and exercise
- Increase physical activity: **ask** about phone time, type of activity
- Avoid excessive salt intake/ increase fruits/ vegetables (K+) → 36% lower risk of HTN in adulthood

WHO GUIDELINES ON **PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR**

https://www.who.int/publications

CHILDREN AND ADOLESCENTS
(aged 5–17 years)

In children and adolescents, physical activity confers benefits for the following health outcomes: improved physical fitness (cardiorespiratory and muscular fitness), cardiometabolic health (blood pressure, dyslipidaemia, glucose, and insulin resistance), bone health, cognitive outcomes (academic performance, executive function), mental health (reduced symptoms of depression); and reduced adiposity.

At least 60 minutes a day

moderate- to vigorous-intensity physical activity across the week; most of this physical activity should be aerobic.

It is recommended that:

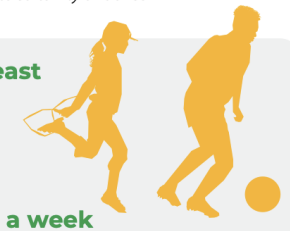
› **Children and adolescents should do at least an average of 60 minutes per day of moderate- to vigorous-intensity, mostly aerobic, physical activity, across the week.**

Strong recommendation, moderate certainty evidence

› **Vigorous-intensity aerobic activities, as well as those that strengthen muscle and bone, should be incorporated at least 3 days a week.**

Strong recommendation, moderate certainty evidence

On at least 3 days a week



vigorous-intensity aerobic activities, as well as those that **strengthen muscle and bone** should be incorporated.

GOOD PRACTICE STATEMENTS

- Doing some physical activity is better than doing none.
- If children and adolescents are not meeting the recommendations, doing some physical activity will benefit their health.
- Children and adolescents should start by doing small amounts of physical activity, and gradually increase the frequency, intensity and duration over time.
- It is important to provide all children and adolescents with safe and equitable opportunities, and encouragement, to participate in physical activities that are enjoyable, offer variety, and are appropriate for their age and ability.

Treatment of Primary Hypertension

- Goal : <90th percentile or <130/80 mm Hg, whichever is lower
- Reduce risk of target organ damage in childhood
- Reduce risk of CV morbidity in adulthood

Non-pharmacologic Treatment (Lifestyle modification

Pharmacologic Treatment (Antihypertensive Rx)

Non-pharmacological therapies

- Weight Loss: Family effort more successful
- Diet: DASH Diet
  - Fruits/ Veg 5 per day
  - Whole grains
  - Low fat milk products 2 or more
  - Meat/ fish/legumes 1-2 per day
  - Sugar and sugary drink not more than 1
  - Dietary sodium < 2.5 gm per day
- Exercise: 40 minutes of moderate, vigorous physican activity → BP reduction by 6mmHg

AAP 2017

Indications for Antihypertensive medications

- Optimal BP level to be achieved with treatment of childhood HTN is <90th percentile or <130/80 mm Hg, whichever is lower
- Use antihypertensive medications if
  - Remain hypertensive despite lifestyle modifications
  - Symptomatic HTN
  - Stage 2 HTN
  - HTN with moderate to severe LVH
- Choice of drug: ACE inhibitors, ARB, Calcium channel blockers

Case: 13 year old boy presents for a mandated school check-up in your OPD. He has no complaints but his mother is concerned that he is addicted to his mobile phone.

On examination, weight = 54kg, height = 152cm, BMI = 23.4 (90^{th} percentile).

BP = 128/82mmHg and 130/76mmHg

- You must document whether BP is normal is his school form
- How would you classify this child's BP? Hypertension
- What is your approach? I-SCREAM

Summary

- HTN is leading modifiable risk factor for CV disease
- Primary HTN in children is underrecognized (misconceptions!)
- Primary HTN is commoner in the outpatient general population than secondary HTN
- I-SCREAM: systematic approach for **I** (pediatricians) to **s**creen, **c**onfirm, ask for **r**isk factors, **e**valuate for cause and target organ damage and **m**anage HTN in children
- Pediatricians are the key!

Thank you!

DO we have time for a quiz?

A 10 year old boy new to your clinic presents for a check up and with a URI. His BMI is 26 (> 95th percentile). BP is at the 95th percentile using an oscillometric machine. His throat is mildly congested but his chest is clear. He has no other significant past history. After prescribing an antihistamine, which of the following is the CORRECT next step in his evaluation?

a) Ask the child to return when he is well to measure BP by auscultation
b) Ask for the birthweight and for a family history of hypertension
c) Instruct the parents to monitor home BPs for a week to diagnose hypertension
d) Refer the child to a pediatric nephrologist to perform ABPM (ambulatory BP monitoring

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c) Instruct the parents to monitor home BPs for a week to diagnose hypertension

d) Refer the child to a pediatric nephrologist to perform ABPM (ambulatory BP monitoring

Answer b) Learning point: Obesity is a risk factor for primary HTN. Take history for other risk factors. Identify possible HTN at the earliest opportunity

You screen the patient's BP using an oscillometric device available in your clinic. His BP is 126/80 mmHg in the right arm which is 5 mm above the > 95th percentile. He has no symptoms of HTN. In addition to obesity, each of the following clinical features is indicative of a diagnosis of **primary** HTN **EXCEPT ?**

a) BPs corresponding to Stage 1 HTN without clinical symptoms
b) Family history of HTN and obesity in father and grandfather
c) Presence of acanthosis nigricans on neck and axilla
d) History of 3 episodes of febrile UTI during infancy

You screen the patient's BP using an oscillometric device available in your clinic. His BP is 126/80 mmHg in the right arm which is 5 mm above the > 95th percentile. He has no symptoms of HTN. In addition to obesity, each of the following clinical features is indicative of a diagnosis of **primary** HTN **EXCEPT ?**

a) BPs corresponding to Stage 1 HTN without clinical symptoms

b) Family history of HTN and obesity in father and grandfather

c) Presence of acanthosis nigricans on neck and axilla

d) History of 3 episodes of febrile UTI during infancy

Answer d) Recurrent UTI is a red flag sign for secondary HTN, CKD etc

You diagnose primary HTN based on repeat BPs on 3 occasions consistently > 95% percentile. Screening urinalysis and renal function tests are normal. Echo shows mild concentric LVH. Each of the following strategies for managing primary HTN is correct EXCEPT:

a) Avoid antihypertensive medications unless lifestyle modifications for 6 months fail
b) Weight loss by following a diet high in fruits, vegetables and legumes
c) Moderate to vigorous physical activity 3-5 days per week
d) ACE inhibitors are a good choice for first line antihypertensive medication if indicated

You diagnose primary HTN based on repeat BPs on 3 occasions consistently > 95% percentile. Screening urinalysis and renal function tests are normal. Echo shows mild concentric LVH. Each of the following strategies for managing primary HTN is correct EXCEPT:

a) **Avoid antihypertensive medications unless lifestyle modifications for 6 months fail**
b) Weight loss by following a diet high in fruits, vegetables and legumes
c) Moderate to vigorous physical activity 3-5 days per week
d) ACE inhibitors are a good choice for first line antihypertensive medication if indicated

Answer a) Since target organ injury (LVH) is already present, begin antihypertensive medications at the same time as lifestyle

You are given government grant funding to set up a primordial prevention program for HTN in your community. Which of the following interventions is likely to be the most successful in preventing the onset of HTN later in the life course?

a) An exercise program for primary school children
b) Screening and follow up of children with history of low birth weight
c) Education about a healthy diet and adherence programs
d) Wellness program including yoga and meditation to reduce stress

You are given government grant funding to set up a primordial prevention program for HTN in your community. Which of the following interventions is likely to be the most successful in preventing the onset of HTN later in the life course?

a) An exercise program for primary school children
b) Screening and follow up of children with history of low birth weight
c) **Education about a healthy diet and adherence programs**
d) Wellness program including yoga and meditation to reduce stress

Answer c) A healthy diet in children has the most

CKD surveillance and referral to a pediatric nephrologist

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Disease burden

- Global prevalence in 2017- 697·5 million cases of CKD
- Almost a third of patients with CKD lived in ***two countries, China*** (132·3 million cases) and ***India*** (115·1 million cases)
- Globally, the prevalence of CKD in the ***5–19 years age group*** is estimated to be around 98.1(85.0–114.43) cases per million, and the incidence is reported to be around 0.30(0.19–0.42) cases per million.

GBD Chronic Kidney Disease Collaboration. 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet.

Disease burden in India

118 (3-18 years) school children screened by single measurement of serum creatinine and urine dipstick

overall prevalence of chronic kidney disease was 9.3%.

Out of all CKD patients in a referral hospital in North India, 5.3% were children

Rai PK. Prevalence Patterns of CKD among School Children and Adolescents in a School in Varanasi, India. Open Access J Urol Nephrol. 2019

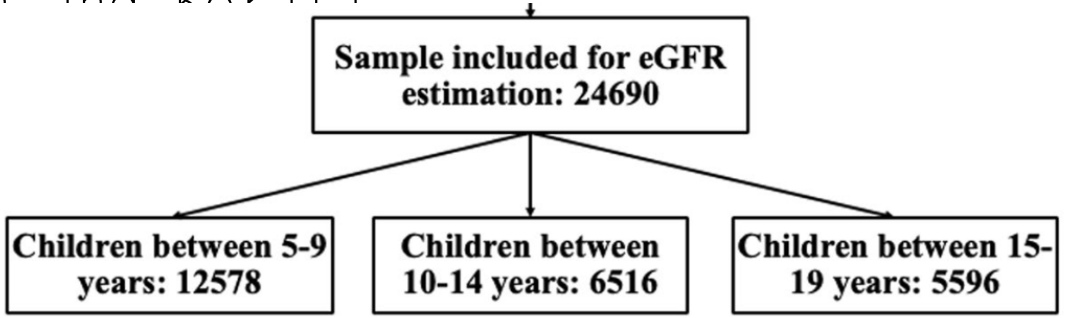
Disease burden in India

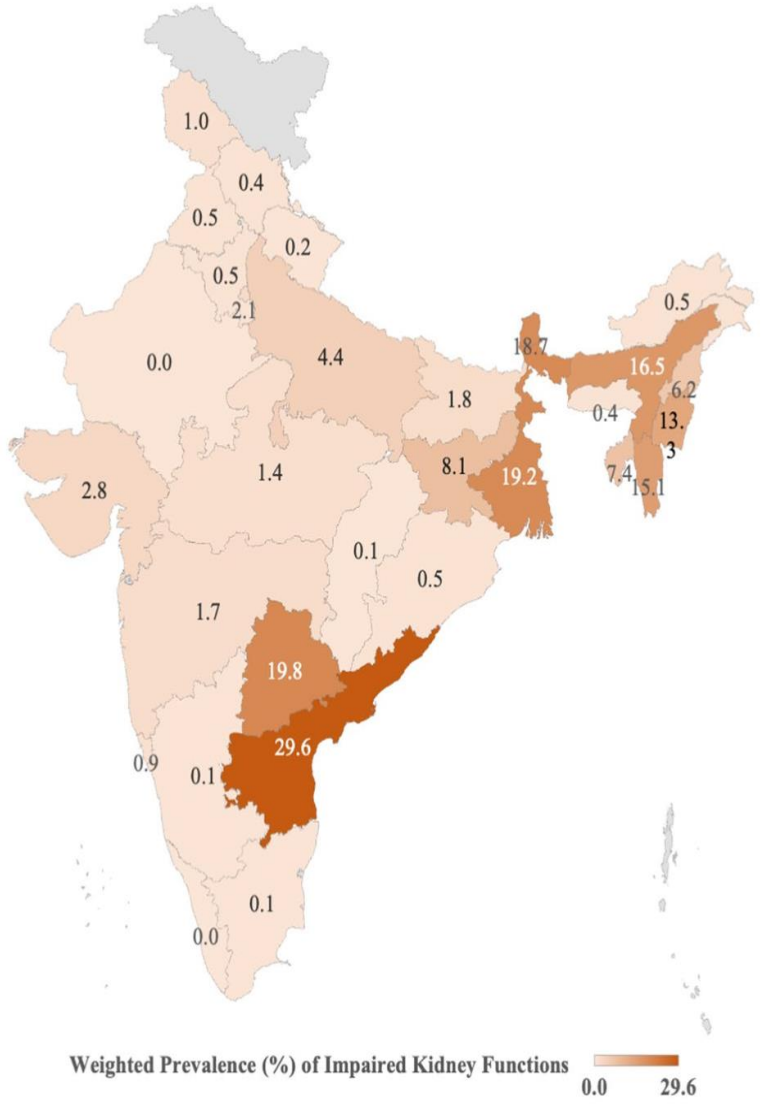
- 1675 children from a North Indian, multiethnic population aged 5-19 years were screened for hematuria and proteinuria by dipstick test, confirmed by microscopy
- 76 children had urinary abnormalities with the prevalence of isolated haematuria in 1.9%, isolated proteinuria in 0.35%, urine microscopy, 44 were observed to have abnormal findings

Urinary Screening in Asymptomatic Indian Children: A Cross Sectional Epidemiological

Disease burden in India

- The overall prevalence of IKF was 4.9%. (single eGFR <60 by modified Schwartz)
- The prevalence in the 5–9, 10–14, and 15–19 year age groups was 5.6%, 3.4% and 5.2%, respectively
- The highest prevalence - AP, Telangana and West Bengal
- prevalence was lowest in TN, Chhattisgarh, Rajasthan and Kerala





How do you do surveillance in healthy children?

- ***Ideal situation ?***
- ***Universal screening ? (Japan, South Korea, Russia)***
- Serum creatinine – at least 2 values
- Proteinuria
- Ultrasound screening

Urinary Screening in Asymptomatic Indian Children: A Cross Sectional Epidemiological

At risk children

🟦 Table 1: Studies 1–9 – Childhood Exposures and Adult Kidney Outcomes

🔷 #	🔷 Country, Year, N	🔷 Childhood Exposure	🔷 Adult Outcome(s)	🔷 Key Finding
🌐 1	🇺🇸 USA, 2002, 2,122	BP & BP change	Microalbuminuria	Linked in Blacks, not Whites
🌐 2	🇨🇳 China, 2008, 412	HTN status change	Microalbuminuria	No significant link
🌐 3	🇺🇸 USA, 2018, 2,512	Long-term BP burden	eGFR	↑ BP burden → ↓ eGFR in Blacks
🌐 4	🇨🇳 China, 2018, 1,222	BP change & HTN transition	Microalbuminuria, eGFR	No association found
🌐 5	🇨🇳 China, 2018, 2,430	BP trajectories	UACR, eGFR, SRD	↑ BP → ↑ UACR, SRD; not eGFR
🌐 6	🇨🇳 China, 2020, 1,738	Childhood hypertension	SRD	HTN in childhood → ↑ SRD risk
🌐 7	🇨🇳 China, 2021, 1,738	Pulsatile stress	SRD	Linked in males, even if normalized later
🌐 8	🇨🇳 China, 2022, 1,771	BP variability (BPV)	SKD, albuminuria	↑ BPV → ↑ SKD and albuminuria risk
🌐 9	🇺🇸 USA, 2010, 2,666	Childhood type 2 diabetes	Macroalbuminuria	Diabetic children → ↑ adult macroalbuminuria incidence

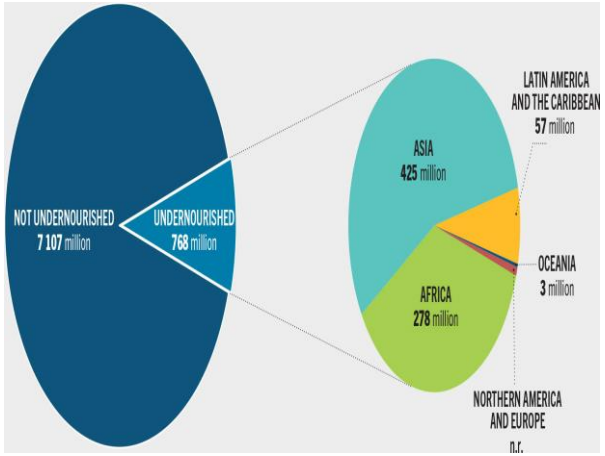
Childhood modifiable risk factors and later life chronic kidney disease: a systematic review. *BMC Nephrol* **24**, 184 (2023).

🟩 Table 2: Studies 10–17 – Childhood Risk Factors and Adult Renal Outcomes

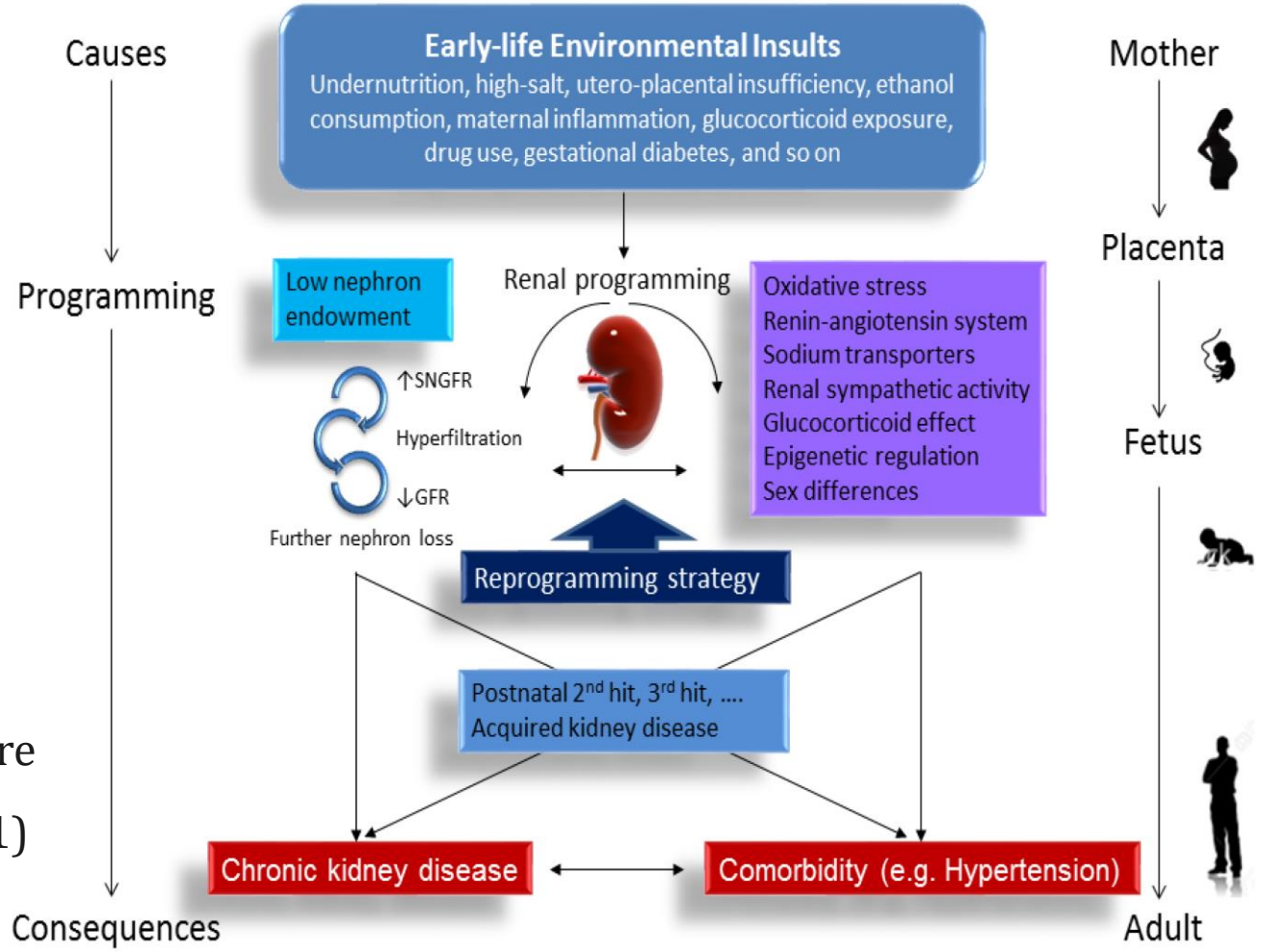
🟢 #	🟢 Country, Year, N	🟢 Childhood Exposure	🟢 Adult Outcome(s)	🟢 Key Finding
🌍 10	🇬🇧 UK, 2013, 4,340	Overweight (ages 2–20)	CKD	Early overweight → ↑ CKD risk
🌍 11	🇨🇳 China, 2021, 2,162	BMI trajectories	SRD, eGFR, UACR	Persistent high BMI → ↑ SRD; no link to eGFR/UACR
🌍 12	🇦🇺 Australia, 2021, 1,442	BMI trajectories	SKD, eGFR, UACR	High BMI → SKD; eGFR inconsistent; no UACR link
🌍 13	🇨🇳 China, 2022, 4,623	BMI trajectories	Albuminuria	↑ BMI → ↑ albuminuria risk
🌍 14	🇮🇪 Ireland, 2018, 4,996	Childhood SEP	CKD	Low SEP → ↑ CKD in women only
🌍 15	🇨🇳 China, 2020, 6,267	Famine exposure	CKD	No significant link
🌍 16	🇦🇺 Australia, 2022, 1,371	Cardiorespiratory fitness (CRF)	GHF, albuminuria	Low CRF → ↑ GHF in women; no albuminuria link
🌍 17	🇦🇺 Australia, 2022, 750	Healthy lifestyle score (HLS)	SKD	No link between childhood HLS and adult SKD

Childhood modifiable risk factors and later life chronic kidney disease: a systematic review. *BMC Nephrol* **24**, 184 (2023).

Nephron endowment – CKD – causal links



In India, an estimated 12% and 18% of children were LBW and PTB, respectively, in 2019–21 (NFHS 2021)

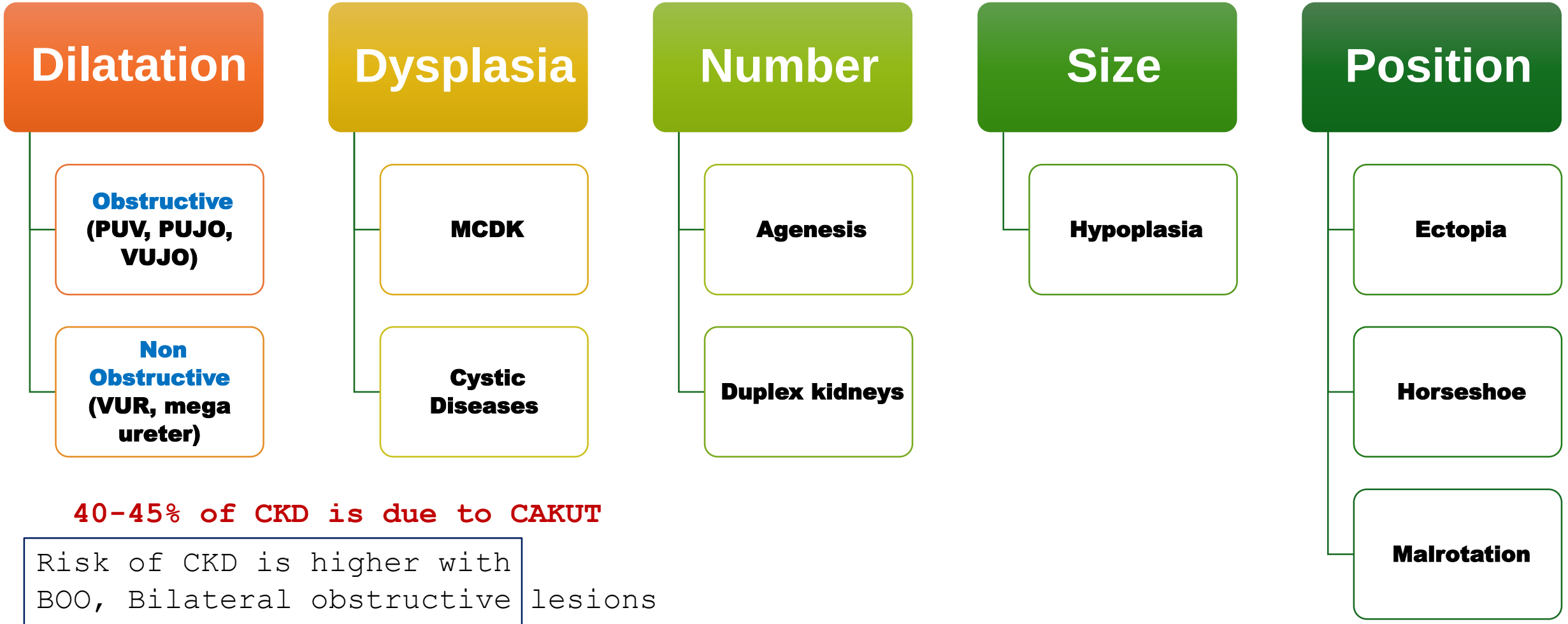


Global burden of disease, 2010

Tain Y-L, Hsu C-N. *Int. J. Mol. Sci.* 2017

THE STATE OF **FOOD SECURITY AND NUTRITION IN THE WORLD**

UMBRELLA OF CAKUT

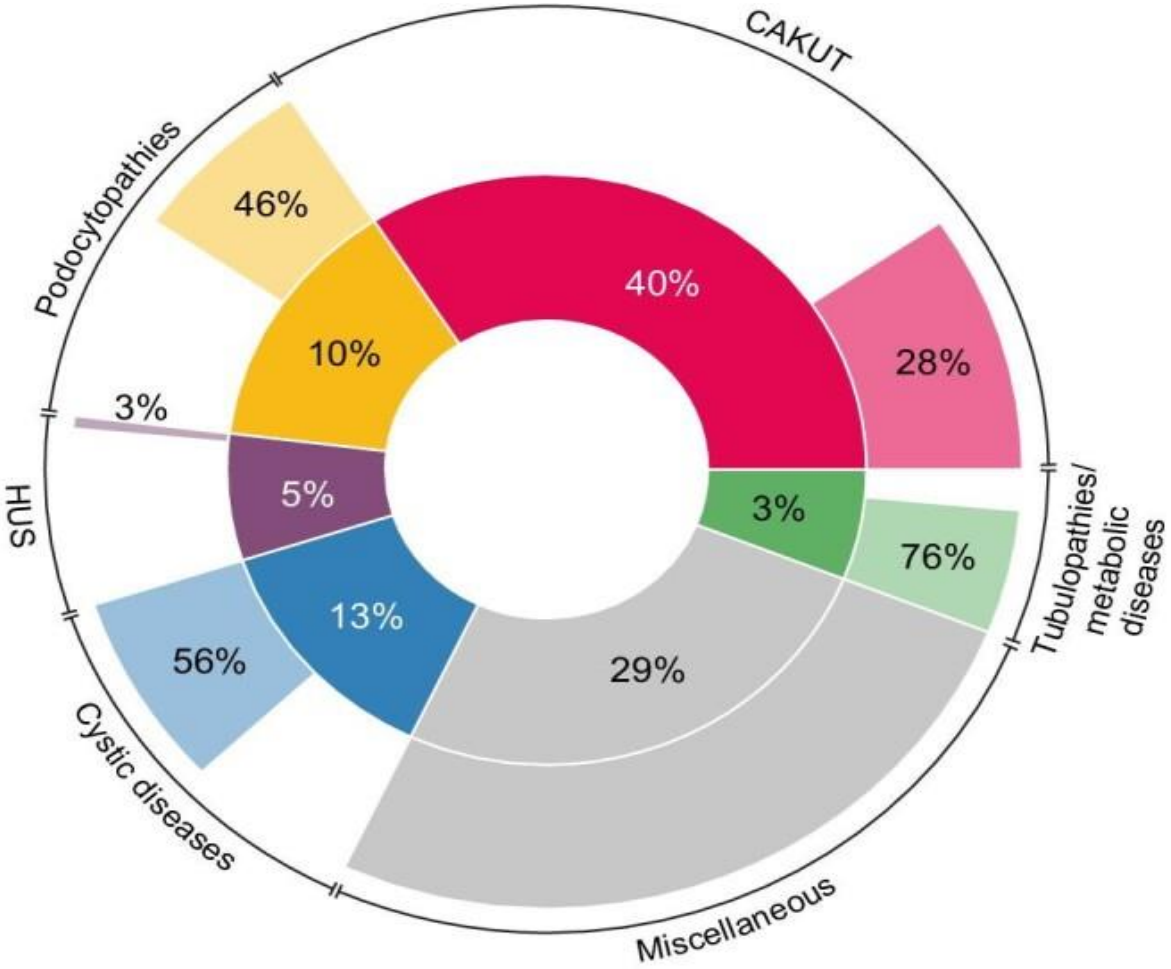


40-45% of CKD is due to CAKUT

Risk of CKD is higher with
BOO, Bilateral obstructive lesions
High grade VUR
Renal dysgenesis or hypoplasia B/L

Modified from An Pediatr

Genetics /family history ?



