Kidney Support Therapy for Acute Kidney Injury

MODERATORS

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Case 1

History

5-month-old boy, known case of transposition of great arteries, underwent arterial switch operation.

On post-op day 2

Developed cardiogenic shock requiring dobutamine and adrenaline

Observed to have low urine output (0.3ml/kg/hr) and edema

General physical examination

PR: 140/min

RR: 40/min

Spo2 99% (under mechanical ventilation)

BP- 88/51 (50^{th}-90^{th} centile) mm Hg

Systemic examination

Respiratory: Bilateral air entry equal, basal crepitations present

Cardiovascular: No gallop

Per abdomen: Liver 2 cm below costal margin

Case 1: Investigations

	POD 0	POD 2	POD 3
Hb	12.3	13.1	11.5
TLC	6560	7880	6490
DLC	56/34	58/32	60/35
Platelet	1.56L	2.31L	2.2L
Urea (mg/dL)	38	78	92
Creatinine (mg/dL)	0.4	0.8	1.7
Na/k (meq/L)	138/4.4	137/4.2	139/4.8
pH/HCO3	7.34/22	7.2/18	7.15/14.4

Dr. Kanav Anand

Is this acute kidney injury?

Must recognize AKI early

Sudden loss of renal function, in hours to days, with altered fluid balance, acid base & electrolytes

Serum creatinine

Varies: age, gender, muscle

Doesn't depict dysfunction immediately; rises after 50% lost

Secretion overestimates function

Effect of fluid overload: Dilutional fall

Methods of estimation vary

Easily dialyzed

Urine output

The canary in the coal mine

Duration: prognostic value
Enables early diagnosis
Improves management

Caveats
Not all AKI is oliguric
Not validated prospectively
Diuretic use
Cumbersome to measure

AKI: Definition & Classification

Staging	Serum creatinine			Urine output (all)
	RIFLE	AKIN	KDIGO	
Definition of AKI	SCr increase ≥50% within 7 days	SCr increase ≥50% or ≥0.3 mg/dL within 48 h	SCr increase ≥50% in 7 days or ≥0.3 mg/dL within 48 h	-
RIFLE-risk; AKIN stage 1; KDIGO stage 1	SCr increase ≥50% or GFR decrease >25% within 7 days	SCr increase ≥50% or ≥0.3 mg/dL within 48 h	SCr increase ≥50% in 7 days or ≥0.3 mg/dL within 48 h	<0.5 mL/kg/h for 6-12 h
RIFLE-injury; AKIN stage 2; KDIGO stage 2	SCr increase ≥100% or GFR decrease >50% within 7 days	SCr increase ≥100%	SCr increase ≥100%	<0.5 mL/kg/h for ≥12 h
RIFLE-failure; AKIN stage 3; KDIGO stage 3	SCr increase ≥200% or GFR decrease >75% or SCr increase ≥4 mg/dL (with acute rise ≥0.5 mg/dL)	SCr increase ≥200% or ≥4 mg/dL (with acute rise ≥0.5 mg/dL) or need for RRT	SCr increase ≥200% or ≥4 mg/dL or need for RRT	<0.3 mL/kg/h for ≥24 h or anuria for 12 h
RIFLE-loss	Need for RRT >4 weeks	-	-	-
RIFLE-end stage	Need for RRT >3 months	-	-	-

GFR=glomerular filtration rate; RRT=renal replacement therapy; SCr=serum creatinine.

Dr Ramya

Is Kidney support therapy (KST) indicated?
When? Why?

Initiate KST timely; any modality

KDIGO Clinical Practice Guideline for Acute Kidney Injury

VOLUME 2 | ISSUE 1 | MARCH 2012

5.1.1: Initiate
chang
exist.

5.1.2: Consi
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- Fluid overload
- Dyselectrolytemia
- Acid-base imbalance
- Anuria/Oliguria
- Removal of dialyzable toxins
- Optimization of fluid balance and nutrition

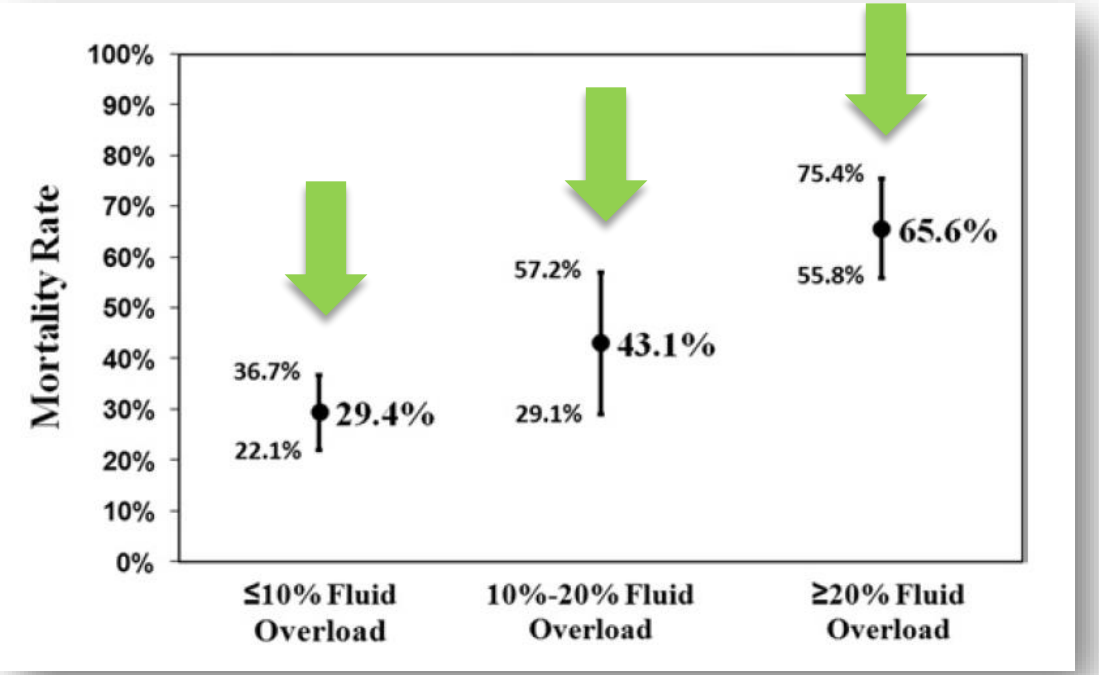
Indications for Kidney support therapy

Refractory hyperkalemia (serum potassium >6 mEq/L despite medical measures)
Refractory metabolic acidosis (pH <7.15)
Uremia (blood urea nitrogen >100 mg/dl) or complications (encephalopathy, pericarditis)
Pulmonary edema
Fluid overload >10-15% since admission
Refractory or symptomatic hypo- or hypernatremia
Severe hyperuricemia or hyperphosphatemia associated with tumor lysis syndrome
Poisoning and drug intoxications (e.g., lithium, salicylate, valproic acid, metformin)
Hyperammonemia and metabolic decompensation in inborn errors of metabolism (e.g., propionic acidemia, methylmalonic acidemia)

Timing of KST: Fluid overload matters..

% Fluid Overload

Σ (fluid input – fluid output) / admission weight X 100



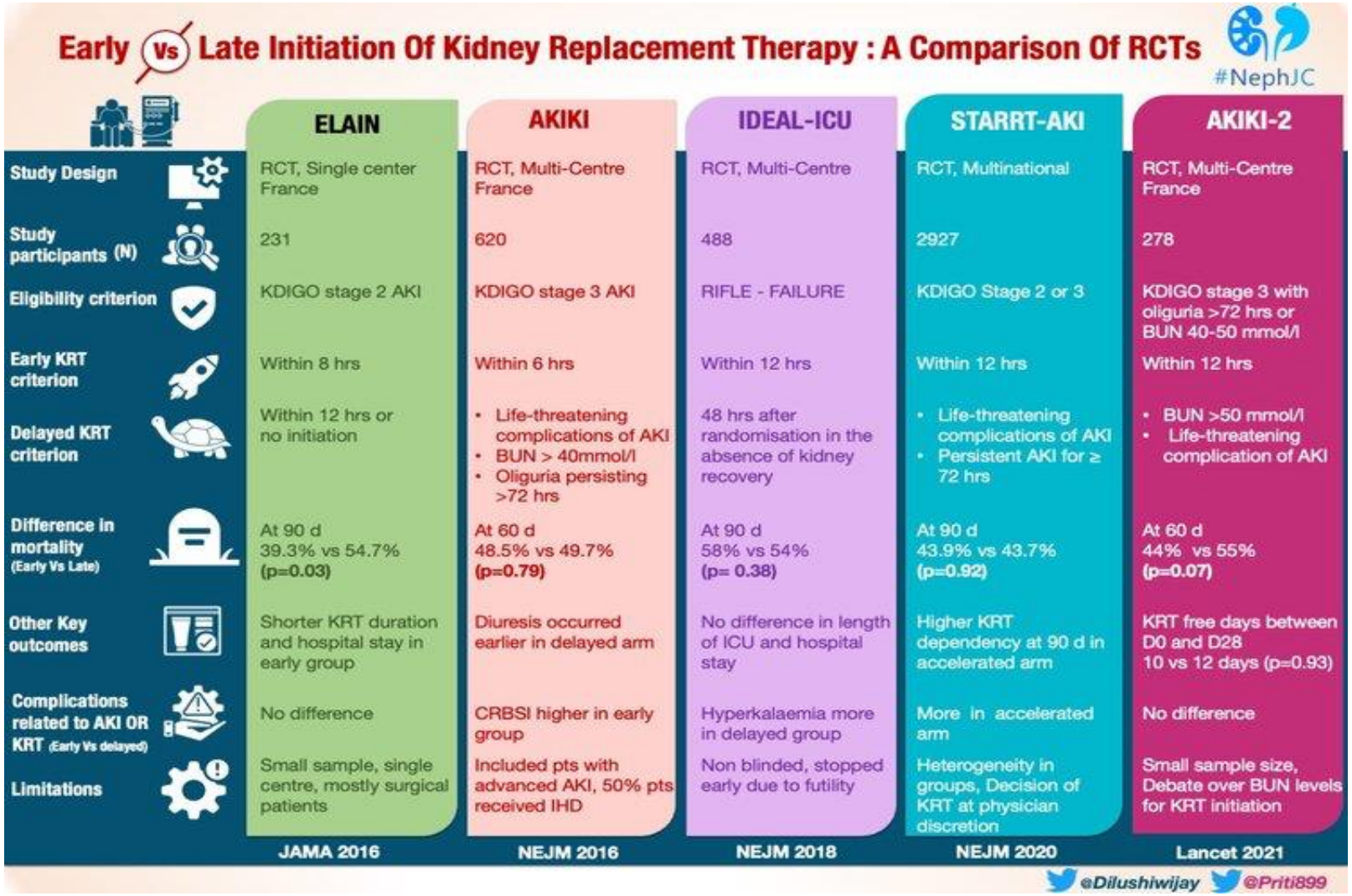
Adjusted mortality with FO >20%: 8.5 times high

PPCRRT Registry
13 centers
Nat Rev Nephrol 2010;6:190

Clinically significant if ≥10%

Independently associated with increased risk of mortality

Timing of KST: Early may not be the best..



IPNA

Dr. Chandrashekar Singha

What modality will you choose? Why?

Modalities of Kidney Support Therapy

Intermittent

IHD
Intermittent hemodialysis

HF
Isolated Ultrafiltration

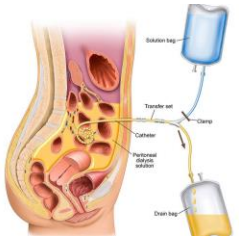
Hybrid

SLED
Sustained (or slow) low efficiency dialysis

SLED-F
Sustained (or slow) low efficiency dialysis with filtration

Continuous

PD
Peritoneal Dialysis



CKRT
Continuous Kidney Replacement Therapy

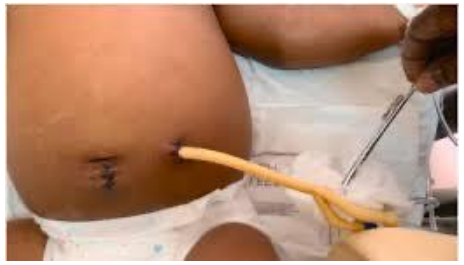
Peritoneal dialysis: Almost always feasible

Challenges of HD/CRRT in sick newborns

Vascular access

Technical skills, equipment for CRRT

Anticoagulation..



Less expertise, equipment

Resource limited regions

Need intact peritoneal cavity

No other absolute contraindication

Can be initiated rapidly

Gradual, continuous clearance

PD is successful in most, but…

Not efficient: severe fluid overload, lactic acidosis

Pulmonary compromise; abdominal surgery

Manual PD: labor intensive, messy

No control on ultrafiltration; clearances

Dr. Karan Raheja

- How will you prescribe PD in this case?

Prescribing peritoneal dialysis

Dialysate composition **(Ensure to WARM to body temperature)**	Dextrose for gradient; lactate based vs bicarbonate based 1.7%, 2.5% or higher; customised
Fill Volume	Start low (10 ml/kg, 200-300 ml/m^2) & hike (800-1100 ml/m^2)
Dwell time	15 min-longer (*as per need*)
Inflow time & outflow time	10 min & 20 min (*varies*)
Ultrafiltrate volume	As per indication
Additives	Heparin, potassium, antimicrobials
Monitoring and recording	Therapy, clinical & lab parameters

Modalities of peritoneal dialysis

	Intermittent Peritoneal Dialysis	Continuous Peritoneal Dialysis/Continuous Flow Peritoneal Dialysis	Tidal Peritoneal Dialysis
Mechanism	Cycling in and out of fluids at regular intervals.	Continuous exchange across the membrane with low dialysate flow.	Only 25-50% of dwell volume is drained, giving a tidal volume of 50-75%.
Advantage	Rapid clearance of small molecules (eg, Potassium).	Increased solute clearance of larger molecules and higher ultrafiltration.	Better clearance of small and middle molecules.
Disadvantages		Inadequate nitrogen balance in preexisting hypercatabolic state. Technically more complex and costly	Always requires the use of a cycler.

PD prescription

Categories	Prescription (Weight- 5kg)
PD catheter	31cm soft PD catheter
PD fluid	1.7% Dextrose
Reservoir	100ml (20-30ml/kg)
Dwell volume	50-100ml (10-20ml/kg), increase upto 150 ml (30 ml/kg)
Dwell duration	30 mins
Inflow, outflow time	5-10 mins
Ultrafiltration	5-10 ml per cycle (depends on hemodynamic status)
Additives	None
Monitoring	VBG for electrolytes, PD fluid cells
Drugs	Appropriate renal modification

Ensure antibiotic within 1 hour of insertion

Follow up

POD 4

No evidence of fluid overload, dwell duration increased to 60 mins

POD 7

Urine output started to increase

Dwell duration increased to 90mins

POD 8

Off dialysis trial - tolerated

Case 2

13-year-old boy, history of

- vomiting, fever for 15 days,
- cola colored urine for 4 days,
- oliguria for 2 days, anuric for 6 hours
- generalized body swelling for 1 day

Anthropometry:

- Weight: 42 kg (+1.45 SDS)
- Height: 150 cm (+1.1 SDS)
- BMI: 18.6 kg/m^2

Examination:

PR: 80/min

RR: 18/min

BP: 145/90 (stage 2 hypertension)

Systemic examination: normal

Case 2

Inv	1/3/24	3/3/24	4/3/24
Hb	12.1	12.2	11.8
TLC	4890	6330	5770
Platelet	2.4L	2.3L	2.5L
Urea (mg/dL)	80	159	250
Creatinine (mg/dL)	2.5	5.6	8.9
Na/k	138/4.2	140/5.1	142/6.2
Ca/PO4	8.5/5.6	8.3/6.1	8.4/6.7
Ph/ HCO3			7.24/18.1

Inv	Reports
USG KUB	RK: 9.8 cm, LK: 9.1cm, CMD: intact
C3/C4	9/28 mg/dL
Urine microscopy	full field RBCs/HPF
ANA/ANCA	negative

RPGN ?C3 glomerulopathy
Acute kidney injury stage 3
Refractory hyperkalemia, Metabolic acidosis, stage 2 hypertension, uremia

Kidney support therapy- Modality?

Intermittent hemodialysis

IPNA

Dr. Kanav

What modality of KST here?

How would you prescribe it?

Hemodialysis:

Allows rapid ultrafiltration and solute removal
Can be coupled to plasma exchanges

Requirements

HD machines, dialyzers

Access: internal jugular; femoral vein

Heparin, saline HD

Ultrafiltration (UF)

Technical expertise

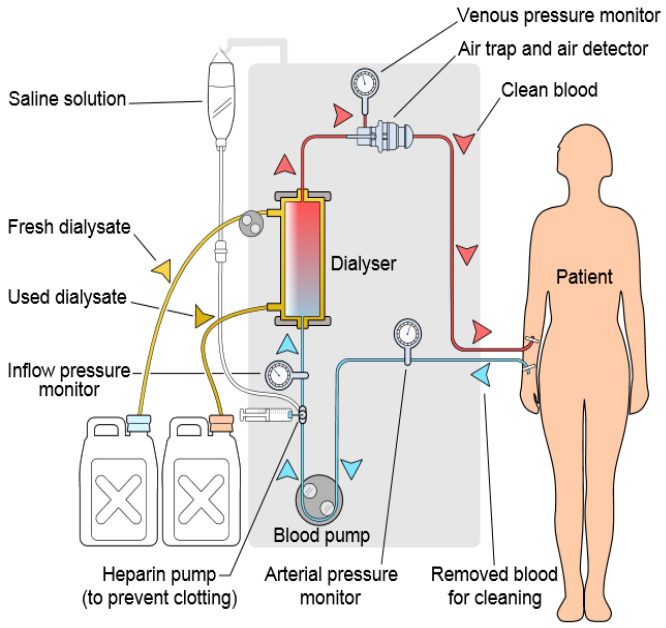
Patient size matters…..

Table 1. Catheter and Patient Size Options

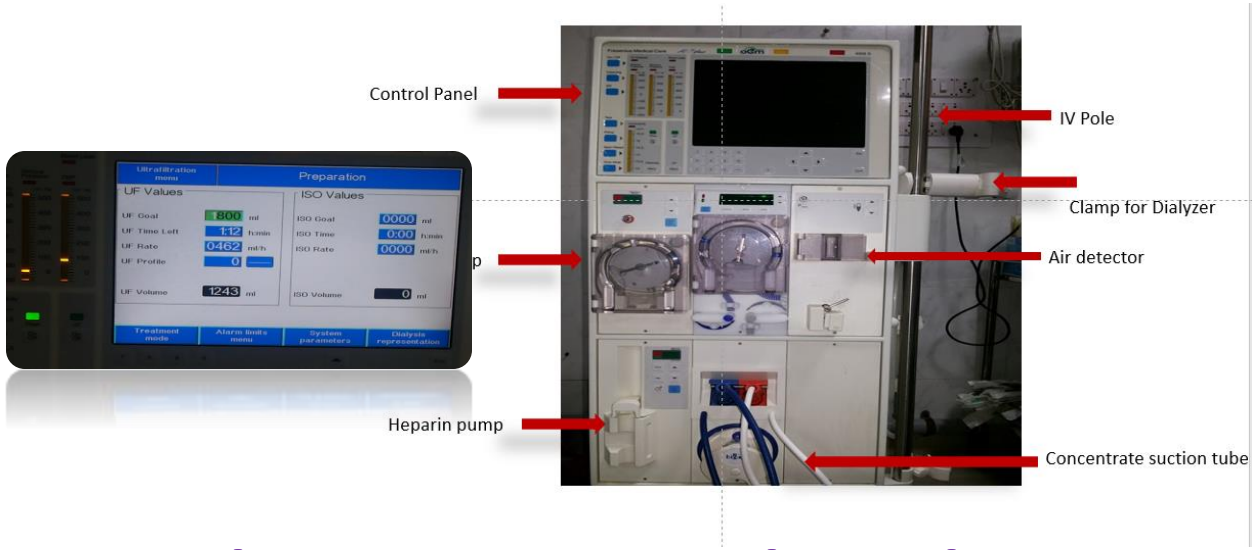
Patient Size	Catheter Size and Source
Neonate	Single-lumen 5F (Cook Medical, Bloomington, IN) Dual-lumen 7.0F (Cook/Medcomp, Harleysville, PA)
3-6 kg	Dual-lumen 7.0F (Cook/Medcomp) Triple-lumen 7.0F (Medcomp; Arrow, Reading, PA)
6-30 kg	Dual-lumen 8.0F (Kendall, Mansfield, MA; Arrow)
>15 kg	Dual-lumen 9.0F (Medcomp)
>30 kg	Dual-lumen 10.0F (Arrow, Kendall)
>30 kg	Triple-lumen 12F (Arrow, Kendall)

Hemodialysis apparatus

Dialysis Circuit



Hemodialysis Machine

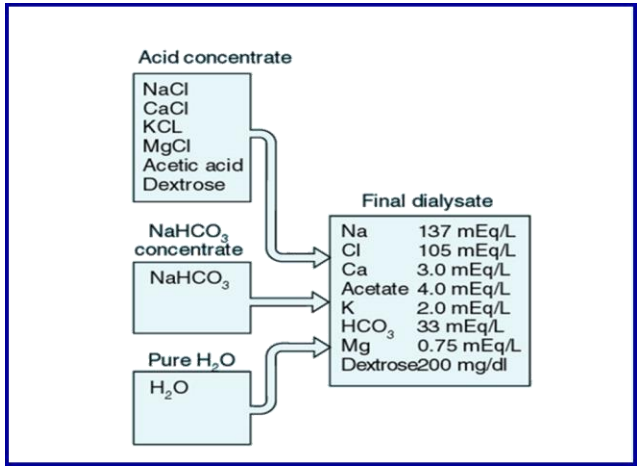


Dialysate: Water & electrolytes

Part A: 1 mL

Part B: 1.83 mL

Water: 34 mL



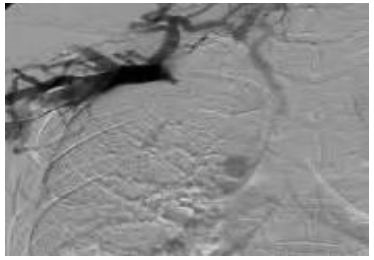
Hemodialysis apparatus

Vascular Access

Non tunneled central venous catheter: AKI

Arteriovenous fistula or tunneled catheter: ESKD

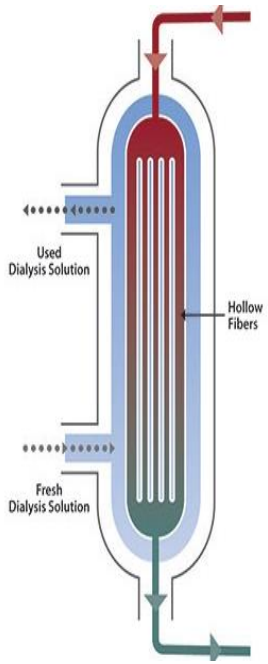
Prefer Right IJV >Femoral >Left IJV

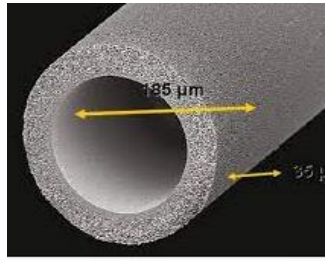


<u>AVOID</u> subclavian

Risk of stenosis

Dialyzer: The membrane





Cellulose & substituted cellulose

Cellulosynthetic

Synthetic: Polysulfone, PAN, PMMA, Polycarbonate

Acute Hemodialysis Prescription

Dialyzer	•Size: Surface area 0.8-1 * BSA (Fx ped 0.2, F4 0.7, F5: 1) •Type: Clearance and middle molecule clearance •Tubing: Pediatric/Adult
Priming with blood or 5% albumin or saline	If extracorporeal volume > 10% of blood volume
Blood Flow rate Q_B	5-7 ml/kg/min (6-8 ml/kg/min later subsequently)
Dialysate Flow rate Q_D	300 or 500 ml/min

Acute Hemodialysis Prescription

Ultrafiltration Volume	• Do NOT exceed 0.2 ml/kg/min • No more than 10 % of the body weight per session • Adjust by state of fluid overload
Session Duration	• Initial short session, avoid disequilibrium • Subsequently 4 to 6 hours per session • Urea reduction ratio < 40% initial session
Frequency	• Daily initially • Tailor according to needs

Acute Hemodialysis Prescription: anticoagulation

- Rinse the circuit with heparinised saline
- Heparin UFH (or LMW)
  - Patient assessment
  - Constant infusion- Bolus 20 U/kg followed by infusion 10U/ kg/h
  - Intermittent bolus doses 25-50 U/kg f/b 10-20/kg hourly

Assessment of Clotting

- Extremely dark blood
- Foaming & clot formation in drip chamber
- High circuit pressures

Citrate anticoagulation: regional anticoagulation

- Chelates calcium
- Calcium chloride infused in the venous line

Hemodialysis prescription

Categories	Prescription (Weight- 42kg)
HD catheter	11.5 Fr
HD access	Right internal jugular vein
Dialyzer, tubing	F6, Adult
Blood flow rate	200ml/min (5ml/kg/min) (increase upto 6-8ml/kg/min)
Dialysate flow rate	500ml/min
Duration	45-60 mins, Increase duration subsequently
Ultrafiltrate	500ml (not to exceed 0.2ml/kg/min or 10%)
Frequency	Daily initially
Anticoagulation	Heparin loading dose: 50U/kg , maintenance dose: 20U/kg/hour
Drugs	Appropriate renal modification

Follow up

Inv	5/3/24	7/3/24	9/3/24	11/3/24	13/3/24
Urine output	150ml	480ml	800ml	1500ml	1800ml
Urea	210	168	121	86	80
Creatinine	7.7	6.5	5.5	3.2	2.2
Na/K	140/5.6	138/4.2	142/4.1	140/4.5	136/4.3
pH/ HCO3	7.3/19	7.33/20.1	7.38/22	7.39/22	7.36/23.1

Spacing out sessions

Stop

CASE 3

- 9 years old male child came with complaints of
  - Fever & Vomiting since last 3 days
  - Breathing difficulty & loss of appetite since last 2 days

He was admitted with above complaints in other hospital

- Child was given IV antibiotics (Ceftriaxone & Amikacin)
- Child was on CPAP support
- Child was in shock on inotropic support (Dopamine, Dobutamine)
- IV antibiotics were changed to Meropenem and Vancomycin on Day 2

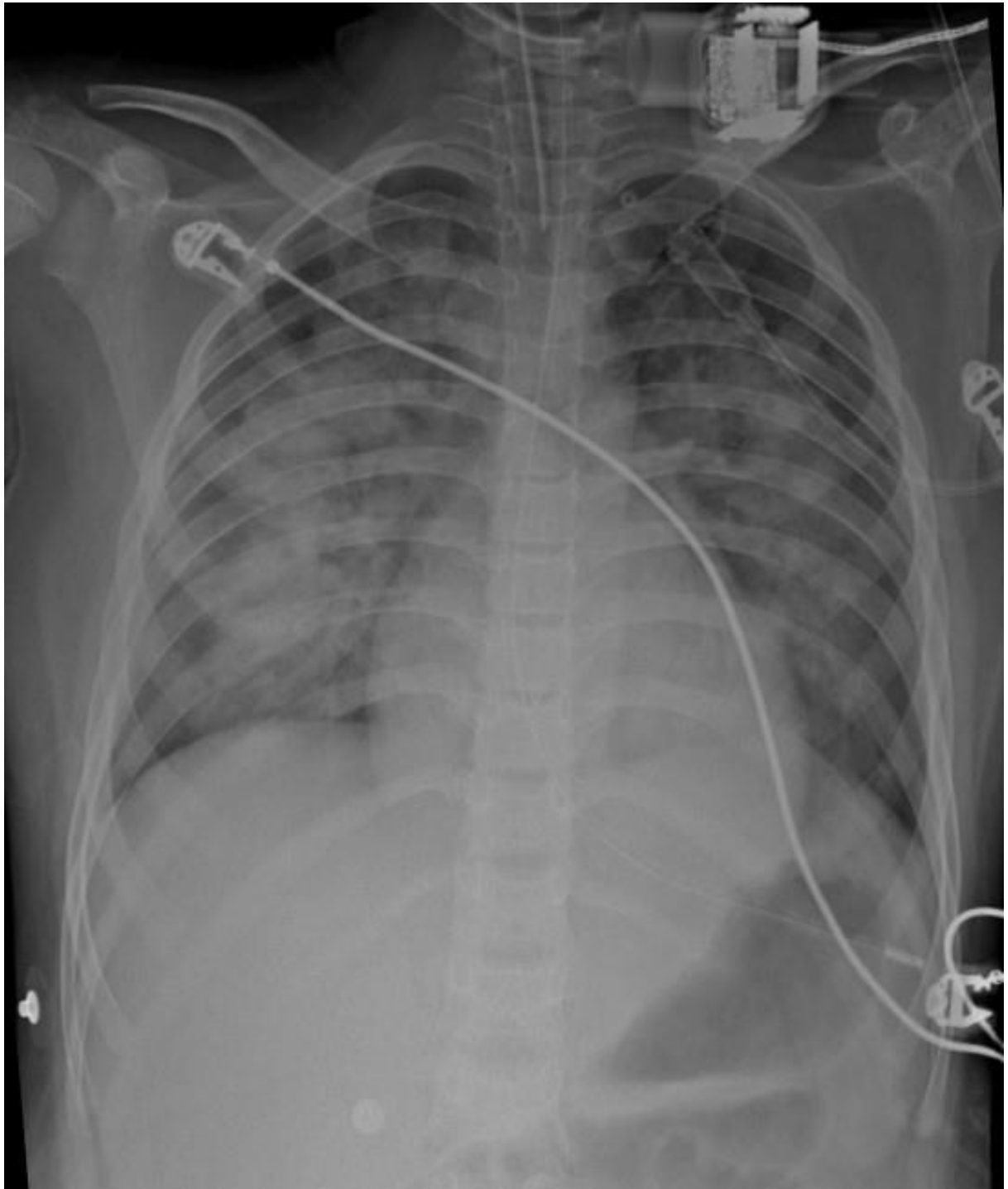
ON PRESENTATION

- Child was transported on oxygen by mask and inotropic support.
- Child was sick, HR- 140 bpm, SpO2- 90% at 10 L/min, BP- 80/38 mm of Hg.
- PP weak, CRT =4 secs, periphery cold.
- CVS- tachycardia, P/A- distended, Liver- 5 cm, CNS- Irritable, GCS-14/15.
- R/S- B/L crepts present.
- Maculopapular rashes all over the body.