To screen or not to screen siblings and first -degree relatives (asymptomatic)

- Cystic kidney disease
- Tubular disorders
- HUS
- Podocytopathies
- ?? CAKUT

Treatment availability
Early detection – cure
Major non-renal implications
Future pregnancies

Chronic kidney disease in children: an update. Clin Kidney J. 2023

Genetics in CAKUT

- Genetic heterogeneity
- Reduced penetrance
- Lack phenotype –genotype correlation
- Environmental and epigenetic modifiers
- Not all defects are functionally relevant

At risk children

- Preterm or low birth weight, CAKUT
- Obesity and metabolic syndrome

(increased prevalence of Type 2 DM, primary hypertension

- Voiding dysfunction, neurological disorders
- Irrational drug use – CIN, recurrent AKI
- Family history of kidney disease including metabolic renal stones
- Chronic diseases– lung, liver, heart, short bowel, type 1 DM, MODY

Annual renal function monit
proteinuria estimation
BP at every clinic visit

Diagnosing CKD

- Modified Schwartz – height, serum creatinine
- CKiD U25
  - It employs ***serum creatinine and cystatin C, patient age and gender*** without including height
  - avoiding anthropometric data as limiting factors of the bedside Schwartz's equation
  - more reliable in assessing CKD in adolescents and young adults in comparison
  - shown to underestimate (Schwartz formula) or overestimate (CKD-EPI) GFR
- Proteinuria – assessment of microalbuminuria (ACR). PCR
- BP

DEFINING CHRONIC KIDNEY DISEASE

Kidney damage for ≥3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR or

GFR <60 mL/min/1.73m^2 for ≥3 months, with or without kidney damage

KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

DEFINING CHRONIC KIDNEY DISEASE

MARKERS OF KIDNEY DAMAGE

1. ALBUMINURIA > 30 mg/day

2. URINARY ABNORMALITIES (hematuria, red cell casts)

3. ELECTROLYTE AND OTHER ABNORMALITIES

4. ABNORMAL HISTOLOGY

5. STRUCTURAL ABNORMALITIES IN IMAGING

6. HISTORY OF KIDNEY TRANSPLANT

KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

WHY GFR <60 mL/min/1.73m^2 ?

1. Increased risk for CVD
2. Increased risk of all-cause mortality
3. Increased risk of drug dosing errors
4. Increased risk of metabolic complications

CLASSIFICATION OF CKD

Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

GREEN – LOW RISK OR NO CKD

YELLOW – MODERATE RISK

ORANGE – HIGH RISK

RED – VERY HIGH RISK

Risk increases

Death

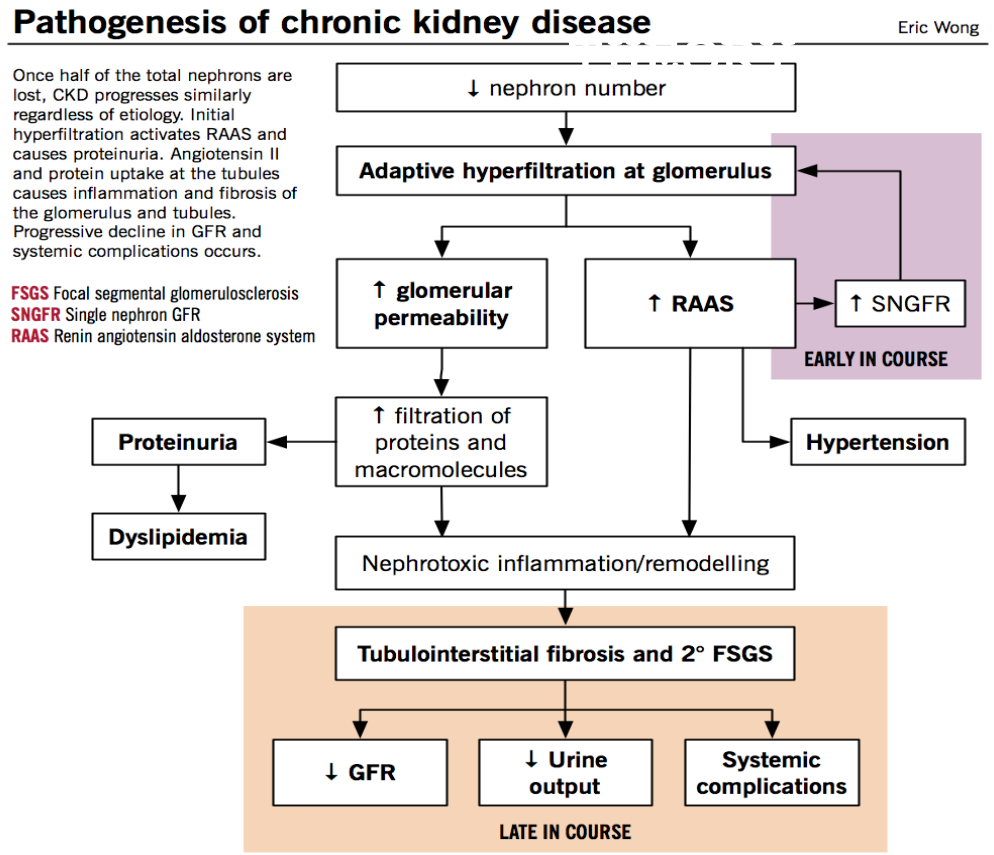
Infections

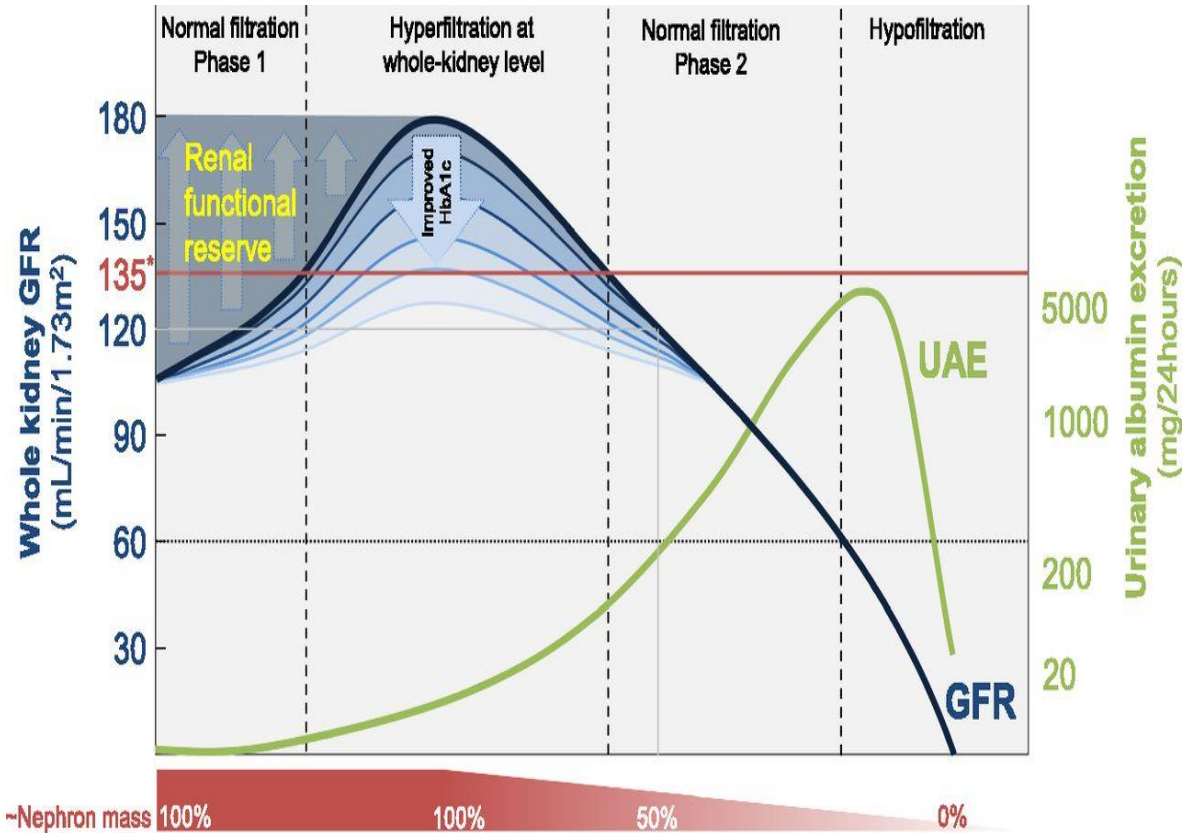
Cardiovascular morbidity

Complications

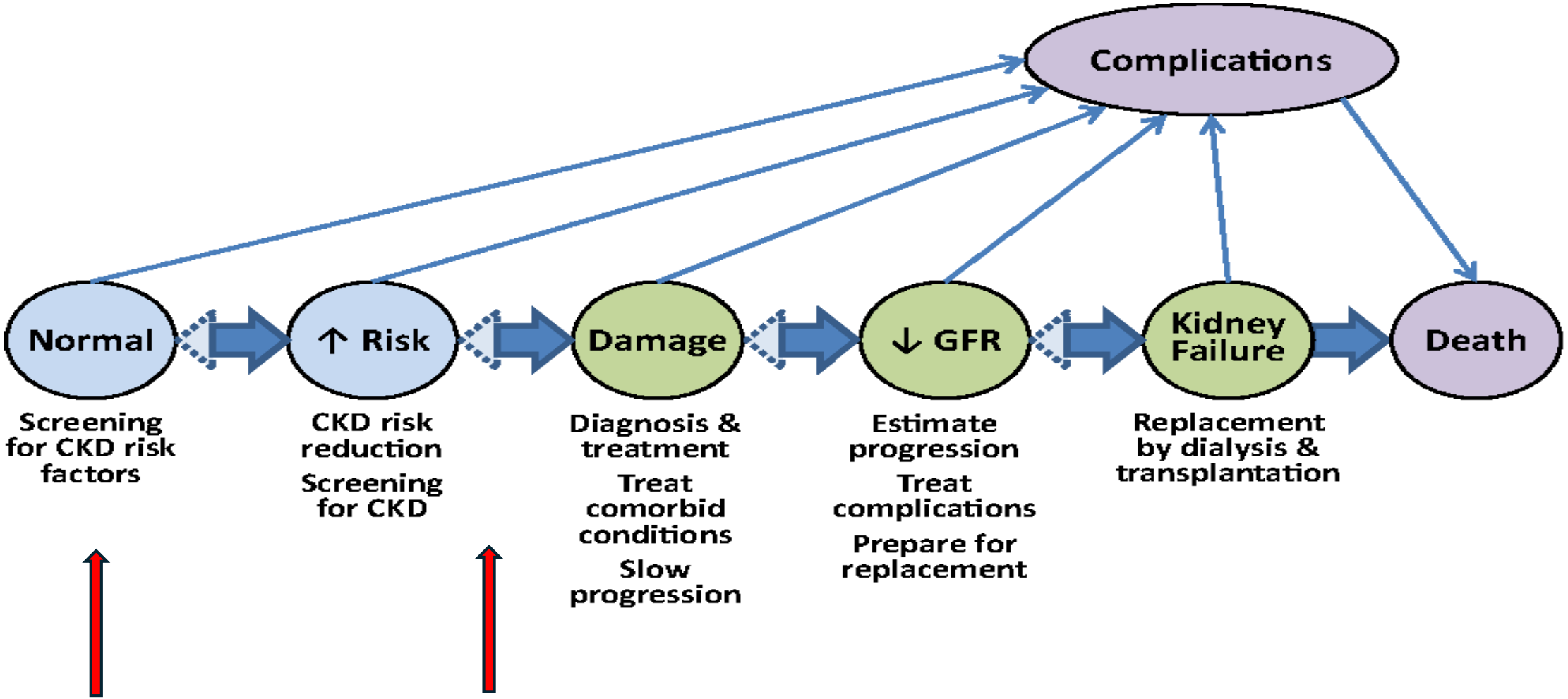
KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

PATHOPHYSIOLOGY OF CKD





PROGRESSION OF CKD



Late presentation

- 1/3rd of children in India present at CKD -3b or more
- Predominantly asymptomatic for kidney related symptoms
  - Anemia (not responding to iron supplements)
  - Bone deformities, rickets with or without metabolic acidosis
  - Short stature

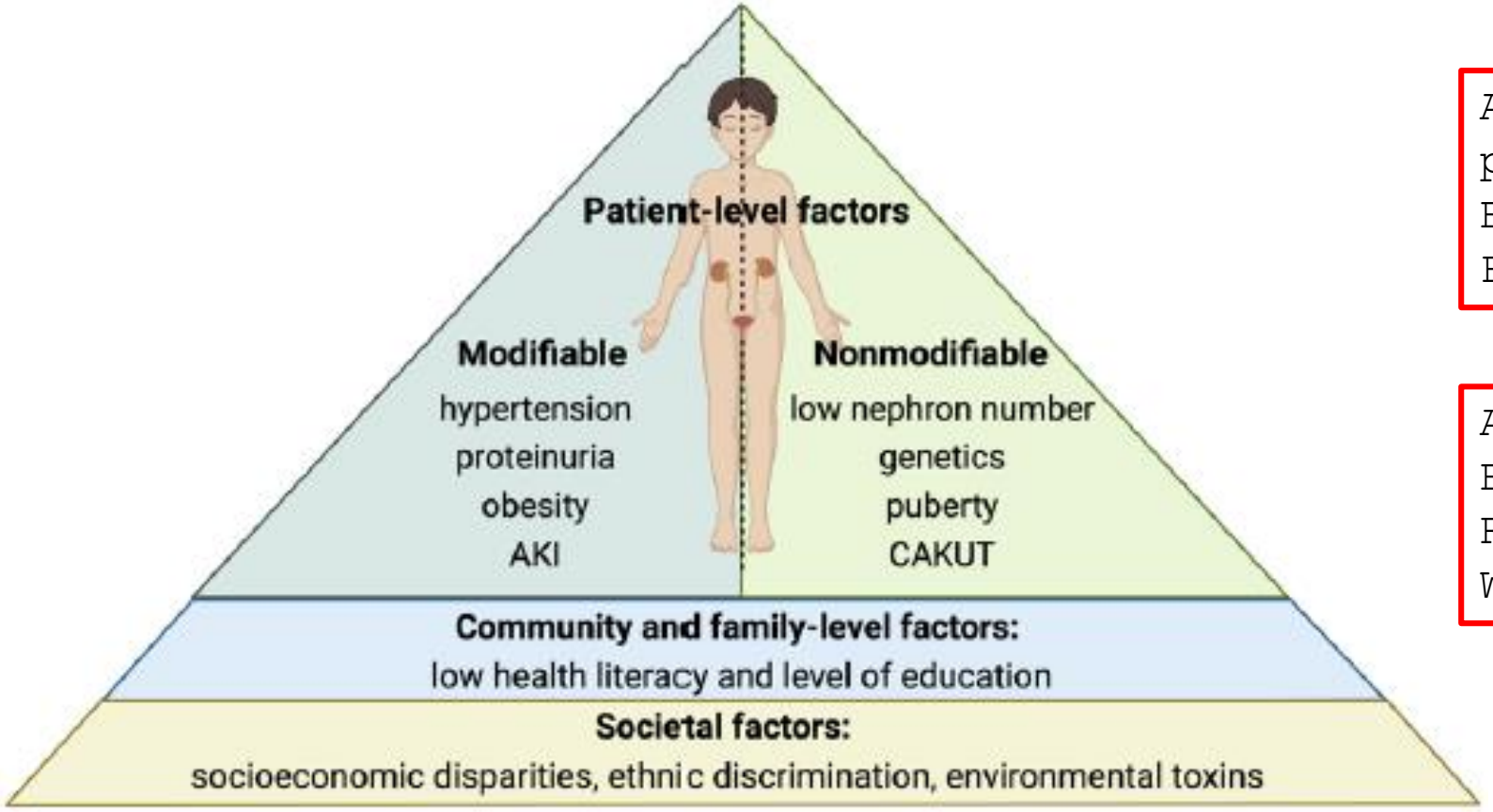
Kamath N, Iyengar A, George N, Luyckx VA. Risk Factors and Rate of Progression of CKD in Children. Kidney Int Rep. 2019

Risk factors for progression

- ~ 500 children (1-16 years) with eGFR 30-90 ml/min
- followed prospectively for composite event of renal replacement therapy or 50% decline in GFR
  - 398 patients had non glomerular disease and 98 had glomerular disease
  - 29% and 41% progressed after median follow-ups of 5.2 and 3.7 years, respectively
- urinary PCR >2mg/mg, hypoalbuminemia, and elevated blood pressure were associated with significantly reduced times to the composite event
- Non-glomerular – male, increased age and anemia additional

Predictors of Rapid Progression of Glomerular and Nonglomerular Kidney Disease in Children and Adolescents: The CKiD Cohort. *American journal of kidney diseases 2022*

Risk factors for progression



BEST PRACTICES

Annual renal function monitoring
proteinuria estimation
BP at every clinic visit
Frequent monitoring during adoles

Avoiding nephrotoxic medications
Emphasize hydration
Remove treat risk factors – BP, P
Weight reduction

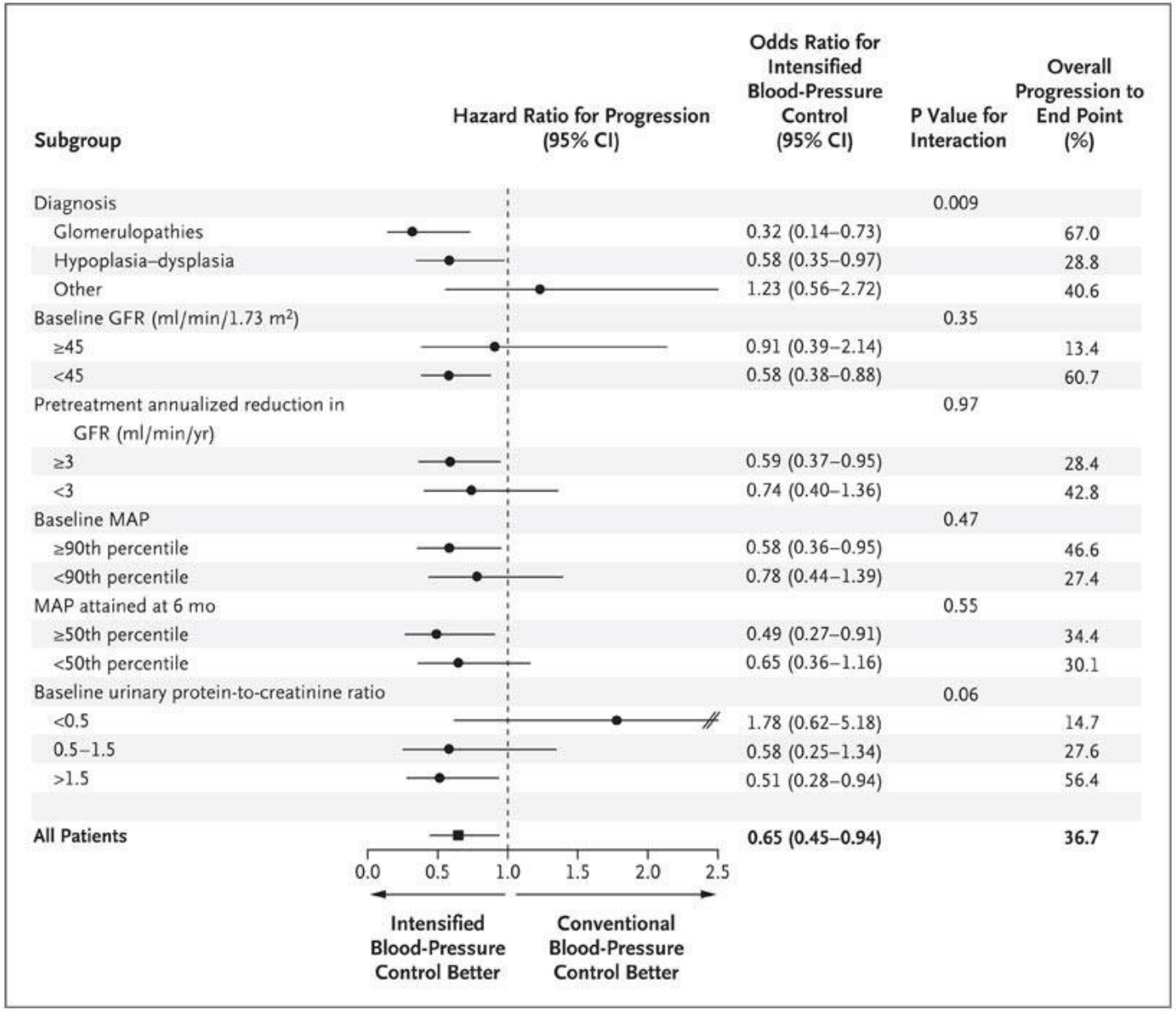
Kamath N, Iyengar A, George N, Luyckx VA. Risk Factors and Rate of Progression of CKD in Children. Kidney Int Rep. 2019

ETIOLOGY OF KIDNEY DISEASE

CKDu (CIN)

- young age
- lack of known CKD risk
- reduced glomerular filtration rate
- minimal proteinuria
- no or slight increase in blood pressure
- chronic interstitial nephritis

ESCAPE Trial



TIMING OF REFERRAL

- CKD stages 1-2 -Management by pediatrician
- Consider adequate hydration, treat or prevent UTI episodes
- Avoid nephrotoxic medications
- Vaccinations
- 6-12 monthly follow up
  - BP, proteinuria and serum creatinine, electrolytes (salt wasting, ACEI/ARBs)
- Monitor frequently after AKI episodes, stresses like

TIMING OF REFERRAL

- CKD stages 3-5 - Referral to pediatric nephrologist
- Complications of CKD
  - Anemia, bone disease, HTN and fluid vigilance in some
  - Delayed puberty, malnutrition
- Rapid progression
  - ***(38% progress over 2 years, median rate of decline in GFR was 3.5 ml/yr, almost twice that in the CKiD study (1.8 ml/yr)- St. John's Hospital, Bangalore)***
- More episodes of AKI, non recovery of renal function to baseline
- Dose modification of drugs
  - Nephrotoxic drugs
  - Non renal effects of non-nephrotoxic drugs

Kamath N, Iyengar A, George N, Luyckx VA. Risk Factors and Rate of Progression of CKD in Children. Kidney Int Rep. 2019

TIMING OF REFERRAL

- CKD stages 3-5 - Referral to pediatric nephrologist
- Disease progression needs closer monitoring
- Drugs for delaying progression
  - ***ACEI/ARBS – hyperkalemia***
  - ***Dapaglifozin, Finerenone, combination therapies***
- Nutritional management challenging - Dietary restrictions, poor apetite

Summary

- Screening of asymptomatic children – who have risk factors
- All at risk children – practically possible, economical schedule for follow up
- Frequent follow up during critical period
- BP control and early proteinuria management is beneficial
- Avoid dehydration, nephrotoxic medications in early CKD
- Referral to pediatric nephrologist at CKD stage III or

CYSTIC KIDNEY DISEASES: HOW TO APPROACH

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Division of Pediatric Nephrology

Institute of Child Health Kolkata

OBJECTIVES

- Brief overview of various cystic kidney diseases
- Case study guided discussion about presentation of cystic kidney diseases
- Summarising the approach to cystic kidney diseases

Classification of renal cysts

Table 11. The Liapis and Winyard[121] (2006) Classification of Renal Cystic Disease

A. Polycystic kidney disease
   1. Autosomal-dominant polycystic kidney disease
      Classic ADPKD
      Early onset ADPKD in children
   2. Autosomal-recessive polycystic kidney disease
      Classic ARPKD in neonates and infants
      Medullary duct ectasia in older children with hepatic fibrosis
   3. Glomerulocystic kidney disease
      Familial GCKD
      Renal hypoplasia and *UROM* mutation
      Associated with *HNFB1* mutations
      Hereditary GCKD
      Associated with ADPKD/ARPKD/TSC
      Syndromic nonhereditary GCKD
      Sporadic GCKD
      Acquired GCKD

B. Renal medullary cysts
   1. Nephronophthisis
      Nephronophthisis, autosomal recessive
      Juvenile nephronophthisis
      NPH1, NPH4
      NPH1, NPH5 associated with Senior-Loken syndrome
      Infantile NPH2
   2. Medullary cystic diseases
      Autosomal dominant MCKD
      MCKD associated with hyperuricemia
   3. Medullary sponge kidney

C. Cysts in hereditary cancer syndromes
   1. von Hippel-Lindau disease
   2. Tuberous sclerosis

D. Multilocular renal cyst

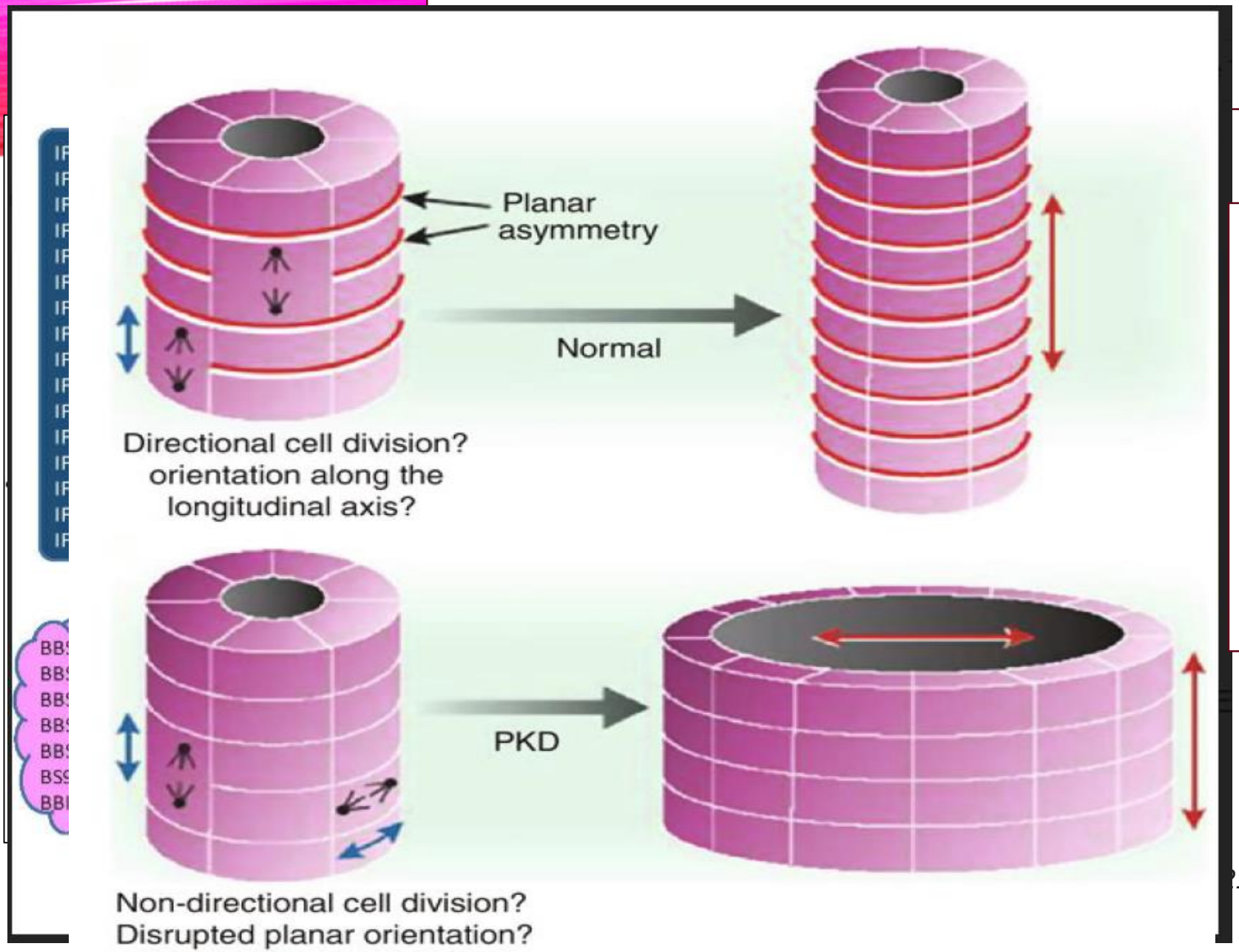
E. Localized cystic disease

F. Simple cortical cysts

G. Acquired (dialysis-induced) cysts

H. Miscellaneous
   1. Pyelocaliceal diverticula
   2. Perinephric pseudocysts
   3. Hygroma renalis

Bonsib SM. The classification of renal cystic diseases and other congenital malformations of the kidney and urinary tract. Arch Pathol Lab Med. 2010 Apr;134(4):554-68.



Unified theory of cystogenesis

21 Mar;77(3):410-419

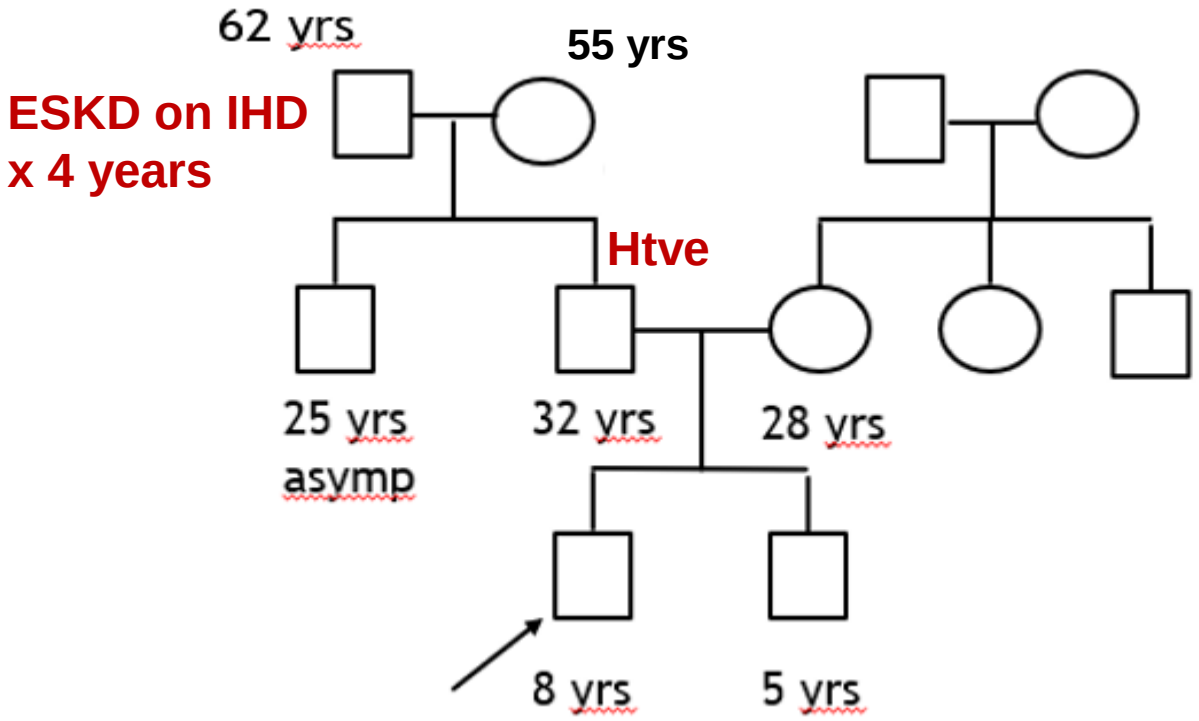
CASE STUDIES

CLINICAL CASE 1

- 8 yr old male, born out of non consanguineous marriage
- Incidentally detected solitary cyst in RK by USG

(RK – 10cm, LK – 9.8 cm, increased cortical echogenicity B/L, cortical cyst 1.2 cm in RK)

- Anthropometry – normal
- Normotensive
- Normal renal function test,1+ proteinuria in urine dipstick, early morning UPCR – 0.4
- No extra-renal manifestations, eye and hearing assessments normal



- USG of father - bilateral enlarged kidneys with 4 cysts in each kidney, largest 1.3 cm
- USG of paternal grandfather - bilateral enlarged kidneys with multiple cysts bilaterally (>1cm)
- USG of mother, paternal uncle: normal

Probable Diagnosis?