MANAGEMENT

- Child was shifted to PICU for further management
- Child was given fluids bolus at 10 ml/kg
- Continued on Dobutamine infusion and started on Adrenaline infusion.
- VBG- pH-7.1, pCO2-35,HCO3-12, Lactate-4
- Child was intubated under modified RSI with 6 cuffed tubed and started on mechanical ventilation.

CHEST X-RAY



INITIAL INVESTIGATION

- COVID 19 PCR- Negative
- Blood, Urine and ET culture (29/12/21) – Negative.
- Scrub typhus, Weil –Felix, Dengue NS1, IgM- Negative.
- Vitamin D - <3 ng/ml

INITIAL INVESTIGATION

- Ferritin- 1211

  COVID antibody -Positive(2201).
- Pro BNP- >25,000
- Trop I – 5407 (<19)
- 2 D Echo- (29/12/21)
  - Global LV Hypokinesia- 20-25 %
  - Moderate MR,TR
  - Dilated LA, LV.

PROVISIONAL DIAGNOSIS

- Severe Sepsis with Shock (Cardiogenic/Septic) with Myocarditis with suspected post covid 19 MISC

DAY 1-3

- Hemodynamics
  - Inotropic support- adrenaline, dobutamine, milrinone & Lasix infusion
  - Day 1- BP -90/61, Day 3- 112/82 mm of Hg
- Ventilation
  - FIO2- 100 % - 50 %, PEEP- 14, VT- 5ml/kg, VR- 20-35
  - ABG- pH-7.35,PaO2-100,PaCO2-45, HCO3- 24
- Antibiotics
  - Meropenem, Vancomycin (continued).
  - Azithromycin and Doxycycline.
- Hematological
  - PRBC Transfusion, FFP Transfusion
- Feeds started

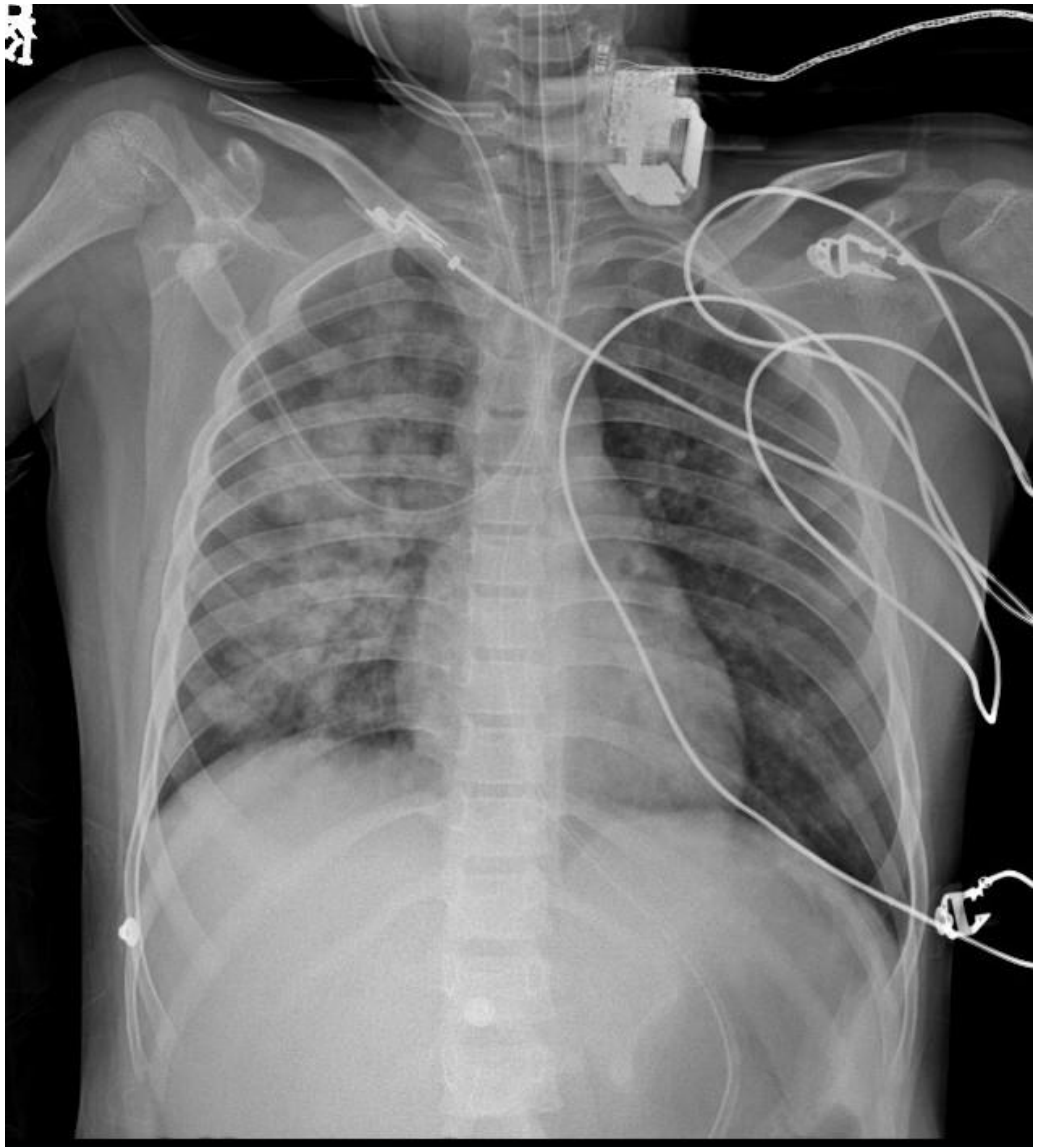
DAY 2

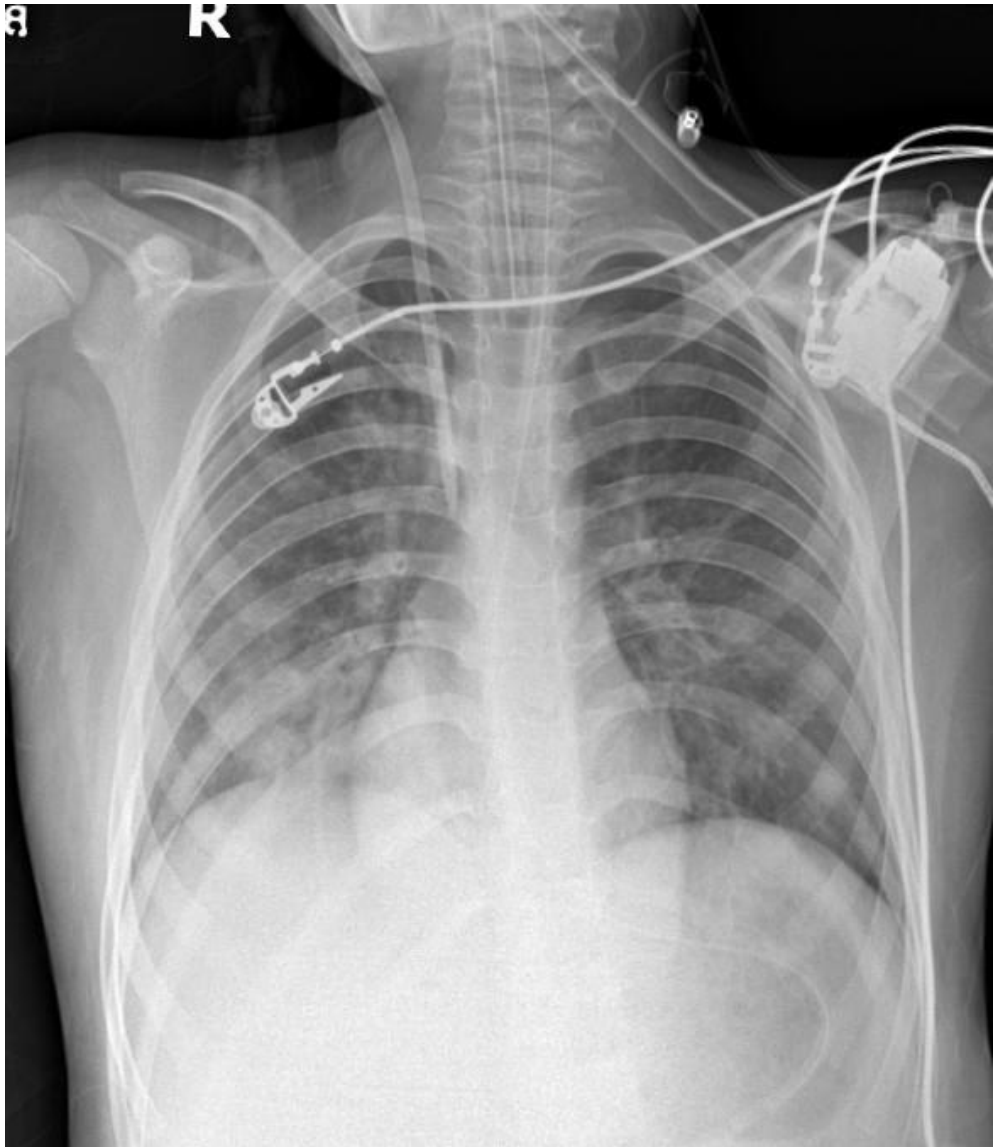
- Child had oliguria and edema
- Albumin transfusion (Sr. Albumin-2.5 g/dl)
- Urea- 88 and Creatinine- 1.05.

- In view of thrombocytopenia and persistent fever
  - Inj Fluconazole and Inj Colistin was started
- Haemodynamics
  - Noradrenaline and vasopressin was started.
  - Hydrocortisone infusion was also started.

Date	29/12	30/12	31/12
Hb	9	11.7	11.6
TLC	12.4	22.3	31.53
Plat	1.80	1.97	0.84
INR	0.95	1.15	
aPTT	28	29	
Urea	**86.9**	**83.3**	**53.6**
Creat	**0.84**	**1.05**	**0.64**
Na	144	148	139
K	4.1	3.6	3.5
Bil	0.33		
SGOT	124.4		
SGPT	38.7		
Alb	2.59	3.54	3.37
CRP	6.15		

CHEST X-RAY DAY 2





Panelist- Dr Kanav Anand

- What kind of renal support thearpy?
- CRRT

DAY 3-5

- IL6- 237, D-Dimer-3429
- Diagnosis-
- **Post COVID 19 Complication-MIS-C (Multiorgan Inflammatory Syndrome in Children) with myocarditis with MODS**
- Inj Methylprednisolone pulse therapy started.(Hydrocortisone stopped)
- IL6-
  - 31/12- 237
  - 01/01-15 (Post Cytosorb)

Date	01/01	02/01	03/01
Hb	12.3	11.4	10.8
TLC	23.16	15.39	8.67
Plat	0.40	0.85	0.80
INR			
aPTT			
Urea	**79.8**	**107**	**135**
Creat	**0.39**	**0.72**	**0.65**
Na	136	141	140
K	4	3.2	3.3
Bil	0.53	0.84	1.13
SGOT	64.6	97.5	
SGPT	34.1	46.1	
Alb	2.71	3.33	3.18
CRP	2.74		

DAY 5-7

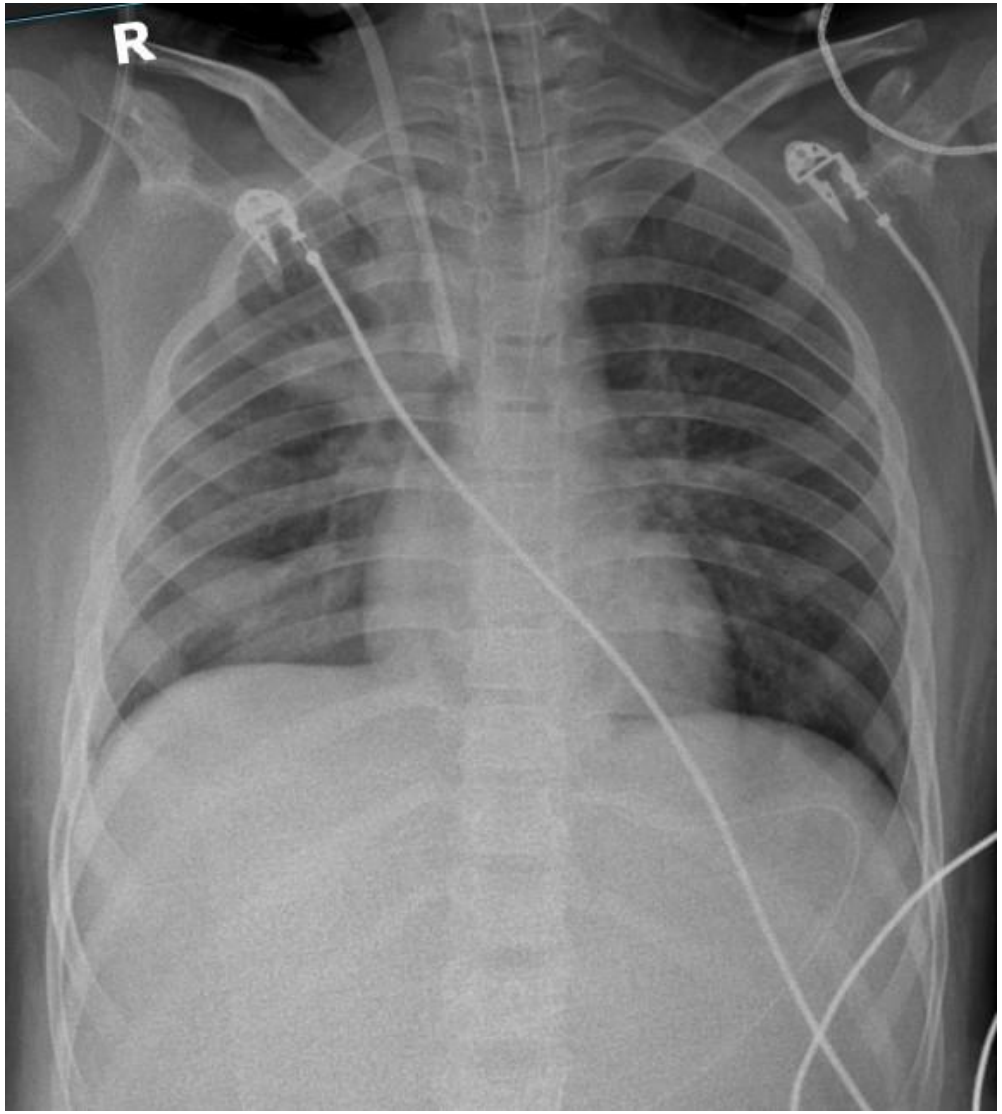
- Hemodynamics
  - Inj Levosimedan was given for 48 hours and Inj Milrinone was stopped.
  - Echo- Ejection fraction improved to 40-50 %
  - Noradrenaline & Vasopressin were tapered and stopped
- Ventilation
  - PEEP- 14 to 7
  - FiO2- 40%
  - ABG- pH-7.44,PaO2-82,PaCO2-45,HCO3-32,Lactate-1.2
- Repeat septic screen- ET culture –NEGATIVE
- Intra Abdominal Hypertension – 40 mm of H20

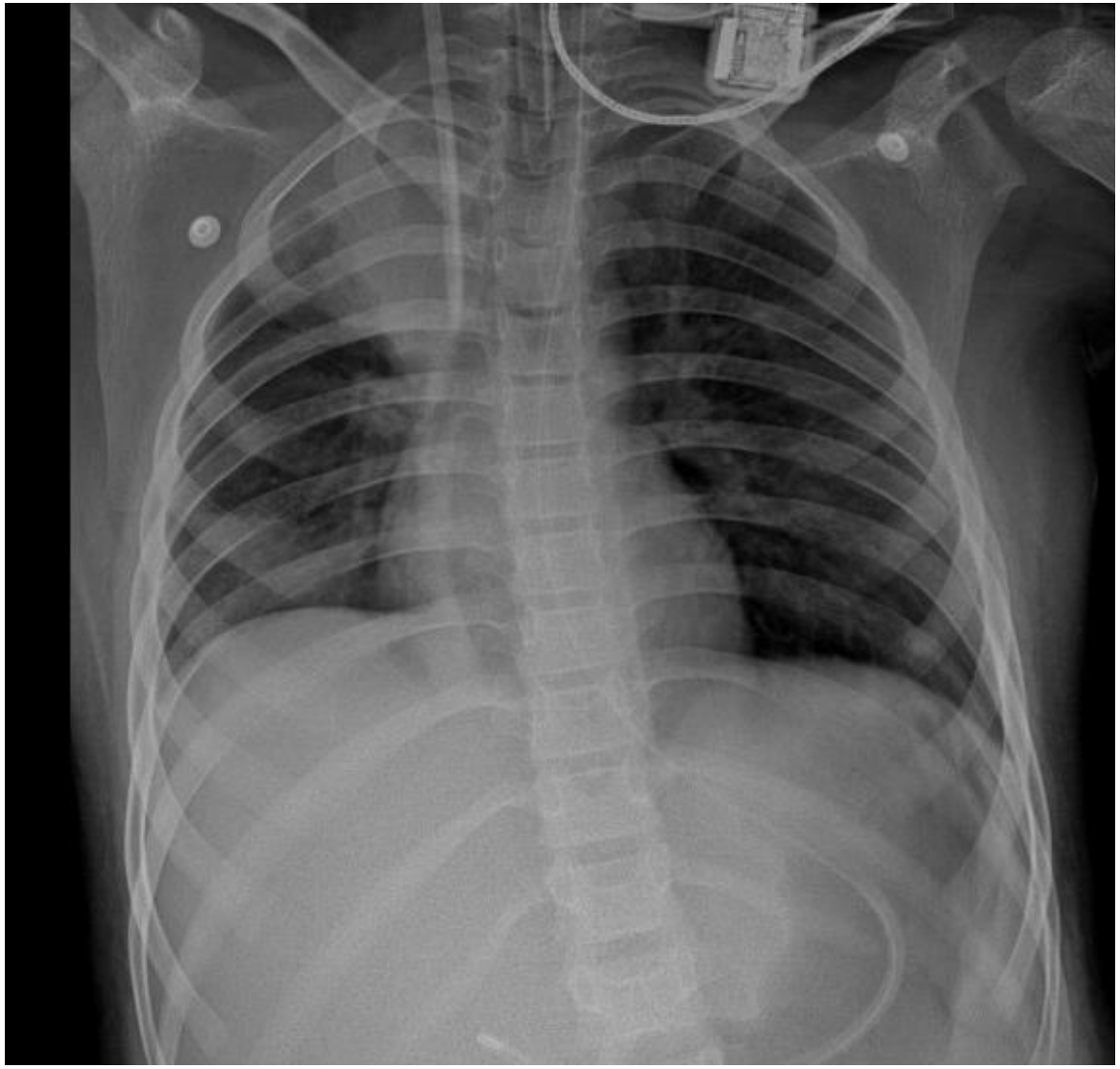
Panelist- Dr Chandrashekar

- Role of PD in intra-abdominal hypertension?

- Peritoneal dialysis
  - Intra abdominal hypertension
  - RRT.

CHEST X-RAY DAY 5-10





DAY 11-13

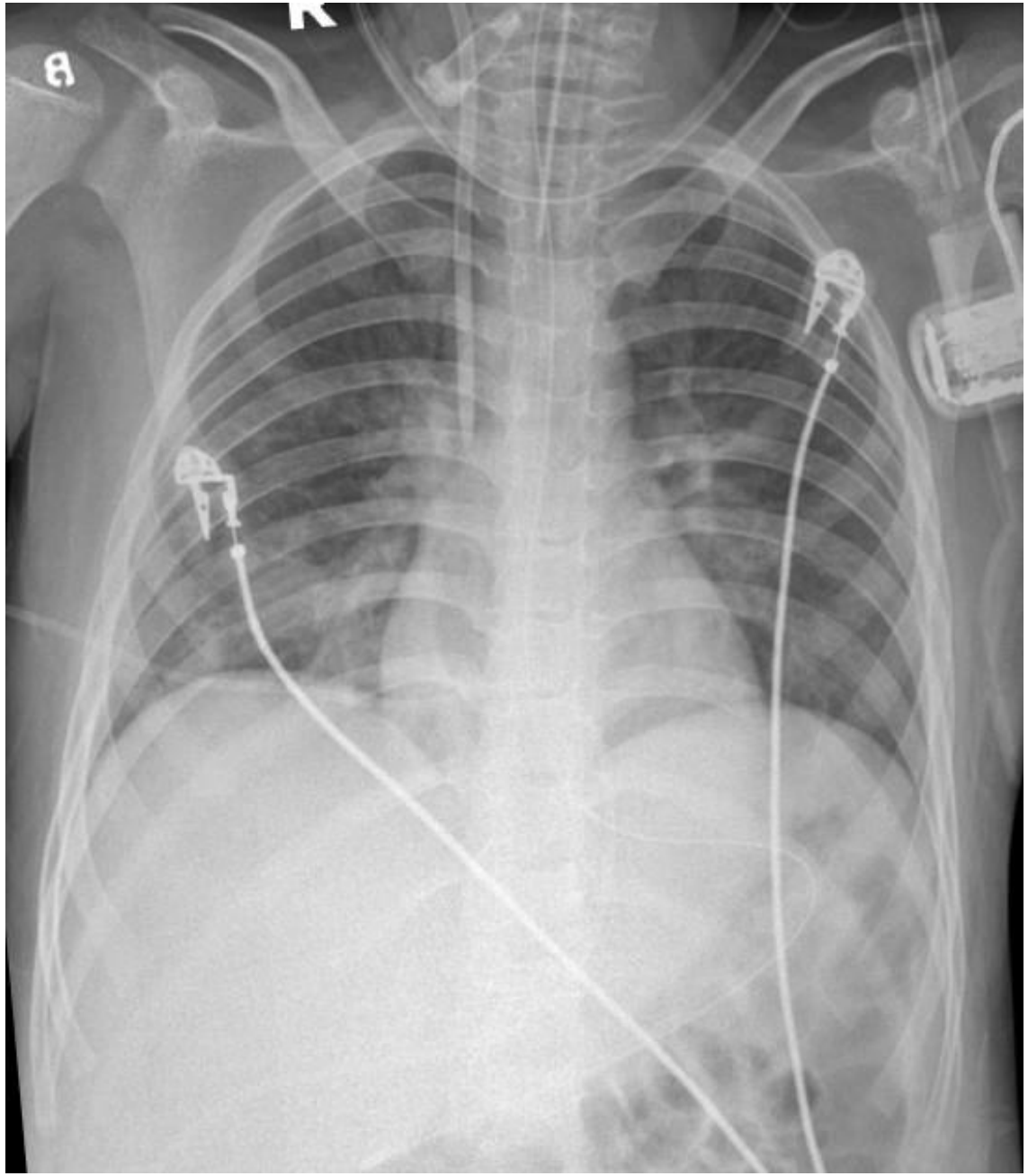
- Spontaneous breathing trial (SBT) was given on day 11,day12 which failed.
- Inotrope- Dobutamine at 5 mcg/kg/min, Echo- EF-50-55%
- MRI Brain was done (pre extubation)
  - Cytotoxic lesion of corpus callosum with mild restricted diffusion involving subcortical white matter of bilateral parieto-occipital region- Post COVID inflammatory response.
- EEG- Intermittent suppression.
- Neurology consult- No active intervention
- Day 13 child tolerated the SBT well.
- ABG- pH-7.41,PaO2-80,PaCO2-40,HCO3-28,Lactate-0.8

Panelist- Dr. Karan Raheja

- What role of SLED?

Date	08/01	09/01	10/01
Hb	10.7	12	10.9
TLC	14.45	13.74	15.15
Plat	1.55	1.73	1.75
INR			
aPTT			
Urea	34.7	43.8	47.3
Creat	0.29	0.34	0.4
Na	135	145	145
K	2.2	3/6	3.9
Bil	1.41	1.2	
SGOT	76.5	71.8	
SGPT	151	137	
Alb	3.41	3.11	2.96
CRP			

CHEST X-RAY (PRE EXTUBATION)



DAY 14-16

- BiPap were also tapered and stopped and child was shifted to wards for completion of therapy.
- Review Echo prior to discharge was normal.

Take home message

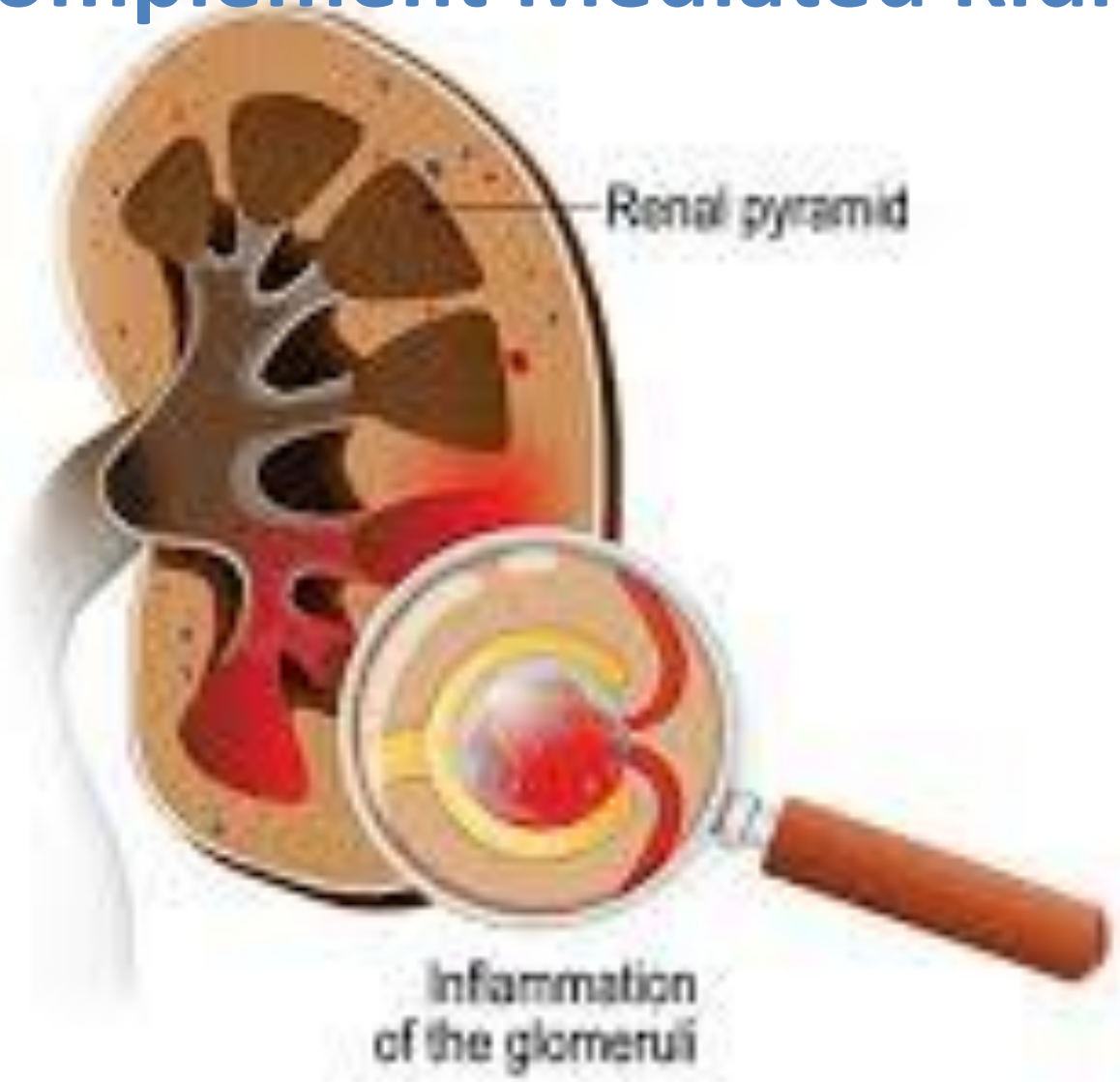
- Optimize modalities as per clinical scenario
- Important to know when to start and stop kidney support therapy
- Proper prescription charting and monitoring is essential

Take Home Message

- Early recognition of AKI.
- Different modalities you can choose from.
- Limitations and advantage of every dialysis.