ADPKD : DIAGNOSTIC CRITERIA

Age (years)	Number of cysts
Ultrasonography (at-risk of ADPKD type 1)	
< 30	≥ 2 in one or both kidneys
30 to 59	≥ 2 in each kidney
≥ 60	≥ 4 in each kidney
Ultrasonography (at risk and unknown genotype)	
15 to 39	≥ 3 in one or both kidneys
40 to 59	≥ 2 in each kidney
≥ 60	≥ 4 in each kidney
Magnetic resonance imaging (at risk)	
< 30	≥ 5 in each kidney
30 to 44	≥ 6 in each kidney
45 to 59 (females)	> 6 in each kidney
45 to 59 (males)	> 9 in each kidney

Am Fam Physician. 2014;90(5):303-307

International consensus statement on the diagnosis and management of autosomal dominant polycystic kidney disease in children and young people

Charlotte Gimpel[1], Carsten Bergmann[2,3], Detlef Bockenhauer[4], Luc Breysem[5], Melissa A. Cadnapaphornchai[6], Metin Cetiner[7], Jan Dudley[8], Francesco Emma[9], Martin Konrad[10], Tess Harris[11,12], Peter C. Harris[13], Jens König[10], Max C. Liebau[14], Matko Marlais[4], Djalila Mekahli[15,16], Alison M. Metcalfe[17], Jun Oh[18], Ronald D. Perrone[19], Manish D. Sinha[20], Andrea Titieni[10], Roser Torra[21], Stefanie Weber[22], Paul J. D. Winyard[4] and Franz Schaefer[23]*

Recommendation 2.2

In a child under 15 years with a positive family history of ADPKD, sonographic detection of one or more kidney cysts is highly suggestive of ADPKD (evidence level B, recommendation level moderate). In a fetus or neonate

For PKD1, diagnostic specificity ≥ 1 cysts on US = 89% in < 5 years and 100% in >5 years

Gabow, P at al. Utility of ultrasonography in the diagnosis of autosomal dominant polycystic kidney disease in children. Am. Soc. Nephrol. ***8****, 1 (1997)*

Indications of genetic testing

a) young at-risk patients, asymptomatic, negative findings on US (post-counselling)
b) at-risk patients who wish to be considered as live kidney transplant donors.
c) patients with unknown family history and enlarged kidneys with renal cysts
d) very early onset disease or rapid progression (homozygous, compound heterozygous, digenic, contiguous gene deletions e.g. PKD1/TSC2)

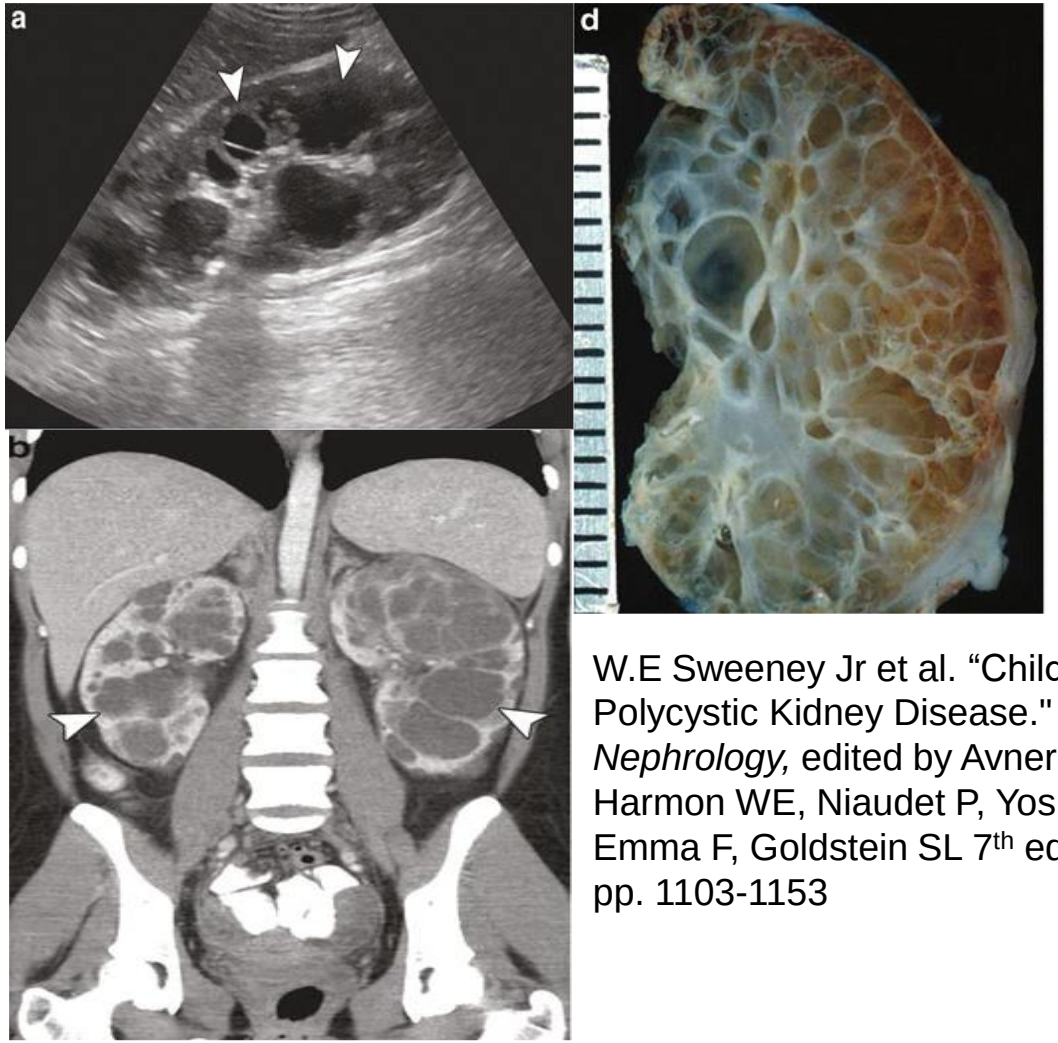
ADPKD: BRIEF OVERVIEW

- 1 in 500-2500
- Cysts start forming in-utero, macrocysts often visible in childhood

  All parts of nephron

  Cortex + medulla
- Typically asymptomatic/symptomatic with unilateral/bilateral cysts ± enlarged kidneys in childhood; ESKD in adulthood

3% - Very Early Onset Disease



W.E Sweeney Jr et al. “Childhood Polycystic Kidney Disease." *Pediatric Nephrology,* edited by Avner ED, Harmon WE, Niaudet P, Yoshikawa M, Emma F, Goldstein SL 7th ed, 2016, pp. 1103-1153

Renal manifestations

- Hypertension (20%)
- Proteinuria (20%)
- ↓ GFR (8%, 2-39%)
- Polyuria, polydipsia (58%)
- Gross hematuria (5-15%)
- UTI (15-25%), cyst infection (rare)
- Abdominal/flank pain (10-20%; non specific, cyst rupture/cyst hemorrhage/nephrolithiasis)
- Nephrolithiasis (rare)

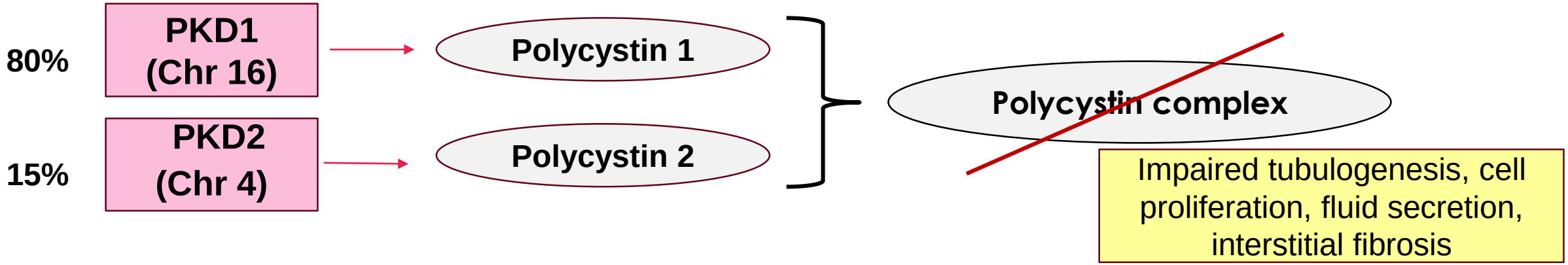
Extrarenal manifestations

- Liver cysts
- Ovarian cysts
- Splenic cysts
- Pancreatic cysts
- Diverticulosis
- Bronchiectasis
- Male infertility, seminal vesical cyst

- LV hypertrophy and diastolic dysfunction
- MV prolapse (12%)
- Pericardial effusion

- IC aneurysm (9% if negative family history, 20-27% if positive family history; prevalence in children unknown)
- Arachnoid cyst

GENETICS OF ADPKD



- Approx 7% - no variants in PKD1/PKD2 (GANAB, DNAJB11, ALG9 variants)
- 8-10% - de novo disease

INTRAFAMILIAL VARIABILITY

Modifier genes

Epigenetic mechanisms

Environmental factors

VEOD/ RAPIDLY PROGRESSIVE DISEASE

- ✓ Homozygous hypomorphic variants
- ✓ Truncating + hypomorphic variants
- ✓ Digenic (truncating/hypomorphic + GANAB/DNAJB11/ALG9)
- ✓ Coexisting HNF1B, PKHD1 gene variants

MANAGEMENT OF ADPKD

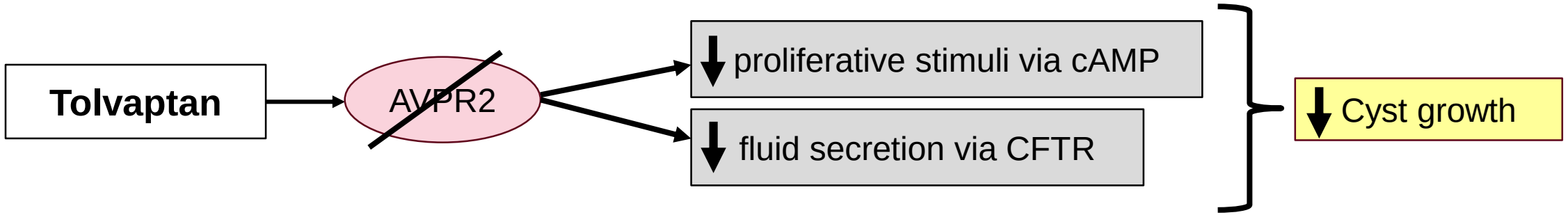
- Hypertension screening: Yearly; ABPM for diagnosis; BP target: <75th centile; ACEI/ARBs>BB, CCB. Diuretics (caution)
- Screening for albuminuria; ACEI/ARBs
- M
- M
  c
- L

Recommendation 8.5

Do not routinely offer vasopressin antagonists to children and young people with ADPKD. Off-label use of vasopressin antagonists can be considered at clinician discretion in children at high risk of early progression based on large total kidney volume, rapid kidney growth, family history, etc. (evidence level D, recommendation level weak).

International consensus statement on the diagnosis and management of ADPKD in children and young people. Gimpel et al, Nat Rev Nephrol. 2019

DELAYING DISEASE PROGRESSION



TEMPO 3:4 – tolvaptan reduced rate of GFR loss and TKV in rapid progressors

Polyuria, thirst, nocturia – discontinuation
Idiosyncratic liver damage
? Ill sustain efficacy over long term use

Post hoc analysis (Raina et al) – slower increase of TKV in 18-24 yrs with tolvaptan vs placebo

RCT examining effect of tolvaptan in 12-17 yrs old ongoing

Studies defining rapid progressors in children lacking

International consensus statement on the diagnosis and management of ADPKD in children and young people. Gimpel et al, Nat Rev Nephrol. 2019

Recommendation 8.5
Do not routinely offer vasopressin antagonists to children and young people with ADPKD. Off-label use of vasopressin antagonists can be considered at clinician discretion in children at high risk of early progression based on large total kidney volume, rapid kidney growth, family history, etc. (evidence level D, recommendation level weak).

OTHER PHARMACOLOGICAL OPTIONS

- Statins – lack of consensus regarding use
- mTORi – not recommended for routine use
- Somatostatin analogues – not recommended in children with ADPKD
- Metformin
- Tyrosine kinase inhibitors
- Proglitazone
- Venglustat
- Lixivaptan

Clinical trials ongoing

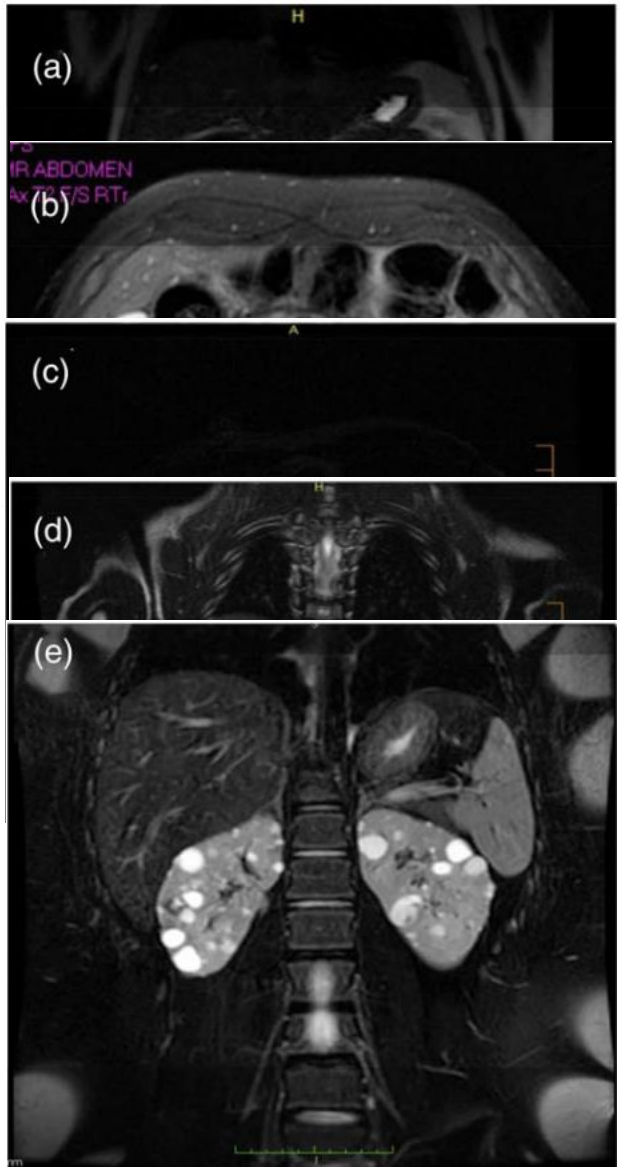
Other Autosomal Dominant Cystic Kidney Disease

Disorder	Family History	Clinical Features
Tuberous sclerosis complex (TSC)	Absent in 2/3 of cases	Affects ~1 in 10,000 live births; skin lesions (facial angiofibromas, periungual fibroma, hypomelanotic macules, shagreen patch); >90% have cerebral pathology (cortical tuber, subependymal nodules, giant cell astrocytoma); 90% have kidney manifestations (polycystic kidneys, angiomyolipomas); 50%-70% have retinal hamartomas; 50% have pulmonary lymphangioleiomyomatosis
PKD1-TSC contiguous gene syndrome	Spontaneous presentation frequent	Presentation with polycystic kidneys at an early age, with kidney angiomyolipomas frequently presenting after the first year of life
von Hippel-Lindau syndrome	~20% de novo	Affects ~1 in 36,000, cerebellar and spinal hemangioblastoma, retinal angiomas, serous cystadenomas and neuroendocrine tumors of pancreas, pheochromocytoma, renal cell carcinoma
Medullary sponge kidney (MSK)	Familial clustering reported	Affects ~1 in 5,000, tubular dilatation of the collecting ducts giving the appearance of "brush" or linear striations on intravenous pyelogram, medullary nephrocalcinosis, kidney stones, kidney cortex spared on CT or MRI
Medullary cystic kidney disease (MCKD[a])	Rare	Slowly progressive kidney disease, medullary cysts (but uncommon in families with type 2 MCKD[a]), hyperuricemia and gout (in type 2 MCKD[a]), small to normal-sized kidneys
Renal cysts and diabetes syndrome (RCAD/MODY5/ HNF-1B[b])	Spontaneous mutations (often deletions) in 50%	Kidney cysts or malformation in 90%, diabetes mellitus in 45%, hypomagnesemia in 40%, genital tract abnormalities in 20%, hyperuricemia in 20%, elevated liver enzymes in 15%

AJKD: Core curriculum in nephrology, 2016

Cystic kidney diseases in TSC

- **Polycystic kidney disease** (2%): mostly seen in CGS, rarely in TSC1
- **Cortical microcystic kidney disease**: associated with rapid decline in eGFR (CKD 2-3 by teens to early twenties), hypertension appear late
- **Focal cystic kidney disease**: cysts in one renal pyramid
- **Cortical cystic kidney disease**: cysts arise from cortex and columns of bertin, are uniform in size and can be present in early childhood
- **TSC multicystic kidney disease:** resemble polycystic disease, cysts in both cortex and medulla.



Ref: Bissler JJ, Christopher Kingswood J. Renal manifestation of tuberous sclerosis complex. Am J Med Genet C Semin Med Genet. 2018 Sep;178(3):338-347

AD TUBULOINTERSTITIAL KIDNEY DISEASE

Type	Age of CKD onset	Other features
ADTKD-UMOD	Adolescence-early adulthood	Hyperuricemia, gout
ADTKD-REN	Variable (childhood-adulthood)	Anemia, mild hyperkalemia, polyuria, mild hypotension, low plasma renin, hyperuricemia
ADTKD-HNF1B	3rd decade (early infancy-adulthood)	MODY, CAKUT, genital anomalies, hyperuricemia and gout, low Mg

Confirmation with genetic testing (NGS/WES)

NF1B

- Cystic
- Fetal –

  73% - r

  Variabl

  U/L ren

anomalie

- AD, 5

  HNF1

  no ge

  17q1

tem

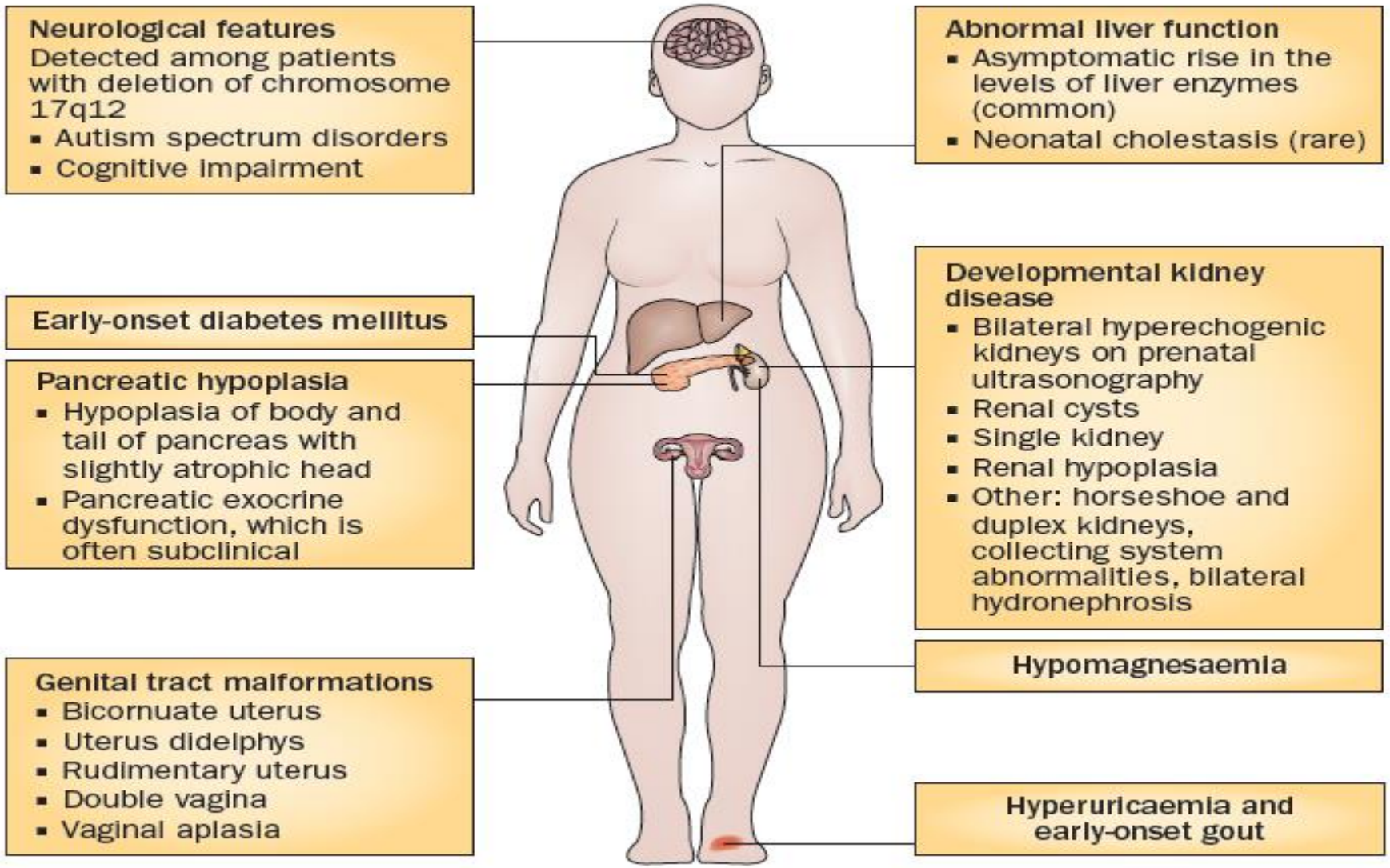


Figure 1 | Renal and extra-renal phenotypes frequently observed among patients with hepatocyte nuclear factor 1β-associated disease.

CLINICAL CASE 2

- 4 hours old male neonate, 36 weeks/2.5 kg, born out of non consanguineous marriage
- Antenatally detected bilateral enlarged hyperechogenic kidneys with oligohydramnios in 3rd trimester
- Respiratory distress soon after birth – Mechanical ventilation
- Abdominal distension, with bimanually palpable and ballotable kidneys
- No dysmorphism
- Hypertensive, Oliguric, creatinine 1.2 mg/dl
- Postnatal USG – bilateral enlarged kidneys (RK – 8.9 cm, LK – 9.2 cm) with increased cortical echogenicity and poor CMD; tiny (1-2 mm) multiple cysts B/L radially arranged in medulla

- 3rd in birth order, no h/o previous sibling loss
- No family h/o renal disease
- Parents USG – normal (Mother 35 years, Father 42 years)

Probable Diagnosis?

Likely pathogenic variant causative of the reported phenotype was identified

*Correlation with clinical profile and family history is required

FINDINGS RELATED TO PHENOTYPE

Gene & Transcript	Variant	Location	Zygosity	Disorder (OMIM)	Inheritance	Classification
PKHD1 NM_138694.4	c.6274delG (p.Glu2092ArgfsTer19)	Exon 38	Homozygous	Polycystic kidney disease 4, with or without hepatic disease (263200)	Autosomal Recessive	Likely Pathogenic

VARIANT INTERPRETATIONS

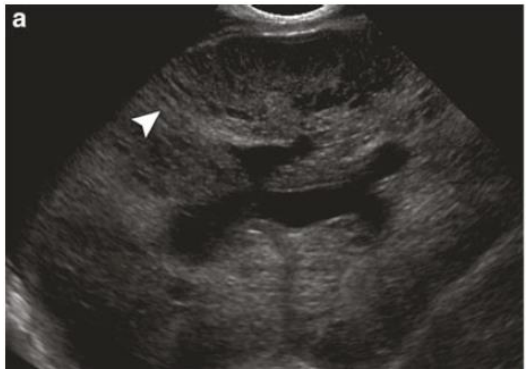
PKHD1 chr6:51777222delC - Likely Pathogenic.

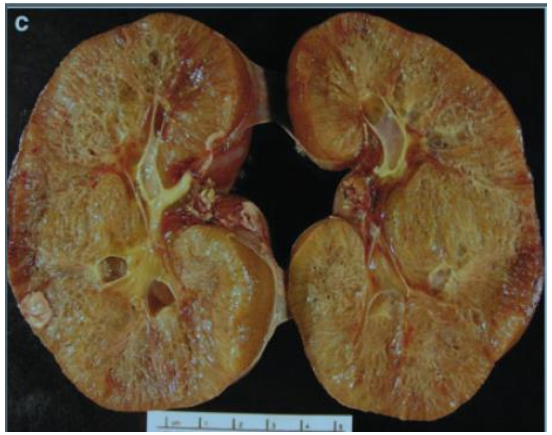
The frameshift deletion NM_138694.4 (*PKHD1*):c.6274delG (p.Glu2092ArgfsTer19) has not been reported previously as a pathogenic variant nor as a benign variant, to our knowledge. The p.Glu2092ArgfsTer19 variant is novel (not in any individuals) in gnomAD South Asian Background in gnomAD. The p.Glu2092ArgfsTer19 variant is novel (not in any individuals) in 1kG. This variant is predicted to cause loss of normal protein function through protein truncation caused a frameshift mutation. The frame shifted sequence continues 19 residues until a stop codon is reached. This variant is a frameshift variant which occurs in an exon of *PKHD1* upstream of where nonsense mediated decay is predicted to occur. There are 181 downstream pathogenic loss of function variants, with the furthest variant being 1984 residues downstream of this variant. This indicates that the region is critical to protein function. The p.Glu2092ArgfsTer19 variant is a loss of function variant in the gene *PKHD1*, which is intolerant of Loss of Function variants, as indicated by the presence of existing pathogenic loss of function variant NP_619639.3:p.M1V and 174 others. **For these reasons, this variant has been classified as Likely Pathogenic.**

ARPKD: BRIEF OVERVIEW

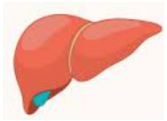
1:6000-1:20000

Hepatorenal fibrocystic disease





Fusiform cystic dilatations from collecting ducts



Ductal plate malformation: Congenital hepatic fibrosis/ periportal fibrosis ± intrahepatic biliary radicle dilatation / Carolis disease

Clinical Spectrum

Kidney

- 70-80% survive the neonatal period
- Survival at 1 yr – 85%, 10 yrs – 82%, 15 yrs – 79%
- Renal survival at 1 yr – 86%, 15 yrs – 67%
- Progression to ESKD slower in children with non perinatal (26.3+/-9.2 years, range 15-36 years) vs perinatal presentation (7.6+/-6.8 years, range 0.5-18 years)

Liver

Firm Hepatomegaly
Portal hypertension, variceal bleeding, splenomegaly, absence of hepatocellular dysfunction
Biliary ductal ectasia, Ascending bacterial cholangitis

Important determinant of mortality and morbidity post KT

Genetics

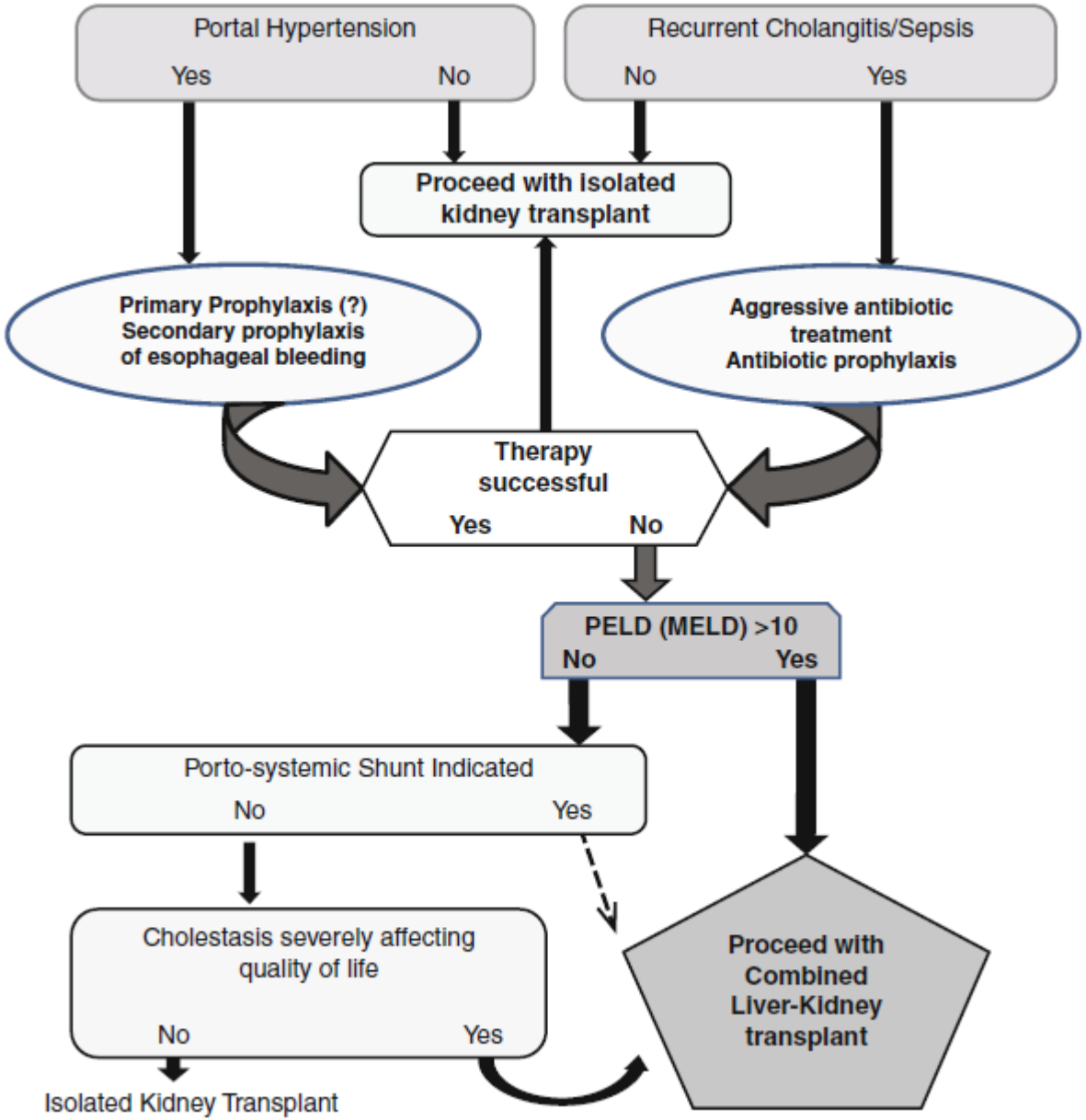
- *PKHD1* (6p12.2-3)→ fibrocystin
- DZIP1L gene – 2nd locus (ciliary membrane translocation of PC complex)
- Truncating vs missense mutations
- Intrafamilial phenotypic variability
- Mutation detection rate approx. 90%

Management

Fetal Monitoring	• 2-3 weekly USG – Renal size and AF volume • Prenatal imaging characteristics don't reliably predict chances of lethal pulmonary hypoplasia
Perinatal management	• Delivery in well equipped NICUs • Multidisciplinary management – Fetal-maternal medicine expert, neonatologist, ped nephrologist • Decisions regarding aggressive interventions, dialysis in conjunction with parents
Postnatal management	• **Hypertension** – ACEI/ARBs • **Hyponatremia** – fluid restriction, concentrated feeds • **Feeding** – Gastrostomy/NG tube feeds, Vit A,D,E,K supplementation ± UDCA administration, regular anthropometric & nutritional assessments • **Nephrectomies** – pre/during KT. No evidence to support nephrectomy for resp distress or nutritional management or severe HTn in early ARPKD

H

Ne
anc



Telega G, Cronin D, Avner ED. New approaches to the autosomal recessive polycystic kidney disease patient with dual kidney-liver complications. Pediatr Transplant. 2013;17:328–35.