Thank you

Complement Mediated Kidney Diseases



IPNA

CASE 1

Dr. Mahesh Kiran
Clinical Director, Nephrologist
& Transplant Physician
KIMS, IKON Hospital
Vishakhapatnam

6-year-old male child

- Facial puffiness and bilateral lower limb edema - 5 days
- Passage of cola-coloured urine and decreased urine output - 5 days
- Headache - 5 days
- No history of seizures, blurring of vision, difficulty in breathing
- History of preceding pyoderma over bilateral lower limbs - 4 weeks back

Examination

- Mild pallor
- Hypertension : BP 128/90 mm Hg
- Urine examination : urine protein 2+,
- M/E: plenty of RBCs
- Urine protein: creatinine ratio = 0.4 (normal <0.2 mg/mg

What is the probable diagnosis ?

Investigations

Laboratory parameters	Observed	Normal values
Hemoglobin(g/dl)	10.2	> 12.5 g/dl
Total leukocyte count	7300	4000-11000/mm^3
Platelet count (lacs)	1.8	1.5-4.5 lacs
Blood urea(mg/dl)	68	15-40 mg/dl
Se. Creatinine(mg/dl)	1.0	0.3-0.6mg/dl
Se. Albumin (mg/dl)	3.5	> 3 g/dl
Se cholesterol Anti-nuclear antibody Anti ds-DNA antibody C3 C4 Anti streptolysin O antibody titre	180 10 15 54 32 350	<200 mg/dl <25 IU/ml <20 IU/ml 75-180 mg/dl 10-40 mg/dl < 200 IU/ml

What is the line of management ?

How will you follow up this case?

CASE 2

Dr. Vikram Kalra
Director,
Akash Healthcare Super speciality Hospital, Dwarka
New Delhi

9-year-old female child

- Facial puffiness and decreased urine output for 10 days
- Pain in both knee joints and mild arthritis
- History of photosensitivity and oral ulcers are present
- Moderate Pallor, hypertension- BP 130/88mm Hg (between 90-95th centile)
- Urine examination showed proteinuria++ and hematuria (RBCs 8-12/hpf)

Diagnosis & Investigations

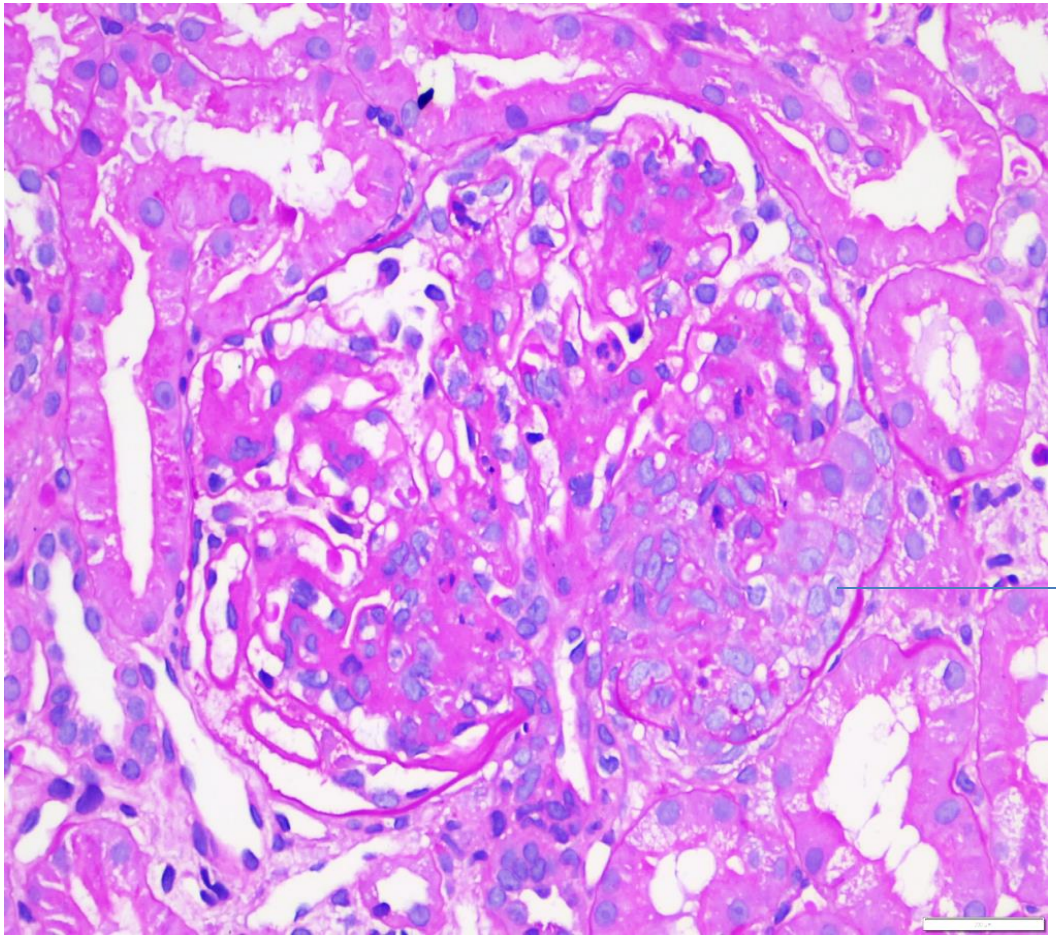
- What is the likely diagnosis?
- What investigations are required to confirm the diagnosis

Investigations

Laboratory parameters	Observed	Normal values
Hemoglobin(g/dl)	8.4	> 12.5 g/dl
Total leukocyte count	6800	4000-11000/mm^3
Platelet count	2.3	1.5-4.5 lacs
Blood urea	68	15-40 (mg/dl)
Se. Creatinine	0.9	0.3-0.6(mg/dl)
Se. Albumin	3.6	> 3 g/dl
Se cholesterol **Anti-nuclear antibody** **Anti ds-DNA antibody** **C3** **C4** **Anti streptolysin O (ASO) antibody titre**	180 150 250 4 8 **150 IU/ml**	<200 mg/dl <25 IU/ml <20 IU/ml 75-180 mg/dl 10-40 mg/dl < 200IU/ml

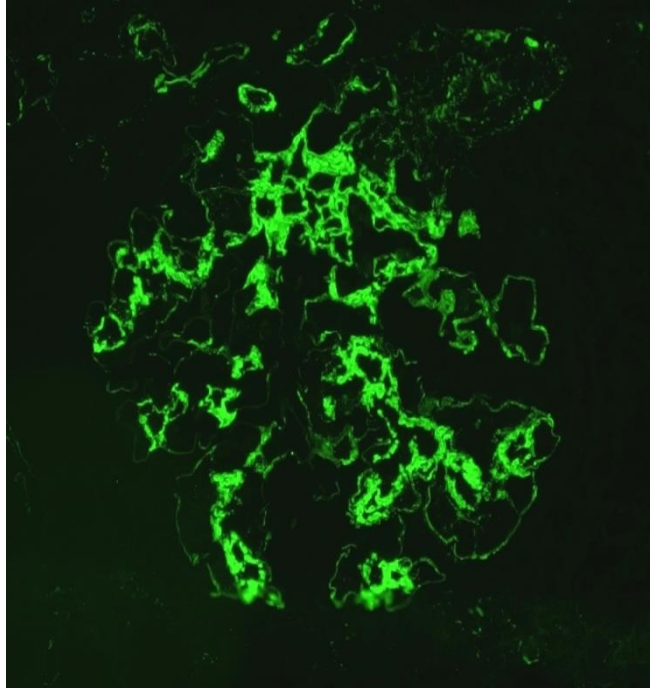
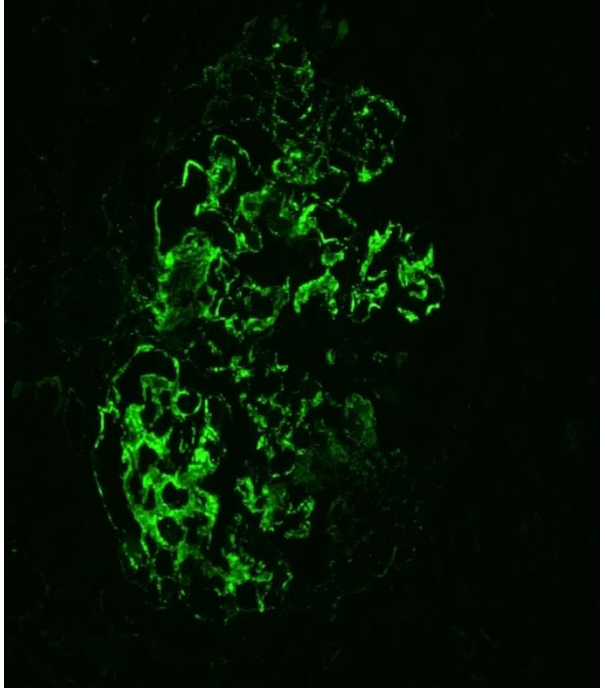
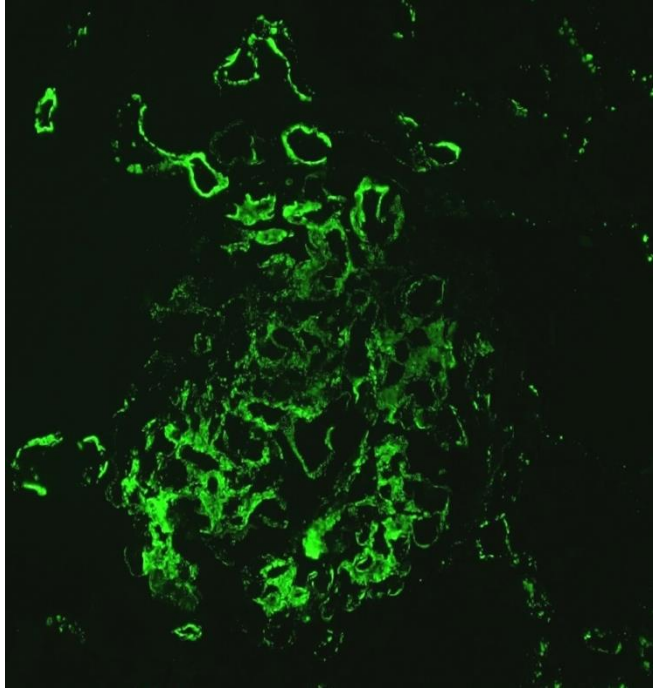
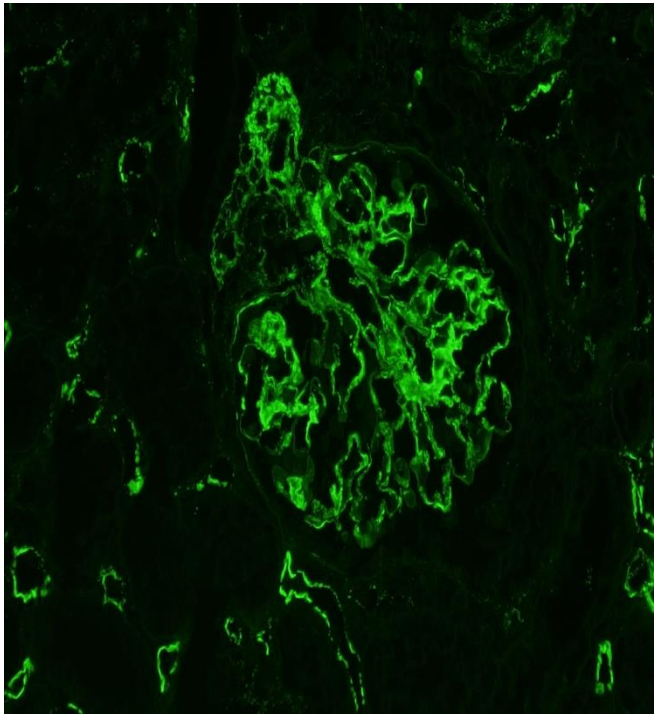
What other investigations are required ?

- Kidney biopsy



Light microscopy 40x
Fibrous crescents
Wire loop lesion

Courtesy: Prof. Vineeta V Batra, New Delhi

Immunofluorescence staining of glomeruli in 20x magnification : IgA, C3, C1q and IgG full house deposits of immune complexes

Courtesy: Prof. Vineeta V Batra, New Delhi

What would be management of this case?

- Salt restricted diet, ACE inhibitors
- Hydroxychloroquine (HCQs)

Induction therapy

- IV Methylprednisolone (500mg/m2,maximum 1g for 3-5 doses
- Thereafter, switched to prednisolone (1-2 mg/kg/d), maximum 60 mg

Induction phase

- IV Cyclophosphamide(500mg/m2) monthly for 6 months
- After 8 weeks ,dose of prednisolone is gradually reduced

Maintenance therapy

- Mycophenolate mofetil (MMF)1000 mg/m2 daily in 2 divided doses
- Alternate doses of low dose prednisolone

CASE 3

Prof. Rajiv Sinha
Department of Pediatrics
Institute of Child Health
Kolkata

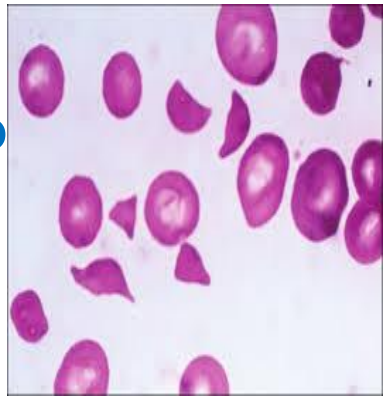
13-years-old female

- Fever for 5 days
- Pain abdomen for 5 days
- Decreased urine output for 3 days.
- No history of preceding diarrhoea, dysentery, rash over face, oral ulcers, joint pain, bleeding from any site, blurring of vision and headache.
- Examination: Pallor, Petechiae and Edema were present

Investigations

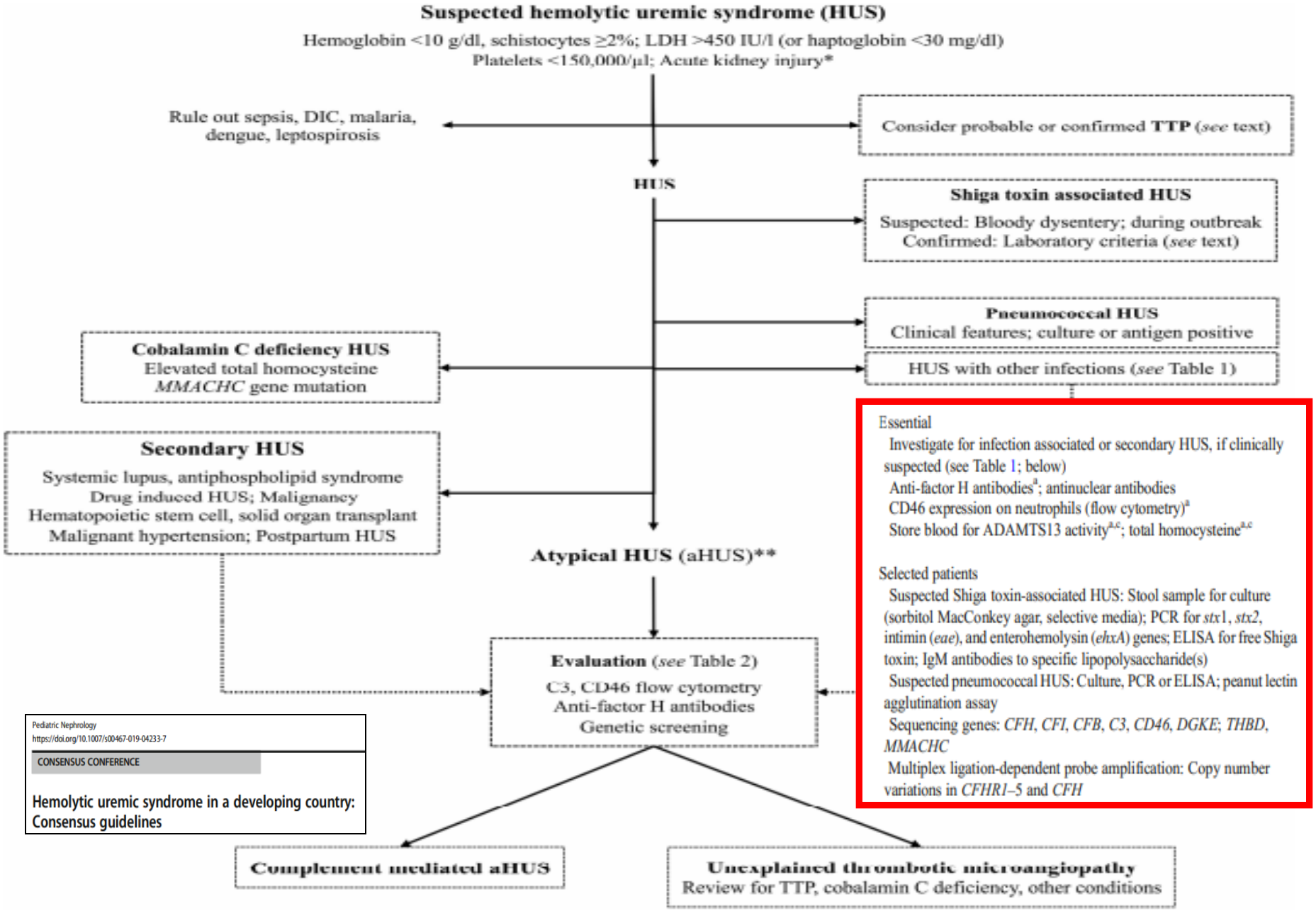
Laboratory parameters	Observed	Normal values
Hemoglobin(g/dL)	7.4	> 12.5 g/dl
Total leukocyte count	9300	4000-11000/mm^3
Platelet count	1.06	1.5-4.5 lacs
Blood urea	256	15-40 (mg/dl)
Se. Creatinine	19.2	0.3-0.6(mg/dl)
Se. Albumin	3.6	> 3 g/dl
Se cholesterol Anti-nuclear antibody Anti ds-DNA antibody C3 C4 Anti streptolysin O (ASO) antibody titre	180 10 11 76 34 22	<200 mg/dl <25 IU/ml <20 IU/ml 75-180 mg/dl 10-40 mg/dl < 200IU/ml

What other investigations required?



- **Peripheral blood smear**
  Dimorphic anaemia with features of haemolytic anaemia (Schistocytes -3%) with
- **Platelets count** : 78,000/mm3
- **Reticulocyte count**-6 %
- **LDH-**2087 IU/L, **CRP**-4.7 mg/dL
- **Dengue serology** (NS1Ag and Ig M)-Negative,
- **Para check for MP-** negative, **Scrub typhus** IgM-negative

Other specific tests required to confirm the etiology ?



What would be management of this child?

Pediatric Nephrology
https://doi.org/10.1007/s00467-019-04233-7

CONSENSUS CONFERENCE

Hemolytic uremic syndrome in a developing country: Consensus guidelines

Guideline 7: Therapy of Shiga toxin-associated HUS

7.1 We recommend maintaining hydration by early use of isotonic fluids in patients with dysentery, starting from onset of bloody diarrhea to the day of onset of HUS, and monitoring for fluid overload in patients with renal failure. [**1B**]

7.2 We recommend therapy with appropriate antibiotics for bloody diarrhea. [**1A**]

7.3 While we do not suggest the use of PEX in patients with Shiga toxin-associated HUS, therapy may be considered for patients with severe neurological or cardiac involvement. [**2D**]

7.4 We do not recommend the use of plasma infusions, heparin, urokinase, dipyridamole, antimotility agents, glucocorticoids, and Shiga toxin binders. [**1B**]

Guideline 8: Managing atypical HUS without anti-FH antibodies

8.1 In the absence of eculizumab, we recommend prompt initiation of PEX in patients with aHUS. For initial therapy, we recommend that PEX be preferred to plasma infusions. [**1C**]

8.2 We suggest that PEX be administered daily until hematological remission and then tapered over 4–6 weeks (Table 3). [**2D**]

8.3 Patients on plasma therapy should be monitored for plasma or filter reactions, complications of catheter insertion, infection or thrombosis, and blood-borne infections. [**1C**]

8.4 We recommend efforts to enable therapy with eculizumab in the following: (i) lack of remission despite 7–10 days of PEX, (ii) life-threatening features (seizures, cardiac dysfunction), (iii) complications due to PEX or vascular access, and (iv) inherited defect in complement regulation. [**1C**]

Guideline 9: Managing anti-FH antibody-associated HUS (Fig. 2)

9.1 We recommend a combination of prompt PEX (with fresh frozen plasma as replacement fluid) and immunosuppressive therapy for patients with anti-FH antibodies (Fig. 2). [**1B**]

9.2 We do not recommend use of immunosuppressive medications without confirming the presence of anti-FH antibodies. [**1D**]

9.3 We suggest daily PEX until hematological remission and then taper over 3–5 weeks. We do not recommend plasma infusions as a substitute for PEX. [**2D**]

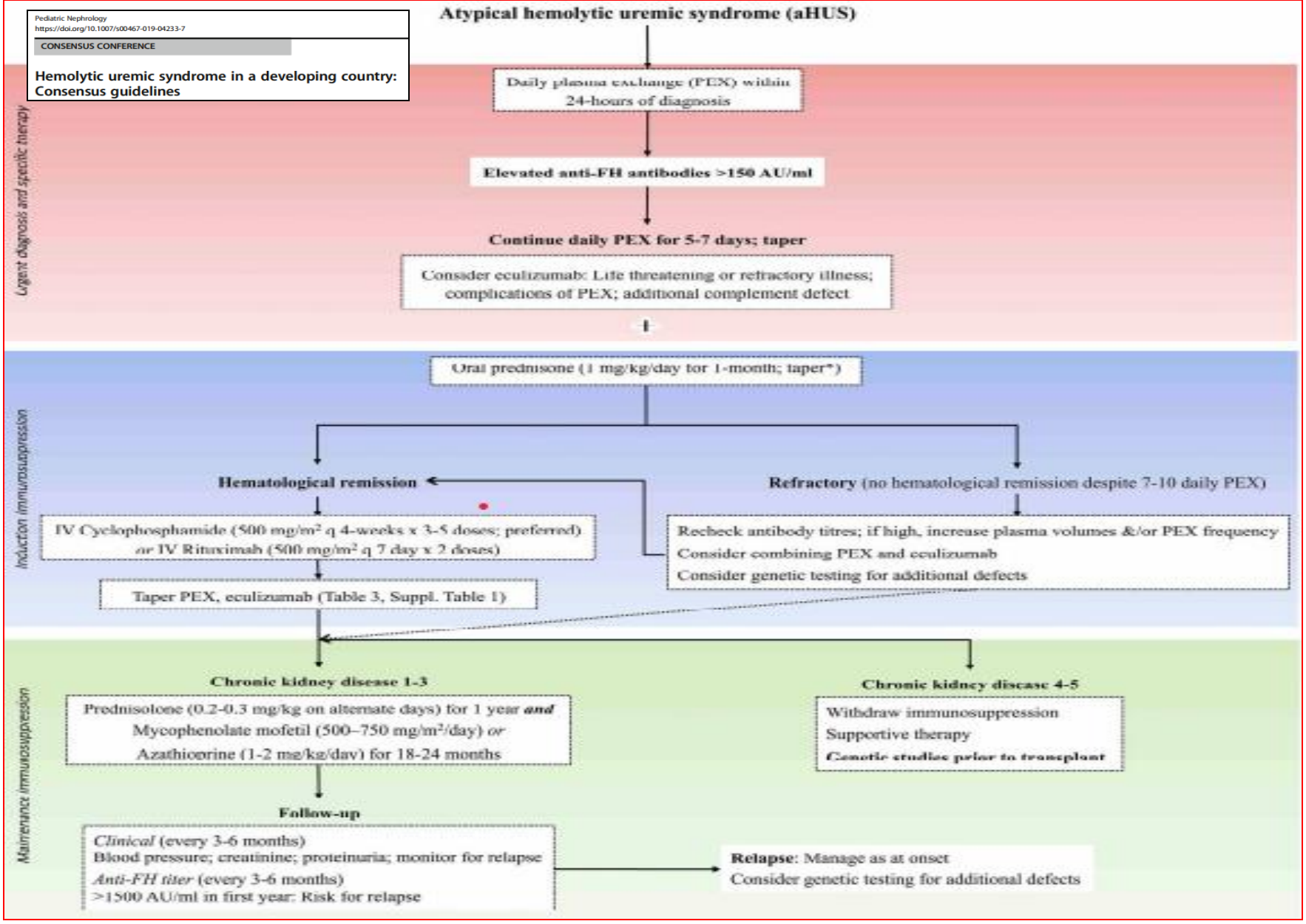
9.4 Since high anti-FH levels might predict a relapse, we recommend monitoring antibody titers frequently during the first 12–24 months. [**1C**]

9.5 We suggest therapy with eculizumab in the following: *(*i) lack of remission despite 7–10 PEX; (ii) life-threatening features (seizures, cardiac dysfunction); (iii) complications due to PEX or vascular access; and (iv) inherited defect in complement regulation. [**2C**]

What would be management of this child?

Pediatric Nephrology
https://doi.org/10.1007/s00467-019-04233-7
CONSENSUS CONFERENCE

Hemolytic uremic syndrome in a developing country: Consensus guidelines



CASE 4

Dr. Abhinav Prashanth
Consultant, Department
of Nephrology
Ayushman Hospital and Health
Services, Dwarka,
New Delhi.

15-years-old Male

- Generalized swelling for 3 months –insidious in onset gradually progressive started around eyes and involved abdomen and lower limbs.
- Single episode of abnormal body movement with unrolling of eyes - 15 days back
- Decreased urine output- 2 days
- Difficulty breathing- 2 days
- No history of cola-coloured urine
- No similar episode in past

Physical examination

- Pallor
- Facial puffiness, bilateral pedal edema and ascites
- Hypertension 150/99 mmHg (BP > 99TH percentile)
- Decreased urine output < 0.5ml/kg/hr
- Urine dipstick showed proteinuria 2+ , Upr/cr 3.5 mg/mg
- Urine microscopy- RBCs 5-6 /hpf

Investigations

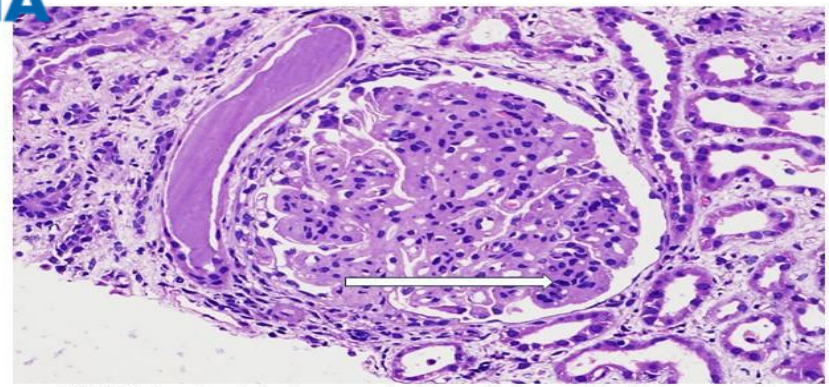
Laboratory parameters	Observed	Normal values
Hemoglobin(g/dl)	10.2	> 12.5 g/dl
Total leukocyte count	7300	4000-11000 /mm^3
Platelet count lacs	1.8 lacs	1.5-4.5 Lacs/mm3
Blood urea(mg/dl)	128 mg/dl	15-40 mg/dL
Serum Creatinine(mg/dl) Na K	3.77 mg/dl 128 mq/L 5.2 mq/L	0.3-0.6 mg/dL 130-150 meq/L 3.5-4.5 meq/L
Serum Albumin (mg/dl)	1.81 mg/dl	> 3 g/dl
Serum cholesterol Anti-nuclear antibody Anti ds-DNA antibody C3 C4 Anti streptolysin O ASO antibody titre	180 10 15 11 32 43	<200 mg/dl <25 IU/ml <20 IU/ml 75-180 mg/dl 10-40 mg/dl < 200IU/ml

Confirmation of Diagnosis

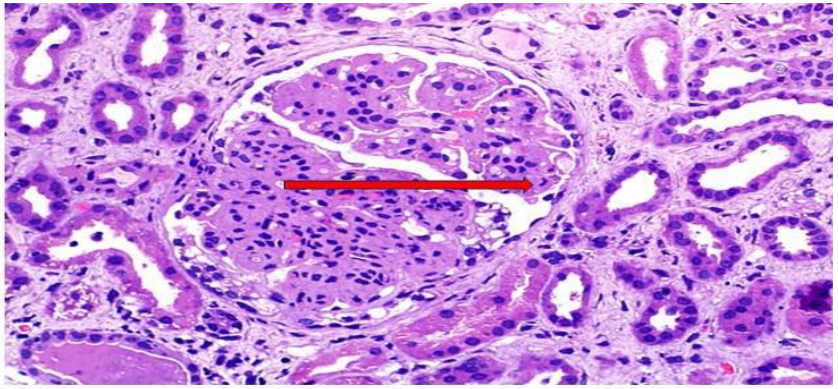
- What is the differential diagnosis
  -Nephritic syndrome

- What should be done to confirm the diagnosis?
  -Blood tests
  -Kidney biopsy

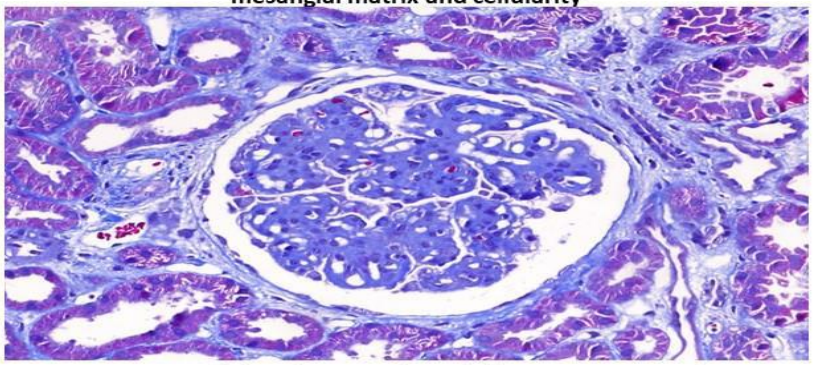
Kidney Biopsy Findings



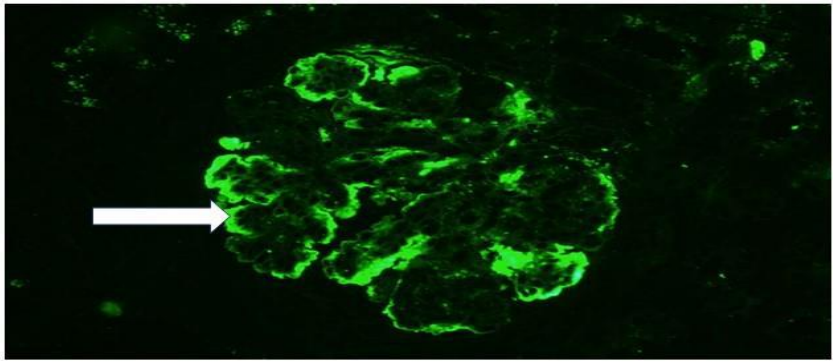
HE 20X showing lobular accentuation of glomeruli with increased mesangial matrix and cellularity



HE 20X showing enlarged glomeruli with partial crescents



40 – 50% chronic parenchymal damage on MT stain



IF showing C3 deposits (2-3+) along the peripheral capillary wall

Light microscopy: - Glomerular sclerosis (≈60%)

Immunoflorescence: - C3 deposits along the glomerular capillary wall (2+ to 3+). No deposits of IgA, IgG, IgM and C1q.

Electron Microscopy: - Focal but extensive effacement of foot process of podocytes and granular electron dense deposits in sub-epithelial, intra-membranous and mesangium

Courtesy: Prof. Vineeta V Batra, New Delhi

Final Diagnosis

- **What is the diagnosis based on biopsy findings**

  C 3 Glomerulopathy - Dense deposit disease

- **Outline the management of this case**

  - Supportive

  - Immunosuppressive therapy

Dense Deposit disease

- Rare, more common in younger population
- Variable presentation
- Association - retinal drusen, acquired partial lipodystrophy
- Management
- Supportive

  - Salt restriction.
  - Protein restriction
  - ACEi / ARB
  - B P control
  - Lipid control

Immunosuppression

- MMF plus prednisolone x 6 months
- With RPRF - Cyclophosphamide plus Prednisolone
- No response with the above treatment - Eculizumab
- PEX with FFP - removes antibodies and replaces factor H
- Kidney Tx - high incidence of recurrence

Thank you

Growing tall with Kidney disease

IPNA

SLOW CAR

Speed limit

Poor visibility - fog

No petrol

Bad driver

Poor road

Bad tyres

Over next 20 minutes

- Basics of growth assessment
- 2 cases – and evidence based management
- Sum up and learning pearls

Growth assessment

- Barometer of well being in a given child.
- Important pillar of preventive care.

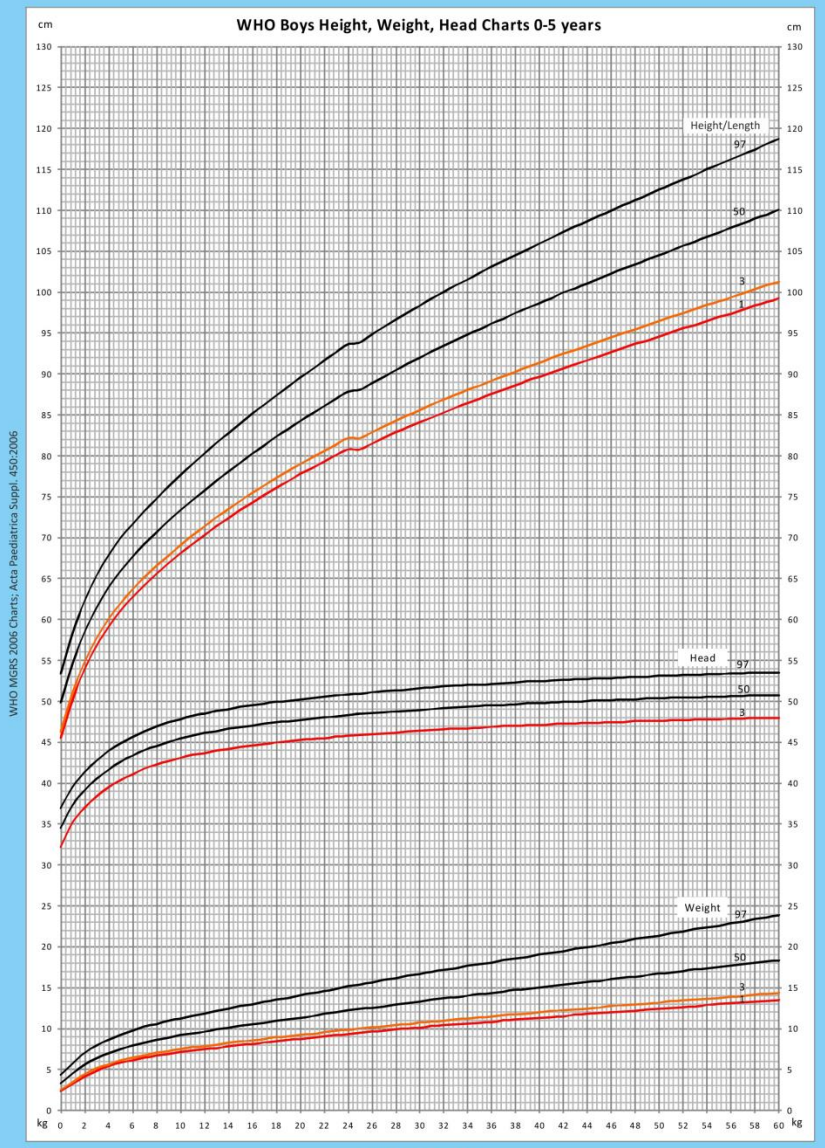
Growth monitoring in CKD children

	<1 year	1-2 years	>2 years
Weight	Q1-2m	Q3	Q3
Height	Q2m	Q3	A3
Head circumference	Q2m	Q3	A3
BMI			Annually
SMR			Annually >12y

0 to 5 Years : WHO Boys Length/Height, Weight and Head Circumference Charts

Name : _____

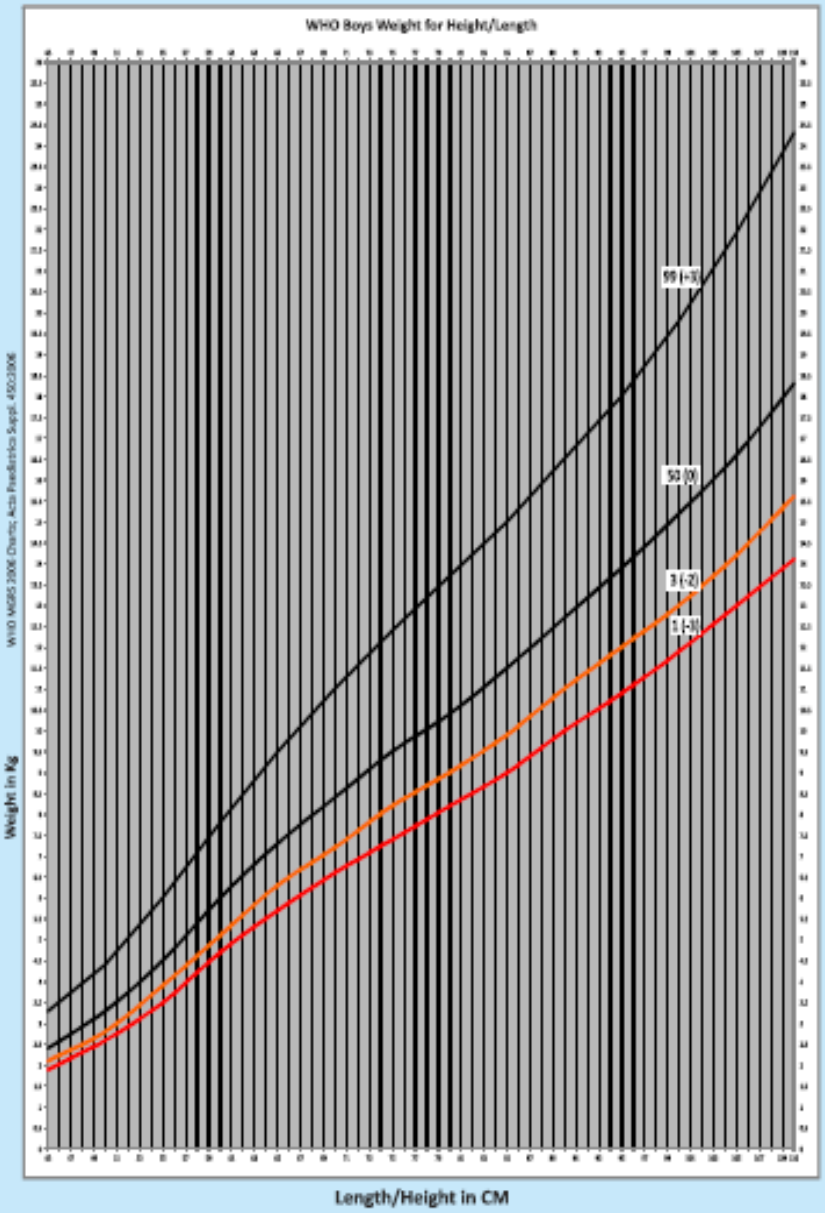
DOB : _____



WHO Boys Weight for Height/Length Charts
(Z Scores are in Parenthesis)

Name : _____

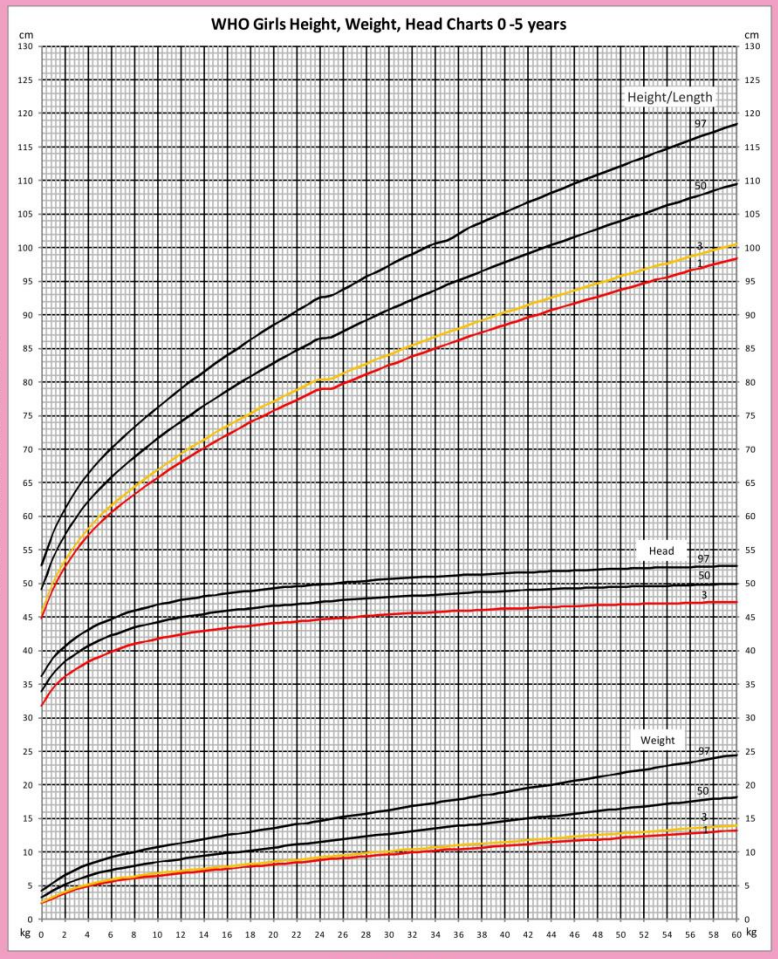
DOB : _____



0 to 5 Years : WHO Girls Length/Height, Weight and Head Circumference Charts

Name : _____

DOB : _____

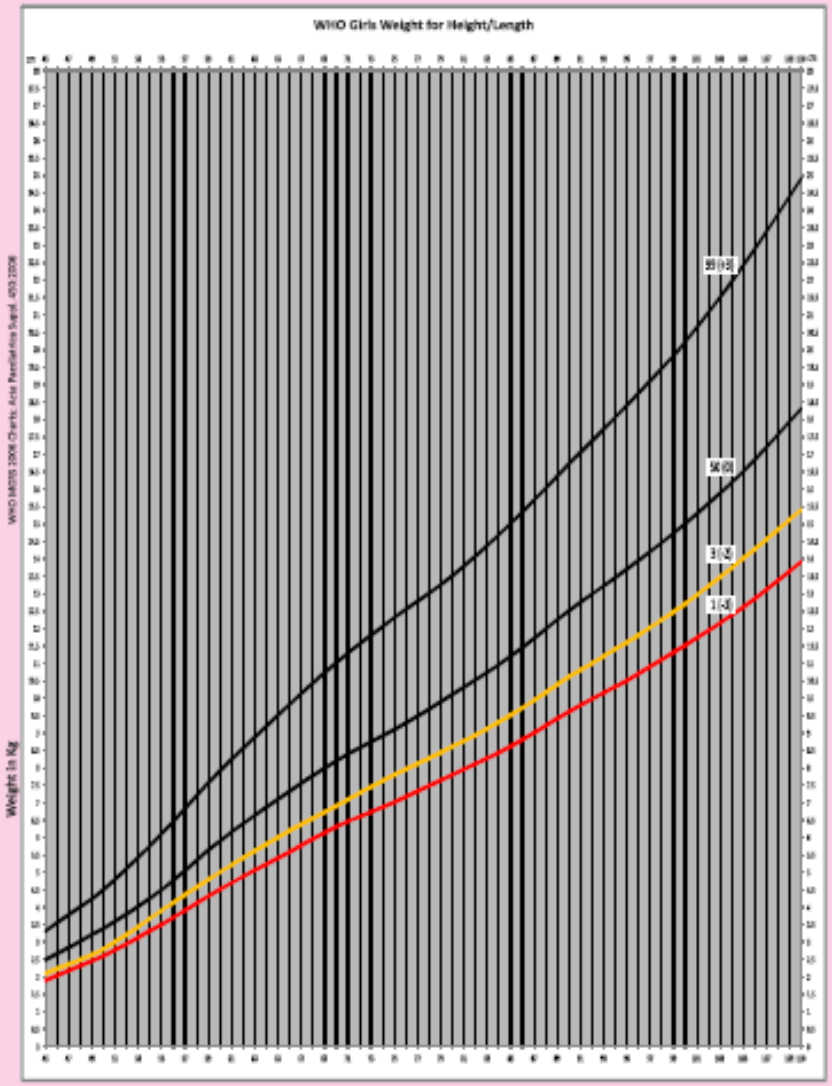


WHO Girls Weight for Height/Length Charts

(Z Scores are in Parenthesis)

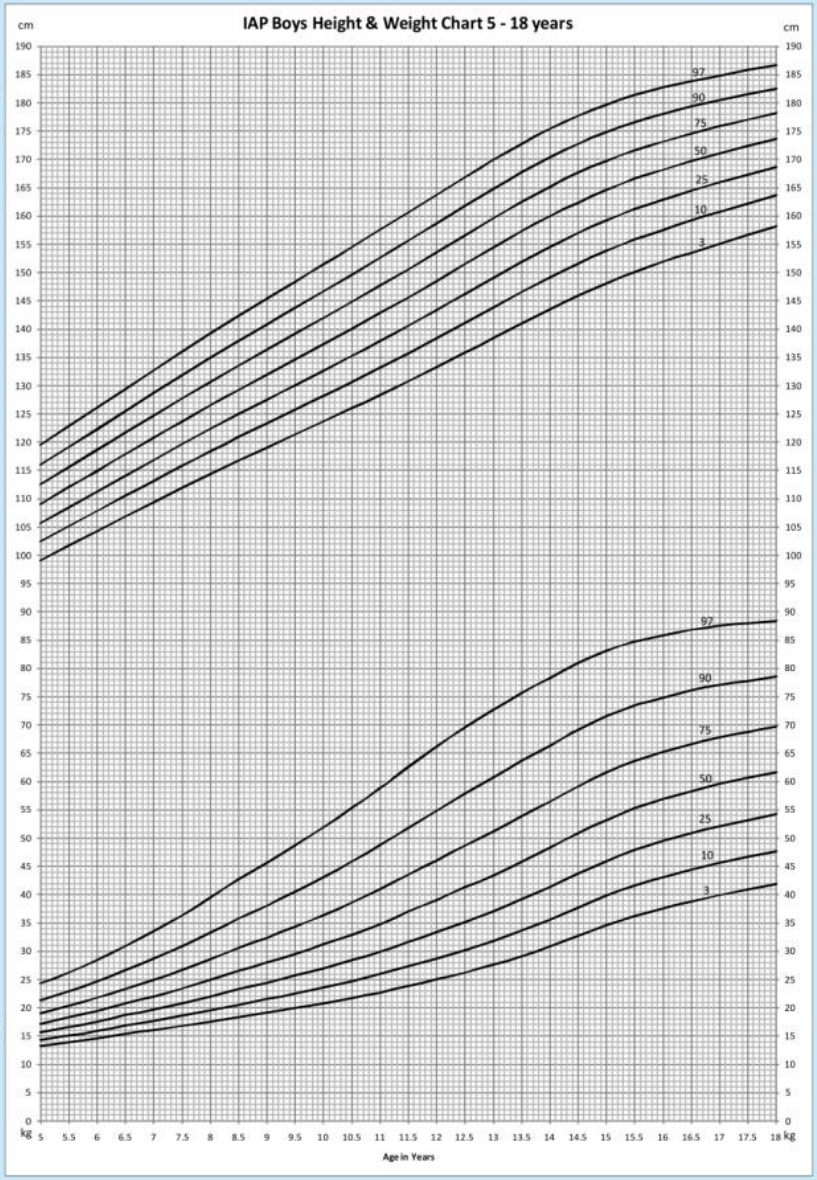
Name : _____

DOB : _____



5 to 18 Years : IAP Boys Height and Weight Charts

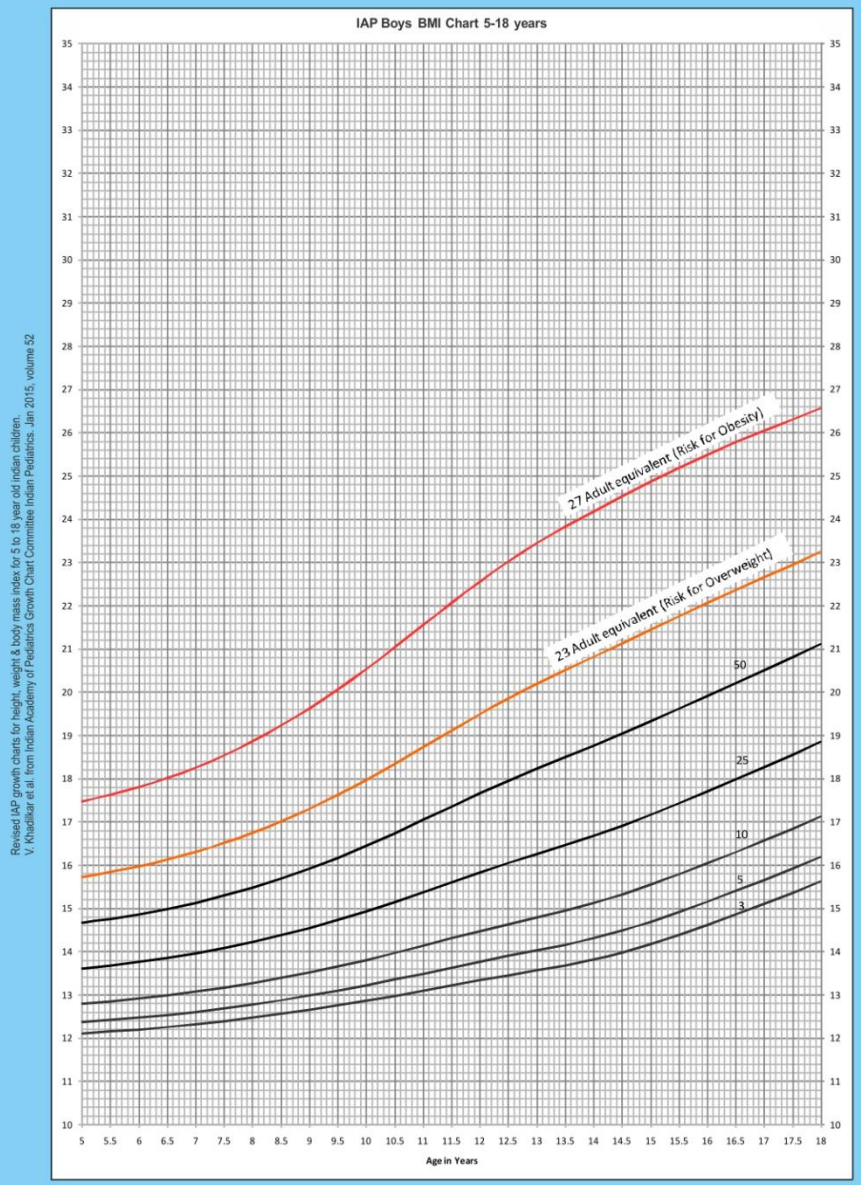
Father's Height _____, Mother's Height_____, Target Height_____



5 to 18 Years : IAP Boys Body Mass Index Charts

Name _____

DOB _____

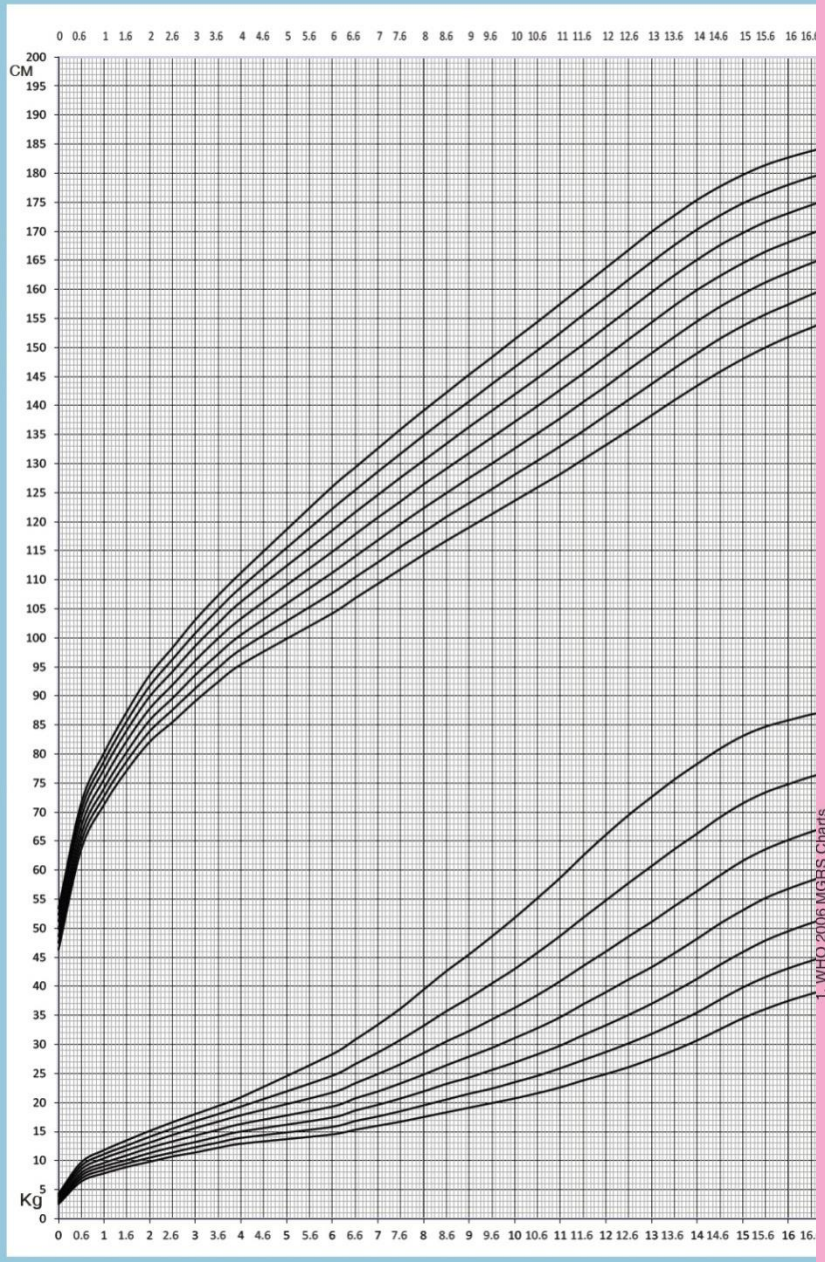


0 to 18 Years: Boys

WHO 2006 & IAP 2015 Combined Height & Weight Charts

NAME _____

DOB _____



AGE (Years)