DIFFERENTIAL DIAGNOSIS

D/D	Differentiating features
HNF1B	Structural renal abnormalities, genital anomalies, family h/o kidney cysts/MODY + parental USG, low Mg, hyperuricemia
VEO ADPKD	Family history, parental USG
Infantile Nephronophthisis	Cortical cysts ± Hypertension, Situs inversus, VSD,
Bardet Biedl Syndrome	Polydactyly, developmental anomalies of kidney, urinary tract malformations, genital anomalies
Meckel Gruber Syndrome	Occipital encephalocele, polydactyly, hepatic abnormalities

Table 1 Diagnostic features and prevalence in BBS

Primary features	
Rod-cone dystrophy	
Polydactyly	
Obesity	
Genital anomalies	
Renal anomalies	
Learning difficulties	
Secondary features	
Speech delay	
Developmental delay	
Diabetes mellitus	
Dental anomalies	
Congenital heart disease	7%
Brachydactyly/ syndactyly	46–100%/8–95%
Ataxia/ poor coordination	40–86%
Anosmia/hyposmia	60%

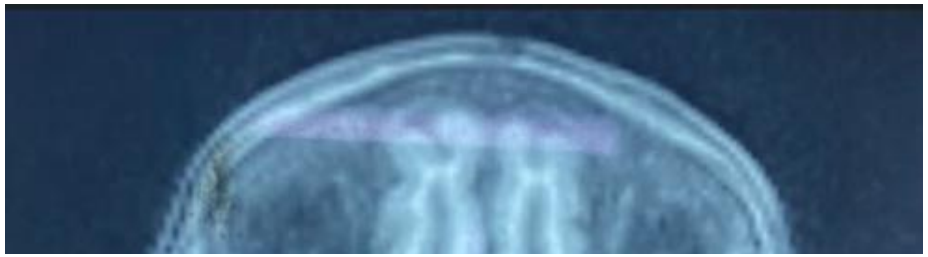
Four primary features or three primary features and two secondary features are required for a clinical diagnosis of Bardet–Biedl syndrome.[4,16,18]

- Abnormal ERG – earliest 1st 2 years, significant > 5 yrs
- Cystic kidney disease (microcysts at CMJ, 10-72%), dysplastic kidneys, developmental anomalies, urinary tract malformations
- Impaired urinary concentration
- Advanced CKD by 5 years or persist into adulthood with normal/near normal renal functions
- BBS10, truncating variants, structural renal anomalies, hypertension predict progression to advanced CKD

CLINICAL CASE 3

- 6 yrs old female, born out of non consanguineous marriage
- Presented with fever, short stature, serum creat 2.13 mg/dl
- Polyuria
- Normotensive
- USG – normal sized kidneys with increased cortical echogenicity and altered CMD; multiple small cysts 3-4 mm B/L along CMJ
- Spastic diplegia, GDD, ptosis, nystagmus, strabismus
- Hearing evaluation by BERA normal
- No family h/o renal disease; Parents USG normal (Mother – 28 yrs, Father – 35 yrs)

Probable Diagnosis?



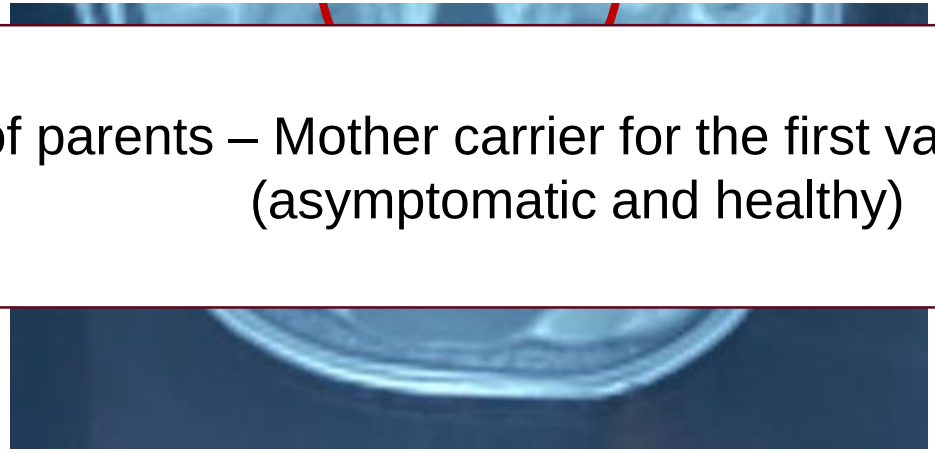
RESULT SUMMARY

Likely compound heterozygous variants causative of the reported phenotype were identified

*Correlation with clinical profile and family history is required

FINDINGS RELATED TO PHENOTYPE

Gene & Transcript	Variant	Location	Zygosity	Disorder (OMIM)	Inheritance	Classification
RPGRIP1L NM_015272.5	c.2480C>G (p.Thr827Arg)	Exon 17	Heterozygous	Joubert syndrome 7 (611560)	Autosomal Recessive	Uncertain Significance
RPGRIP1L NM_015272.5	c.1945C>T (p.Arg649Ter)	Exon 15	Heterozygous	Joubert syndrome 7 (611560)	Autosomal Recessive	Pathogenic



Sanger sequencing of parents – Mother carrier for the first variant and father for the second (asymptomatic and healthy)

Extrarenal manifestation associated with NPHP	Syndrome
Retinitis pigmentosa/retinal dystrophy	Senior–Løken syndrome
	Alström syndrome
	Arima syndrome
Oculomotor apraxia	Cogan syndrome
Nystagmus	Joubert syndrome and related disorders
Ocular coloboma	Joubert syndrome and related disorders
Posterior encephalocele	Meckel–Gruber syndrome
Abnormal respiratory pattern	Joubert syndrome and related disorders
Cerebellar vermis aplasia/hypoplasia	Joubert syndrome and related disorders
Liver fibrosis	Joubert syndrome and related disorders
	Meckel–Gruber syndrome
	Arima syndrome
Postaxial polydactyly	Bardet–Biedl syndrome
	Joubert syndrome and related disorders
Skeletal dysplasia	Ellis–van Creveld syndrome
	Sensenbrenner syndrome
	Jeune syndrome
	Mainzer–Saldino syndrome
Situs inversus/cardiac malformation	Infantile NPHP

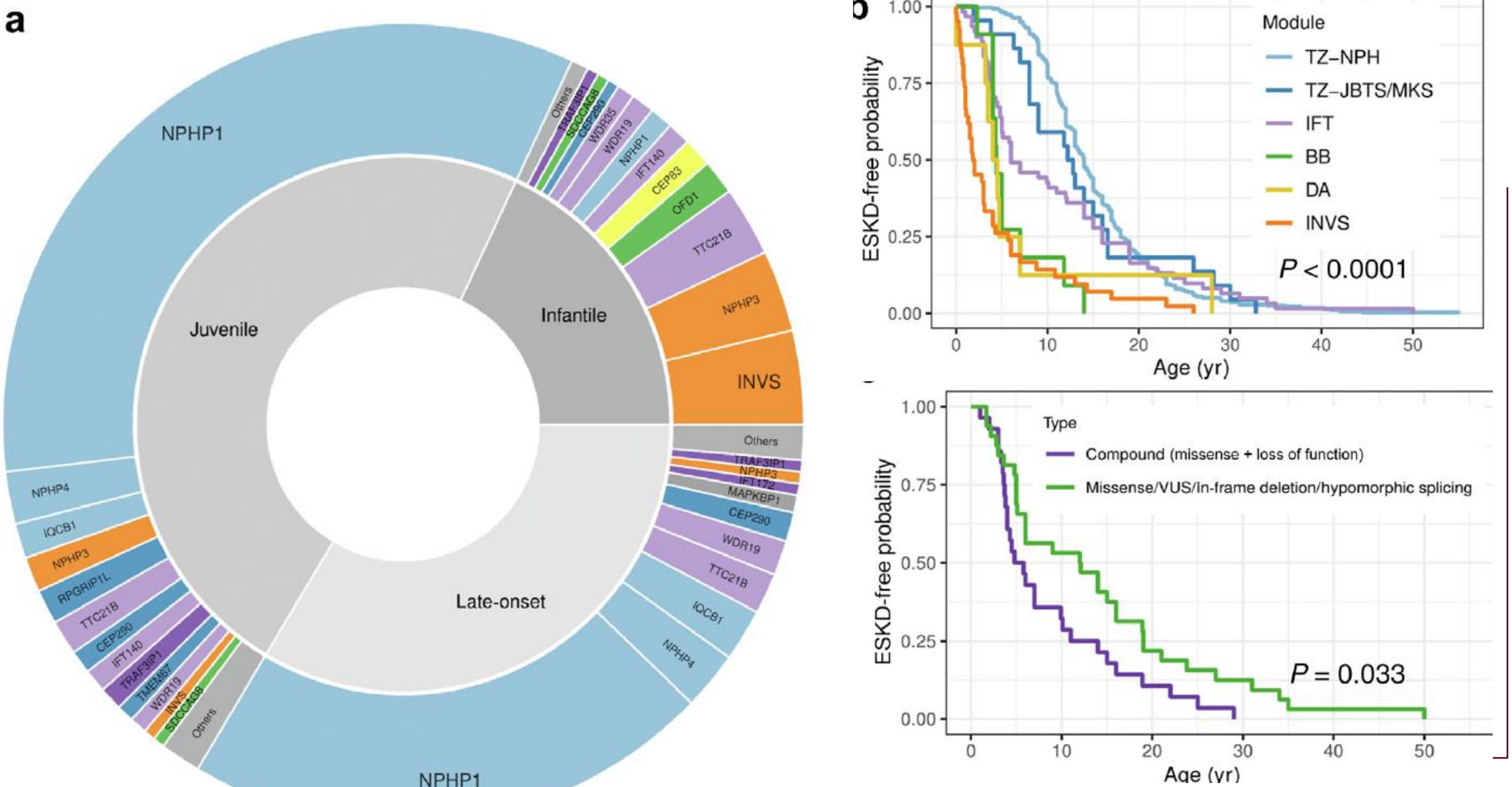
Srivastava S et al. Many Genes-One Disease? Genetics of Nephronophthisis (NPHP) and NPHP-Associated Disorders. Front Pediatr. 2018 Jan 5;5:287.

n age of ESKD

yrs

13 yrs

19 yrs


a
NPHP1
Juvenile
Infantile
Late-onset
INVS
NPHP3
TTC21B
CEP83
OFD1
IFT140
NPHP1
WDR19
WDR35
CEP290
SDCCAG8
TRAF3IP1
Others
NPHP4
IQCB1
NPHP3
RPGRIP1L
TTC21B
CEP290
IFT140
TRAF3IP1
TMEM67
WDR19
INVS
SDCCAG8
Others
NPHP1
IQCB1
NPHP4
TTC21B
WDR19
CEP290
MAPKBP1
IFT172
NPHP3
TRAF3IP1
Others
b
ESKD-free probability
1.00
0.75
0.50
0.25
0.00
0
10
20
30
40
50
Age (yr)
Module
TZ–NPH
TZ–JBTS/MKS
IFT
BB
DA
INVS
P < 0.0001
ESKD-free probability
Type
Compound (missense + loss of function)
Missense/VUS/in-frame deletion/hypomorphic splicing
P = 0.033
Age (yr)

JOUBERT AND NEPHRONOPHTHISIS

- Cerebellar vermis hypoplasia
  Hypotonia, cerebellar ataxia, neonatal tachypnea, developmental delay
  ± ocular coloboma, polydactyly, hepatic fibrosis
- 30% - kidney involvement – classical nephronophthisis
  infantile nephronophthisis
  indeterminate cystic kidney disease phenotype
  unilateral multicystic dysplastic kidney
- NPHP genes including TMEM67 (most common), CEP290, AHI1

SUMMARY OF APPROACH TO CYSTIC KIDNEY DISEASE

- **History** – polyuria, polydipsia, flank pain, hematuria, UTI
  Age of presentation
  Extrarenal involvement
  Family History – 3 generation pedigree; kidney disease/
  IC bleed/blindness/ hearing loss/ liver disease etc

- **Examination** – Anthropometry
  BP, volume status
  Dysmorphism
  Extrarenal involvement (CNS, eye, heart, hepatosplenomegaly, genitourinary abnormalities, skeletal)

- **Investigations**: Renal function test

  Serum electrolytes (Na, K, Mg), Serum uric acid

  Urine routine, proteinuria quantification

  Liver function test, Ophthalmological evaluation, hearing evaluation, FBS/PPBS, echocardiography, MRI Brain, skeletal survey (if indicated by clinical evaluation and imaging)

- **USG abdomen:** Renal – Kidney size, echogenicity & CMD; cyst size, number, distribution & characteristics; associated CAKUTs

  Evidence of hepatic fibrosis, Portal hypertension

  Pancreatic cyst, ovarian cyst etc, Genital anomalies

- **Parents' USG KUB**

IMAGING FINDINGS

- **Kidney Size** – Large – ADPKD, ARPKD, Infantile NPHP, TSC, PKD1-TSC CGS
  Normal/Small – NPHP, ADTKD, dysplastic kidneys

- **Cyst location** – Diffuse – ADPKD, ARPKD
  Cortical – ADPKD, Infantile NPHP, HNF1B, TSC
  Medullary – ARPKD, medullary sponge kidney

Confirmation with Genetic testing – Next Generation sequencing (gene panel/WES)

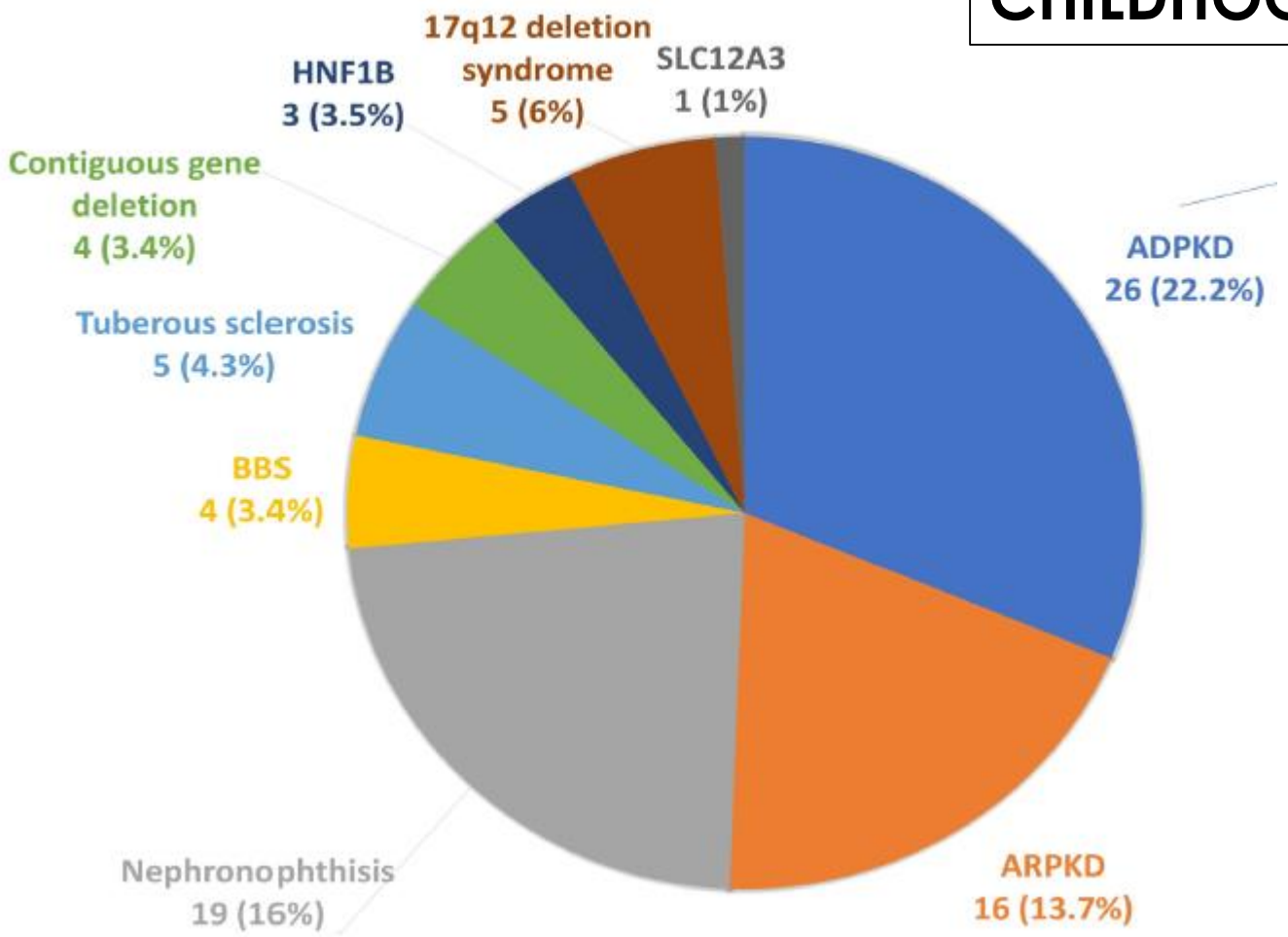
pancreatic dysplasia, BBS

- **Pancreatic cyst, ovarian cyst etc** – ADPKD
- **Genital anomalies:** HNF1B, BBS

TAKE HOME MESSAGE

- Cystic kidney diseases in children are mostly inherited
- Radiological appearance of the kidneys, distribution and size of cysts in the kidneys along with the extrarenal manifestations and family history help to narrow down on the diagnosis
- Due to considerable phenotypic variability and overlap, and lack of genotype-phenotype correlation, confirmation has to be sought through genetic analysis
- Management is often multidisciplinary. Therapeutic modalities to prevent cyst progression are yet to be approved in children

A MULTICENTRE OBSERVATIONAL STUDY TO EXPLORE THE GENETIC ETIOLOGY OF CHILDHOOD CYSTIC KIDNEY DISEASES



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Dr Sriram Krishnamurthy
Dr Manoj Matnani
Dr Subal Pradhan
Dr Kausik Mandal

CYSTIC KIDNEY DISEASES: HOW TO APPROACH

Dr Deblina Dasgupta (MD, FNB)

Assistant Professor

Division of Pediatric Nephrology

Institute of Child Health Kolkata

OBJECTIVES

- Brief overview of various cystic kidney diseases
- Case study guided discussion about presentation of cystic kidney diseases
- Summarising the approach to cystic kidney diseases

Classification of renal cysts

Table 11. The Liapis and Winyard[121] (2006) Classification of Renal Cystic Disease

A. Polycystic kidney disease
   1. Autosomal-dominant polycystic kidney disease
      Classic ADPKD
      Early onset ADPKD in children
   2. Autosomal-recessive polycystic kidney disease
      Classic ARPKD in neonates and infants
      Medullary duct ectasia in older children with hepatic fibrosis
   3. Glomerulocystic kidney disease
      Familial GCKD
      Renal hypoplasia and *UROM* mutation
      Associated with *HNFB1* mutations
      Hereditary GCKD
      Associated with ADPKD/ARPKD/TSC
      Syndromic nonhereditary GCKD
      Sporadic GCKD
      Acquired GCKD

B. Renal medullary cysts
   1. Nephronophthisis
      Nephronophthisis, autosomal recessive
      Juvenile nephronophthisis
      NPH1, NPH4
      NPH1, NPH5 associated with Senior-Loken syndrome
      Infantile NPH2
   2. Medullary cystic diseases
      Autosomal dominant MCKD
      MCKD associated with hyperuricemia
   3. Medullary sponge kidney

C. Cysts in hereditary cancer syndromes
   1. von Hippel-Lindau disease
   2. Tuberous sclerosis

D. Multilocular renal cyst

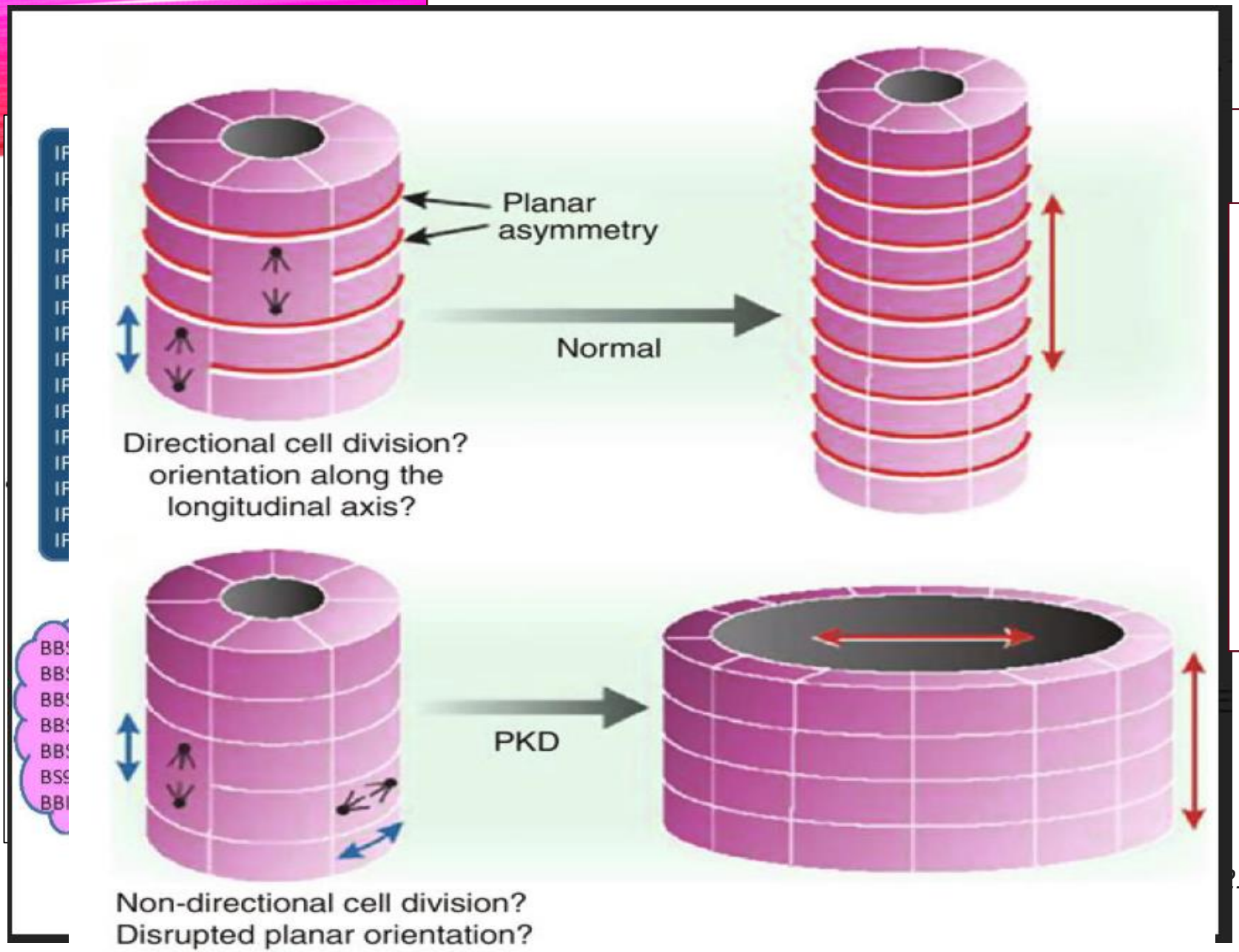
E. Localized cystic disease

F. Simple cortical cysts

G. Acquired (dialysis-induced) cysts

H. Miscellaneous
   1. Pyelocaliceal diverticula
   2. Perinephric pseudocysts
   3. Hygroma renalis

Bonsib SM. The classification of renal cystic diseases and other congenital malformations of the kidney and urinary tract. Arch Pathol Lab Med. 2010 Apr;134(4):554-68.



Unified theory of cystogenesis

21 Mar;77(3):410-419

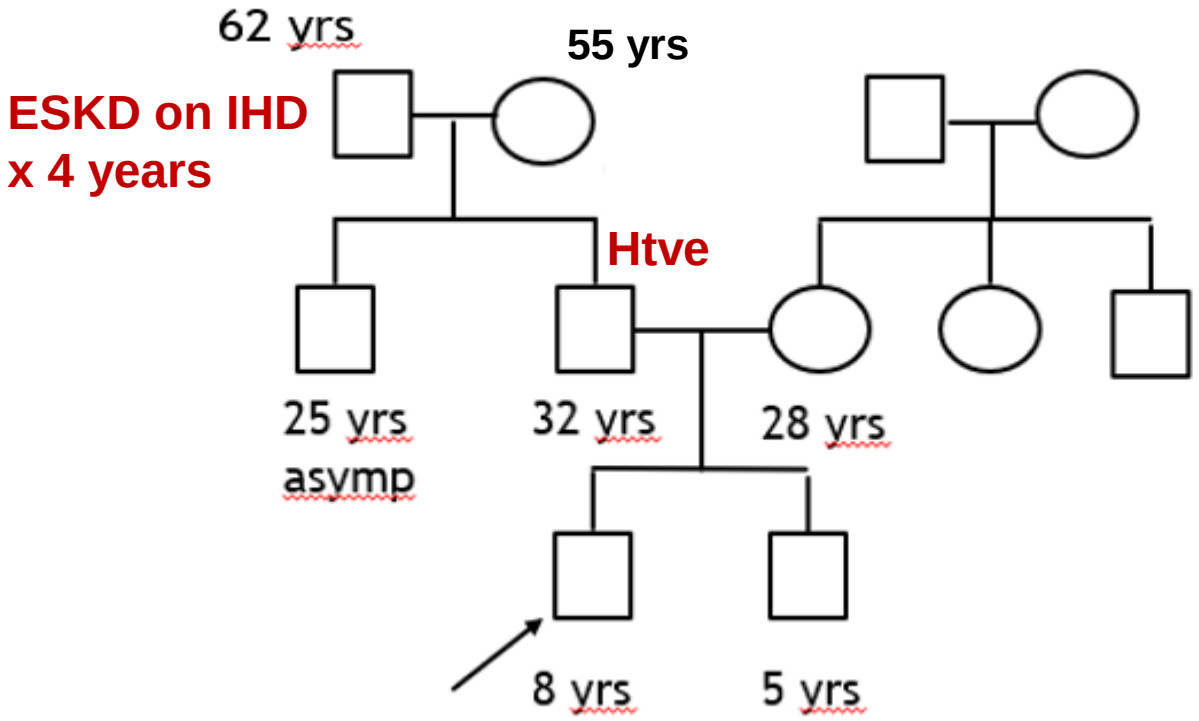
CASE STUDIES

CLINICAL CASE 1

- 8 yr old male, born out of non consanguineous marriage
- Incidentally detected solitary cyst in RK by USG

(RK – 10cm, LK – 9.8 cm, increased cortical echogenicity B/L, cortical cyst 1.2 cm in RK)

- Anthropometry – normal
- Normotensive
- Normal renal function test,1+ proteinuria in urine dipstick, early morning UPCR – 0.4
- No extra-renal manifestations, eye and hearing assessments normal



- USG of father - bilateral enlarged kidneys with 4 cysts in each kidney, largest 1.3 cm
- USG of paternal grandfather - bilateral enlarged kidneys with multiple cysts bilaterally (>1cm)
- USG of mother, paternal uncle: normal

Probable Diagnosis?

ADPKD : DIAGNOSTIC CRITERIA

Age (years)	Number of cysts
Ultrasonography (at-risk of ADPKD type 1)	
< 30	≥ 2 in one or both kidneys
30 to 59	≥ 2 in each kidney
≥ 60	≥ 4 in each kidney
Ultrasonography (at risk and unknown genotype)	
15 to 39	≥ 3 in one or both kidneys
40 to 59	≥ 2 in each kidney
≥ 60	≥ 4 in each kidney
Magnetic resonance imaging (at risk)	
< 30	≥ 5 in each kidney
30 to 44	≥ 6 in each kidney
45 to 59 (females)	> 6 in each kidney
45 to 59 (males)	> 9 in each kidney

Am Fam Physician. 2014;90(5):303-307

International consensus statement on the diagnosis and management of autosomal dominant polycystic kidney disease in children and young people

Charlotte Gimpel[1], Carsten Bergmann[2,3], Detlef Bockenhauer[4], Luc Breysem[5], Melissa A. Cadnapaphornchai[6], Metin Cetiner[7], Jan Dudley[8], Francesco Emma[9], Martin Konrad[10], Tess Harris[11,12], Peter C. Harris[13], Jens König[10], Max C. Liebau[14], Matko Marlais[4], Djalila Mekahli[15,16], Alison M. Metcalfe[17], Jun Oh[18], Ronald D. Perrone[19], Manish D. Sinha[20], Andrea Titieni[10], Roser Torra[21], Stefanie Weber[22], Paul J. D. Winyard[4] and Franz Schaefer[23]*

Recommendation 2.2

In a child under 15 years with a positive family history of ADPKD, sonographic detection of one or more kidney cysts is highly suggestive of ADPKD (evidence level B, recommendation level moderate). In a fetus or neonate

For PKD1, diagnostic specificity ≥ 1 cysts on US = 89% in < 5 years and 100% in >5 years

Gabow, P at al. Utility of ultrasonography in the diagnosis of autosomal dominant polycystic kidney disease in children. Am. Soc. Nephrol. ***8****, 1 (1997)*

Indications of genetic testing

a) young at-risk patients, asymptomatic, negative findings on US (post-counselling)
b) at-risk patients who wish to be considered as live kidney transplant donors.
c) patients with unknown family history and enlarged kidneys with renal cysts
d) very early onset disease or rapid progression (homozygous, compound heterozygous, digenic, contiguous gene deletions e.g. PKD1/TSC2)

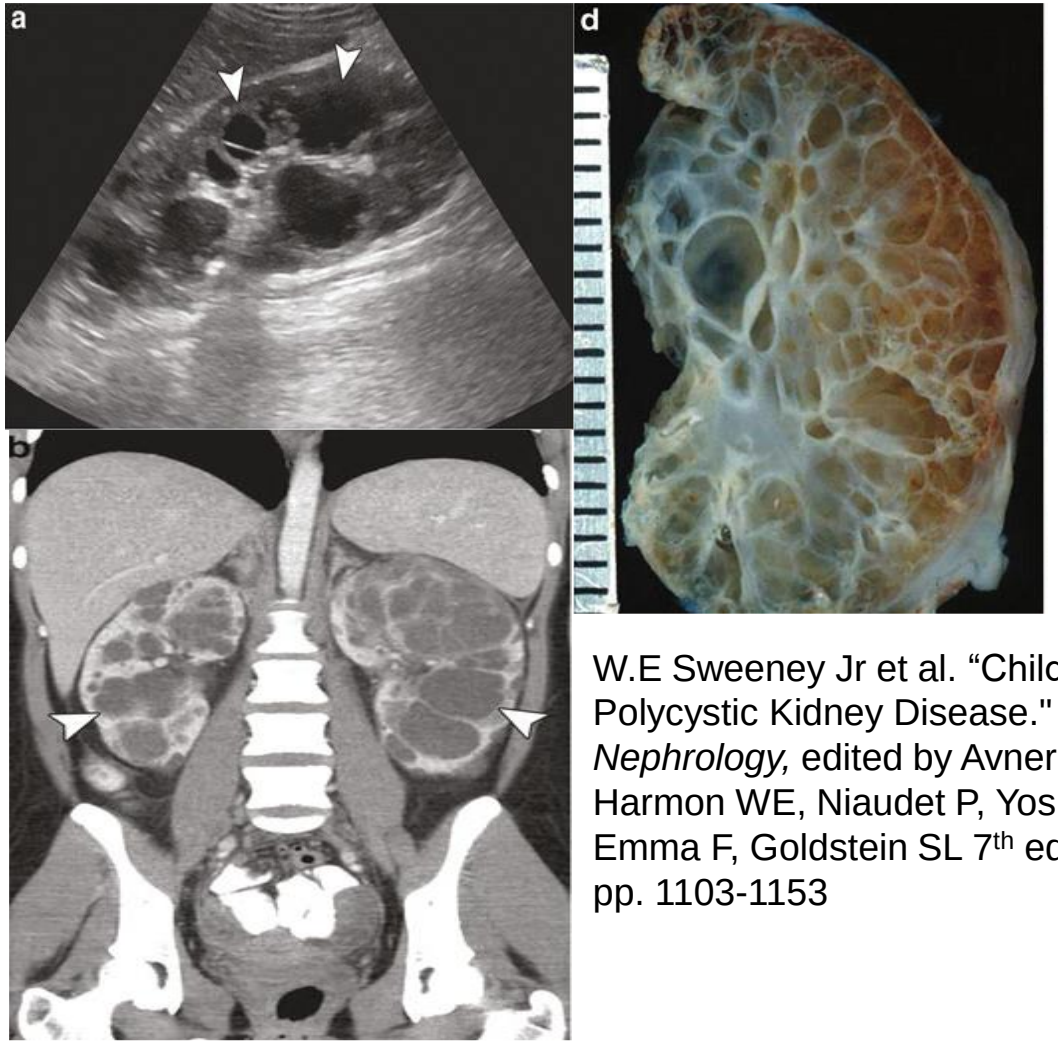
ADPKD: BRIEF OVERVIEW

- 1 in 500-2500
- Cysts start forming in-utero, macrocysts often visible in childhood

  All parts of nephron

  Cortex + medulla
- Typically asymptomatic/symptomatic with unilateral/bilateral cysts ± enlarged kidneys in childhood; ESKD in adulthood

3% - Very Early Onset Disease



W.E Sweeney Jr et al. “Childhood Polycystic Kidney Disease." *Pediatric Nephrology,* edited by Avner ED, Harmon WE, Niaudet P, Yoshikawa M, Emma F, Goldstein SL 7th ed, 2016, pp. 1103-1153

Renal manifestations

- Hypertension (20%)
- Proteinuria (20%)
- ↓ GFR (8%, 2-39%)
- Polyuria, polydipsia (58%)
- Gross hematuria (5-15%)
- UTI (15-25%), cyst infection (rare)
- Abdominal/flank pain (10-20%; non specific, cyst rupture/cyst hemorrhage/nephrolithiasis)
- Nephrolithiasis (rare)

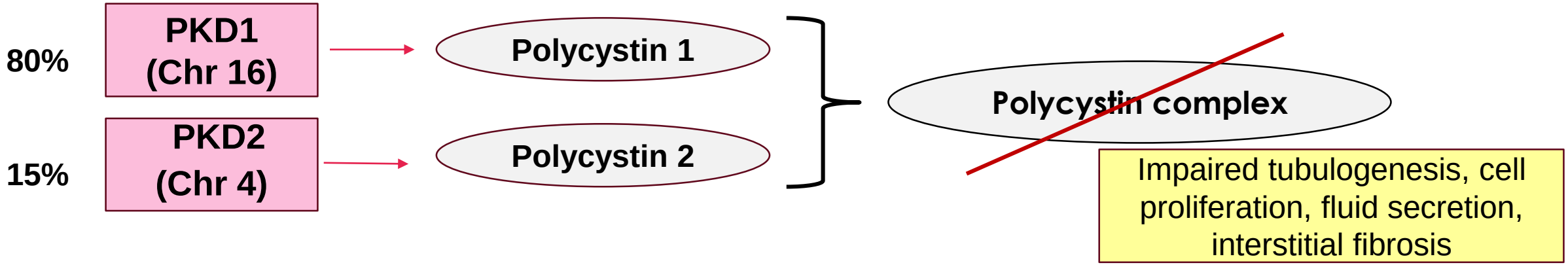
Extrarenal manifestations

- Liver cysts
- Ovarian cysts
- Splenic cysts
- Pancreatic cysts
- Diverticulosis
- Bronchiectasis
- Male infertility, seminal vesical cyst

- LV hypertrophy and diastolic dysfunction
- MV prolapse (12%)
- Pericardial effusion

- IC aneurysm (9% if negative family history, 20-27% if positive family history; prevalence in children unknown)
- Arachnoid cyst

GENETICS OF ADPKD



- Approx 7% - no variants in PKD1/PKD2 (GANAB, DNAJB11, ALG9 variants)
- 8-10% - de novo disease

INTRAFAMILIAL VARIABILITY

Modifier genes

Epigenetic mechanisms

Environmental factors

VEOD/ RAPIDLY PROGRESSIVE DISEASE

- ✓ Homozygous hypomorphic variants
- ✓ Truncating + hypomorphic variants
- ✓ Digenic (truncating/hypomorphic + GANAB/DNAJB11/ALG9)
- ✓ Coexisting HNF1B, PKHD1 gene variants

MANAGEMENT OF ADPKD

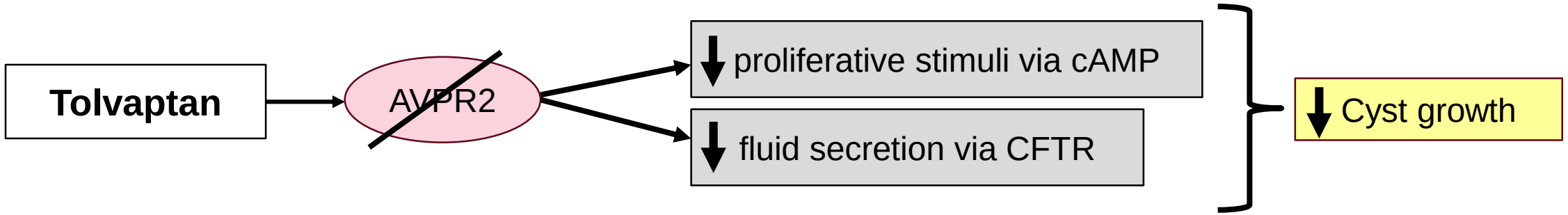
- Hypertension screening: Yearly; ABPM for diagnosis; BP target: <75th centile; ACEI/ARBs>BB, CCB. Diuretics (caution)
- Screening for albuminuria; ACEI/ARBs
- M
- M
  c
- L

Recommendation 8.5

Do not routinely offer vasopressin antagonists to children and young people with ADPKD. Off-label use of vasopressin antagonists can be considered at clinician discretion in children at high risk of early progression based on large total kidney volume, rapid kidney growth, family history, etc. (evidence level D, recommendation level weak).

International consensus statement on the diagnosis and management of ADPKD in children and young people. Gimpel et al, Nat Rev Nephrol. 2019

DELAYING DISEASE PROGRESSION



TEMPO 3:4 – tolvaptan reduced rate of GFR loss and TKV in rapid progressors

Polyuria, thirst, nocturia – discontinuation
Idiosyncratic liver damage
? Ill sustain efficacy over long term use

Post hoc analysis (Raina et al) – slower increase of TKV in 18-24 yrs with tolvaptan vs placebo

RCT examining effect of tolvaptan in 12-17 yrs old ongoing

Studies defining rapid progressors in children lacking

International consensus statement on the diagnosis and management of ADPKD in children and young people. Gimpel et al, Nat Rev Nephrol. 2019

Recommendation 8.5
Do not routinely offer vasopressin antagonists to children and young people with ADPKD. Off-label use of vasopressin antagonists can be considered at clinician discretion in children at high risk of early progression based on large total kidney volume, rapid kidney growth, family history, etc. (evidence level D, recommendation level weak).

OTHER PHARMACOLOGICAL OPTIONS

- Statins – lack of consensus regarding use
- mTORi – not recommended for routine use
- Somatostatin analogues – not recommended in children with ADPKD
- Metformin
- Tyrosine kinase inhibitors
- Proglitazone
- Venglustat
- Lixivaptan

Clinical trials ongoing

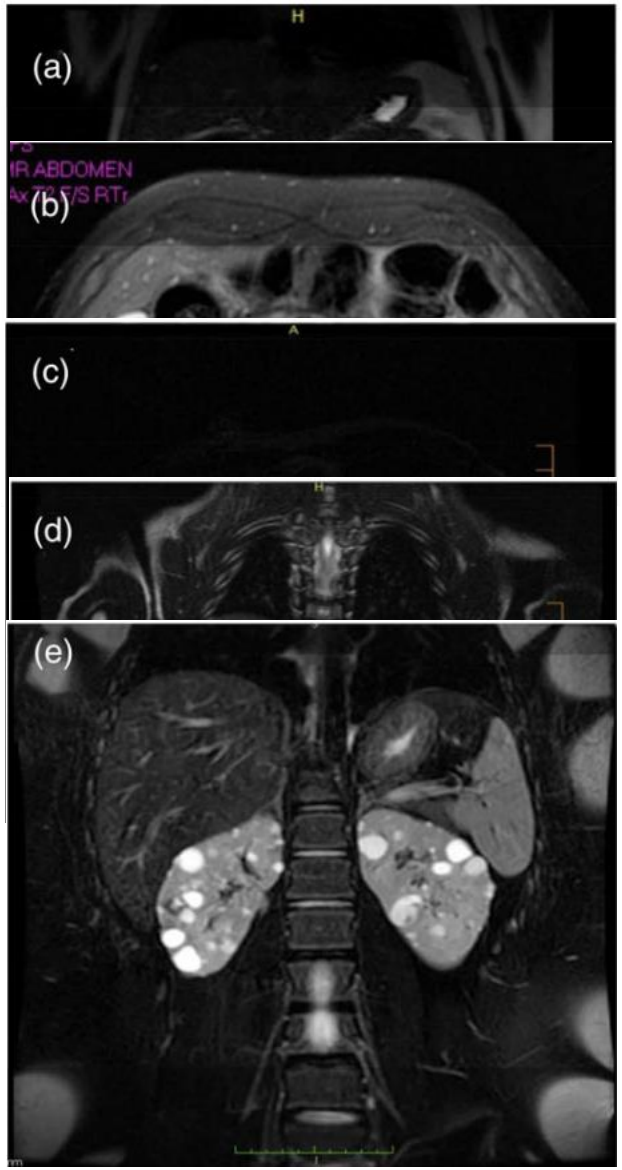
Other Autosomal Dominant Cystic Kidney Disease

Disorder	Family History	Clinical Features
Tuberous sclerosis complex (TSC)	Absent in 2/3 of cases	Affects ~1 in 10,000 live births; skin lesions (facial angiofibromas, periungual fibroma, hypomelanotic macules, shagreen patch); >90% have cerebral pathology (cortical tuber, subependymal nodules, giant cell astrocytoma); 90% have kidney manifestations (polycystic kidneys, angiomyolipomas); 50%-70% have retinal hamartomas; 50% have pulmonary lymphangioleiomyomatosis
PKD1-TSC contiguous gene syndrome	Spontaneous presentation frequent	Presentation with polycystic kidneys at an early age, with kidney angiomyolipomas frequently presenting after the first year of life
von Hippel-Lindau syndrome	~20% de novo	Affects ~1 in 36,000, cerebellar and spinal hemangioblastoma, retinal angiomas, serous cystadenomas and neuroendocrine tumors of pancreas, pheochromocytoma, renal cell carcinoma
Medullary sponge kidney (MSK)	Familial clustering reported	Affects ~1 in 5,000, tubular dilatation of the collecting ducts giving the appearance of "brush" or linear striations on intravenous pyelogram, medullary nephrocalcinosis, kidney stones, kidney cortex spared on CT or MRI
Medullary cystic kidney disease (MCKD[a])	Rare	Slowly progressive kidney disease, medullary cysts (but uncommon in families with type 2 MCKD[a]), hyperuricemia and gout (in type 2 MCKD[a]), small to normal-sized kidneys
Renal cysts and diabetes syndrome (RCAD/MODY5/ HNF-1B[b])	Spontaneous mutations (often deletions) in 50%	Kidney cysts or malformation in 90%, diabetes mellitus in 45%, hypomagnesemia in 40%, genital tract abnormalities in 20%, hyperuricemia in 20%, elevated liver enzymes in 15%

AJKD: Core curriculum in nephrology, 2016

Cystic kidney diseases in TSC

- **Polycystic kidney disease** (2%): mostly seen in CGS, rarely in TSC1
- **Cortical microcystic kidney disease**: associated with rapid decline in eGFR (CKD 2-3 by teens to early twenties), hypertension appear late
- **Focal cystic kidney disease**: cysts in one renal pyramid
- **Cortical cystic kidney disease**: cysts arise from cortex and columns of bertin, are uniform in size and can be present in early childhood
- **TSC multicystic kidney disease:** resemble polycystic disease, cysts in both cortex and medulla.



Ref: Bissler JJ, Christopher Kingswood J. Renal manifestation of tuberous sclerosis complex. Am J Med Genet C Semin Med Genet. 2018 Sep;178(3):338-347

AD TUBULOINTERSTITIAL KIDNEY DISEASE

Type	Age of CKD onset	Other features
ADTKD-UMOD	Adolescence-early adulthood	Hyperuricemia, gout
ADTKD-REN	Variable (childhood-adulthood)	Anemia, mild hyperkalemia, polyuria, mild hypotension, low plasma renin, hyperuricemia
ADTKD-HNF1B	3rd decade (early infancy-adulthood)	MODY, CAKUT, genital anomalies, hyperuricemia and gout, low Mg

Confirmation with genetic testing (NGS/WES)

NF1B

- Cystic
- Fetal –

  73% - r

  Variabl

  U/L ren

anomalie

- AD, 5

  HNF1

  no ge

  17q1

tem

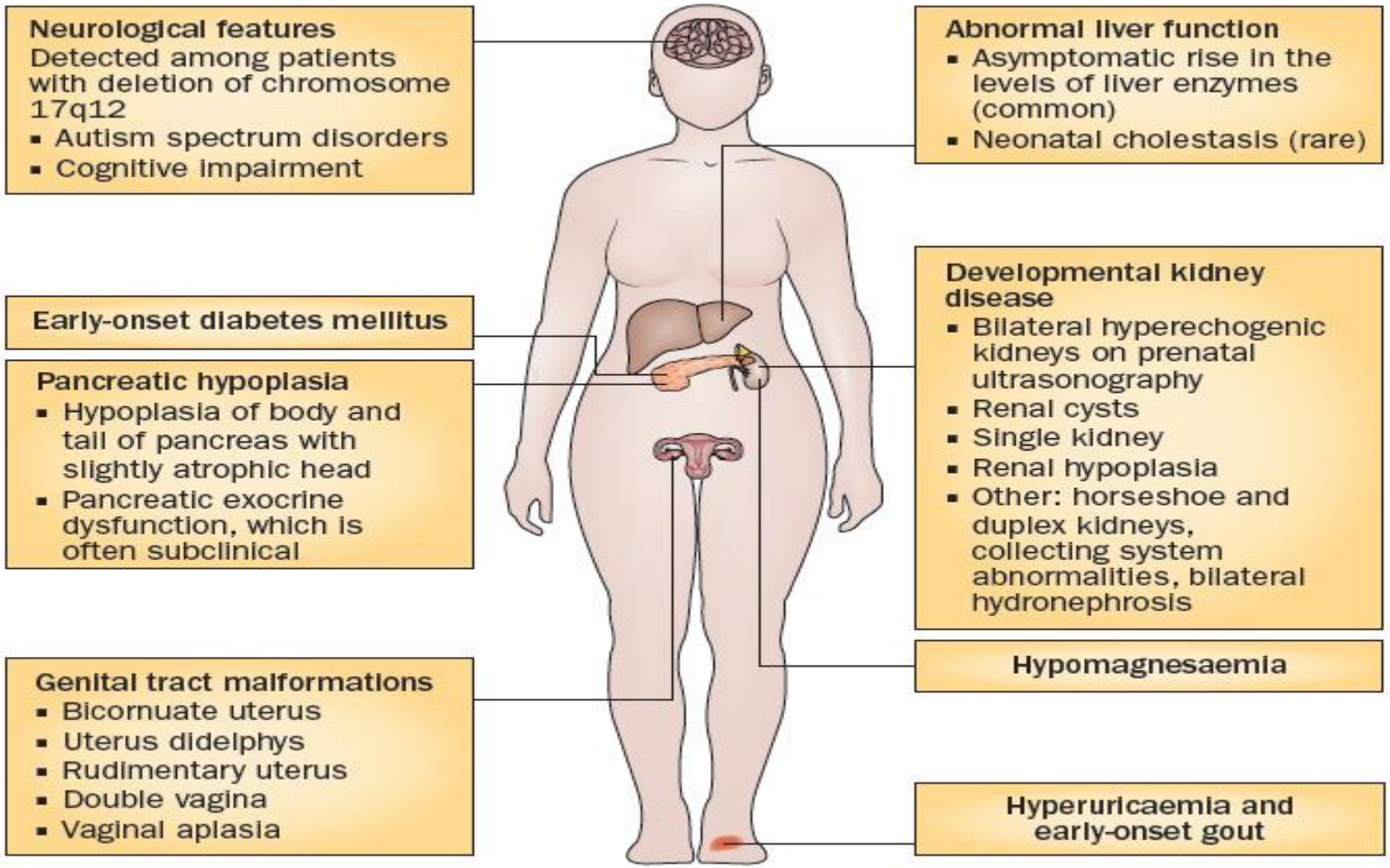


Figure 1 | Renal and extra-renal phenotypes frequently observed among patients with hepatocyte nuclear factor 1β-associated disease.

CLINICAL CASE 2

- 4 hours old male neonate, 36 weeks/2.5 kg, born out of non consanguineous marriage
- Antenatally detected bilateral enlarged hyperechogenic kidneys with oligohydramnios in 3rd trimester
- Respiratory distress soon after birth – Mechanical ventilation
- Abdominal distension, with bimanually palpable and ballotable kidneys
- No dysmorphism
- Hypertensive, Oliguric, creatinine 1.2 mg/dl
- Postnatal USG – bilateral enlarged kidneys (RK – 8.9 cm, LK – 9.2 cm) with increased cortical echogenicity and poor CMD; tiny (1-2 mm) multiple cysts B/L radially arranged in medulla

- 3rd in birth order, no h/o previous sibling loss
- No family h/o renal disease
- Parents USG – normal (Mother 35 years, Father 42 years)

Probable Diagnosis?

Likely pathogenic variant causative of the reported phenotype was identified

*Correlation with clinical profile and family history is required

FINDINGS RELATED TO PHENOTYPE

Gene & Transcript	Variant	Location	Zygosity	Disorder (OMIM)	Inheritance	Classification
PKHD1 NM_138694.4	c.6274delG (p.Glu2092ArgfsTer19)	Exon 38	Homozygous	Polycystic kidney disease 4, with or without hepatic disease (263200)	Autosomal Recessive	Likely Pathogenic

VARIANT INTERPRETATIONS

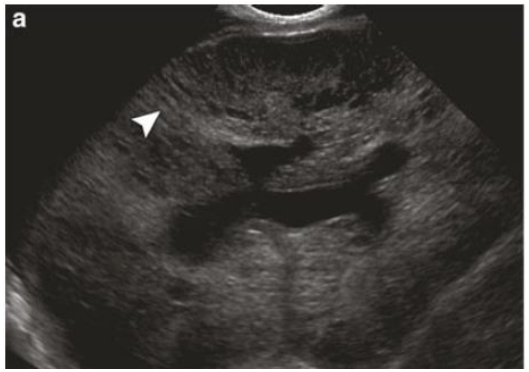
PKHD1 chr6:51777222delC - Likely Pathogenic.

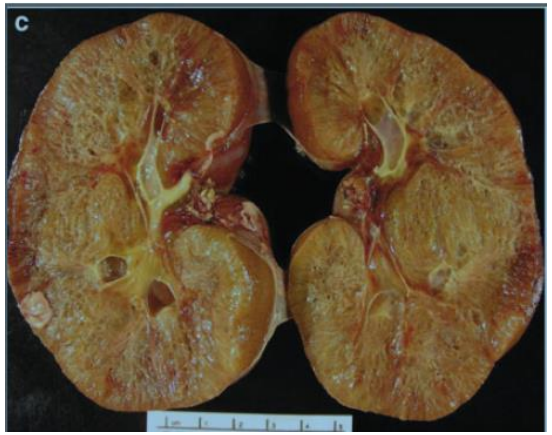
The frameshift deletion NM_138694.4 (*PKHD1*):c.6274delG (p.Glu2092ArgfsTer19) has not been reported previously as a pathogenic variant nor as a benign variant, to our knowledge. The p.Glu2092ArgfsTer19 variant is novel (not in any individuals) in gnomAD South Asian Background in gnomAD. The p.Glu2092ArgfsTer19 variant is novel (not in any individuals) in 1kG. This variant is predicted to cause loss of normal protein function through protein truncation caused a frameshift mutation. The frame shifted sequence continues 19 residues until a stop codon is reached. This variant is a frameshift variant which occurs in an exon of *PKHD1* upstream of where nonsense mediated decay is predicted to occur. There are 181 downstream pathogenic loss of function variants, with the furthest variant being 1984 residues downstream of this variant. This indicates that the region is critical to protein function. The p.Glu2092ArgfsTer19 variant is a loss of function variant in the gene *PKHD1*, which is intolerant of Loss of Function variants, as indicated by the presence of existing pathogenic loss of function variant NP_619639.3:p.M1V and 174 others. **For these reasons, this variant has been classified as Likely Pathogenic.**

ARPKD: BRIEF OVERVIEW

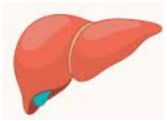
1:6000-1:20000

Hepatorenal fibrocystic disease





Fusiform cystic dilatations from collecting ducts



Ductal plate malformation: Congenital hepatic fibrosis/ periportal fibrosis ± intrahepatic biliary radicle dilatation / Carolis disease

Clinical Spectrum

Kidney

- 70-80% survive the neonatal period
- Survival at 1 yr – 85%, 10 yrs – 82%, 15 yrs – 79%
- Renal survival at 1 yr – 86%, 15 yrs – 67%
- Progression to ESKD slower in children with non perinatal (26.3+/-9.2 years, range 15-36 years) vs perinatal presentation (7.6+/-6.8 years, range 0.5-18 years)

Liver

Firm Hepatomegaly
Portal hypertension, variceal bleeding, splenomegaly, absence of hepatocellular dysfunction
Biliary ductal ectasia, Ascending bacterial cholangitis

Important determinant of mortality and morbidity post KT

Genetics

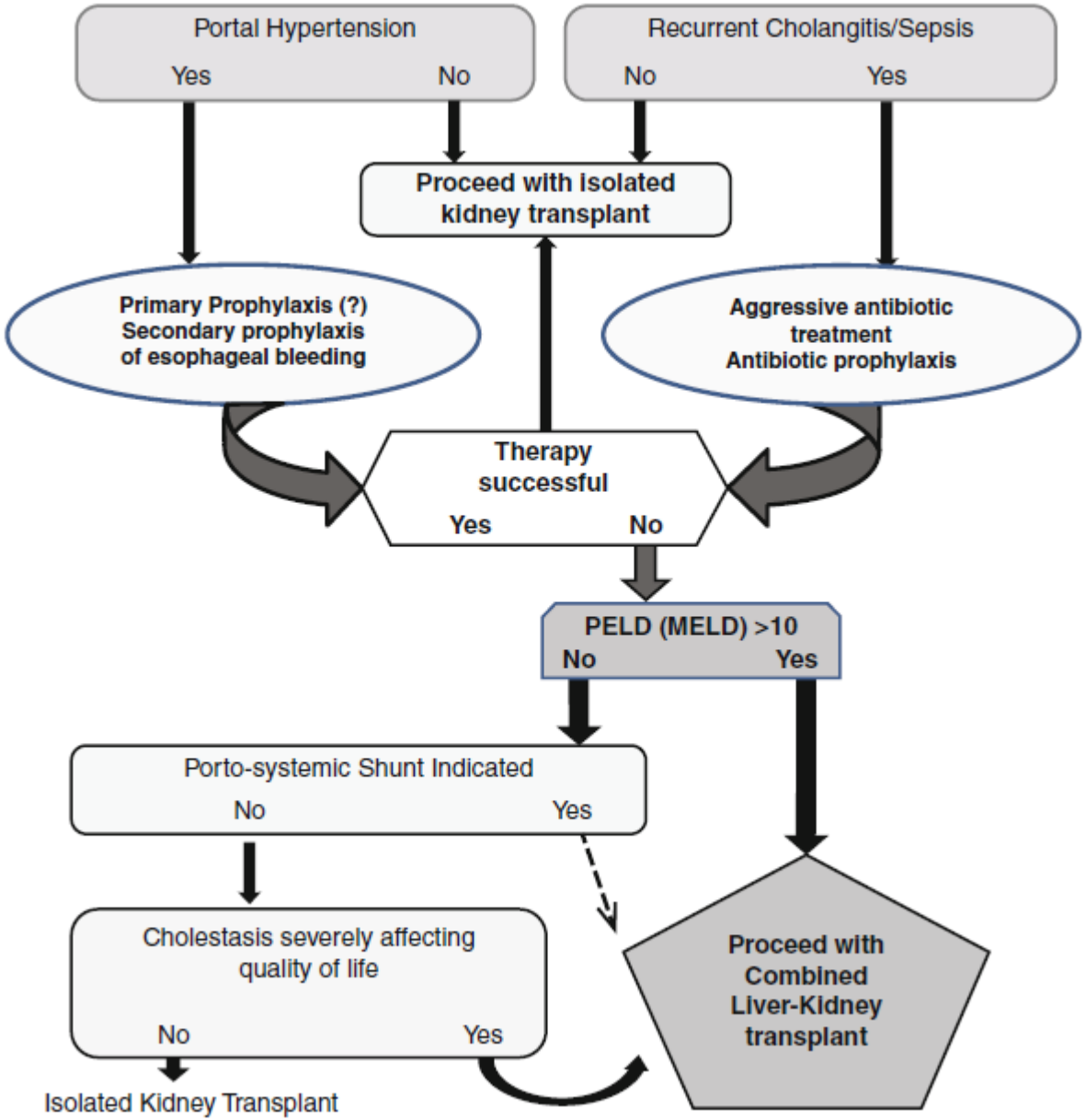
- *PKHD1* (6p12.2-3)→ fibrocystin
- DZIP1L gene – 2nd locus (ciliary membrane translocation of PC complex)
- Truncating vs missense mutations
- Intrafamilial phenotypic variability
- Mutation detection rate approx. 90%

Management

Fetal Monitoring	• 2-3 weekly USG – Renal size and AF volume • Prenatal imaging characteristics don't reliably predict chances of lethal pulmonary hypoplasia
Perinatal management	• Delivery in well equipped NICUs • Multidisciplinary management – Fetal-maternal medicine expert, neonatologist, ped nephrologist • Decisions regarding aggressive interventions, dialysis in conjunction with parents
Postnatal management	• **Hypertension** – ACEI/ARBs • **Hyponatremia** – fluid restriction, concentrated feeds • **Feeding** – Gastrostomy/NG tube feeds, Vit A,D,E,K supplementation ± UDCA administration, regular anthropometric & nutritional assessments • **Nephrectomies** – pre/during KT. No evidence to support nephrectomy for resp distress or nutritional management or severe HTn in early ARPKD

H

Ne
anc



Telega G, Cronin D, Avner ED. New approaches to the autosomal recessive polycystic kidney disease patient with dual kidney-liver complications. Pediatr Transplant. 2013;17:328–35.