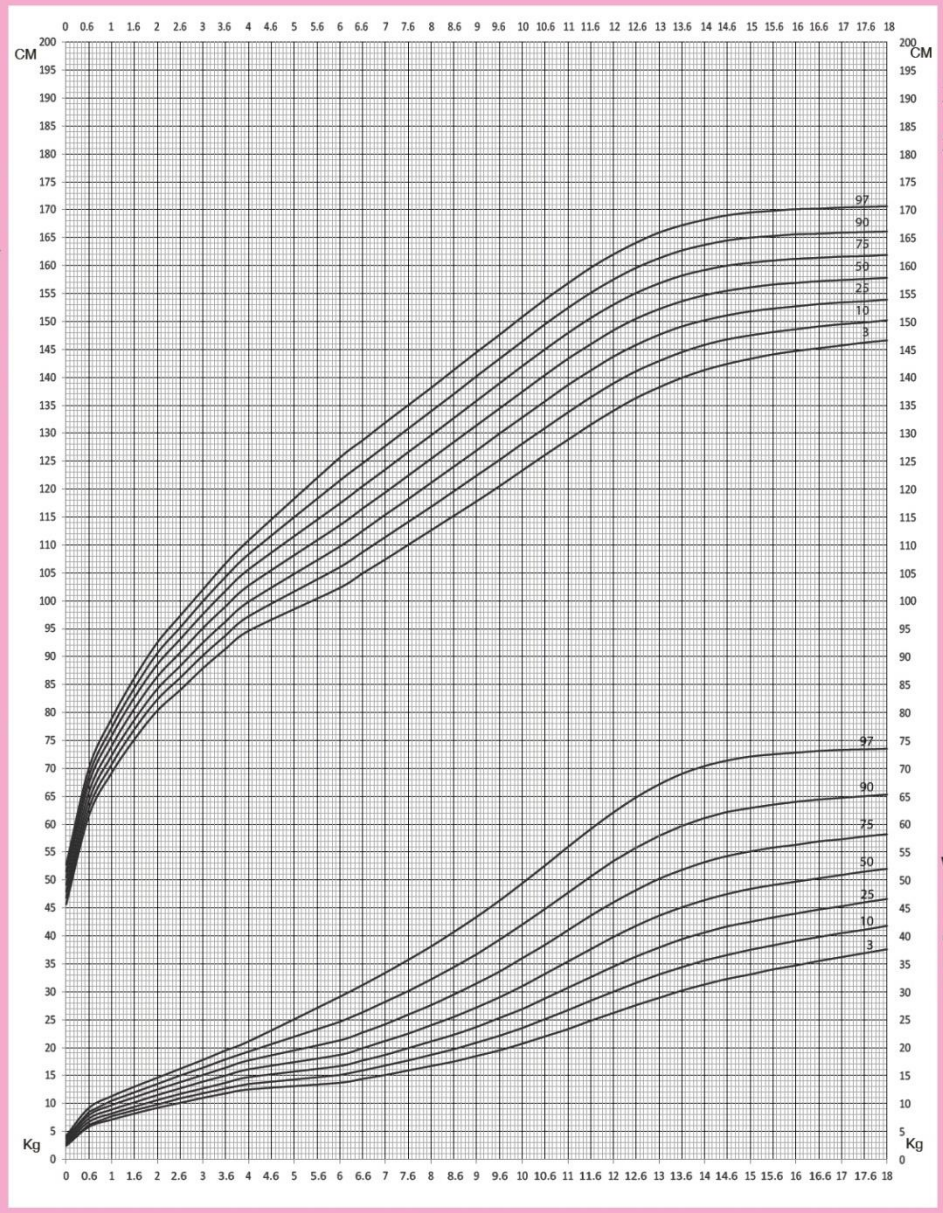
1. WHO 2006 MGRS Charts
2. Revised IAP Growth Charts for Height, Weight and Body Mass Index for 5 to 18 year old Indian Children
V.Khadilkar et al; from Indian Academy of Pediatrics. Growth Chart Committee. Indian Pediatrics. Jan 2015, Volume 52

0 to 18 Years: Girls

WHO 2006 & IAP 2015 Combined Height & Weight Charts

NAME _____

DOB _____



STATURE

WEIGHT

AGE (Years)

1. WHO 2006 MGRS Charts
2. Revised IAP Growth Charts for Height, Weight and Body Mass Index for 5 to 18 year old Indian Children
V.Khadilkar et al; from Indian Academy of Pediatrics. Growth Chart Committee. Indian Pediatrics. Jan 2015, Volume 52

Where to plot

- Please enter the name and DOB
- Single page – assesses – Height/ length, weight and head circumference
- Back side – Weight for height
- ONLY 4 LINES (4 percentiles) – for convenience
- Expressed both percentile and Z score
- Vertically – 1 dark line – 15 days
- Vertically – 1 light line – 1 week
- Horizontally – 1 line represents 1 cm or 1 kg

CASE

3 year old boy

Length = 95 cm

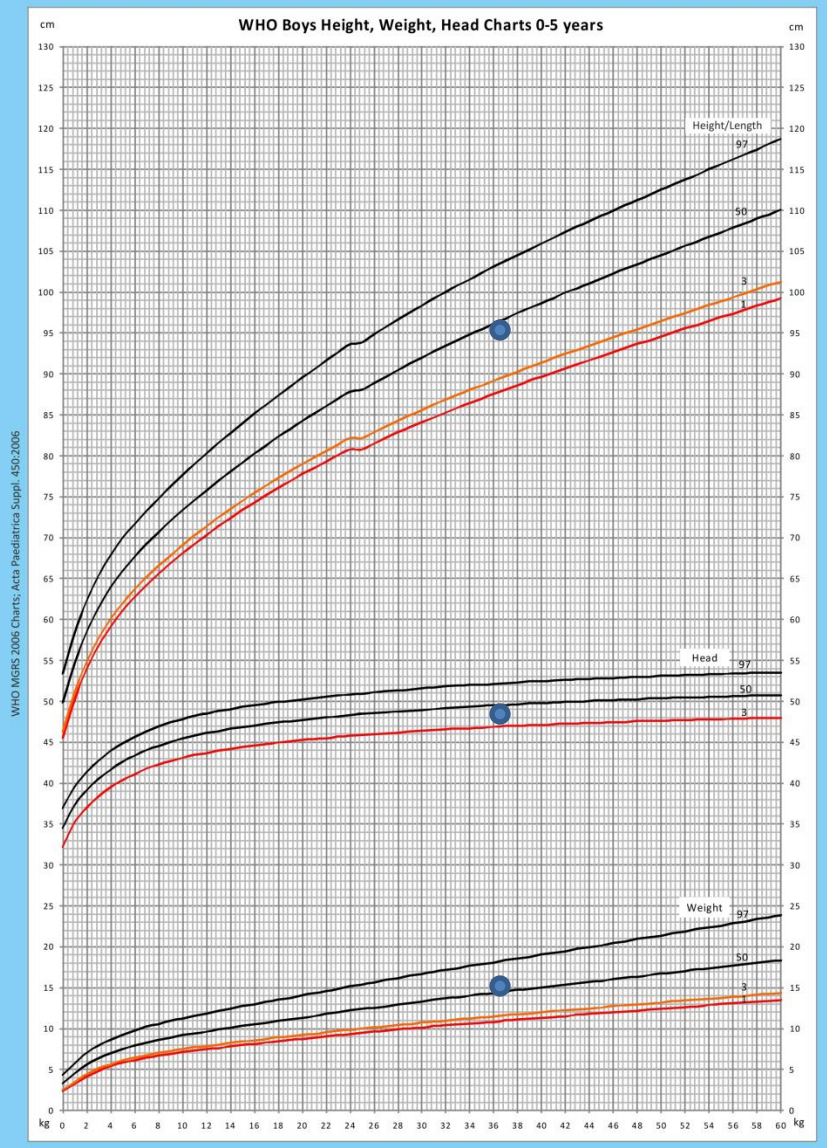
Weight = 15 kg

Head circumference = 48 cm

0 to 5 Years : WHO Boys Length/Height, Weight and Head Circumference Charts

Name : _____

DOB : _____

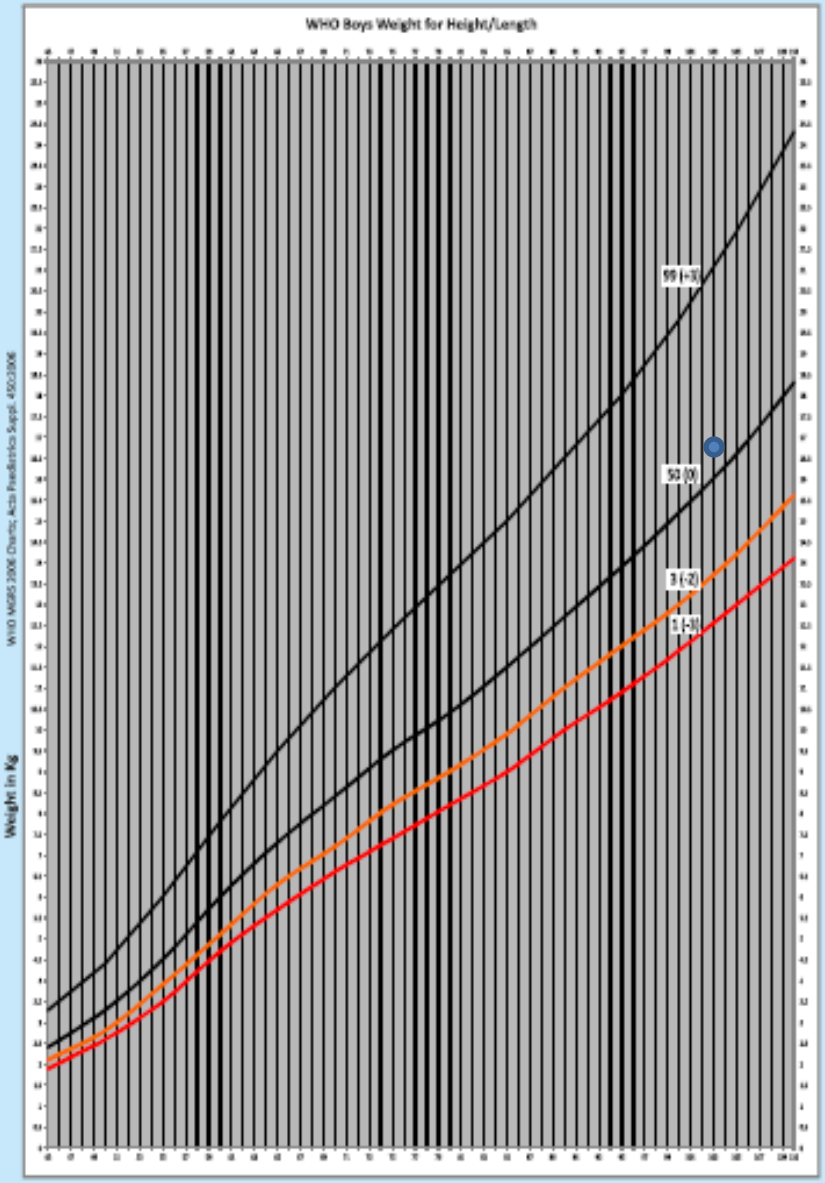


WHO Boys Weight for Height/Length Charts

(Z Scores are in Parenthesis)

Name : _____

DOB : _____



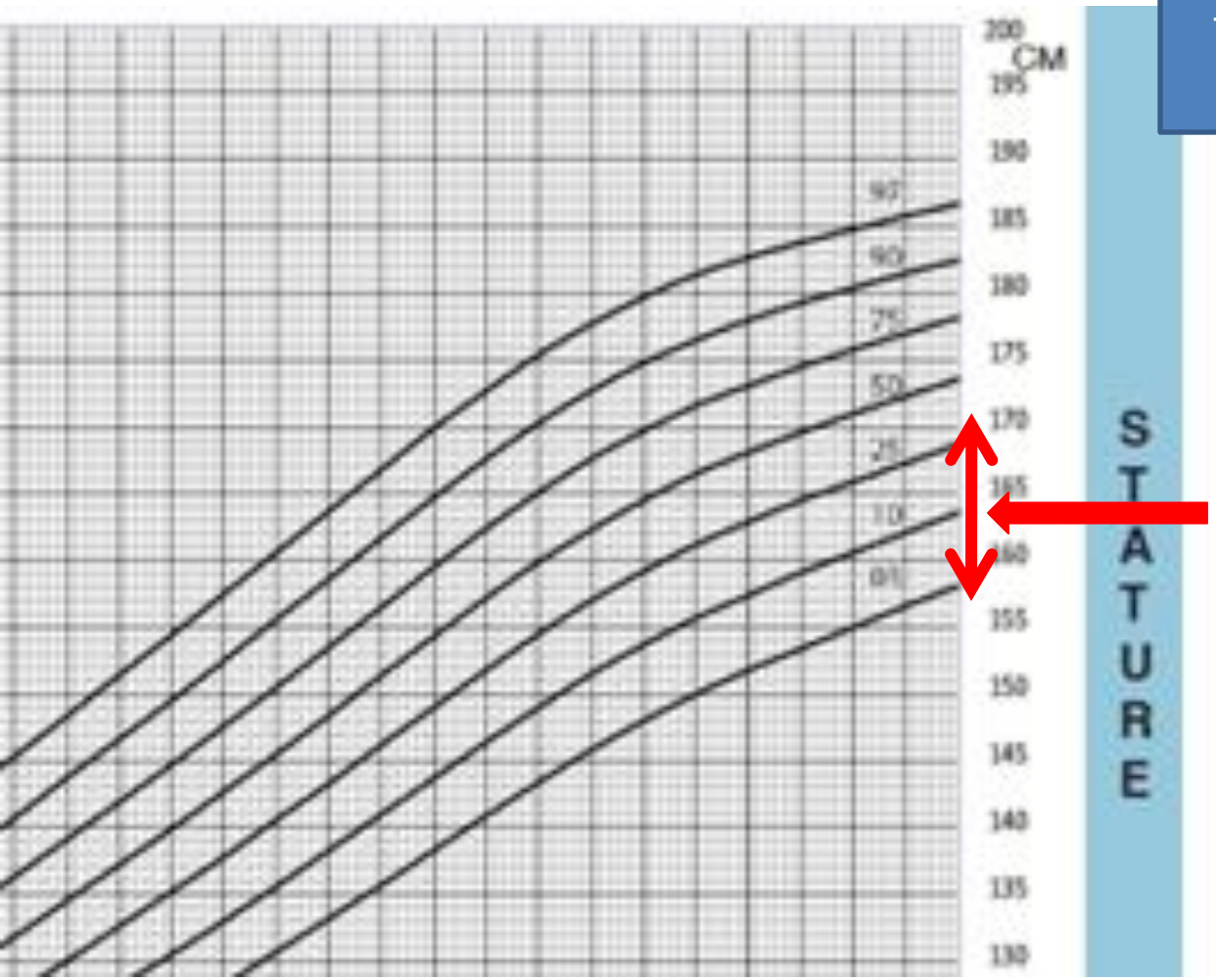
Target height

- Target Height also known as the adjusted mid parental height is calculated as follows:
- Boy: (MHT+FHT+13)/2
- Girl: (MHT+FHT-13)/2
- This height is plotted at **18 years** of age on the chart
- Target range is **6 cms** below and above the target height

IPNA

Target Height of 164 cm

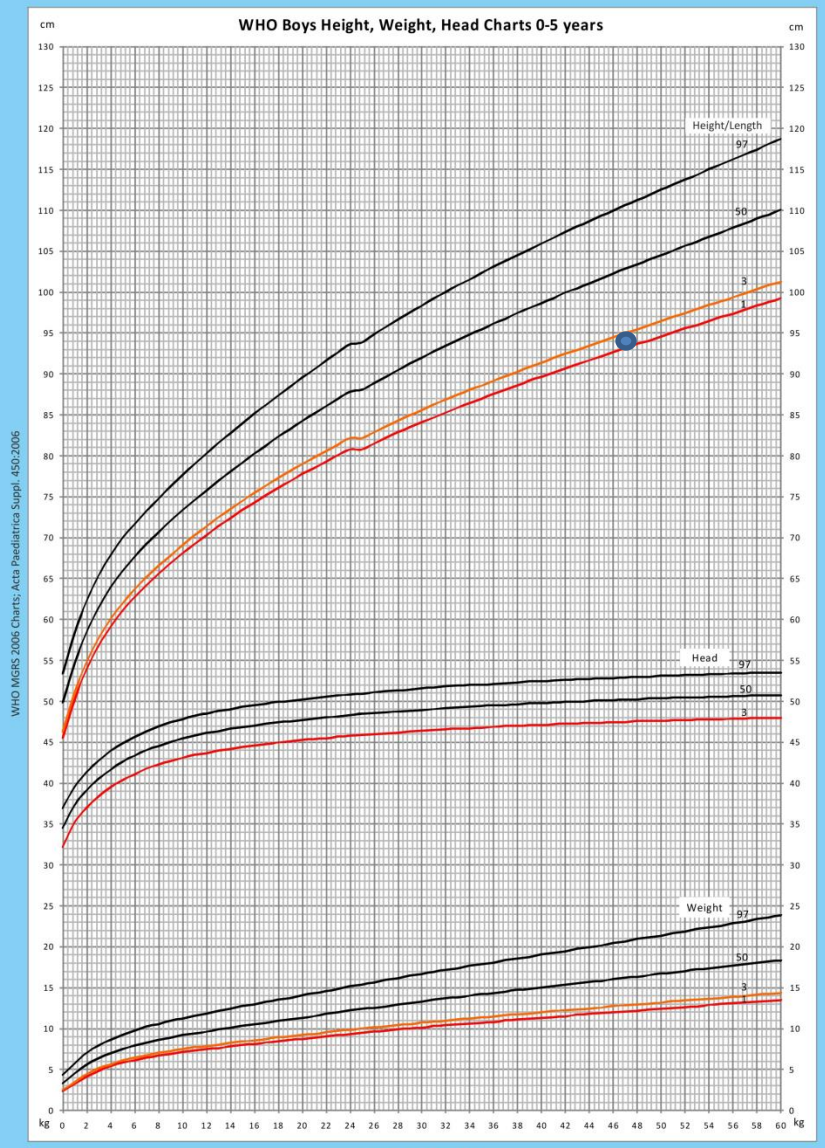
Target range 158 to 170 cm



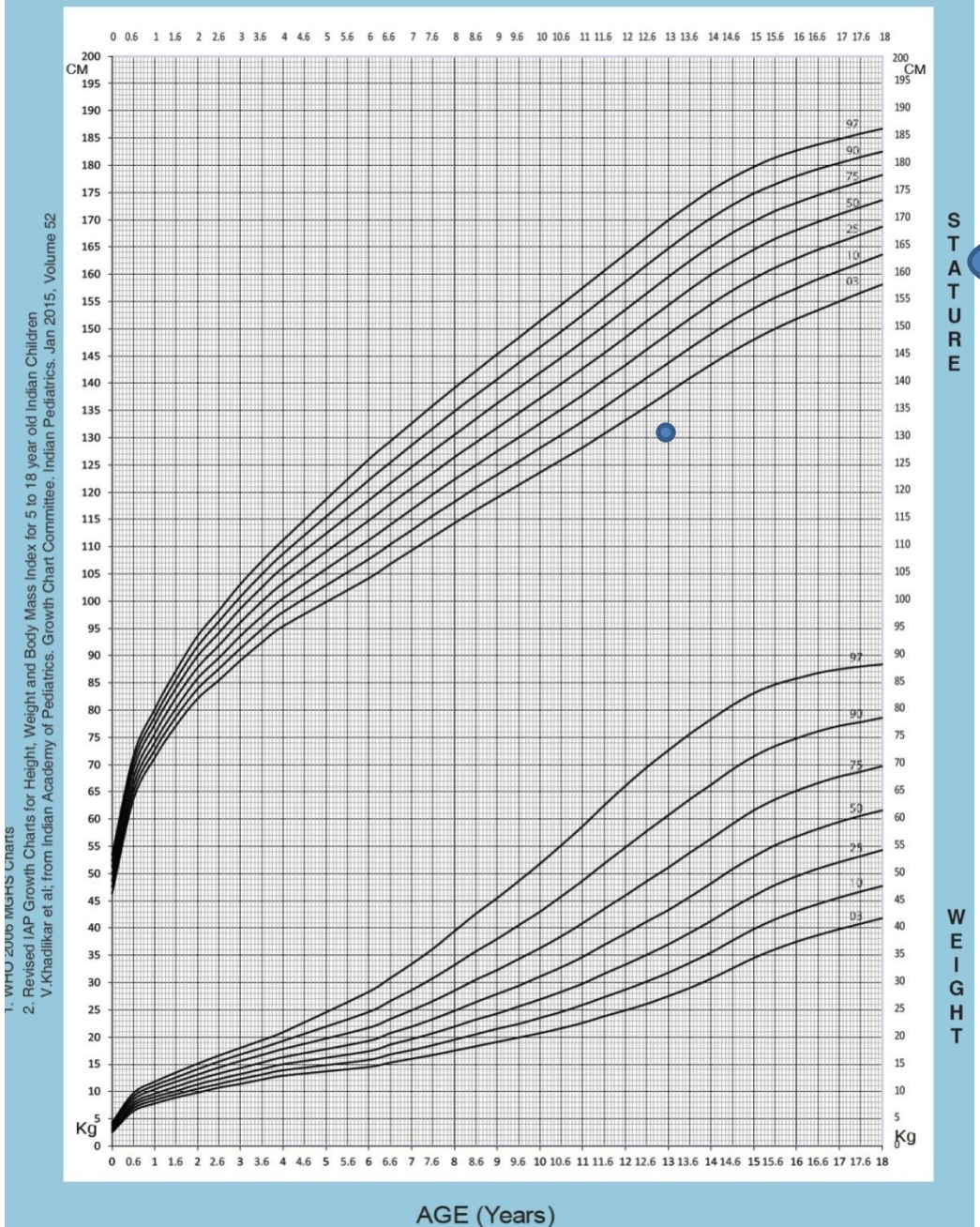
0 to 5 Years : WHO Boys Length/Height, Weight and Head Circumference Charts

Name : _____

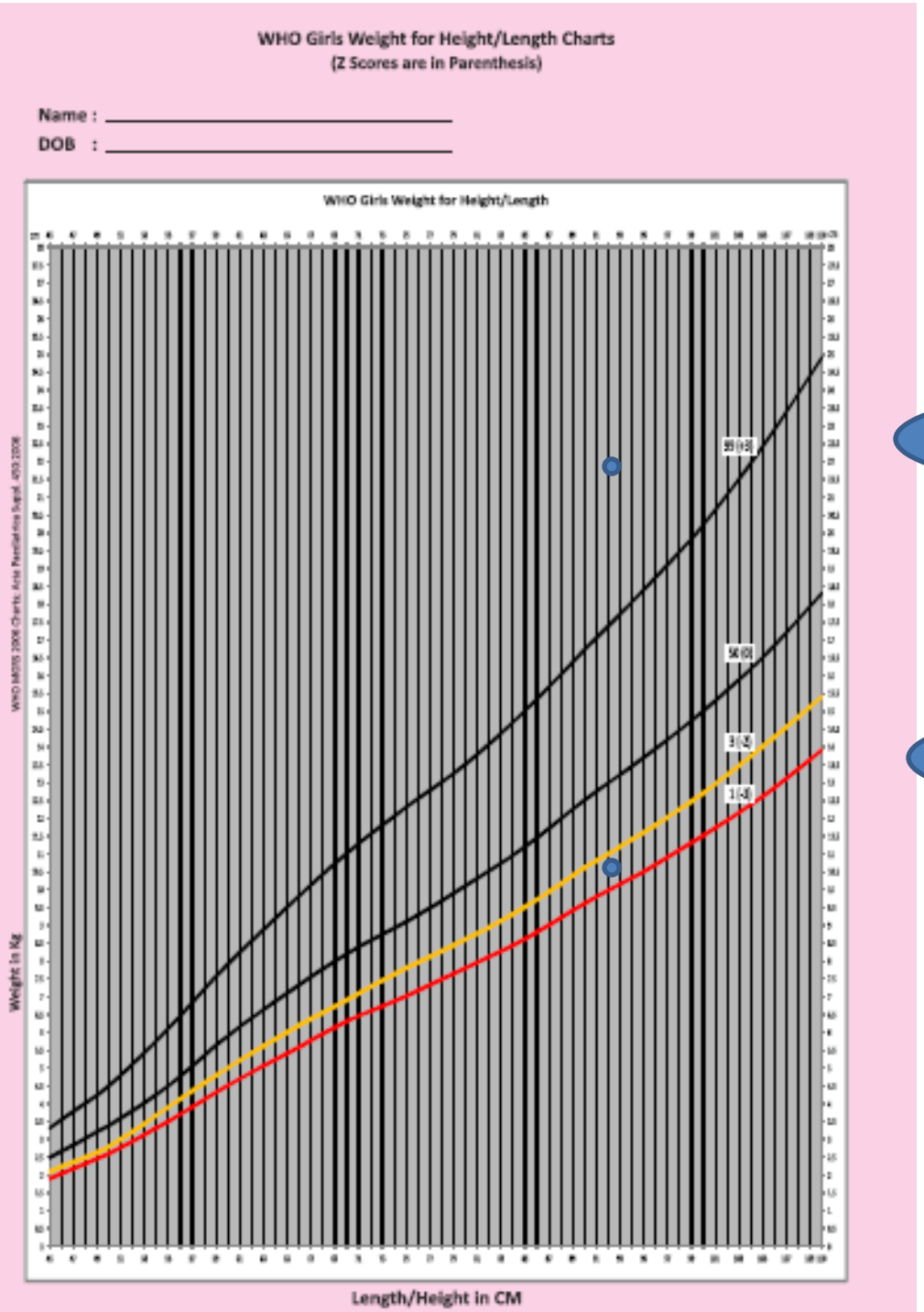
DOB : _____



Height < 3rd percentile - stunting



Height < 3rd percentile - stunting



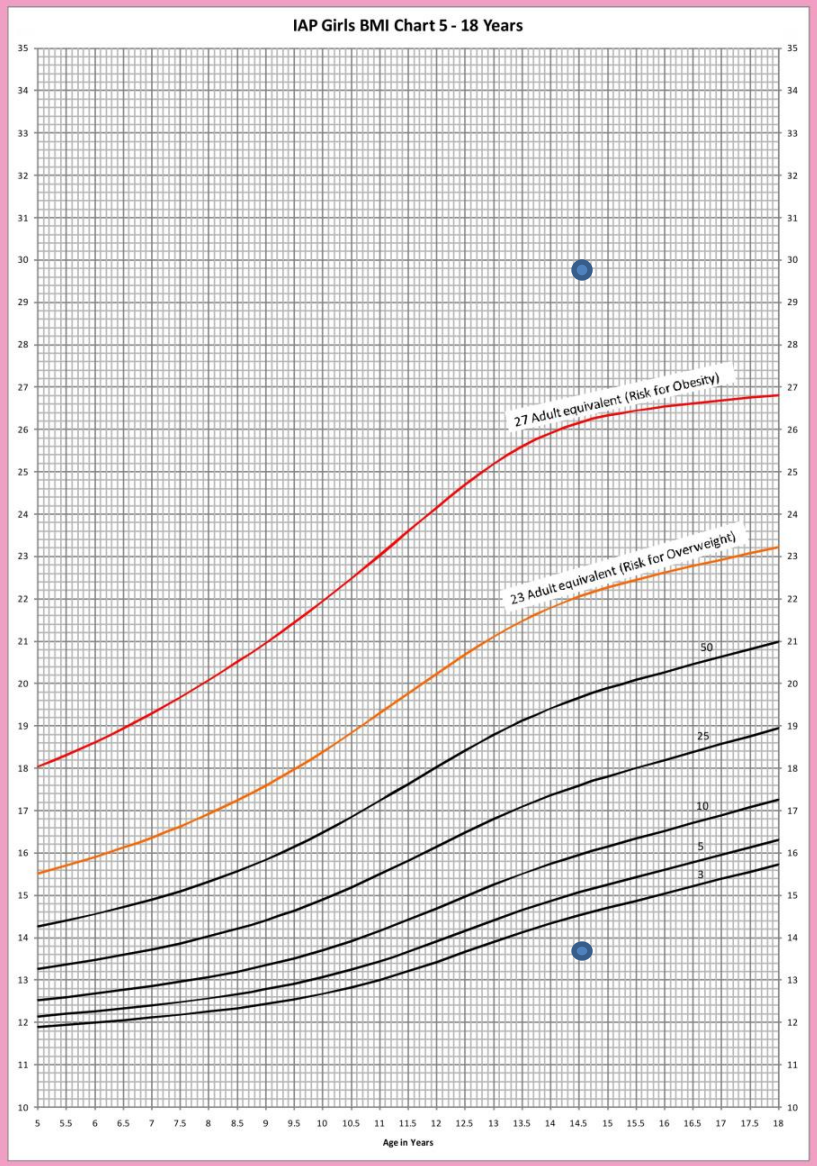
Weight for height > 99th percentile - Obesity