DIFFERENTIAL DIAGNOSIS

D/D	Differentiating features
HNF1B	Structural renal abnormalities, genital anomalies, family h/o kidney cysts/MODY + parental USG, low Mg, hyperuricemia
VEO ADPKD	Family history, parental USG
Infantile Nephronophthisis	Cortical cysts ± Hypertension, Situs inversus, VSD,
Bardet Biedl Syndrome	Polydactyly, developmental anomalies of kidney, urinary tract malformations, genital anomalies
Meckel Gruber Syndrome	Occipital encephalocele, polydactyly, hepatic abnormalities

Table 1 Diagnostic features and prevalence in BBS

Primary features	
Rod-cone dystrophy	
Polydactyly	
Obesity	
Genital anomalies	
Renal anomalies	
Learning difficulties	
Secondary features	
Speech delay	
Developmental delay	
Diabetes mellitus	
Dental anomalies	
Congenital heart disease	7%
Brachydactyly/ syndactyly	46–100%/8–95%
Ataxia/ poor coordination	40–86%
Anosmia/hyposmia	60%

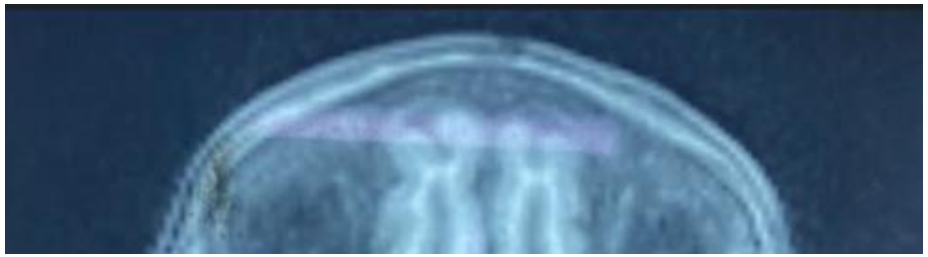
Four primary features or three primary features and two secondary features are required for a clinical diagnosis of Bardet–Biedl syndrome.[4,16,18]

- Abnormal ERG – earliest 1st 2 years, significant > 5 yrs
- Cystic kidney disease (microcysts at CMJ, 10-72%), dysplastic kidneys, developmental anomalies, urinary tract malformations
- Impaired urinary concentration
- Advanced CKD by 5 years or persist into adulthood with normal/near normal renal functions
- BBS10, truncating variants, structural renal anomalies, hypertension predict progression to advanced CKD

CLINICAL CASE 3

- 6 yrs old female, born out of non consanguineous marriage
- Presented with fever, short stature, serum creat 2.13 mg/dl
- Polyuria
- Normotensive
- USG – normal sized kidneys with increased cortical echogenicity and altered CMD; multiple small cysts 3-4 mm B/L along CMJ
- Spastic diplegia, GDD, ptosis, nystagmus, strabismus
- Hearing evaluation by BERA normal
- No family h/o renal disease; Parents USG normal (Mother – 28 yrs, Father – 35 yrs)

Probable Diagnosis?



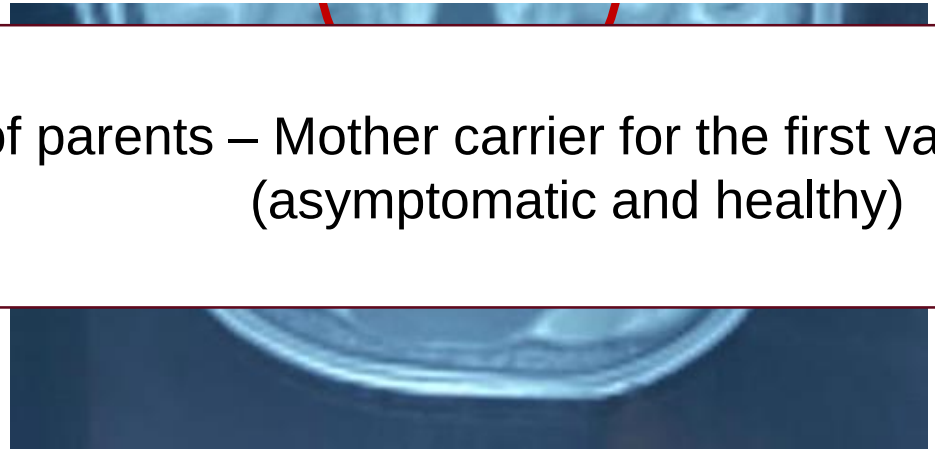
RESULT SUMMARY

Likely compound heterozygous variants causative of the reported phenotype were identified

*Correlation with clinical profile and family history is required

FINDINGS RELATED TO PHENOTYPE

Gene & Transcript	Variant	Location	Zygosity	Disorder (OMIM)	Inheritance	Classification
RPGRIP1L NM_015272.5	c.2480C>G (p.Thr827Arg)	Exon 17	Heterozygous	Joubert syndrome 7 (611560)	Autosomal Recessive	Uncertain Significance
RPGRIP1L NM_015272.5	c.1945C>T (p.Arg649Ter)	Exon 15	Heterozygous	Joubert syndrome 7 (611560)	Autosomal Recessive	Pathogenic



Sanger sequencing of parents – Mother carrier for the first variant and father for the second (asymptomatic and healthy)

Extrarenal manifestation associated with NPHP	Syndrome
Retinitis pigmentosa/retinal dystrophy	Senior–Løken syndrome
	Alström syndrome
	Arima syndrome
Oculomotor apraxia	Cogan syndrome
Nystagmus	Joubert syndrome and related disorders
Ocular coloboma	Joubert syndrome and related disorders
Posterior encephalocele	Meckel–Gruber syndrome
Abnormal respiratory pattern	Joubert syndrome and related disorders
Cerebellar vermis aplasia/hypoplasia	Joubert syndrome and related disorders
Liver fibrosis	Joubert syndrome and related disorders
	Meckel–Gruber syndrome
	Arima syndrome
Postaxial polydactyly	Bardet–Biedl syndrome
	Joubert syndrome and related disorders
Skeletal dysplasia	Ellis–van Creveld syndrome
	Sensenbrenner syndrome
	Jeune syndrome
	Mainzer–Saldino syndrome
Situs inversus/cardiac malformation	Infantile NPHP

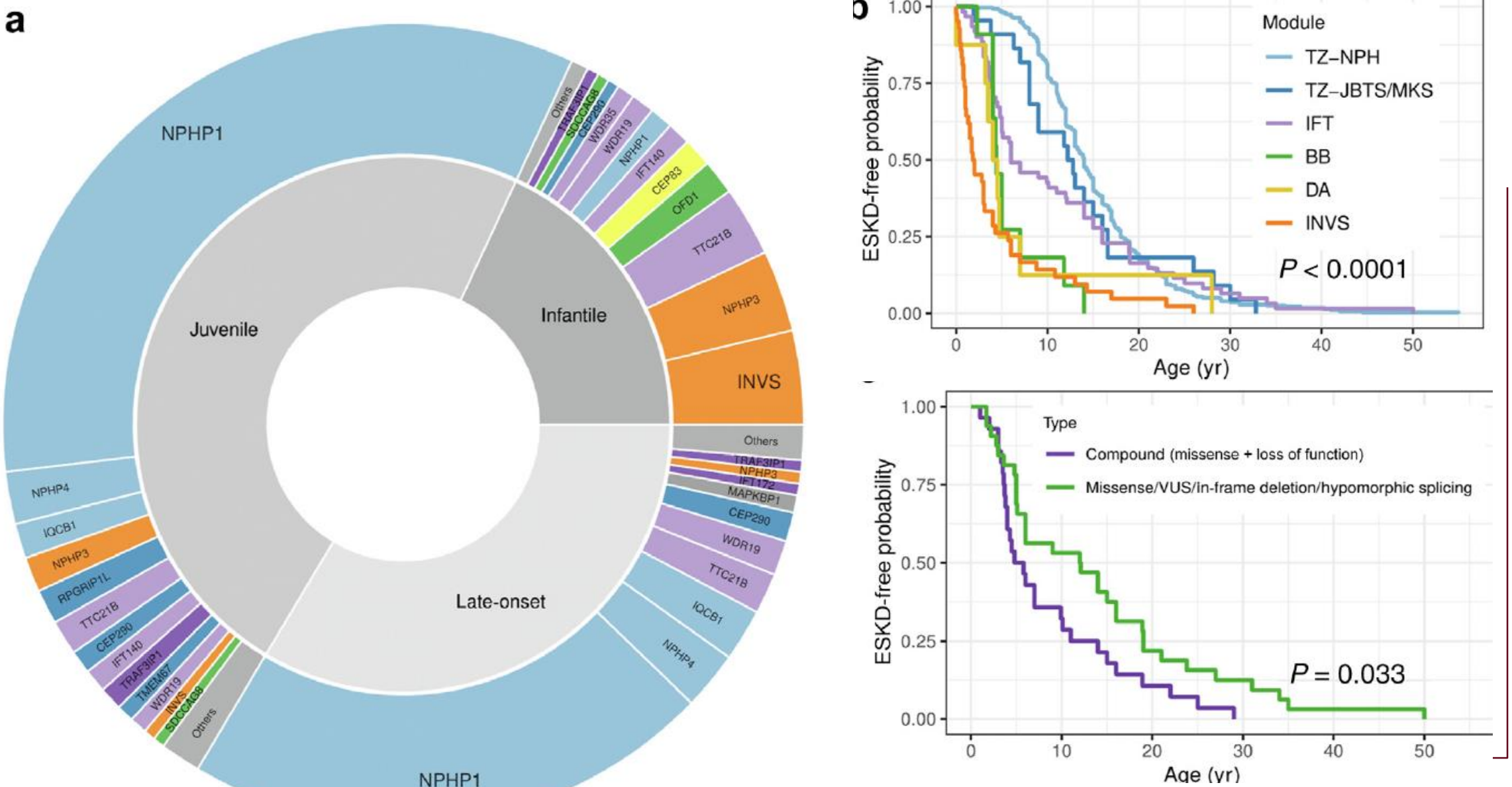
Srivastava S et al. Many Genes-One Disease? Genetics of Nephronophthisis (NPHP) and NPHP-Associated Disorders. Front Pediatr. 2018 Jan 5;5:287.

n age of ESKD

yrs

13 yrs

19 yrs


a
NPHP1
Juvenile
Infantile
Late-onset
INVS
NPHP3
TTC21B
CEP83
OFD1
IFT140
NPHP1
WDR19
WDR35
CEP290
SDCCAG8
TRAF3IP1
Others
NPHP4
IQCB1
NPHP3
RPGRIP1L
TTC21B
CEP290
IFT140
TRAF3IP1
TMEM67
WDR19
INVS
SDCCAG8
Others
NPHP1
IQCB1
NPHP4
TTC21B
WDR19
CEP290
MAPKBP1
IFT172
NPHP3
TRAF3IP1
Others
b
ESKD-free probability
1.00
0.75
0.50
0.25
0.00
0
10
20
30
40
50
Age (yr)
Module
TZ–NPH
TZ–JBTS/MKS
IFT
BB
DA
INVS
P < 0.0001
ESKD-free probability
Type
Compound (missense + loss of function)
Missense/VUS/in-frame deletion/hypomorphic splicing
P = 0.033
Age (yr)

JOUBERT AND NEPHRONOPHTHISIS

- Cerebellar vermis hypoplasia
  Hypotonia, cerebellar ataxia, neonatal tachypnea, developmental delay
  ± ocular coloboma, polydactyly, hepatic fibrosis
- 30% - kidney involvement – classical nephronophthisis
  infantile nephronophthisis
  indeterminate cystic kidney disease phenotype
  unilateral multicystic dysplastic kidney
- NPHP genes including TMEM67 (most common), CEP290, AHI1

SUMMARY OF APPROACH TO CYSTIC KIDNEY DISEASE

- **History** – polyuria, polydipsia, flank pain, hematuria, UTI
  Age of presentation
  Extrarenal involvement
  Family History – 3 generation pedigree; kidney disease/
  IC bleed/blindness/ hearing loss/ liver disease etc

- **Examination** – Anthropometry
  BP, volume status
  Dysmorphism
  Extrarenal involvement (CNS, eye, heart, hepatosplenomegaly, genitourinary abnormalities, skeletal)

- **Investigations**: Renal function test

  Serum electrolytes (Na, K, Mg), Serum uric acid

  Urine routine, proteinuria quantification

  Liver function test, Ophthalmological evaluation, hearing evaluation, FBS/PPBS, echocardiography, MRI Brain, skeletal survey (if indicated by clinical evaluation and imaging)

- **USG abdomen:** Renal – Kidney size, echogenicity & CMD; cyst size, number, distribution & characteristics; associated CAKUTs

  Evidence of hepatic fibrosis, Portal hypertension

  Pancreatic cyst, ovarian cyst etc, Genital anomalies

- **Parents' USG KUB**

IMAGING FINDINGS

- **Kidney Size** – Large – ADPKD, ARPKD, Infantile NPHP, TSC, PKD1-TSC CGS
  Normal/Small – NPHP, ADTKD, dysplastic kidneys

- **Cyst location** – Diffuse – ADPKD, ARPKD
  Cortical – ADPKD, Infantile NPHP, HNF1B, TSC
  Medullary – ARPKD, medullary sponge kidney

Confirmation with Genetic testing – Next Generation sequencing (gene panel/WES)

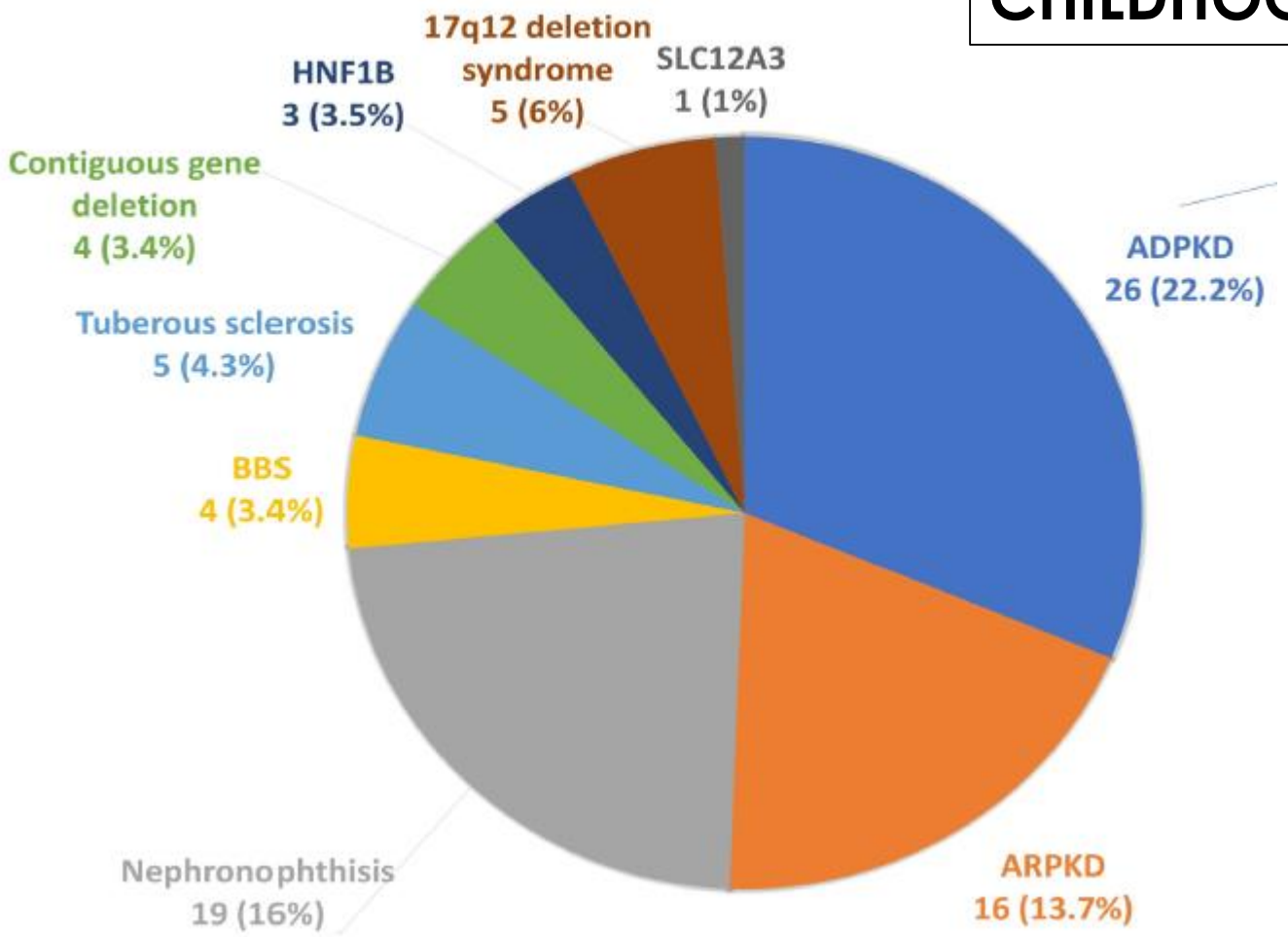
pancreatic dysplasia, BBS

- **Pancreatic cyst, ovarian cyst etc** – ADPKD
- **Genital anomalies:** HNF1B, BBS

TAKE HOME MESSAGE

- Cystic kidney diseases in children are mostly inherited
- Radiological appearance of the kidneys, distribution and size of cysts in the kidneys along with the extrarenal manifestations and family history help to narrow down on the diagnosis
- Due to considerable phenotypic variability and overlap, and lack of genotype-phenotype correlation, confirmation has to be sought through genetic analysis
- Management is often multidisciplinary. Therapeutic modalities to prevent cyst progression are yet to be approved in children

A MULTICENTRE OBSERVATIONAL STUDY TO EXPLORE THE GENETIC ETIOLOGY OF CHILDHOOD CYSTIC KIDNEY DISEASES



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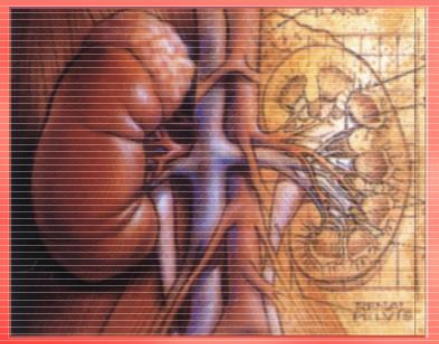
Dr Manoj Matnani
Dr Subal Pradhan
Dr Kausik Mandal

Acute Kidney Injury-Risk Stratification in Children



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Outline of the talk

- AKI – Practical definition
- Organ cross talk
- Identification and Prevention of Risk Factors
- Renal Support
- When, Why and How

Acute Kidney Injury

- Sudden loss of kidney function occurring over hours to days resulting in

- Retention of metabolic waste products

- Dysregulation of fluids, electrolytes and acid base homeostasis

- AKI has largely replaced ARF

- Clearly defines renal dysfunction as a continuum rather than a discrete finding of failed kidney function

Pediatric AKI Criteria

pRIFLE category	Estimated CrCl	Urine output
Risk	eCrCl decrease by 25 %	<0.5 mL/kg/h for 8 h
Injury	%	.5 mL/kg/h for 16 h
Failure	decrease by %	.3 mL/kg/h for 24 h or anuric for 12 h
Loss	Persistent failure >4 weeks	
End-stage renal disease	Persistent failure >3 months	

AKI – KDIGO Guidelines

S No	Serum creatinine criteria	Urine output criteria
1	Increase to 1.5 to 1.9 times baseline, **or** increase of ≥0.3 mg/dL (within 48hrs)	<0.5 mL/kg per hour for 6 to 12 hours
2	Increase to 2 to 2.9 times baseline (within 7 days)	<0.5 mL/kg per hour for ≥12 hours
3	Increase greater than 3 times baseline, **or** SCr ≥4 mg/dL (≥353.6 mcmol/L), **or** Initiation of kidney replacement therapy, **or** eGFR <35 mL/min per 1.73 m^2 (<18 years)	<0.3 mL/kg per hour for ≥24 hours, **or** Anuria for ≥12 hours

Etiology of AKI

- Pre renal

  Decreased effective circulating volume

  GI loss, renal loss, skin loss, hemorrhage, reduced cardiac output, increased leak from vessels, loss of vascular tone

- Intrinsic renal

  Tubular, glomerular, vascular, interstitial ds

- Post renal

  Obstructed system

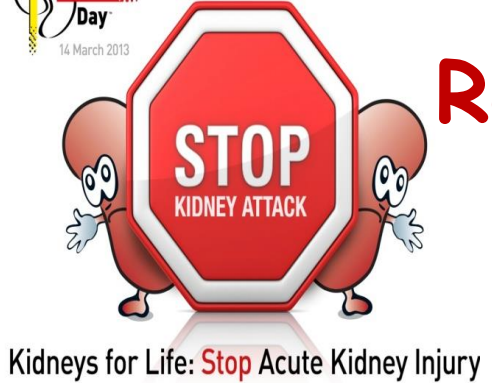
Etiology of AKI

Clinical setting or circumstance	Community-acquired AKI	Associated with a single predominant insult, such as volume depletion
		Often reversible
	Hospital-acquired AKI	Usually in the critical care setting
		Multifactorial and part of multiorgan failure
		Profoundly complicates treatment and outcome

Etiology of AKI in Critically ill children

- Shift in etiology – **Multifactorial**
- Critically ill patient who is intubated and receiving vasoactive medications, AKI incidence exceeds 80%
- Mortality is high in children requiring KRT
- Independent risk factor for both increased hospital stay & mortality
- Modern AKI spectrum -**Multi Organ Dysfunction Syndrome**

Prasad Devarajan. AKI in children. Up to date 2020



Renal Angina & Organ Cross Talk

Brain
- ↑ KC & G-CSF
- ↑ GFAP & microglia
- ↑ Vascular permeability

Heart
- ↑ TNF-α, IL-1
- ↑ Neutrophil trafficking
- ↑ Apoptosis
- ↓ Fractional shortening

Lung
- ↑ Vascular permeability
  Dysregulated channels
- ↑ Cytokines/chemokines
  Transcriptomic changes
- ↑ Leukocyte trafficking
  Altered response to ventilator-associated injury

AKI

Bone marrow
- Anemia
- Coagulation disorders
- Immune dysfunction

Gastrointestinal tract
- ↑ Channel-inducing factor
- ↑ Potassium excretion

Liver
- ↑ Leukocyte influx
- ↑ Oxidation products
- ↓ Antioxidants (GSH)
  Altered liver enzymes

Benjamin R. Critical Care Nephrology: Core Curriculum 2019

Renal angina index (RAI)

Renal angina index – Risk

Patient characteristics	Score
Sepsis or ICU adm	
Stem-cell transplo organ transplant	
Mechanical ventilation and ionotropic support	5

Fluid overload (%) = $\frac{\text{Intake (Liters)} - \text{output (Liters)}}{\text{Weight (kg)}} \times 100$

The RAI score of ≥8 - renal angina positive

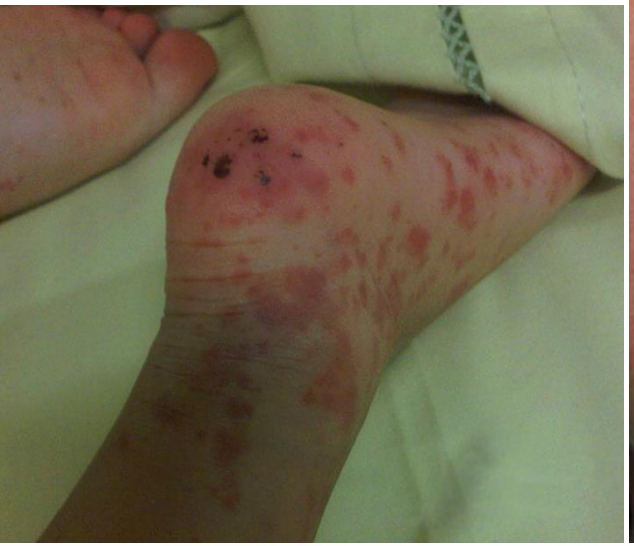
If RAI is negative – NPV 92%

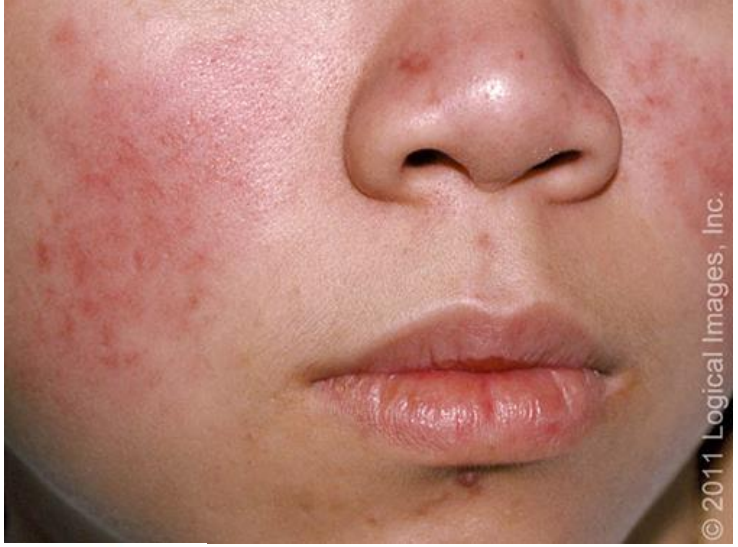
Renal angina index – Injury

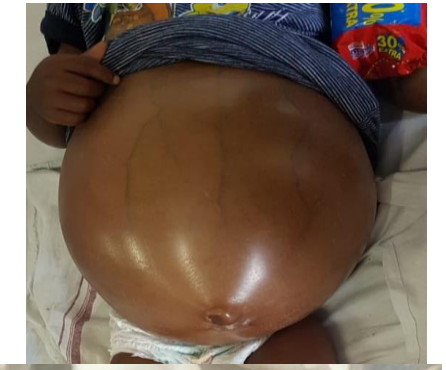
Decrease in creatinine clearance	Percentage of fluid over load	Score
No change	≤5	1
0-24.99%	5-9.99	2
25-49.99%	10-14.99	4
≥50%	≥15	8

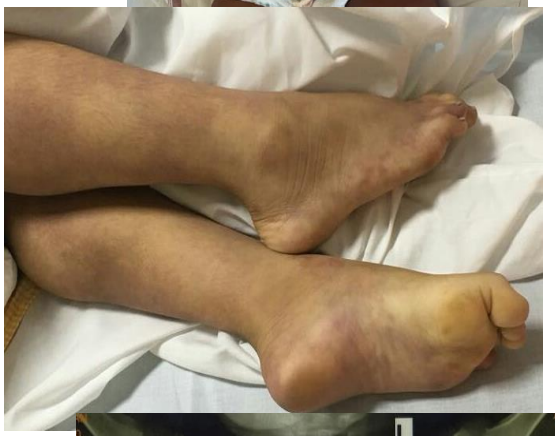
Clinical Features of AKI

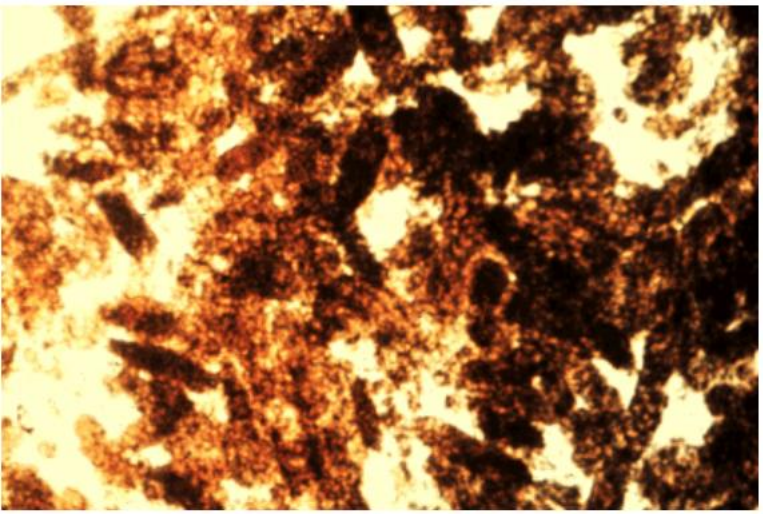
- Detailed fluid balance history – positive/negative
- Serial weights, urine output, medication
- Physical examination pertaining to the underlying disease
- Fluid overload >10–15 % - poor outcome

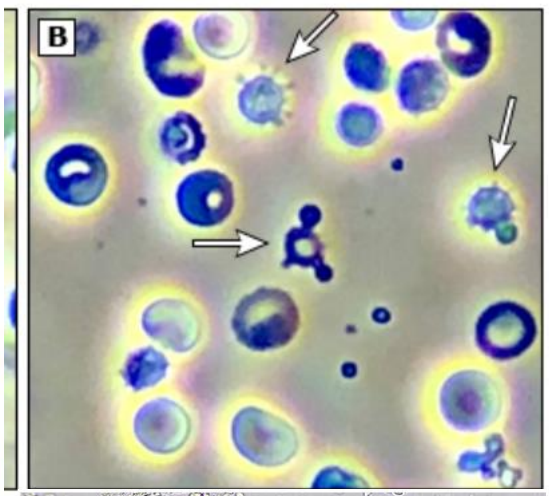


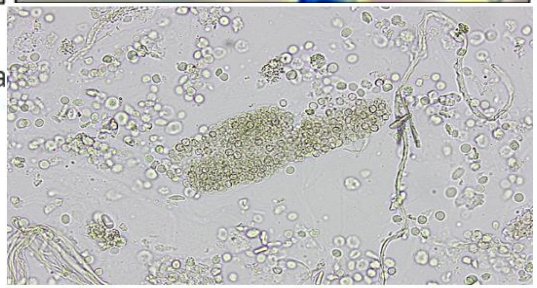




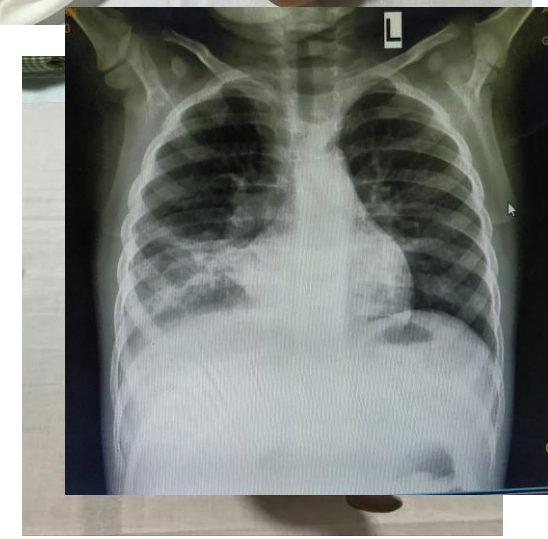








Urine sediment showing multiple muddy brown granular ca



Complications of AKI

Metabolic	Respiratory Cardiovascular	Gastrointestinal	Neurologic	Hematologic	Infectious
Hyperkalemia	Pulmonary edema	Nausea, vomiting, anorexia	Altered mental status	Anemia	Pneumonia
Metabolic acidosis	Arrhythmias	Malnutrition	Irritability	Bleeding	Sepsis
Hyponatremia	Pericarditis	Gastritis	Seizures		Infected IV sites
Hypocalcemia	Myocardial infarction	GI bleeding	Somnolence		
Hyperphosphatemia	Hypertension	GI ulcers	Coma		

Acute kidney injury. Nelson Textbook of Pediatrics, 20th edition.

Laboratory Investigation

- Urinalysis, microscopy, FeNa & FeUrea
- BUN, serum creatinine, electrolytes, ABG, CBC, LFT, CPK, coagulation profile, auto immune work up, drug levels
- Imaging – USG, CT, Doppler, DMSA, MCU
- Renal biopsy

GFR Estimating Equations

	Pediatric estimating equations
Schwartz "bedside"[31,35] (original—1976)	eGFR = k × L (cm)/P_{Cr} (mg/dL) where k ~ 0.33 (preterm infant), k ~ 0.45 (full term), k ~ 0.55 (children and adolescent females), k ~ 0.7 (adolescent males)
Counahan-Barratt[32]	eGFR = 0.43 × L (cm)/P_{Cr} (mg/dL)
Updated Schwartz ($CKiD_{Cr}$)[39]	eGFR = 0.413 × L (cm)/P_{Cr} (mg/dL)
$CKiD_{Cys\text{-}C}$ (Schwartz "bedside" cystatin C)[33]	eGFR = 70.69 × [cystatin C (mg/L)]$^{-0.931}$
$CKiD_{Cr\text{ - }Cys\text{-}C}$[33] (Combined CKiD creatinine—cystatin C)	eGFR = 39.8 × [height (m)/S_{Cr} (mg/dL)]$^{0.456}$ × [1.8/cystatin C (mg/L)]$^{0.418}$ × [30/BUN (mg/dL)]$^{0.079}$ × [1.076]^{gender} × [height (m)/1.4]$^{0.179}$
Pottel and colleagues[56]	eGFR = 107.3/(S_{Cr}/Q) where Q ~ population normalized the estimated GFR
Adult estimating equation $CKD\text{-}EPI_{Cr}$[77]	eGFR = 141 × min [SCr/κ, 1]$^{\alpha}$ × max [SCr/κ, 1]$^{-1.209}$ × 0.993^{age} × 1.108 (if female) × 1.159 (if black) where κ = 0.7, α = −0.329 (females) and κ = 0.9, α = −0.411 (males); min = min of S_{Cr}/κ or 1; max = max of S_{Cr}/κ or 1

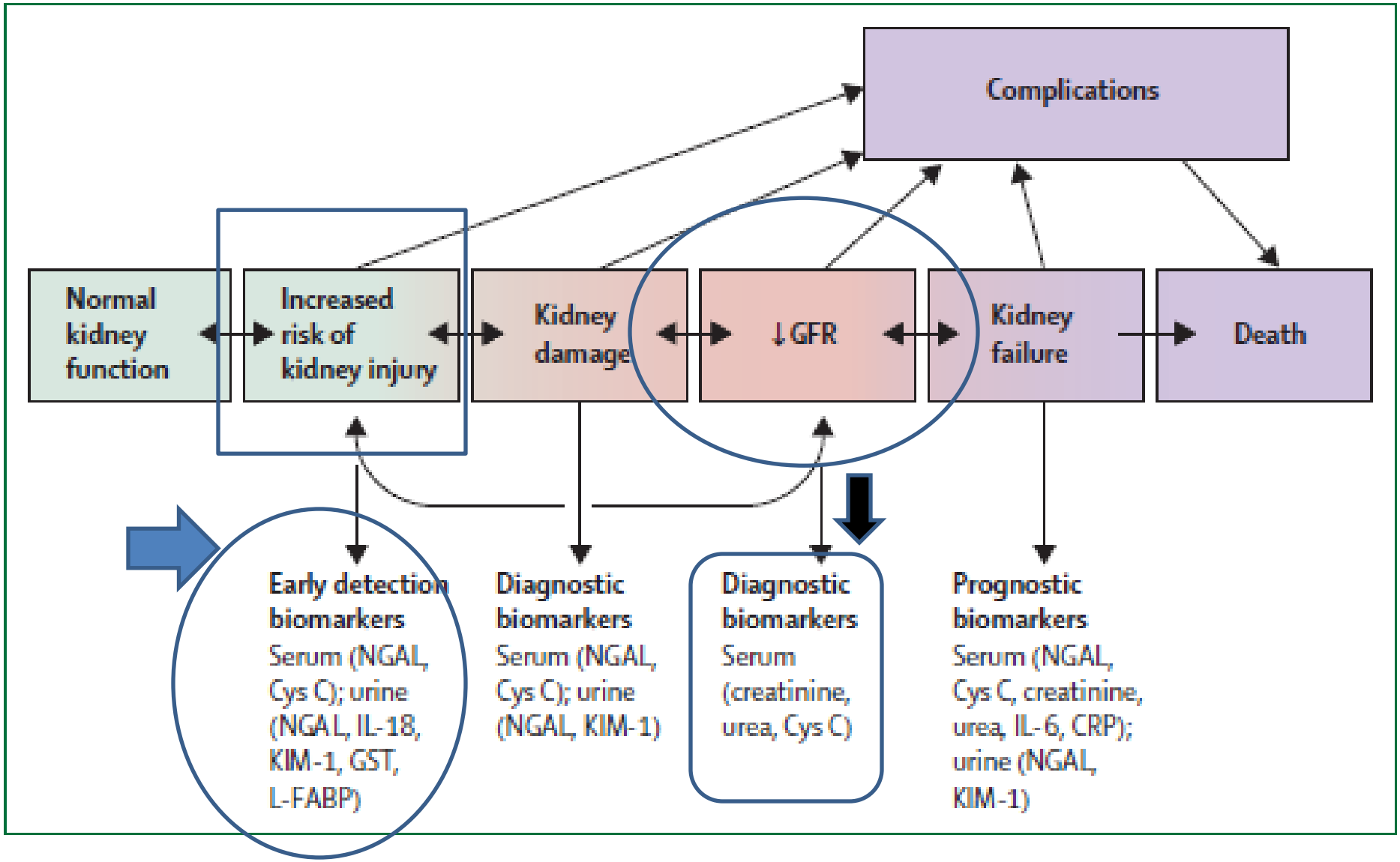
Ranges of normal serum creatinine

- Newborn – 0.3 to 1 mg/dL (27 to 88 micromol/L)
- Infant – 0.2 to 0.4 mg/dL (18 to 35 micromol/L)
- Child – 0.3 to 0.7 mg/dL (27 to 62 micromol/L)
- Adolescent – 0.5 to 1 mg/dL (44 to 88 micromol/L)

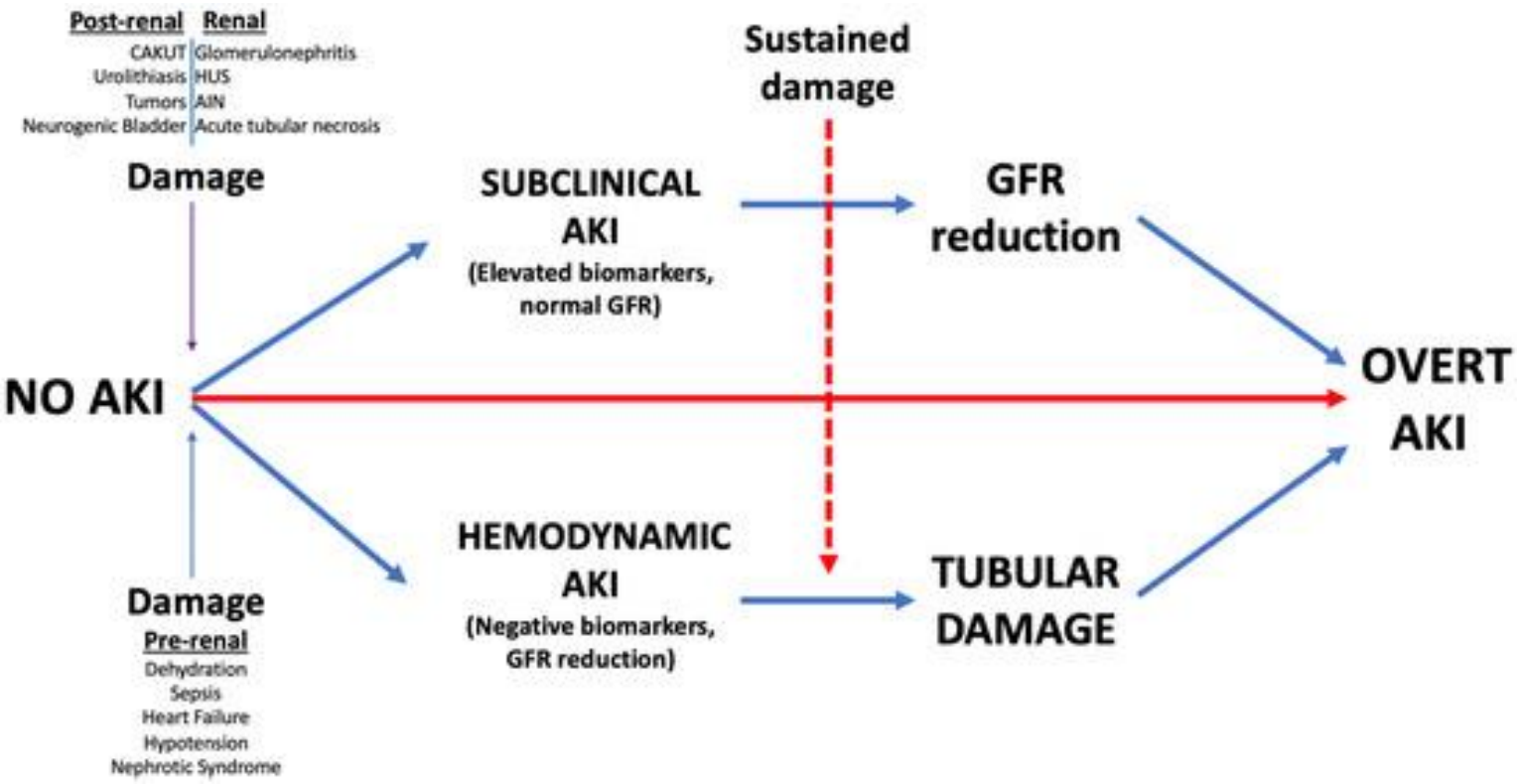
Laboratory Investigation

	Pre-Renal	Intrinsic	Post-Renal
Urinalysis		Dysmorphic RBCs, casts	
Urine Specific Gravity	>1.020	<1.010	
Urine Osmolality	>500 mOsm	<350 mOsm	<350 mOsm
Urine Na	<20 mEq/L	>40 mEq/L	>40 mEq/L
FENa	<1%	>2%	>2%
FEUrea	<35%	>35%	>35%
Serum BUN:Cr	>20:1	10-20:1	10-20:1
Ultrasound	Empty bladder	Increased echogenicity	Hydronephrosis, UB changes

Role of biomarkers



Classification and pathophysiology of AKI on the basis of the novel biomarkers



Rivetti G et al. Acute Kidney Injury in Children: A Focus for the General Pediatrician. *Children*. 2024; 11(8):1004. https://doi.org/10.3390/children11081004

Case Scenario 1

- 2 yrs old child with acute watery diarrhoea has signs of **severe dehydration**. Her wt- 10kg

- **BUN – 30mg/dL,** S.Creat- 0.4mg/dL, Serum Na/K/Cl/HCO3-**120/3.4/98/14mEq/L**
- Urine specific gravity – 1.030, urine osmolality – 660mosm/kg, FeNa- 0.7

1) What is your diagnosis?
2) How do you manage this child?

1. **Pre renal AKI**

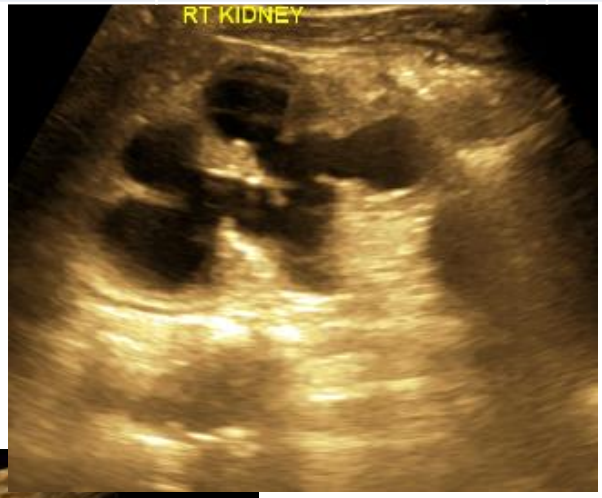
2. Severe dehydration correction **I.V with isotonic fluid**- 30ml/70ml over 30min & 2 $\frac{1}{2}$ hours

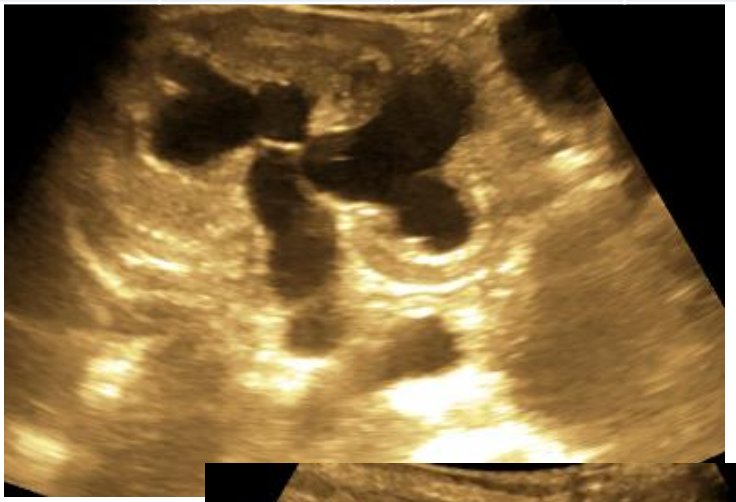
- Re assessment of fluid status with output monitoring
- Initiate on oral feeds

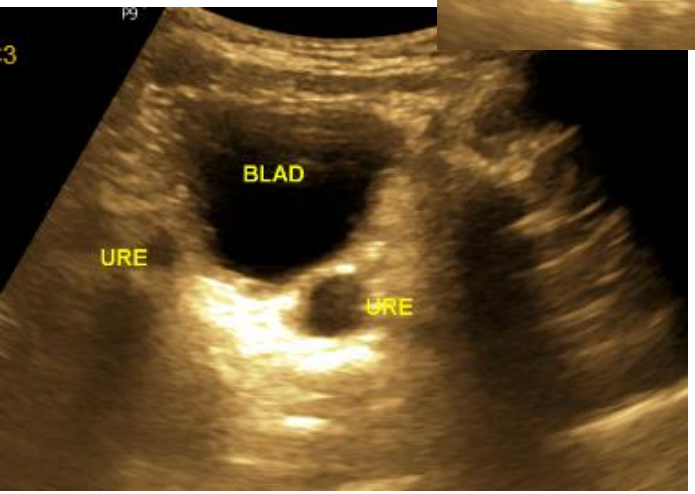
Case Scenario 2

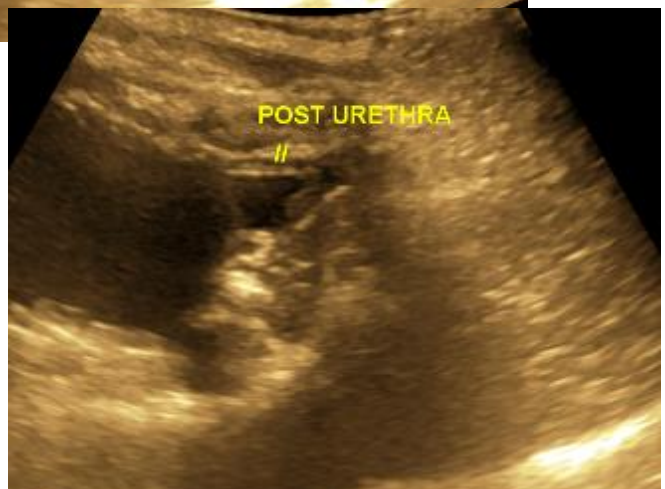
- 5 months old boy presented with history of vacant stare, ?seizures
- O/E – wt – 7kg, length – 62cm, pallor, bilateral kidney ballotable with palpable urinary bladder
- AN scans: oligohydramnios at term. Emergency LSCS. Neonatal period uneventful
- Parents never noticed the stream of urine

Day	BUN mg/dL	S.Creat mg/dL	S.Electrolytes mEq/L	S.Ca mg/dL	S.PO4 mg/dL	SAP (IU)	PTH (pg/mL)
1	98	**3.3**	138/**7.7**/104/**11**	**6.2**	**16.5**	408	**937**
2	56	1.8	142/4.7/109/15	7.1	8.9		
3	34	1.1	145/4.1/107/24	8.2	7.2		
7	18	0.6	144/4.2/104/22	9.6	5.1		

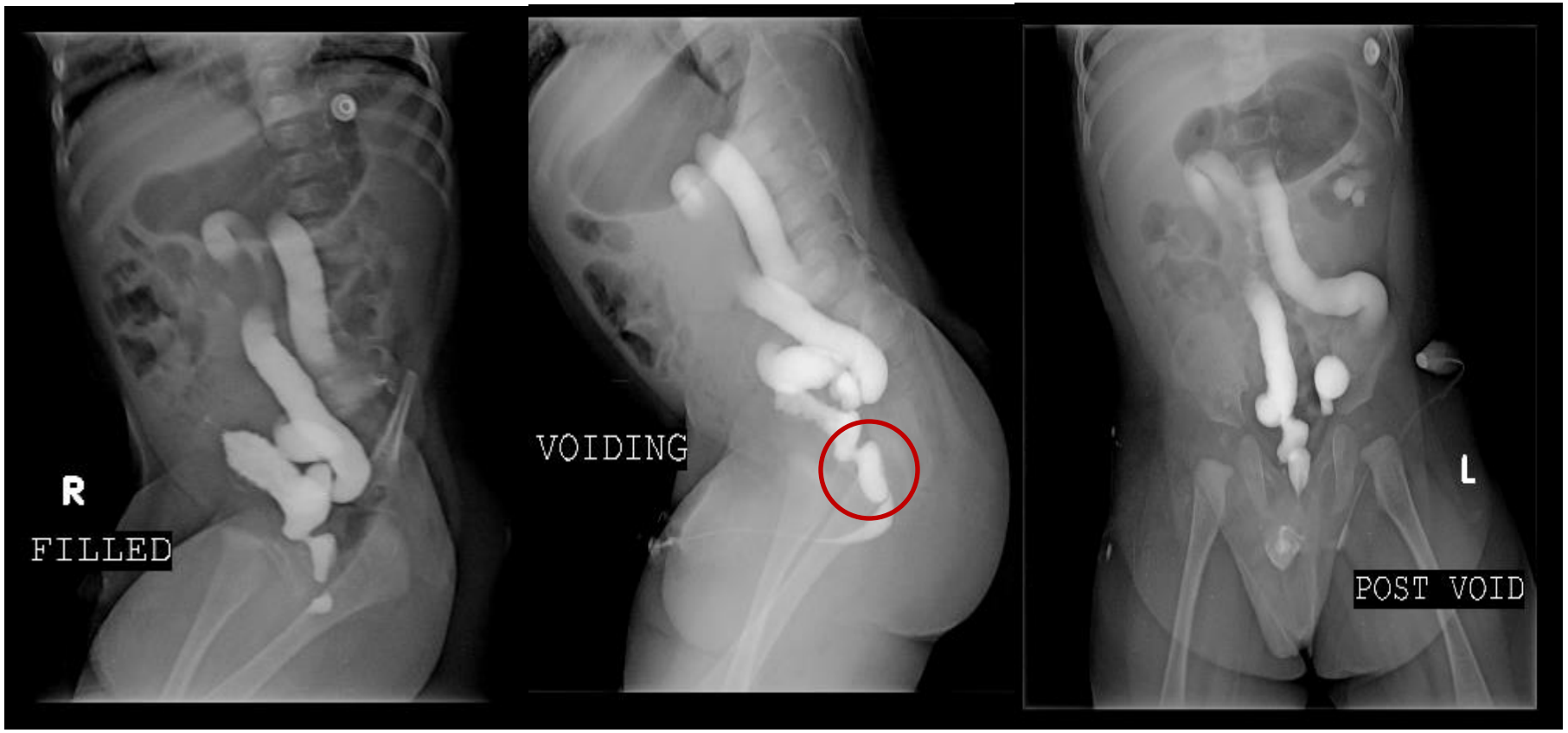








MCU



Management

- Bladder catheterization
- Medical management of hyperkalemia (K binders), metabolic acidosis (Soda bicarb), hyperphosphatemia (sevelamer), hypocalcemia and hyperthyroidism (active vit D and calcium)
- Post renal obstruction - Primary Valve fulguration

Case Scenario 3

- 8 months boy (Post VSD closure and PDA ligation at 5 months of age)

  On Enalapril (0.5 mg/ kg/day), Frusemide (1 mg/ kg/ day) and Spirinolactone (2 mg/kg /day) (Fixed drug combination)
- Presented with loose stools, poor feeding for 2 days and anuric for 12hrs

- On examination, he had hypotension (60/30 mm of Hg) Length 70cm, weight 8kg
- BUN -68 mg/dl, Creatinine-6.1mg/dl
- Na^+-133 mEq/L, K^+- 5.8mEq/L, $HCO3^-$- 13mEq/L

Case Scenario 3

1) What is the diagnosis ?

Acute Kidney Injury – Failure : 3rd stage (KDIGO)

2) Why do you think this child developed AKI ?