Weight for height < 3rd percentile - wasting

5 to 18 Years : IAP Girls Body Mass Index Charts

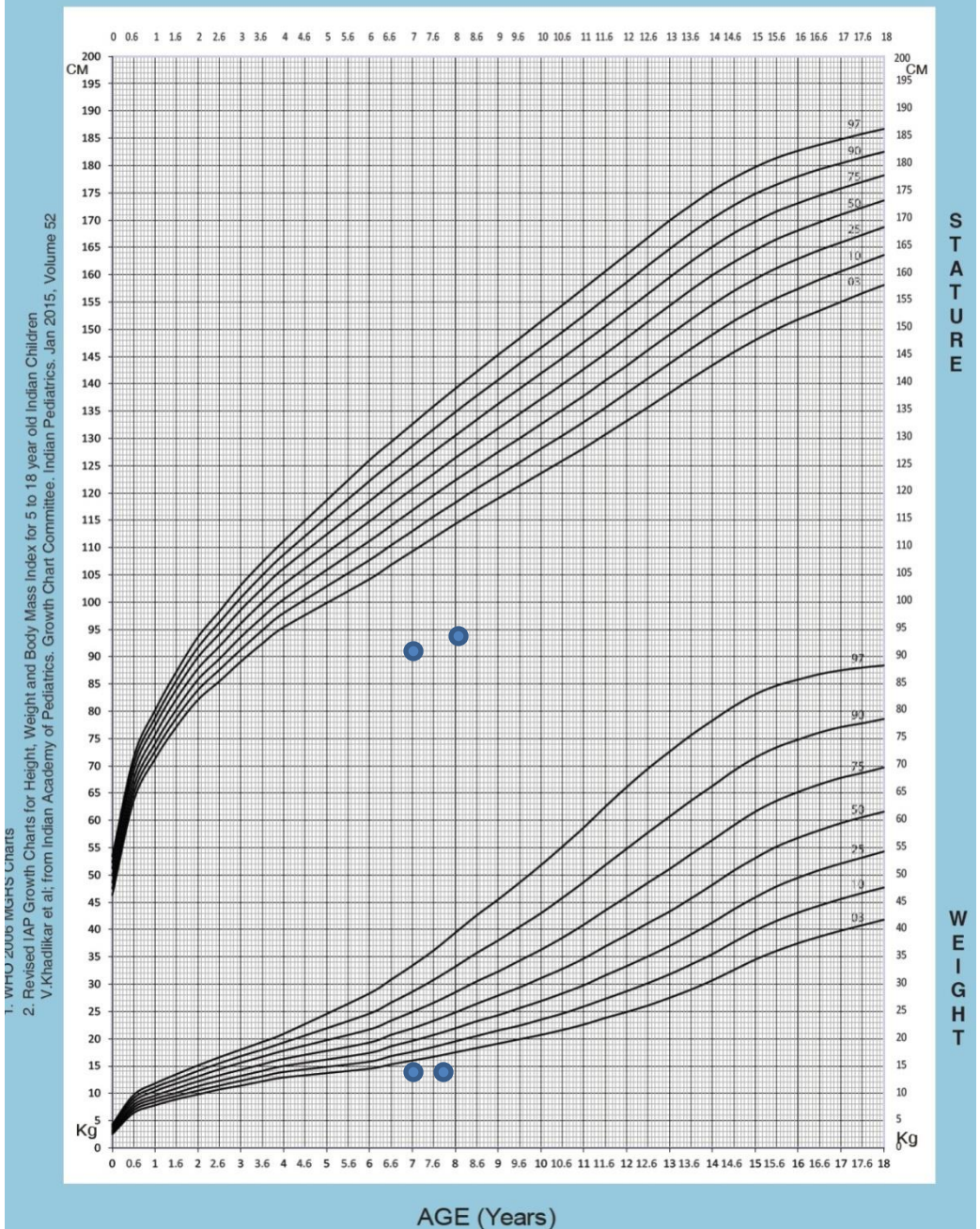
Name _____

DOB _____



BMI > 27th adult equivalent - Obesity

BMI < 3rd percentile - wasting



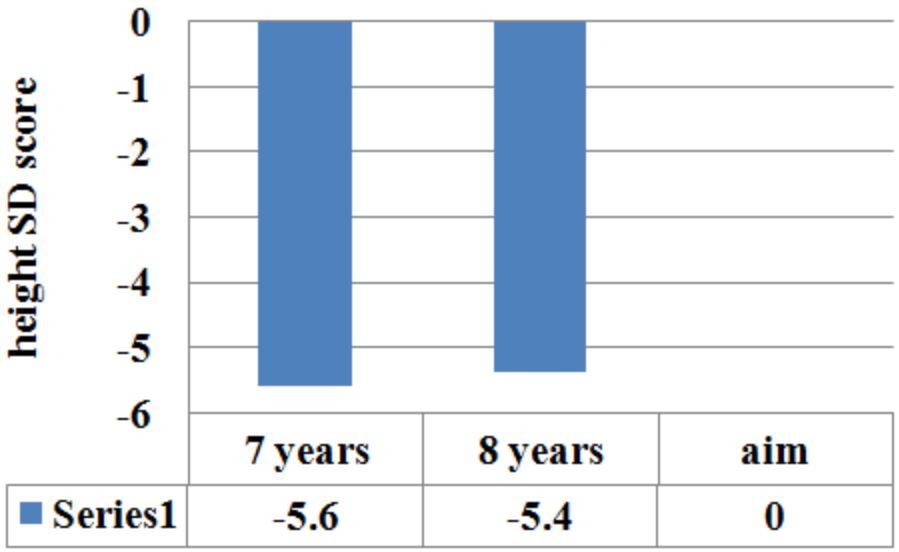
7 year old boy
Height 90 cm
Weight 12 kg

8 year old boy
Height 95 cm
Weight 13 kg

IPNA

A	B	C	D	E	F	P	Q	R	S	T	U	V	W	X	Y	Z	AA
Serial Num	age	gender	Height	Weight	BMI	HtZscore	WtZscore	BmiZscore		Will work for children between 5 -18 years							
					#DIV/0!	#N/A	#N/A	#DIV/0!		Instructions:							
					#DIV/0!	#N/A	#N/A	#DIV/0!		1. Copy or manually fill data in Serial number, Age, Gender (Enter as m or f), height and weight							
					#DIV/0!	#N/A	#N/A	#DIV/0!		2. Results will be displayed in the HtZscore, WtZscore and BmiZscore columns							
					#DIV/0!	#N/A	#N/A	#DIV/0!		3. Copy individual columns (Not 2-3 columns together) and paste the results (Use Paste Special then values) in another							
					#DIV/0!	#N/A	#N/A	#DIV/0!		and use for data analysis							

A	B	C	D	E	F	P	Q	R	S
Serial Num	age	gender	Height	Weight	BMI	HtZscore	WtZscore	BmiZscore	
					#DIV/0!	#N/A	#N/A	#DIV/0!	
	7	m	90	12	14.81481	-5.6804	-4.2843	-0.15709	
	8	m	95	13	14.40443	-5.429	-4.1132	-0.56419	



Delta height SDs = +0.2

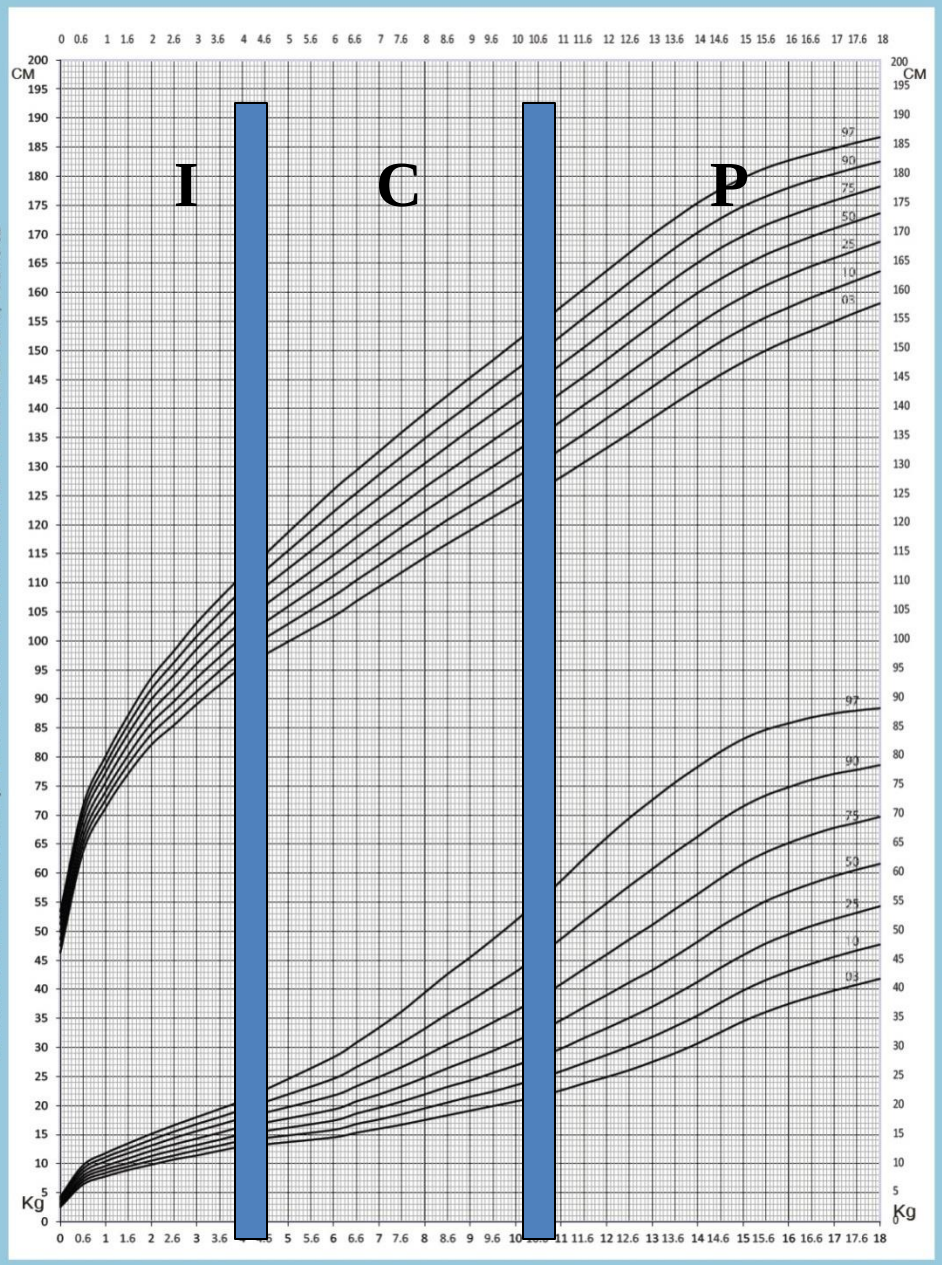
IPNA

0 to 18 Years: Boys

WHO 2006 & IAP 2015 Combined Height & Weight Charts

NAME_____

DOB _____



1. WHO 2006 MGRS Charts
2. Revised IAP Growth Charts for Height, Weight and Body Mass Index for 5 to 18 year old Indian Children
V.Khadilkar et al; from Indian Academy of Pediatrics. Growth Chart Committee. Indian Pediatrics. Jan 2015, Volume 52

Message ICP model – 3 phases

Infancy

Nutrition and in-utero environment bones

Childhood

Childhood GH, genes

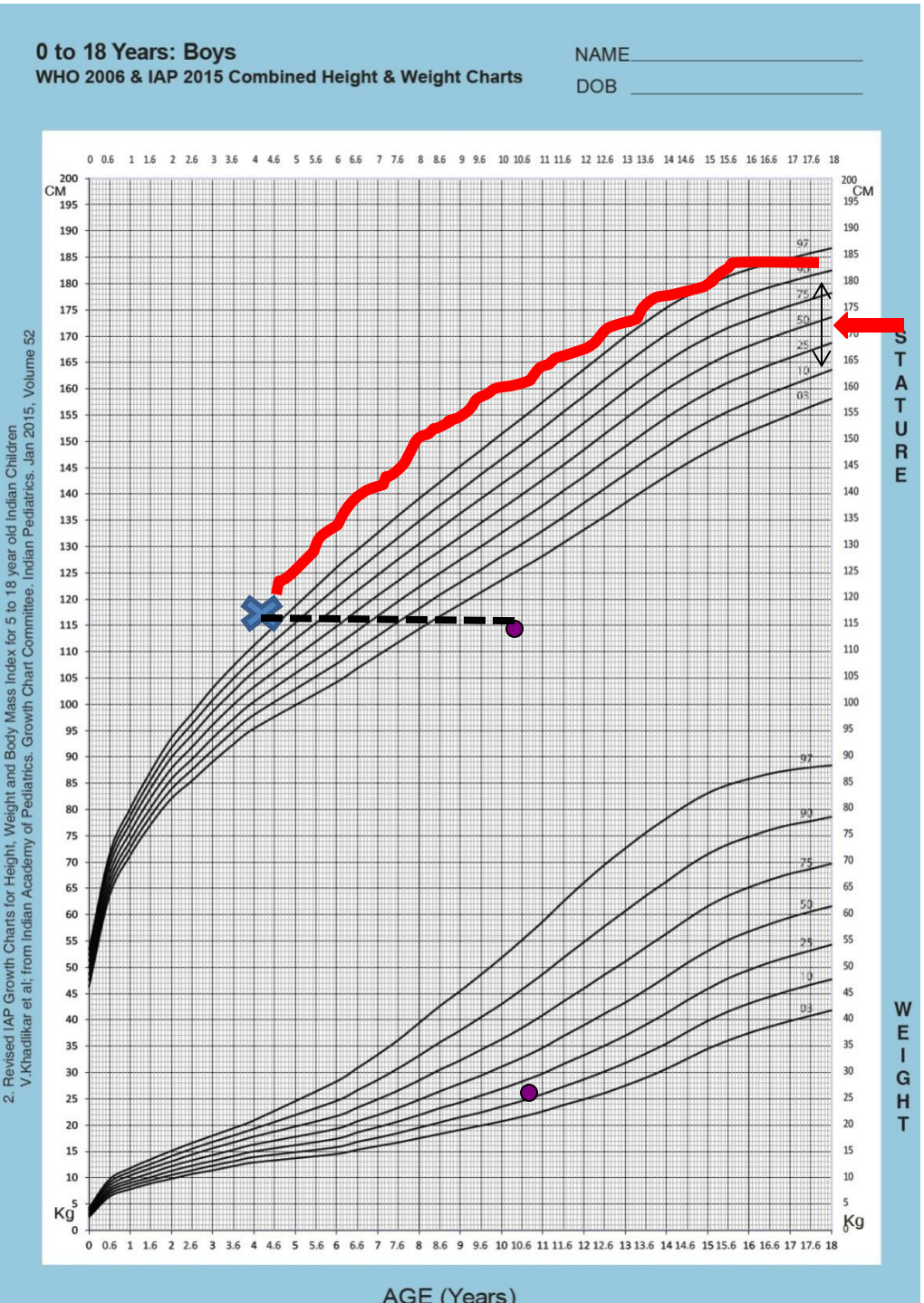
Nutrition

Puberty

Puberty Sex hormone

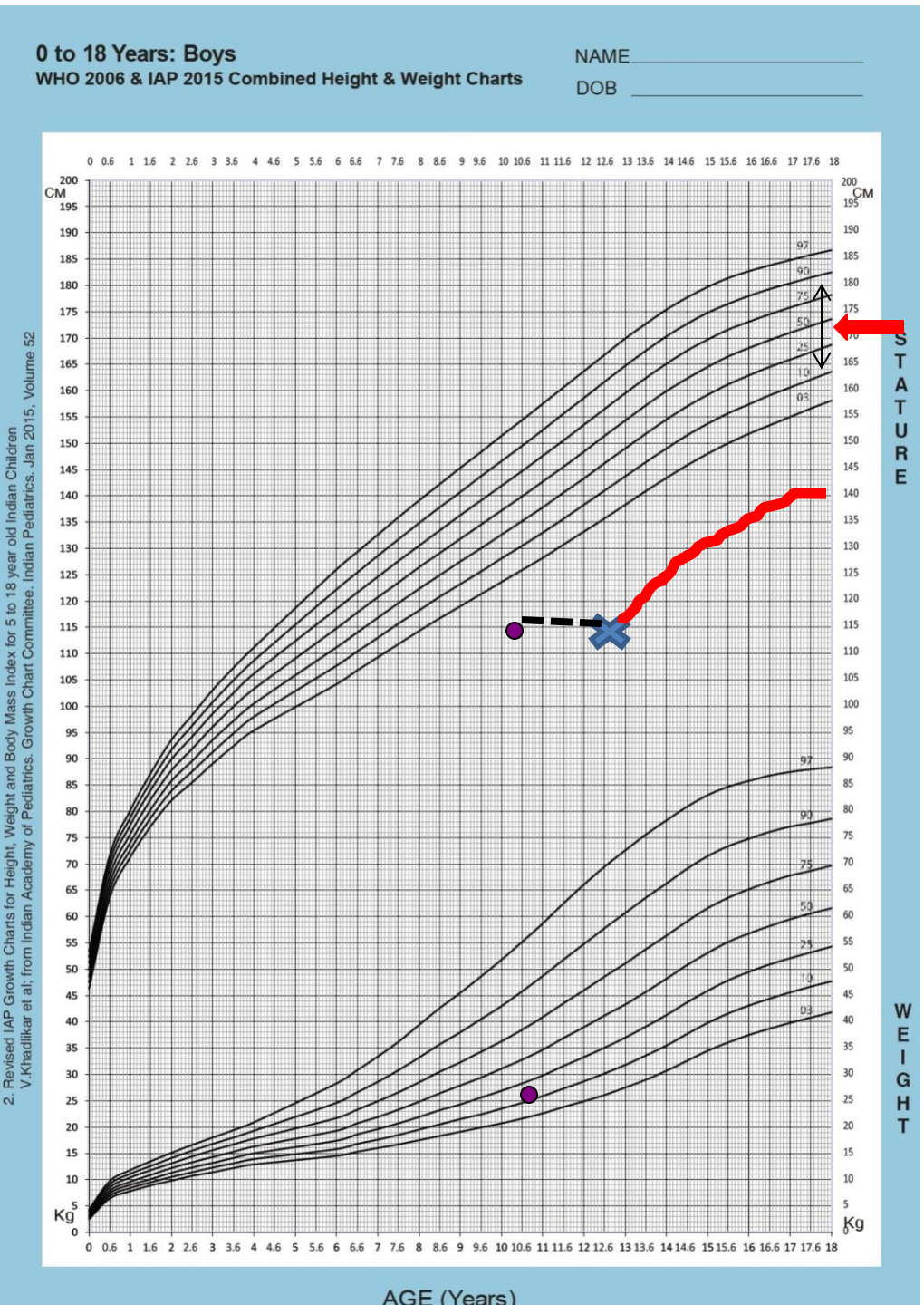
Childhood GH, genes

Nutrition



11 year old boy
Height 115 cm
Bone age = 4.5

Preserved height potential



11 year old boy
Height 115 cm
Bone age = 13y

Compromised height potential

Growth assessment - basics

- Right measurement at right age
- Select the right chart
- Height < 3rd percentile
- Height SD score < -1.8
- Growth velocity < 25th percentile
- What phase of ICP model is the child in?
- What is the Tanners stage?
- What is the bone age?
- What is the height potential left for the child?

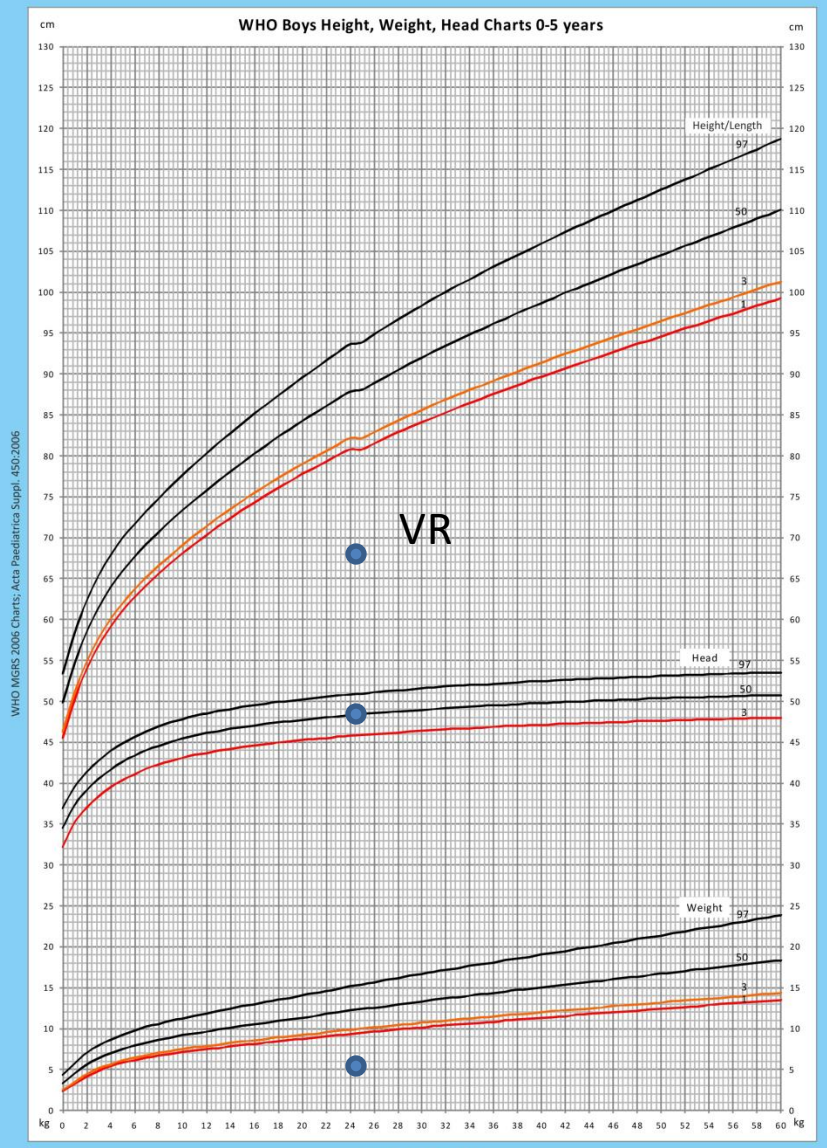
Case 1

A 1.3 year old infant with CKD stage 3 is seen in the growth clinic. The infant is on conservative management. The last venous bicarbonate is 14 meq/dL, hemoglobin is 9 gm/dL. There is history of poor nutritional intake. The last PTH is 340 pg/ml, normal serum calcium. Birth weight is normal.

0 to 5 Years : WHO Boys Length/Height, Weight and Head Circumference Charts

Name : _____

DOB : _____

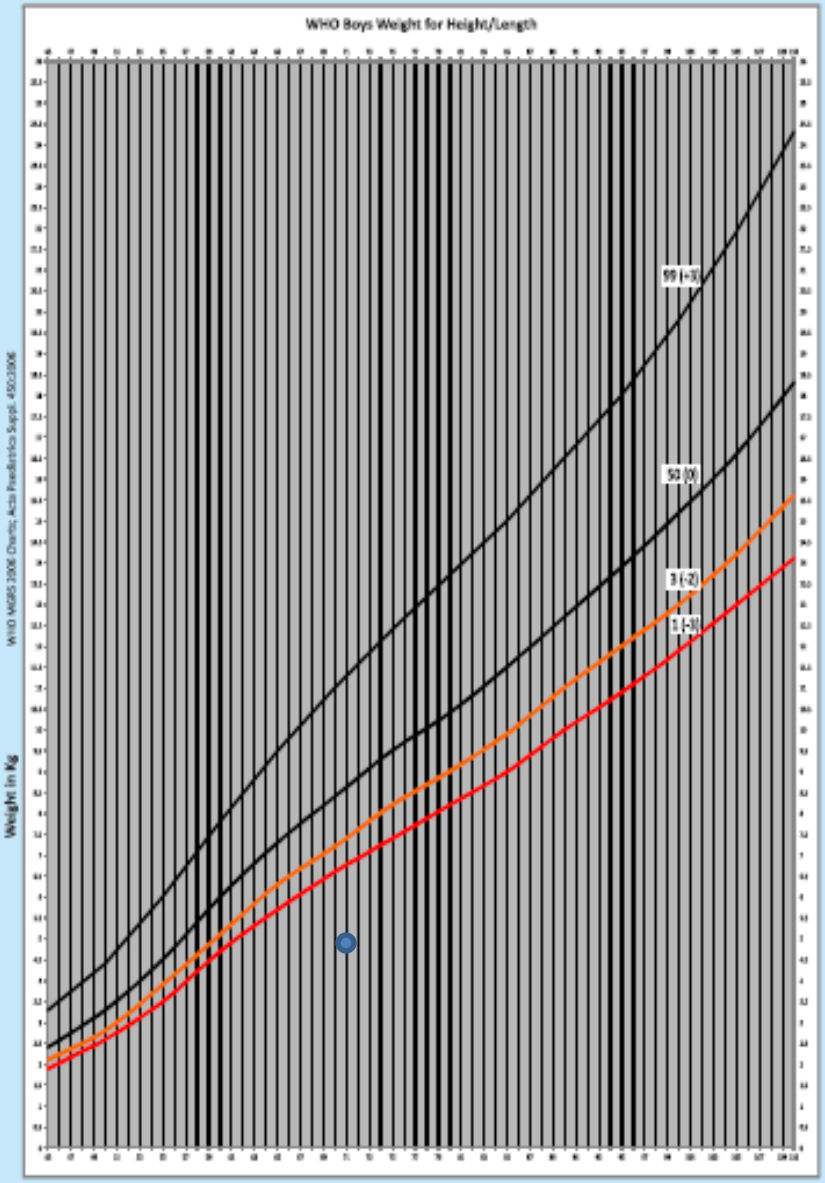


WHO Boys Weight for Height/Length Charts

(Z Scores are in Parenthesis)

Name : _____

DOB : _____



DR HARISH PEMDE

What are the causes of growth failure in infants with CKD

Infancy

- anorexia, nausea, and vomiting (*uremic toxicity, metabolic acisosis*, imbalance of regulatory proteins of energy intake)
- increased basal metabolic rate (IL-1α, IL-6 and TNF-β)
- loss of lean body mass (muscle mass replaced with fat), and
- declining serum proteins (albumin, transferrin {*anemia*}, prealbumin)
- Uncorrected acidosis
- Renal osteodystrophy

IPNA

Evidence for improved growth on conservative therapy – definitely YES

Author	Reference	Study sample	Key observation
Boehm M	Ped nephrol 2007	47 subjects with CKD	36% had Ht SD < -2, 40% catch up+ on conservative management. Determinants of catch up include: improvement in Hb (OR 1.85, p<0.05), erythropoetin therapy (OR 13.6, p<0.05)
Tom A et al	J Pediatr 1999	12 infants for 2.2 years	Replacement of 90.6% energy and 155.9% proteins leads to catch up +0.31 SD per year of therapy. No obesity, no spurt
Coleman J E et al	Adv periton dial 1998	14 subjects	Gastrostomy button feeds lead to height catch up (height SD -2.4 to -1.6) and weight catch up (-2.2 to -0.7). No local infections.
Lesley Rees et al	CJASN	153 infants on peritoneal dialysis < 2 years	Improved growth (catch up SDs) noted in those using biocompatible dialysis fluid, tube feeds for improved nutrition.