ACE Inhibitor induced AKI precipitated by acute illness (dehydration and hypotension)

Case Scenario 3

3) Management

- Anti- failure therapy withheld
- Fluid bolus 20ml/kg (no improvement in output)
- Peritoneal dialysis

Kidney replacement therapy

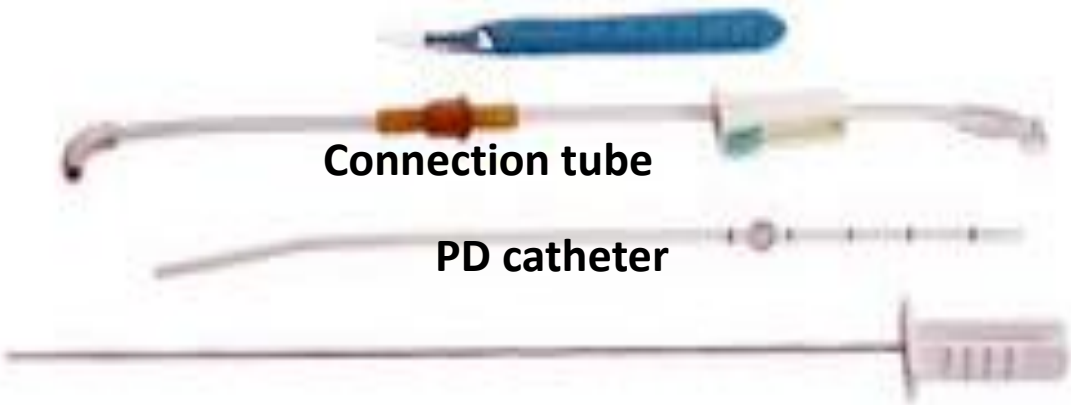
Absolute indications	Relative indications
• Anuria • Fluid overload • Pulmonary oedema • Hypertensive encephalopathy • Uremic pericarditis • Uremic bleeding diathesis	• Persistent hyperkalaemia • Persistent hyponatraemia • Persistentmetabolic acidosis (pH < 7.1 or serum HCO3 < 10 mEq/l) • Uncontrollable hypertension • Severe hyperphosphataemia, hyperuricemia and/or hypercalcaemia

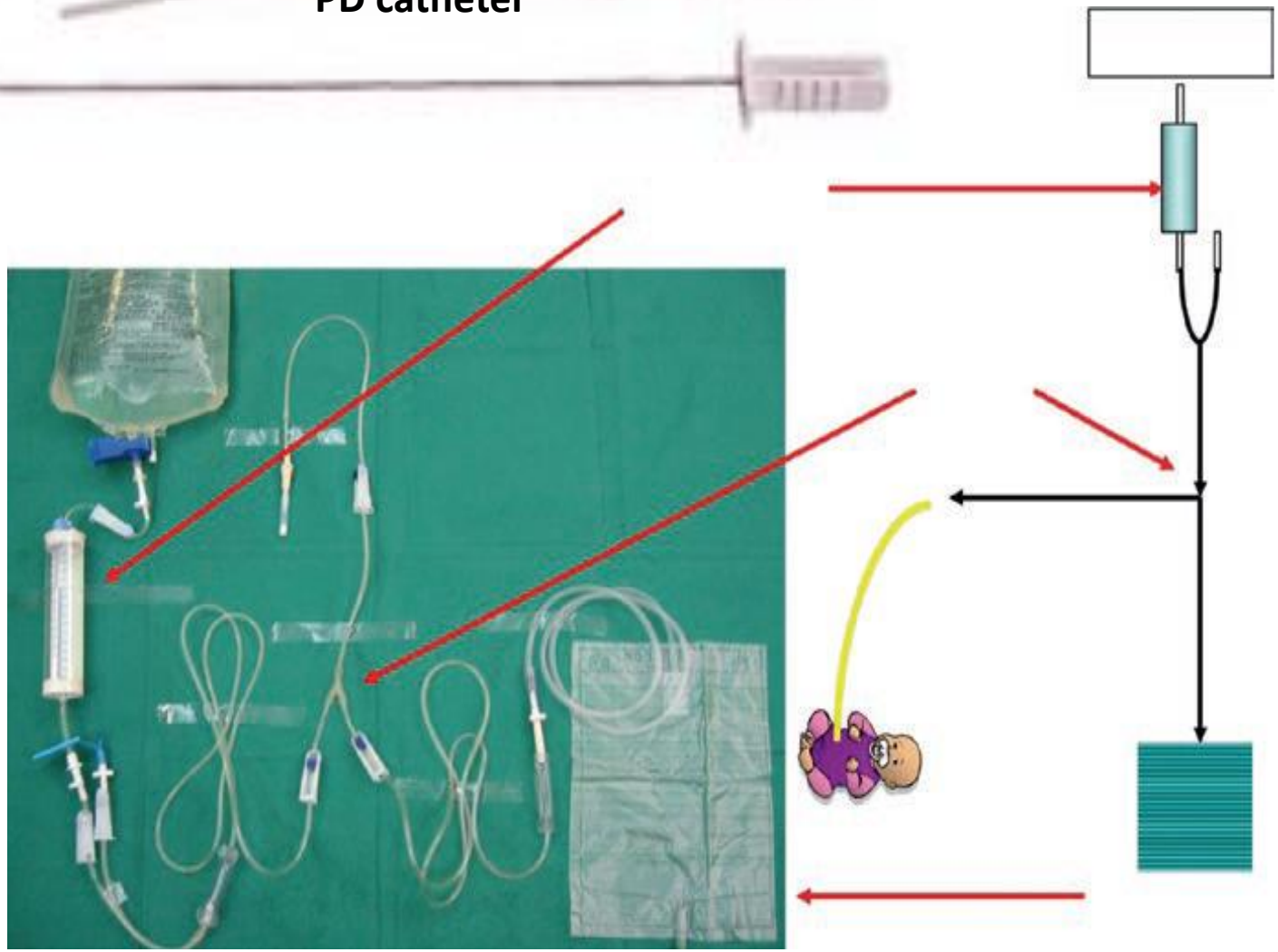
Non renal indication

Immunomodulation in sepsis, IEM with hyper ammonemia

To give adequate nutritional support

Peritoneal dialysis





PD cycle

- Prepare, priming, PD catheter insertion, fluid exchanges
- Peritoneal dialysis prescription

  1.7% Dextrose PD fluid

  Priming of peritoneal cavity with 240ml fluid

  In – 240ml (30ml/kg), 10min

  Dwell time – 30min,

  Out time – 20min(1 hour cycle)
- Duration 72 hrs

Case Scenario 3

Follow up:

- Child's urine output increased progressively and renal parameters normalized after 8 days
- Anti- failure therapy restarted after 2 weeks
- He is currently gaining weight well and has normal renal function

Outcome in ACEI induced AKI

- AKI caused by ACE inhibitors is usually reversible and responds well to correction of volume
- Fluid management and temporary dialysis

- ACE inhibitors can be safely re-started once AKI resolves

Case Scenario 4

- 8 years boy developed facial puffiness, decreased urine output with, breathlessness
- Recently had an infected wound in the leg
- HR 110, RR 36, BP 130/ 88mmHg, pedal edema
- CVS, RS Normal, Mildly enlarged tender liver

Diagnosis?

Case Scenario 4

- IRGN
- Urine routine Protein 1+, 15-20 RBCs/HPF
- BUN 25, Creat 1.2 mg/dL, urine output 0.7ml/kg/hr
- Electrolytes Normal
- Complement C3 – 18 g/L

Management principles ?

Case Scenario 4

- Diet
- Fluid
- Diuretics
- Antihypertensives

Case Scenario 4

- Urine output 0.3ml/kg/hour
- S.Creatinine after 24 hours 3.2 mg/dL
- Serum electrolytes (Na/K/Cl2/HCO3) - 138/6/101/11 mEq/L
- How will you manage?

Hyperkalemia

- Calcium Gluconate 1 ml/kg (max 20ml)over 15 minutes

Shift potassium intracellularly

- Inhaled β_2 adrenergic agonist (Salbutamol)
- Glucose 1 gm/kg plus 0.1 unit/kg regular insulin
- Alkalinize (Sodium bicarbonate 1 mEq/kg IV)

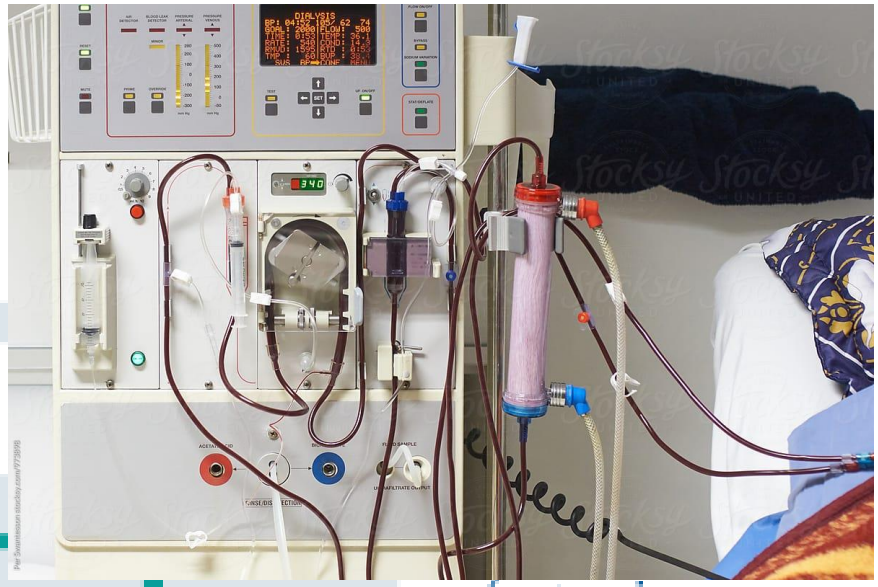
Removal of potassium from the body

- Cation exchange resin: Calcium polystyrene sulfonate 1 gm/kg
- Dialysis

Intermittent Haemodialysis

- Rt IJV catheterized with 10 Fr double lumen HD catheter
- Initiated on IHD
- 4 cycles of HD in 8 days

Intermittent HD



7 Air trap and pressure monitor

8 Filtered blood returns to your body

2 Blood thinner

4 Dialyzer

goes in

1 Blood goes into the machine

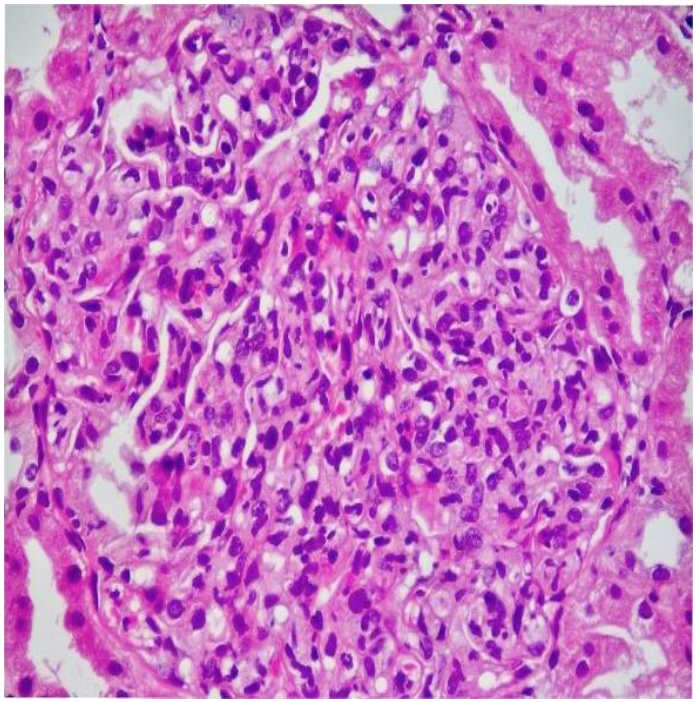
3 Pressure monitor and pump

6 Used dialysate solution pumped out

Case Scenario 4

Course:

- Renal biopsy - IRGN
- D9 S.creat 0.8mg/dL
- Follow up after 3 weeks – S.Cr 0.3mg/dL

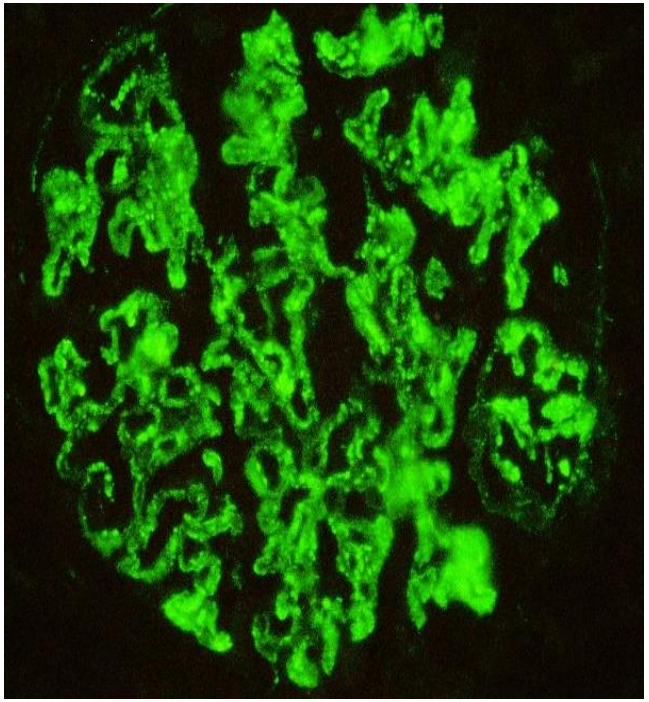


LM study

↑ Cellularity

Endocap proliferation

IF study
"starry-sky"
pattern



Case Scenario 5

- 8 months old baby girl presented with fever, hypotensive shock. Resuscitated with fluid boluses, inotropes and ventilated. Treated with paracetamol & ibubrufen for fever elsewhere

On evaluation

- TC – **28000**/mm^3, P76, L23, platelets- **65000**
- S.Cr- **2**mg/dL, S.E- 130/3.6/98/12 mEq/L
- SGOT/SGPT- **1340/2520U**, **prolonged PT/aPTT/INR**

Case Scenario 5

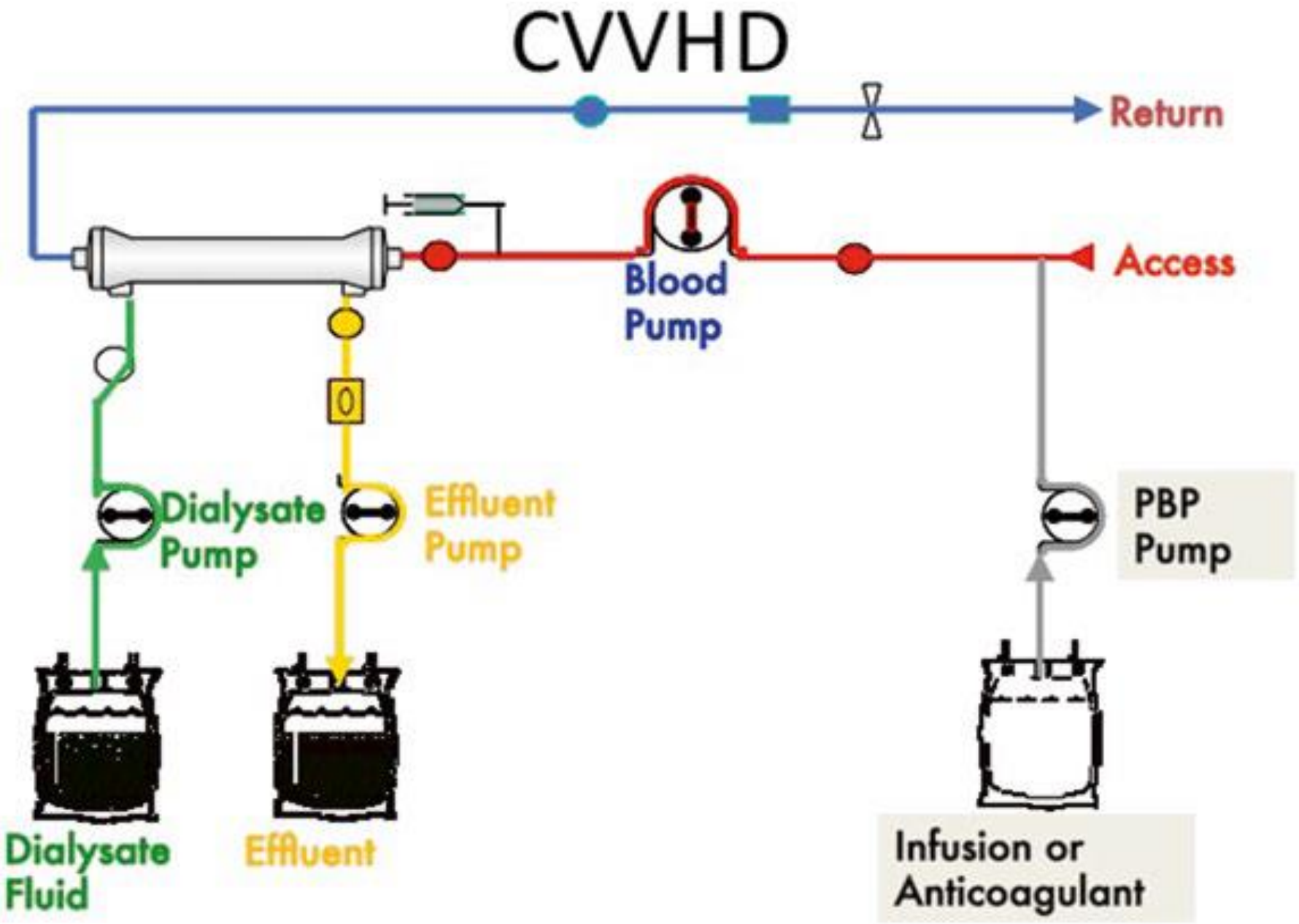
- Broad spectrum antibiotics
- Oliguric for 6hours

- Mode of KRT?

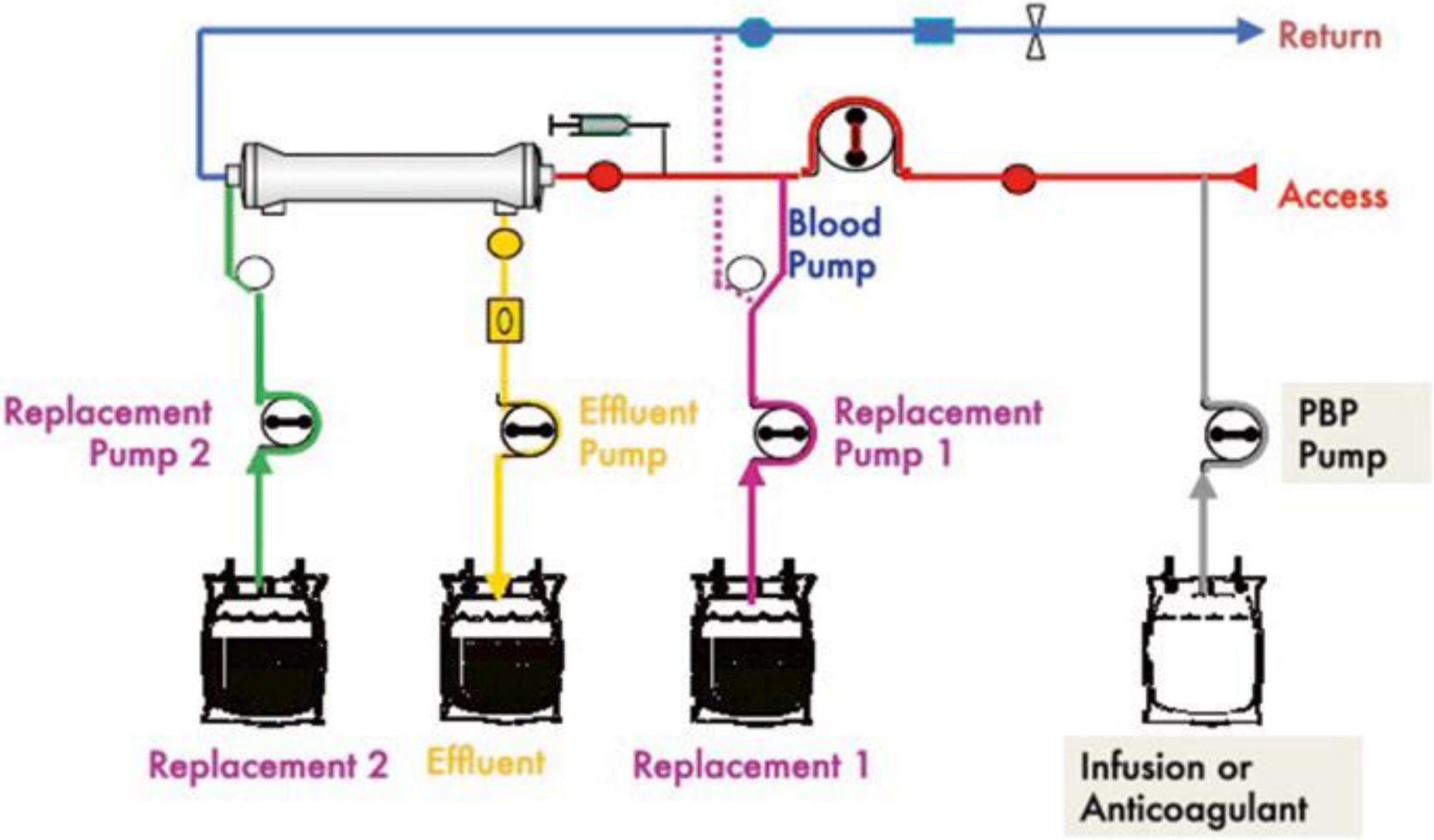
- CRRT

Modes of CRRT

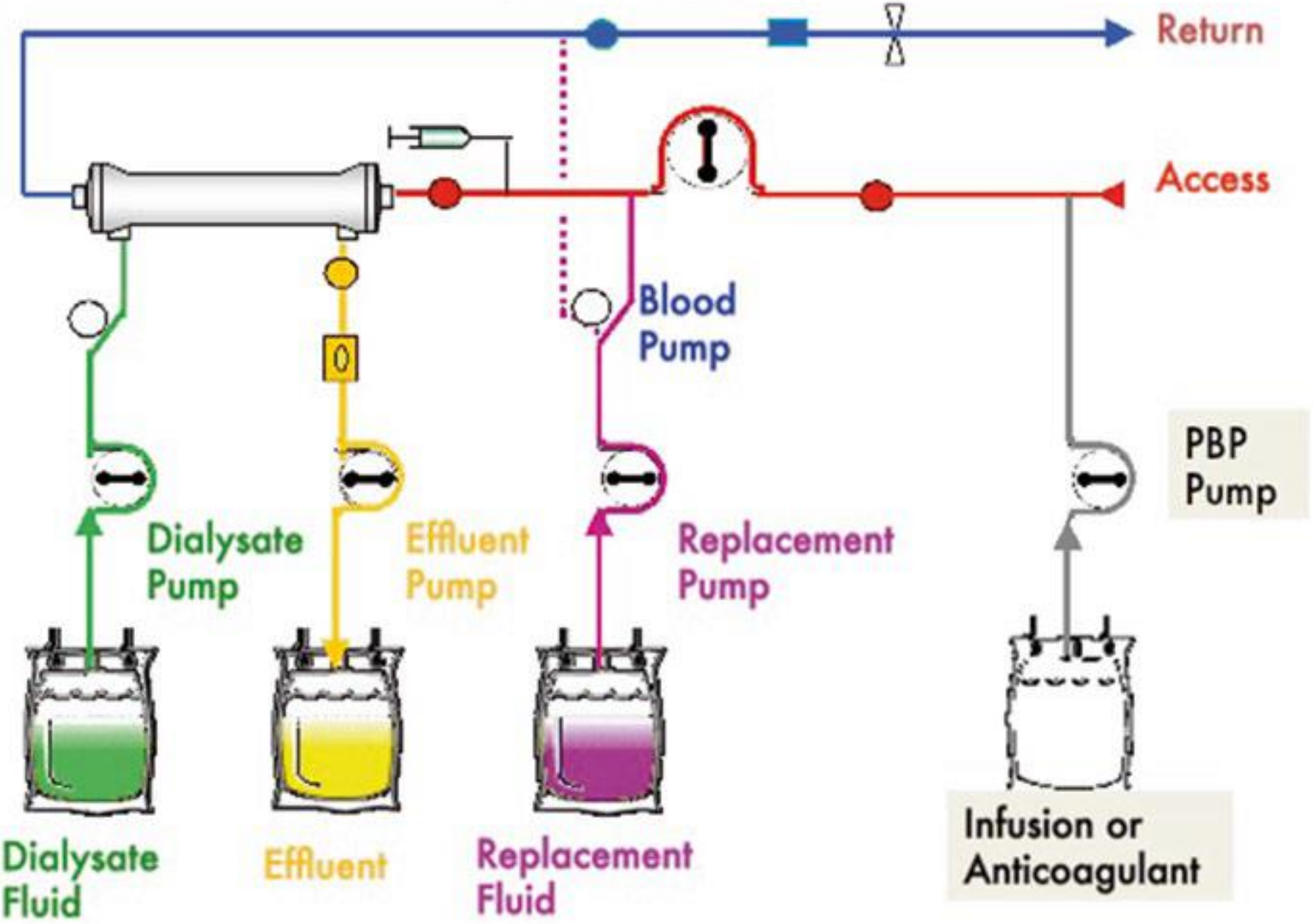
- CVVH: Continuous Veno-Venous Hemofiltration
- CVVHD: Continuous Veno-Venous Hemodialysis
- CVVHDF: Continuous Veno-Venous Hemodiafiltration
- SCUF: Slow Continuous Ultrafiltration


CVVHD
Return
Access
Blood Pump
Dialysate Pump
Effluent Pump
PBP Pump
Dialysate Fluid
Effluent
Infusion or Anticoagulant

CVVH


Return
Access
Blood Pump
Replacement Pump 2
Effluent Pump
Replacement Pump 1
PBP Pump
Replacement 2
Effluent
Replacement 1
Infusion or Anticoagulant

CVVHDF


Return
Access
Blood Pump
PBP Pump
Dialysate Pump
Effluent Pump
Replacement Pump
Dialysate Fluid
Effluent
Replacement Fluid
Infusion or Anticoagulant

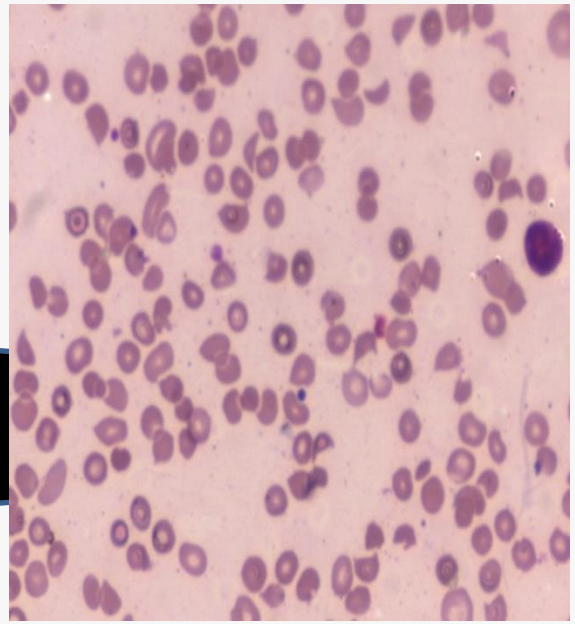
Modality selection

- Volume removal only -SCUF
- Solutes +/- volume - CVVHD/CVVHDF
- Hypercatabolic +/- volume - CVVHDF

Case scenario 6

- A 3 yr old boy had AKI following 5th day of bloody diarrhea

	Hb	TC	Plt	PSS	LDH	S.Creat	C3
D1	10.2	18200	1.47	Normal	900	1.8	
D5	7	27000	47000	32% schistocytes	3476	3.2	51.4



Genetic mutation of complement C3 and Complement factor I

- PD/CAPD/HD/ Plasma exchange
- Developed MODS and succumbed

Hemolytic Uremic Syndrome

- Triad of HUS - Microangiopathic hemolytic anemia, thrombocytopenia and AKI

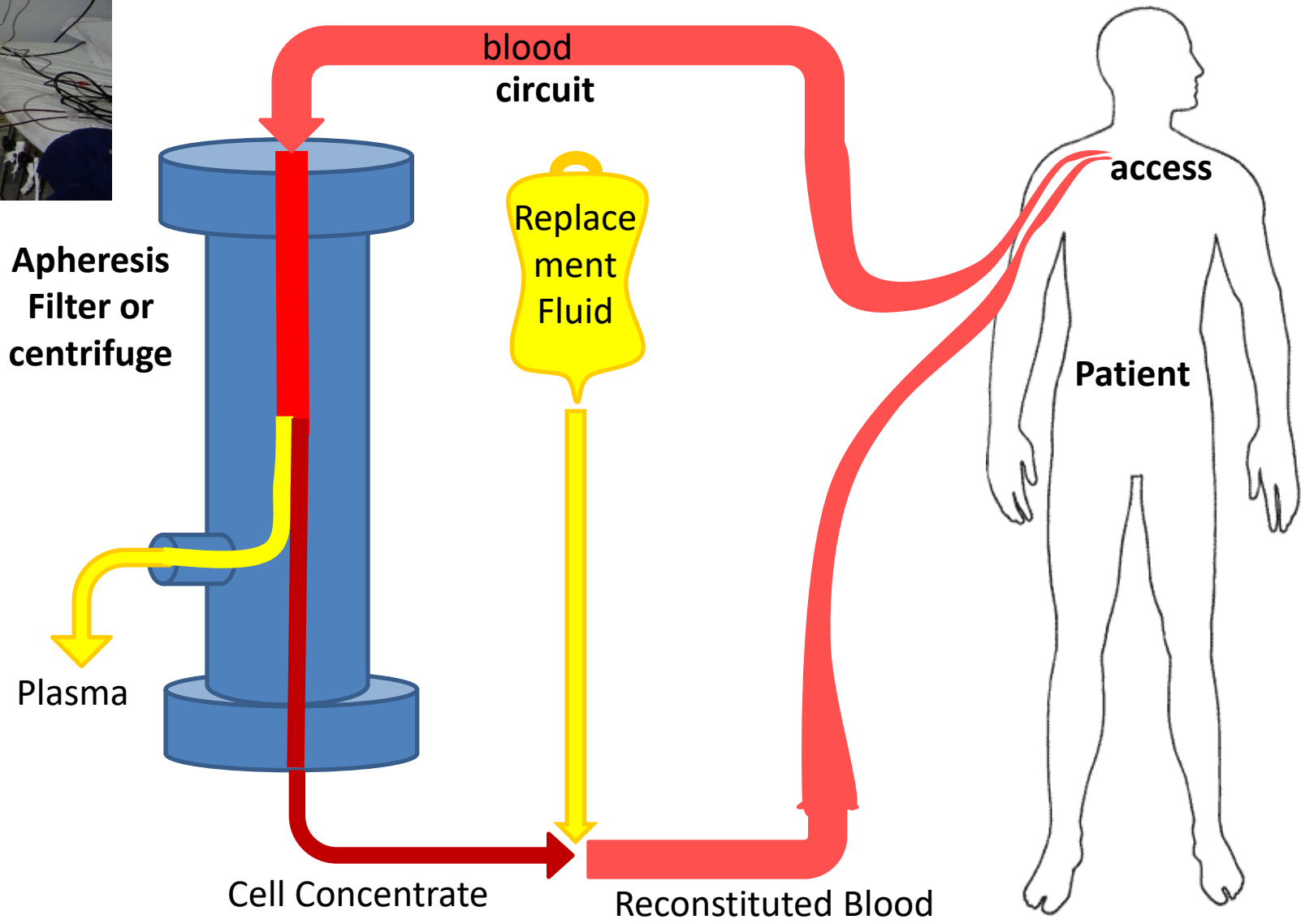
Causes of HUS

- Infection induced: Verotoxin producing E.coli, Shigella dysentriae type1, Streptococcus pneumoniae and HIV
- Genetic: Factor H, I and B, MCP mutation
- Antibody mediated
- Other diseases associated with micro vascular injury- DIVC
- Medication induced- Quinine, Calcineurin inhibitor

Management

- Infection – HUS – Supportive
- Antibody mediated/Genetic mutation – Plasma exchange/ Eculizumab

PLASMAPHERESIS



Take home points

- AKI – Multifactorial, demands prompt recognition and intervention
- Assess and monitor the clinical status of child to diagnose AKI at the early stage
- Goal of Dialysis

  Ultrafiltration v/s solute clearance
- Vascular Access
- KRT mode - Institutional preference & Cost

THANK YOU