What are conservative measures to be taken of growth failure in CKD in infants

DR JYOTI BAGLA

Anemia	Maintain the target hemoglobin for optimal growth
Dialysis	Optimise the dialysis regimen – increase protein and improved urea clearance
MBD	Ensure PTH in recommended target and Vitamin d level > 30 ng/mL
Metabolic control	Ensure bicarbonate level > 22 (oral bicarbonate/ bicarbonate in dialysate); salt and water in tubular disorder
Nutrition	Especially in infants and childhood. Nutritionally appropriate feed – NG tube and gastrostomy

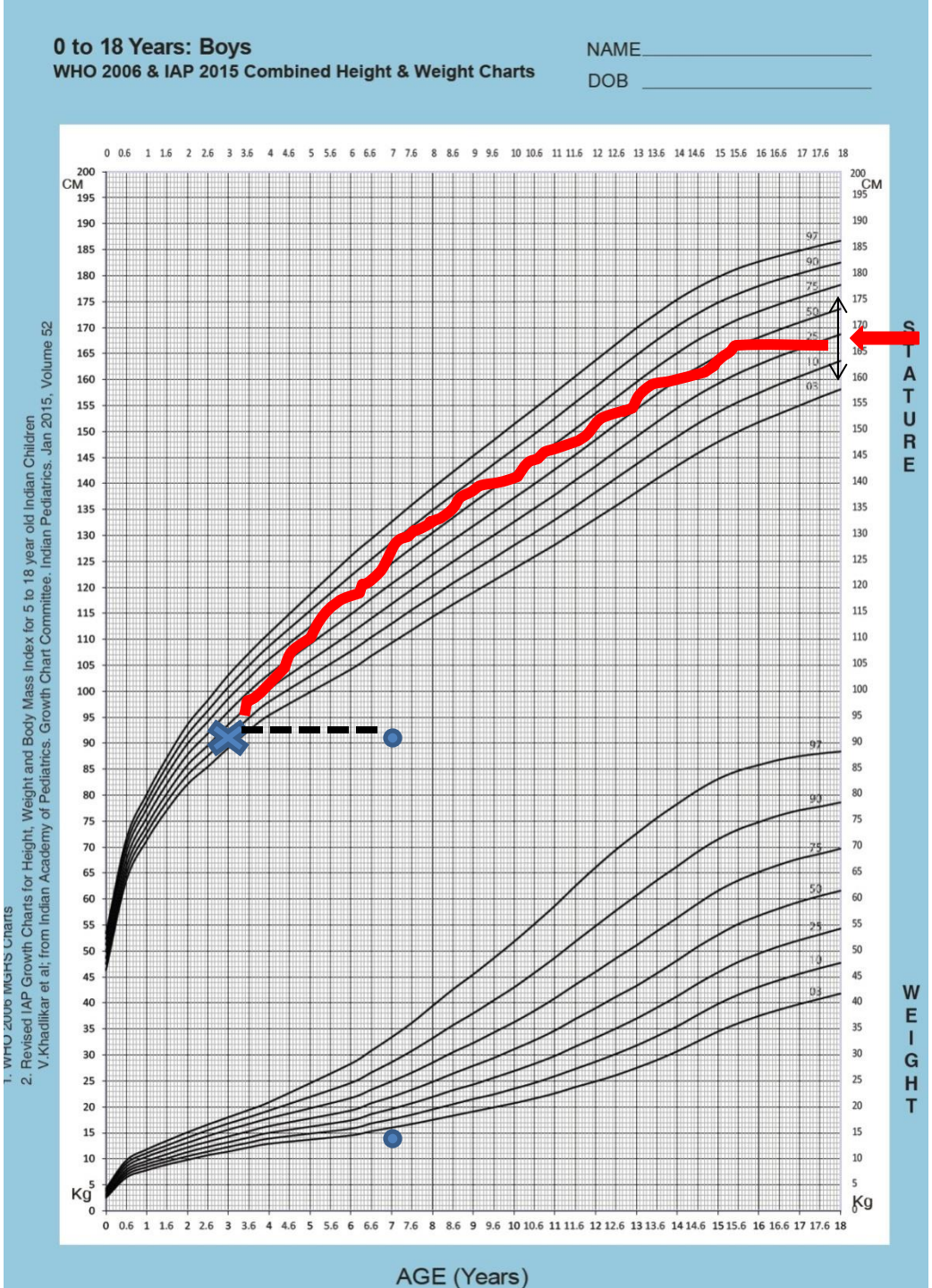
Evidence for GH – may be yes

Author	reference	Sample	Key observation
Mencarelli et al	Ped nephrol 2009	27 infants (standard therapy versus GH)	Good catch up in height SD noted. No adverse effects
Lesley Rees et al	JASN	153 infants (<2 years), 8 received GH	Increased growth by 1.5 SD in 8 infants who received GH
Fernando Santos et al	CJASN	RCT of 16 infants who received GH versus conservative	Increment in height SD in GH therapy +1.4 versus -0.1 in untreated

GH therapy probably safe – advantages:
Low dose – reduced cost
Early transplantation
Increased psychosocial benefit
Improved adult height

Case 2

A 7 year old boy with CKD stage 3 is seen in the growth clinic. The child is on conservative management. Correctable factors like: anemia, ROD, acidosis, thyroid profile, nutrition have been addressed. How can this child be treated?



7 year old boy
Height 90 cm
Weight 12 kg

IPNA

Pertinent questions

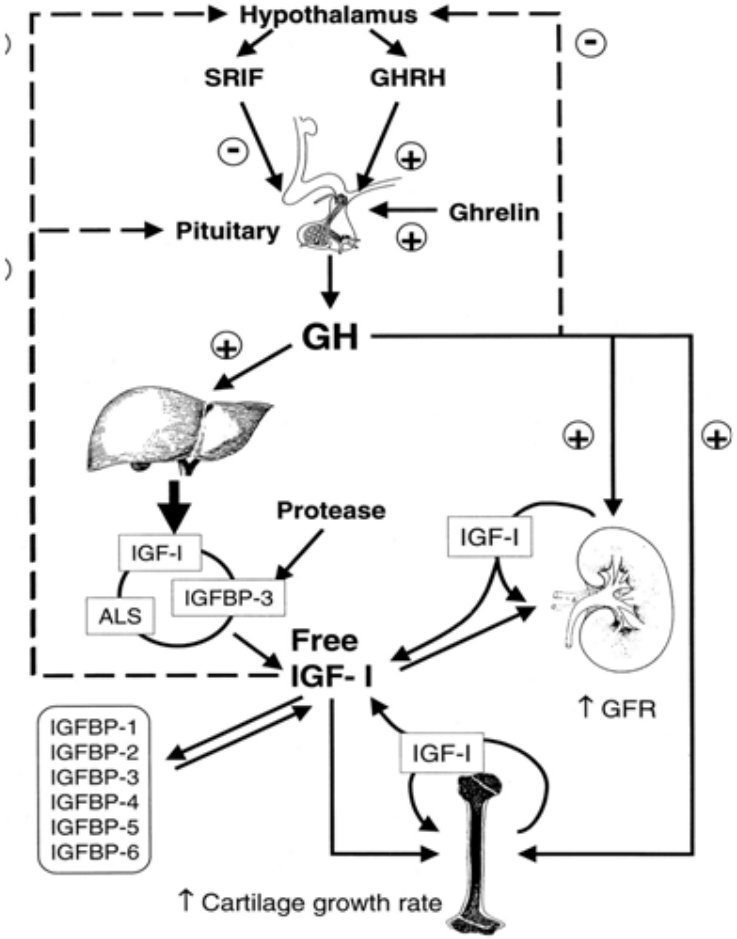
- What can be done?
- What is the rationale?

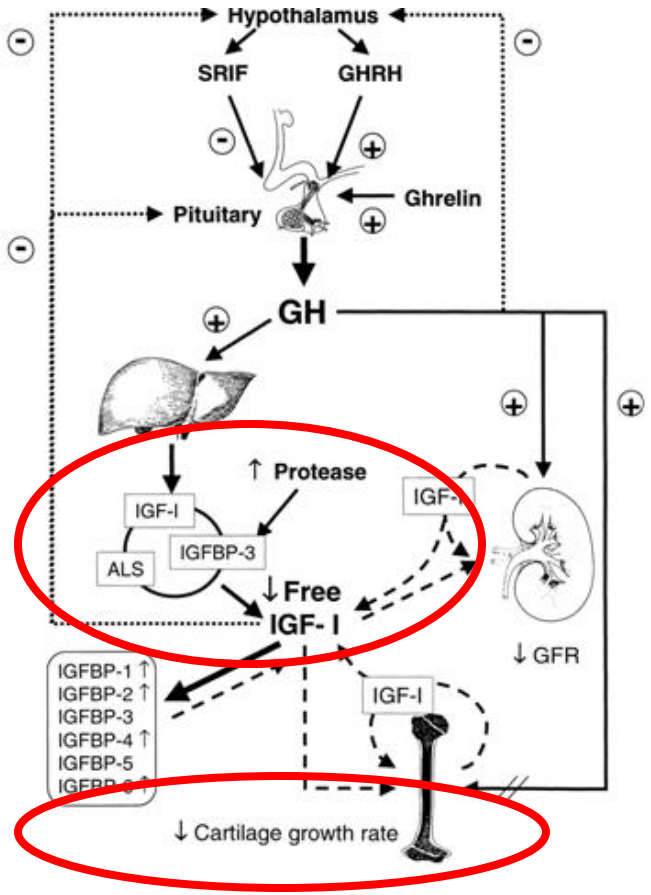
DR RAVINDER KUMAR

What can be done?

- Growth failure in children with CKD, was the first non-GHD growth disorder for which Growth Hormone (GH) was approved for use by the US FDA in 1993 and by the EMEA in 1995.

What is the rationale?



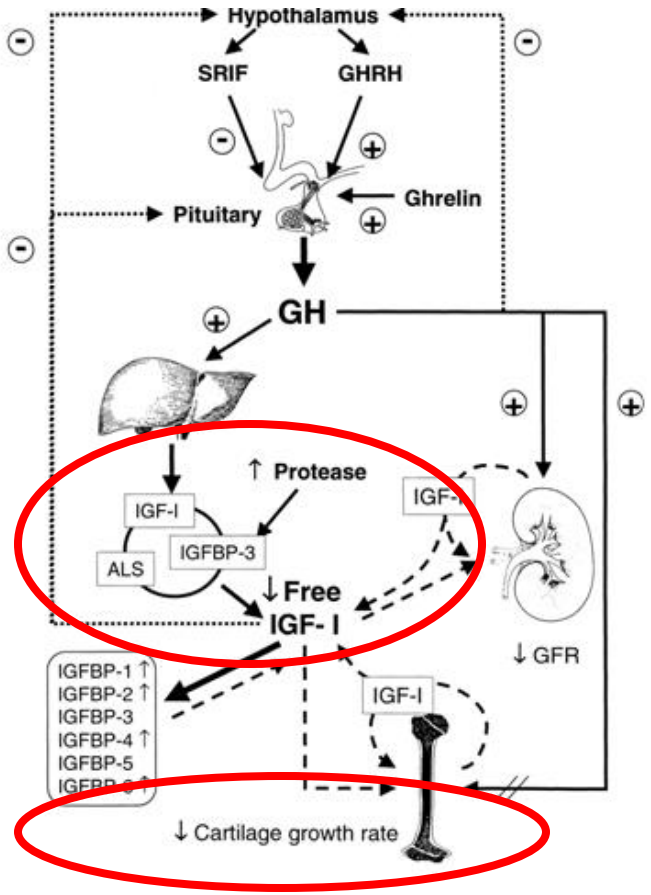


Normal HP-IGF axis

CKD HP-IGF axis

What is the rationale?

- Decrease in the density of GH receptors
- Defect in the defect in the post-receptor GH activated Janus kinase 2 (JAK2) signal transducer and activation of the STAT pathway necessary for IGF-1 production
- increase in levels of circulating IGFBPs-1, -2, -4, and -6, (due to reduced clearance) leading to a reduction in the concentration of bioavailable IGF-I .
- increased proteolysis of IGFBP-3 leads to a decrease in IGF-I available for the formation of IGF-I–ALS–IGFBP-3 complexes



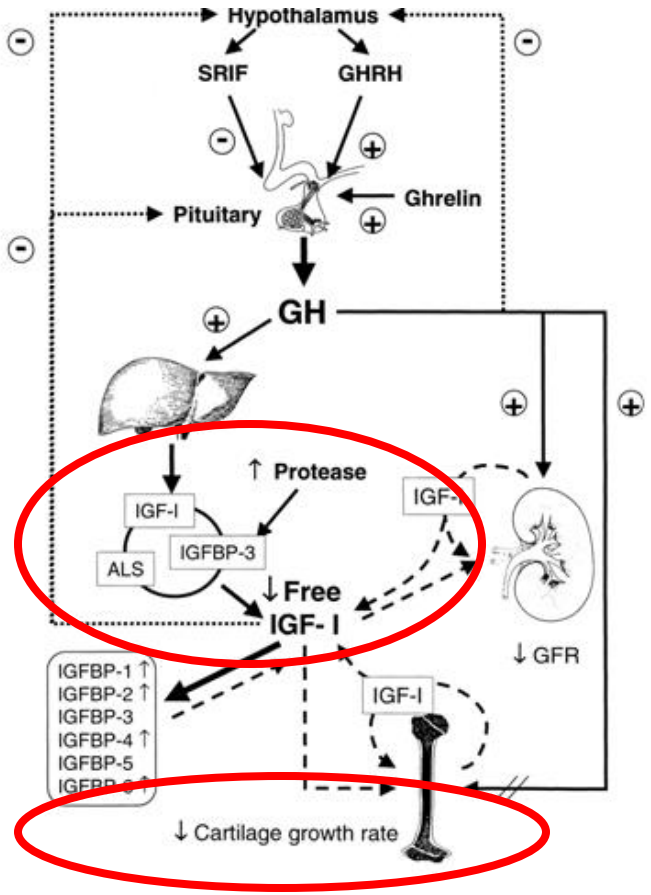
CKD HP-IGF axis

What is the rationale?

Increased IGF levels - anabolic

Direct action on growth plate

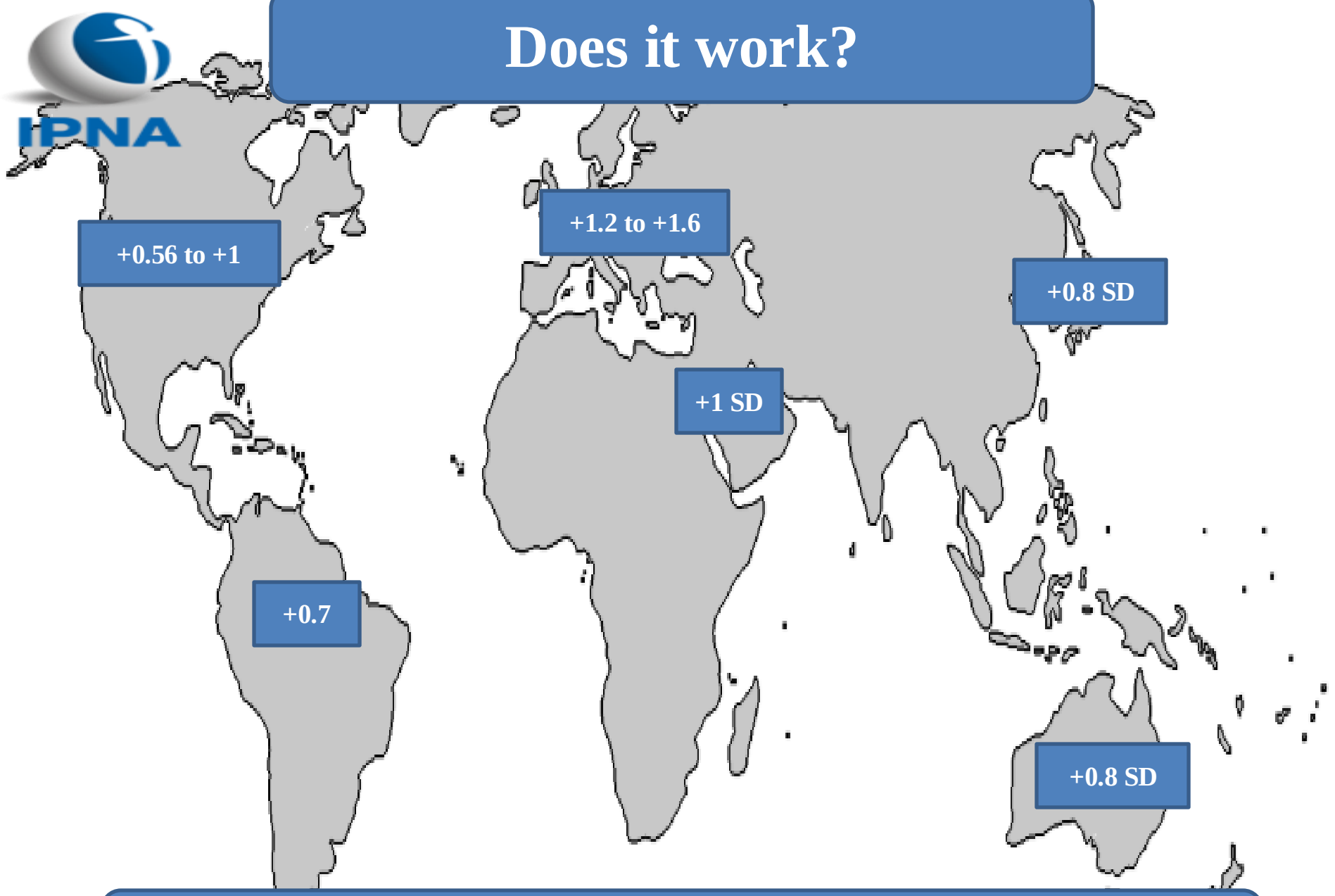
Augmented growth



Does it work?

Author	centre	sample	duration	response
Richard N Fine	California (O)	20 CKD	5 years	-2.6 to -0.7 Ht SDs
Richard Nissel	Germany (O)	240 KIGS database	1 year minimal	+1.2 to +1.6
Dieter Haffner	Germany (O)	Germany (O)	3 years	+1.6 SD (PAH inc 7 cm)
Fene R N et al	17 USA centres	82 GH versus 43 placebo	2 years	+1.4 SD
NAPRTCS (7189 CKD children)	7189 children CKD database (O)	11.5% received GH (757)	4 years	+0.56
Tonshoff B	Europe (O)	10 pre pubertal children	1 year	-2.3 to +3.8 GV SD
Hokken Koelega et al	Dutch ®	45 prepubertal	8 years	Increase Ht SDs
Bernard E et al	42 French children (O)	42 children	2 years	+0.5 SDs
Youssef Dm et al	Saudi Arabia (O)	15 children	1 year	4.1 to 5 cm per year
Katsumi et al	Japan (O)	93 children	2 years	-3.5 to +0.8 SDs (GV)
GH chrompton	Australia (O)	183	5.3	+0.7 to +0.8

Does it work?



Cochrane review 2001, 2012 – 3.8 to 4 cm per year of therapy

Is it safe?

Author	centre	sample	duration	ADR
Richard N Fine	California (O)	20 CKD	5 years	Increase PPI, ccr 32 to 24, 1 avn
Richard Nissel	Germany (O)	240 KIGS database	1 year minimal	Nil
Fene R N et al	17 USA centres	82 GH versus 43 placebo	2 years	Inc PPI, normal sugar CCR
NAPRTCS (7189 CKD children)	7189 children CKD database	11.5% received GH (757)	4 years	No impact on BMI, eGFR
Tonshoff B	Europe	10 pre pubertal children	1 year	Inc FI, PPI. No inc BG
Hokken Koelega et al	Dutch	45 prepubertal	8 years	No accelerated bone age
Bernard E et al	42 French children	42 children	2 years	N accelerated BA, 5 had hyperparathyrodiism
Youssef Dm et al	Saudi Arabia	15 children	1 year	Nil
Katsumi et al	Japan	93 children	2 years	1 gynaecomastia, 2 glucose intolerance
CH chrompton	Australia	183	5.3	Nil

Side effects of GH therapy

BICH	Baseline fundus
SCFE/ AVN	Clinical monitoring
Sugar abnormalities	3 monthly sugar monitoring

What determines response?

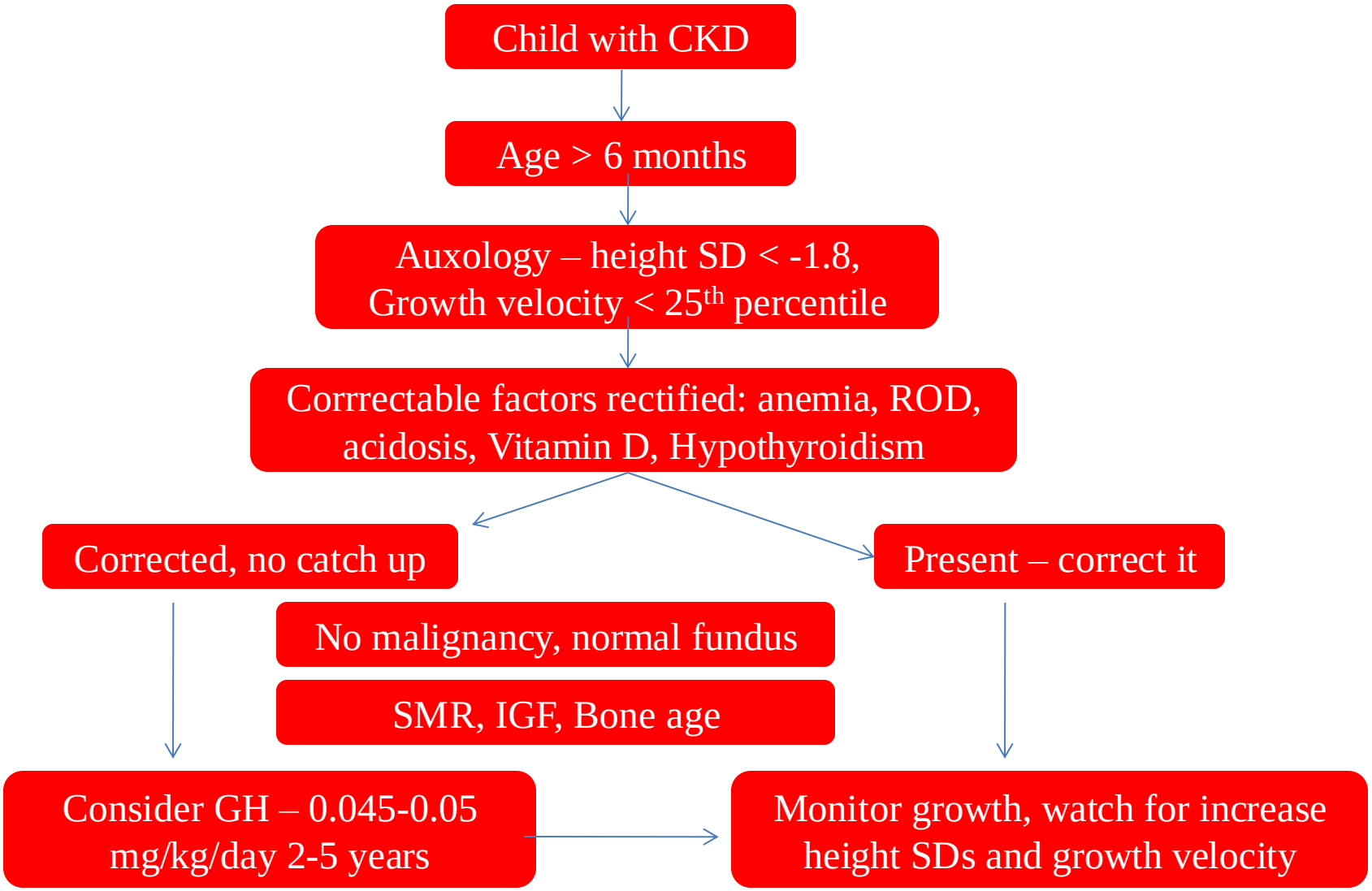
Non modifiable	Modifiable
Target height SDS Female sex Height velocity before GH	Height SDs at start Age Pre pubertal status

Case 2

A 7 year old boy with CKD stage 3 is seen in the growth clinic. The child is on conservative management. Correctable factors like: anemia, ROD, acidosis, thyroid profile, nutrition have been addressed. How can this child be treated?

A trial of GH

How to approach growth abnormality in CKD



Poor growth in CKD

Hypothyroidism

Acidosis anemia

nutrition

GH resistance

ROD

Sex hormone deficiency

IPNA

CAKUT

Dr. M. Bajpai

MS, MCh, PhD,

FRCS, FACS, FAMS, National Board, Fulbright Scholar

Formerly **Dean (Academics);**

Professor & Head

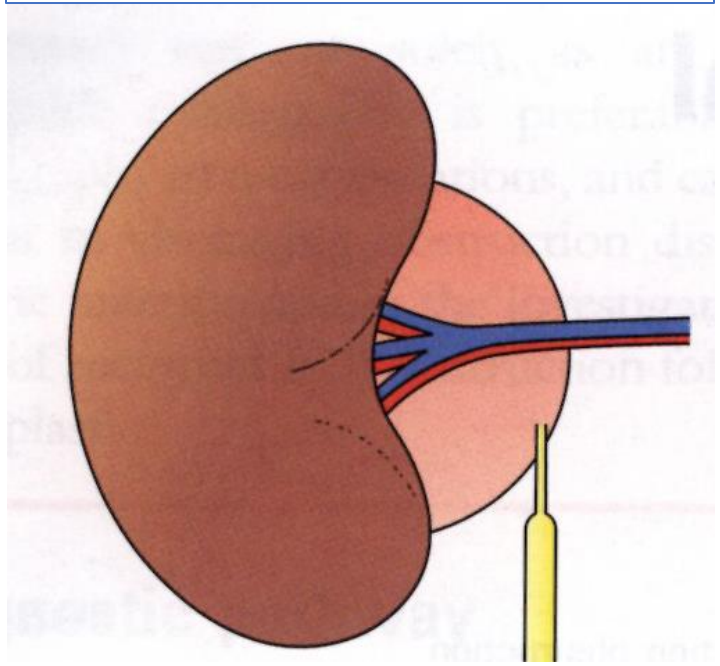
Department of Paediatric Surgery

All India Institute of Medical Sciences

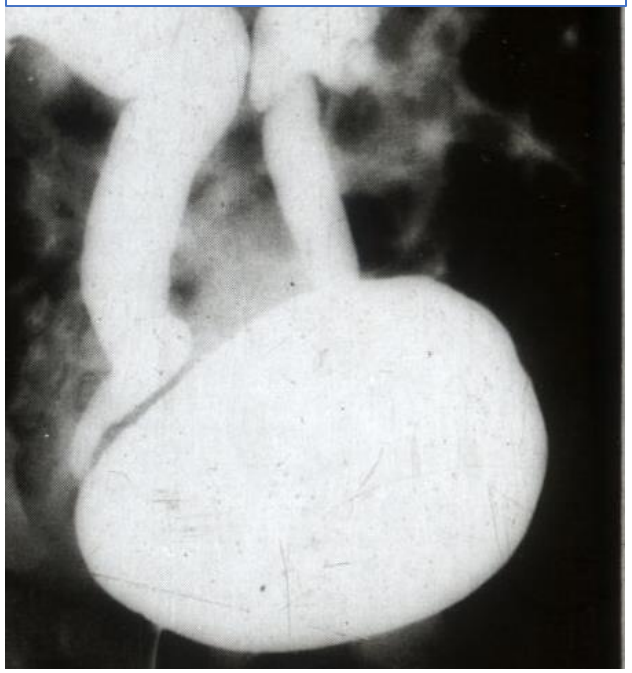
CAKUT/ UTM

- CAKUT- an umbrella term for related abnormalities.
- CAKUT defines -related structural disorders with prenatal origin and
- Shared etiology of CAKUT phenotypes and
- The importance in genetic counseling.

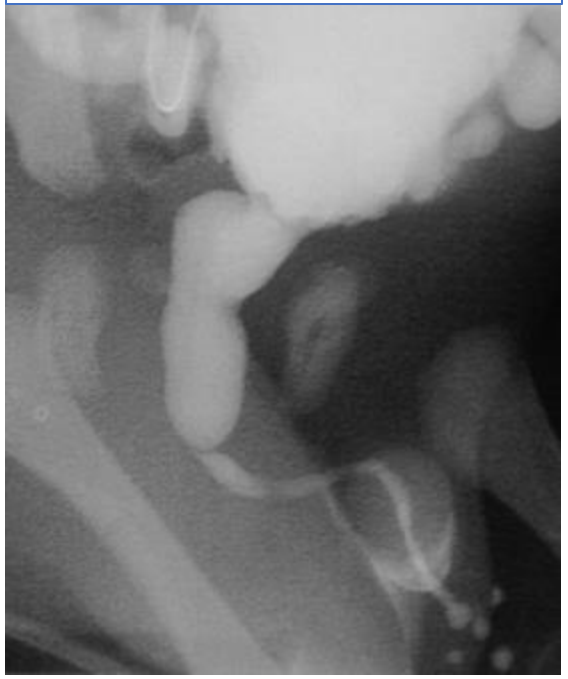
PUJO



VUR



PUV



CAKUT: Some facts to remember

- 3–6 per 1000 live births & 34–59% of CKD
- 70% of them develop hypertension
- All ESKD require renal replacement therapy
- Survival rate- with ESKD is 30 times lower than that of healthy children

- New Strategies Needed
- To Prevent CAKUT,
- Preserve Renal Function, And
- Reduce Associated Cardiovascular Morbidity.

CAKUT: 3 perpetual controversies

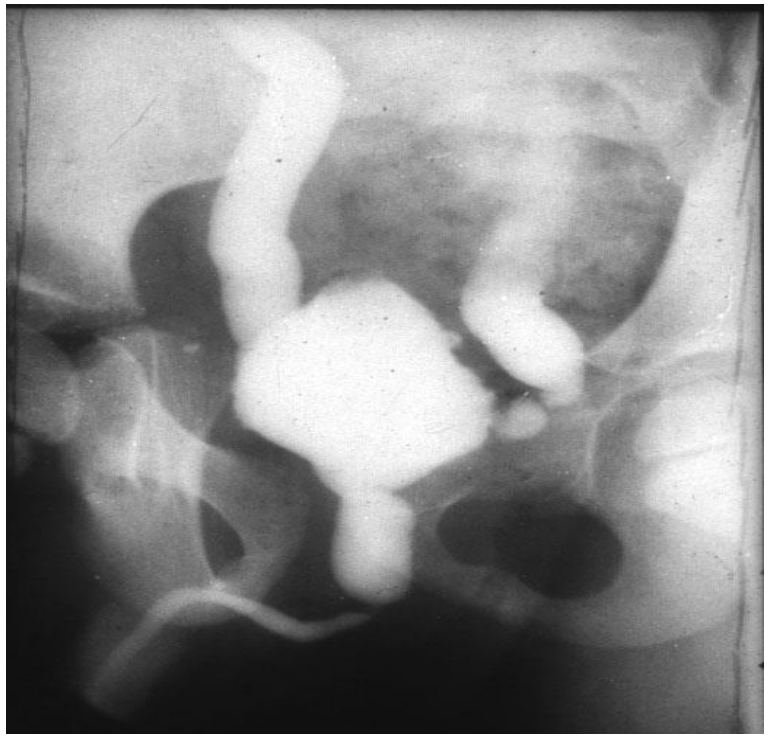
❖Lessons learned

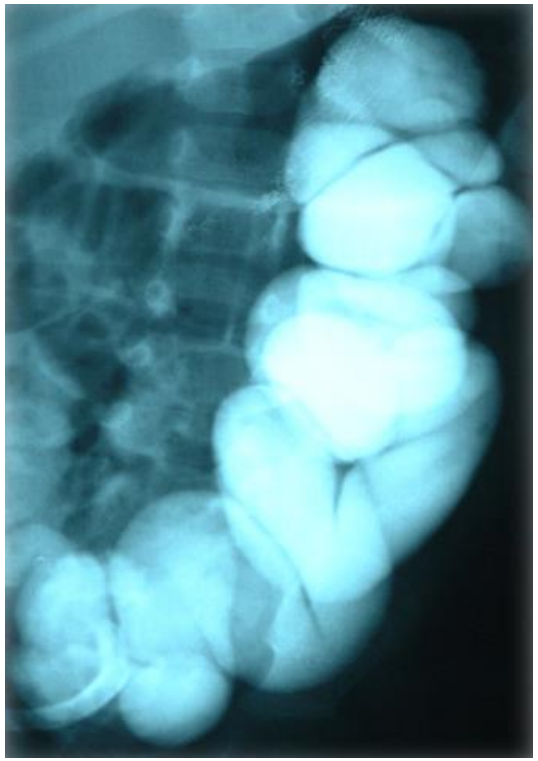
- ❑PUV- 44% CKD by 2nd decade of life;
  - ❖can we retard the pace of renal injury; Cordocentesis; most of my articles
- ❑VUR- Mx vs Sx-
  - ❖pyelonephritis continues despite prophylaxis
- ❑PUJO- When to operate;
  - ❖discriminatory factor; Kaplan meir curve
  - ❖Obstructive stress Injury: tubulo-interstitial compartment
- ❑Genetic influences
- ❑Point of care tests

PUV: Management

Choice of primary therapy

- **Valve ablation or**
- **Ureterostomy**





Role of primary therapy: Controversies

High diversion in all patients

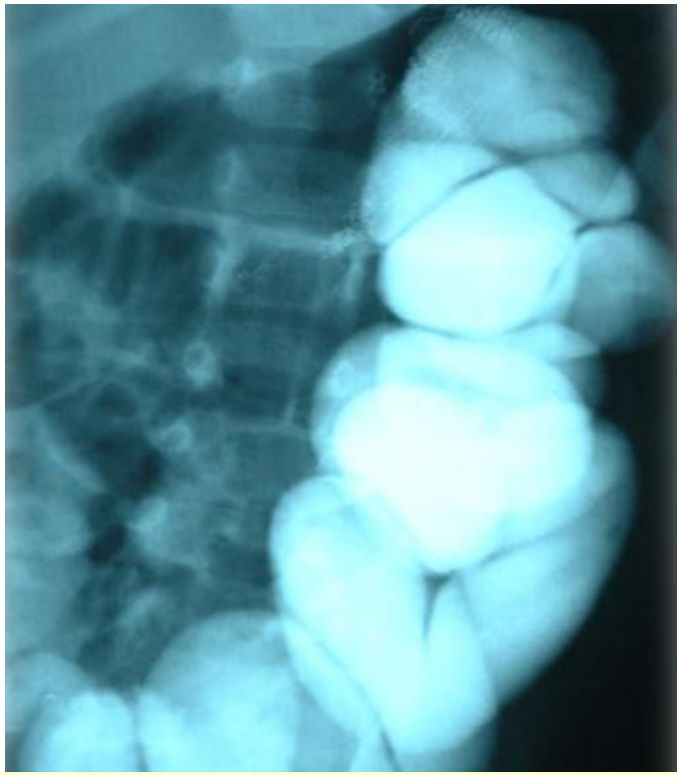
- Krueger,etal(1980):

-maximizes long-term growth & renal function

- Primary Valve ablation

- Duckett (1974),
- Parrot (1976),
- Walker (1990),
- Bajpai (2001):

'Glassberg ureters'



Decision making & The step ladder protocol

IPNA

*The step ladder protocol

Assessment of clinical & biochemical status:
G.C., RFT, ABG, Urosepsis ±

Abnormal ↔ **Normal**

↓ **Catheter drainage**
Serial monitoring

↓ **Primary valve ablation**

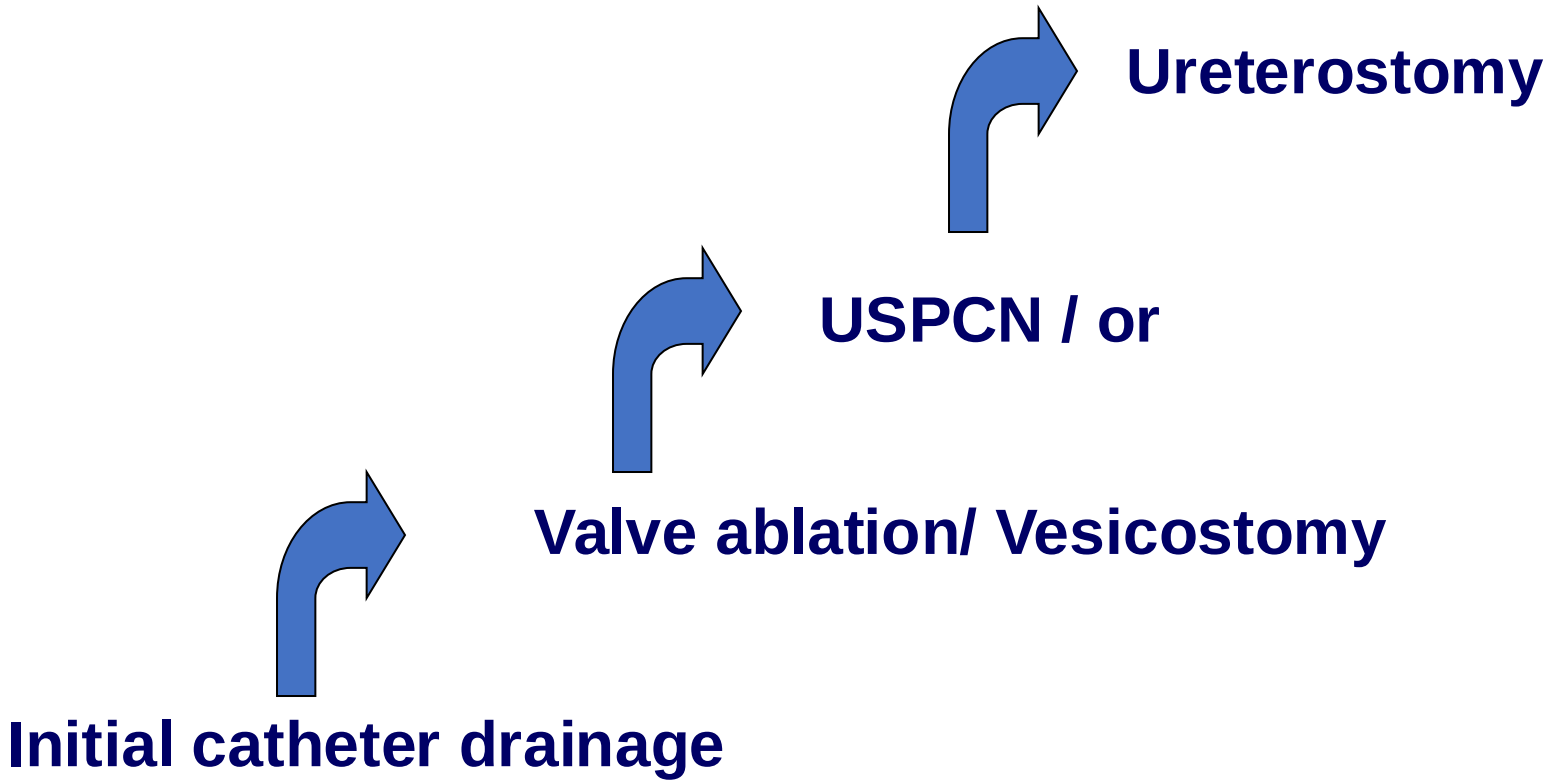
Non Responders ↔ **Responders**

↓ **B/L severe HDUN**

↓ **High ureterostomy, Biopsy**

↓ **Valve ablation**

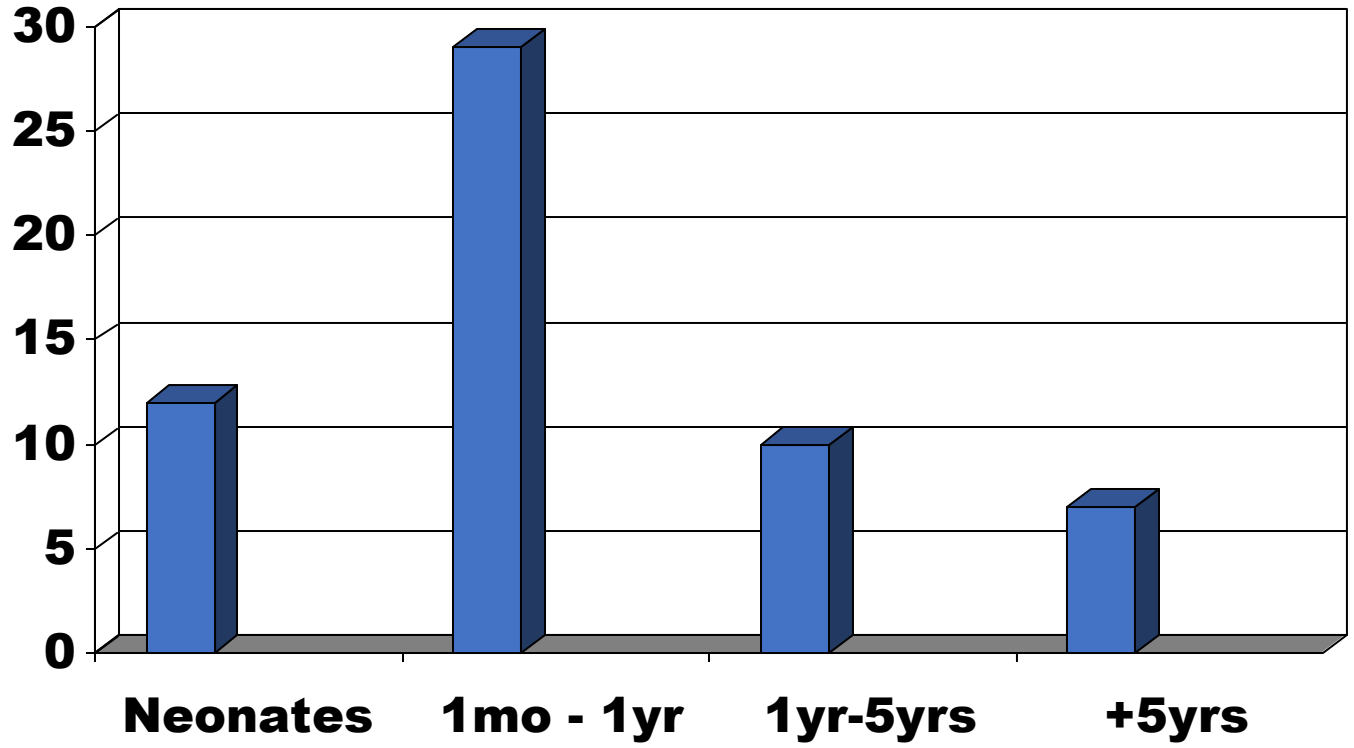
The ***Step Ladder*** Protocol



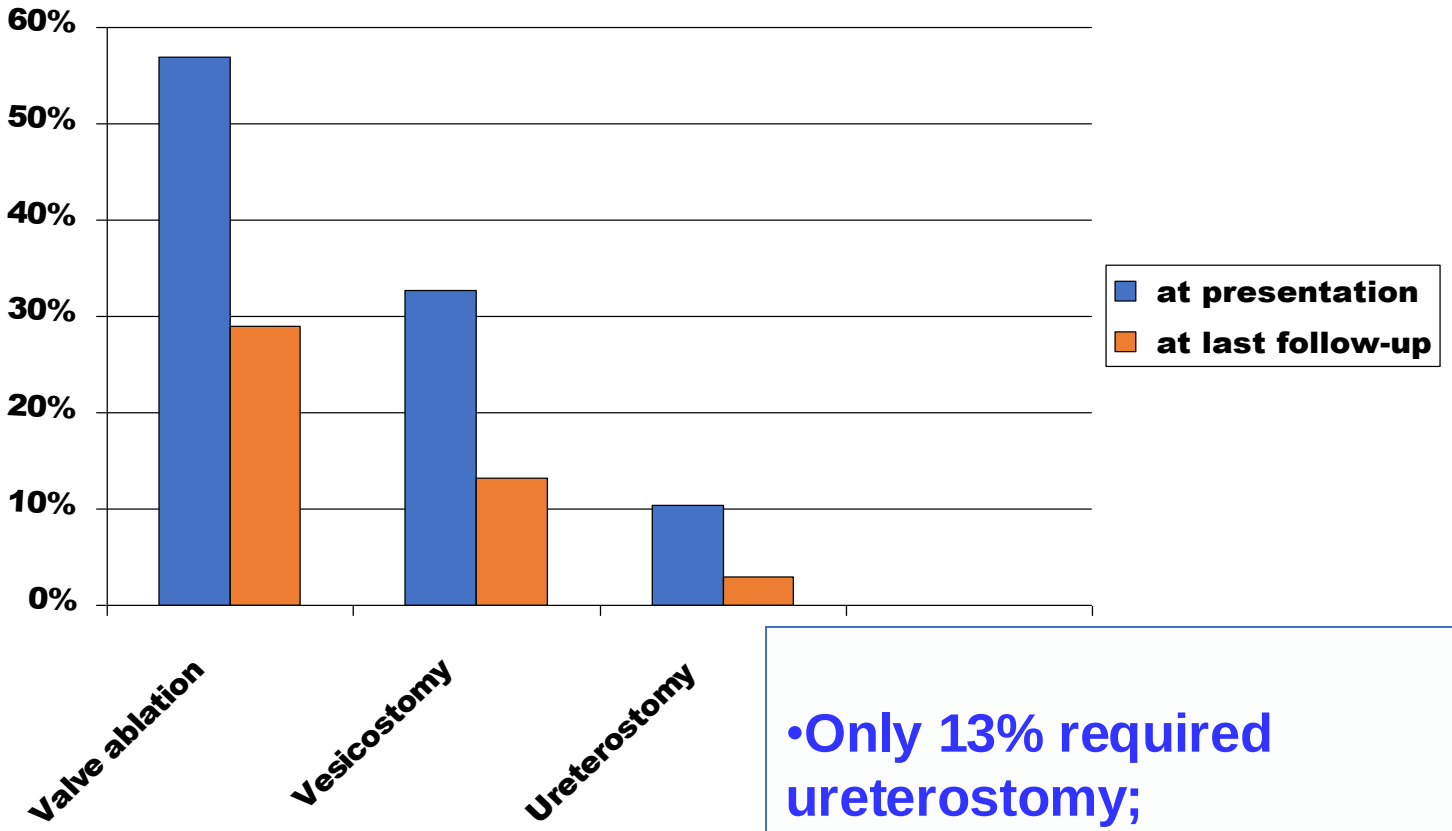
Bajpai M, et al: Factors affecting outcome in the management of PUV**.**
Pediatric Surgery International 1:11-15, 2001

*Age at Presentation: n= 58

Follow-up: Range = 3.6 - 9.0 yrs. ; mean : 6.9 yrs.

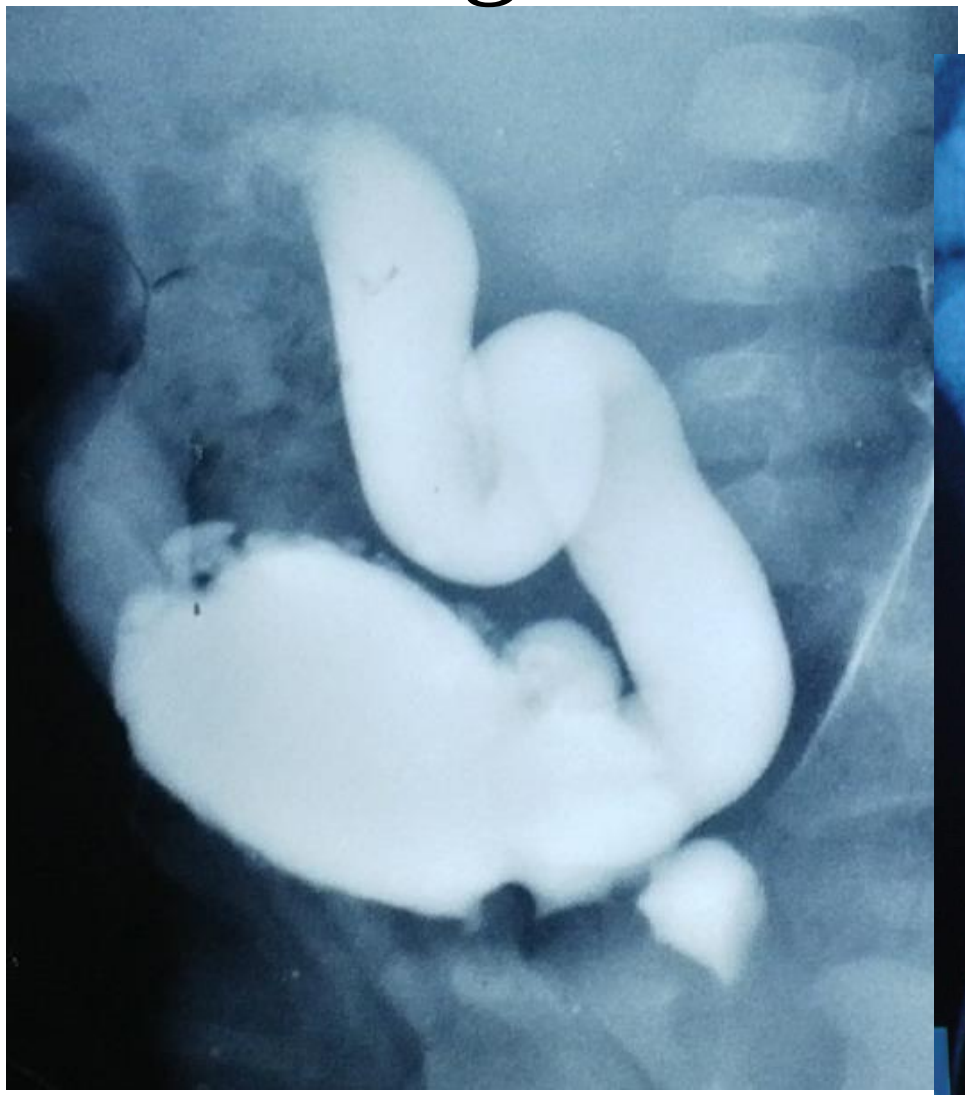


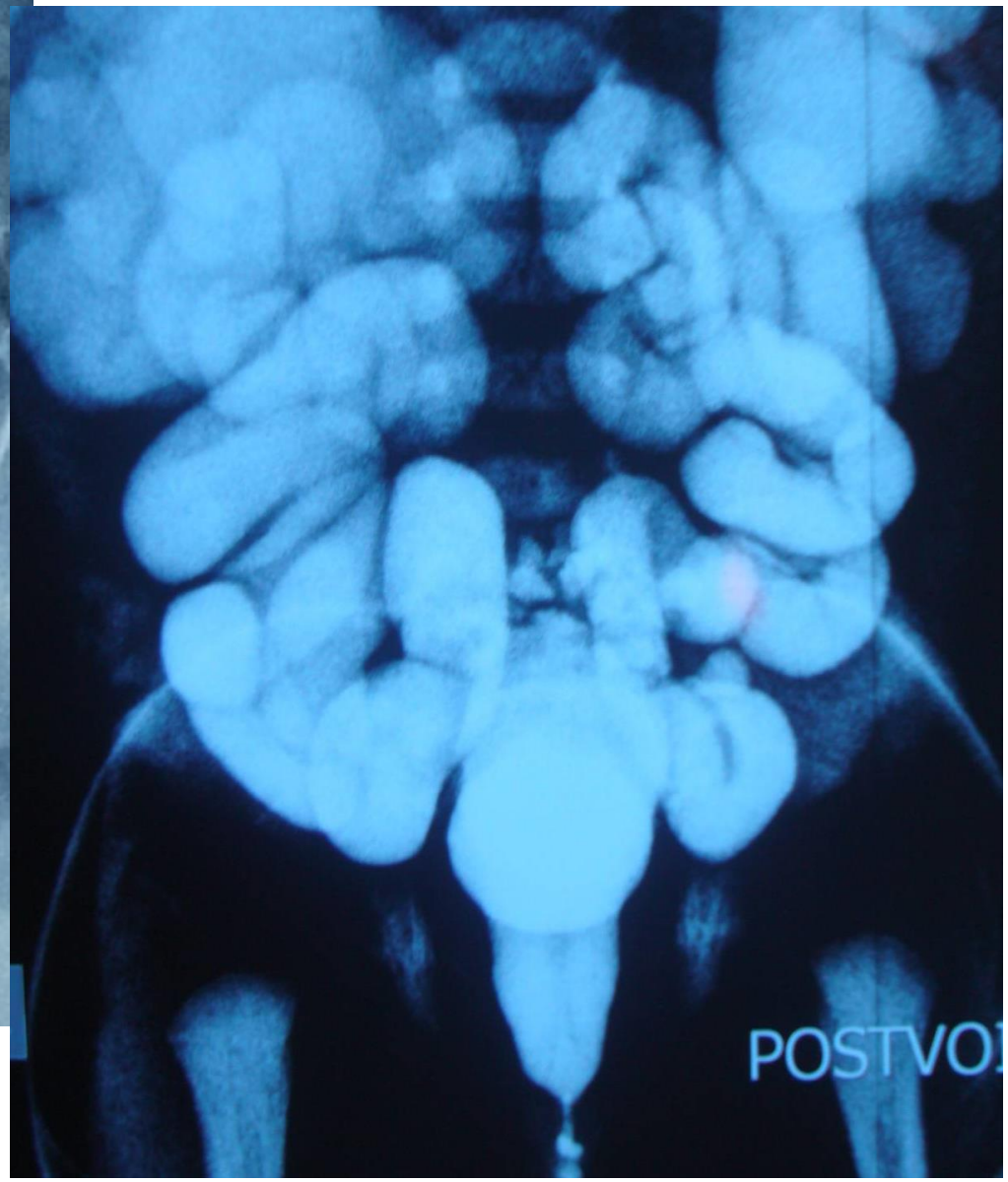
Procedure Related Outcome of Renal Function



- Only 13% required ureterostomy;
- 2/3 recovered renal function

High or low ureterostomy





Post ablation issues

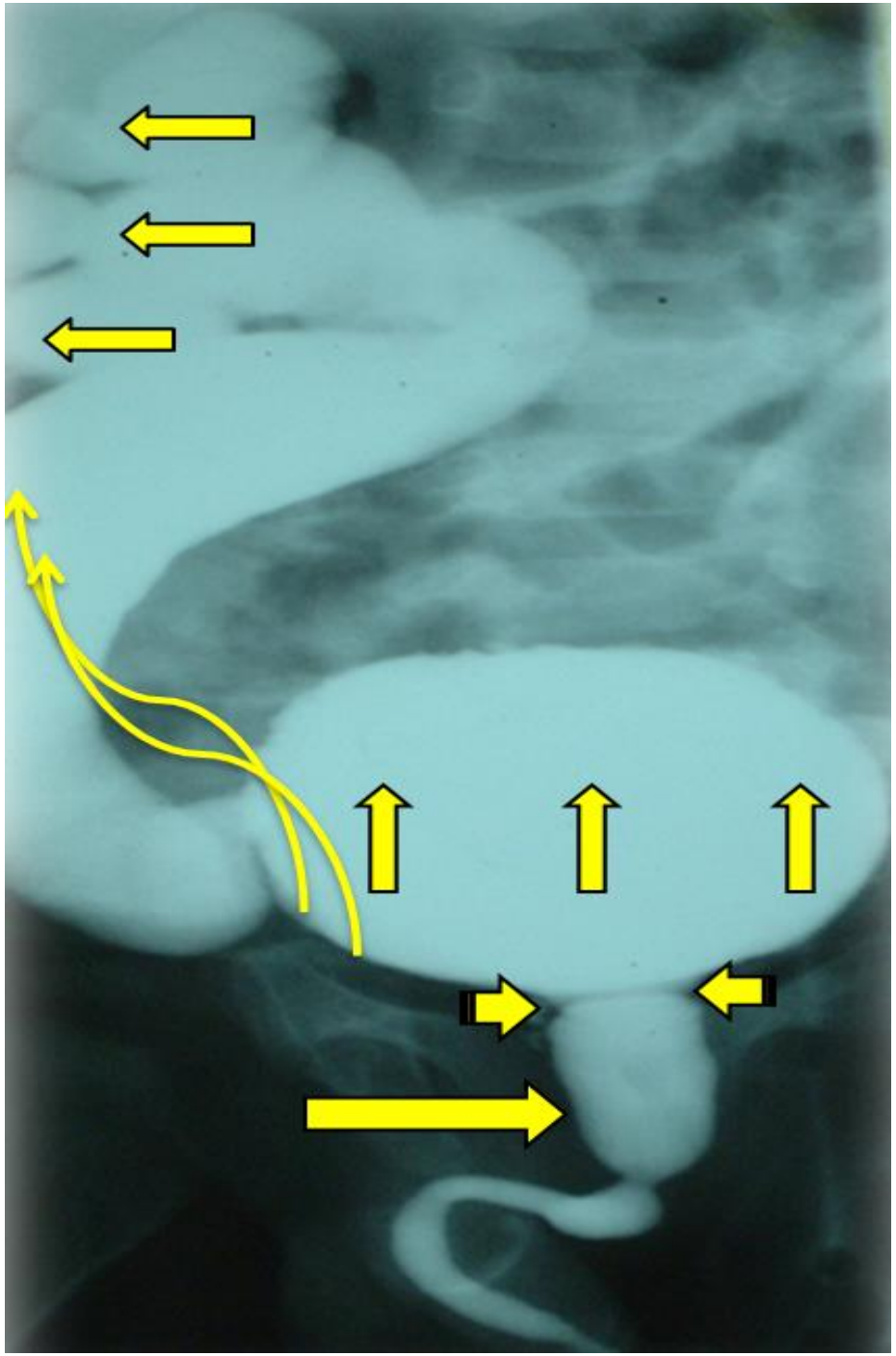
- Management begins **After** Valve ablation

**PUV:

Anatomical & Functional changes

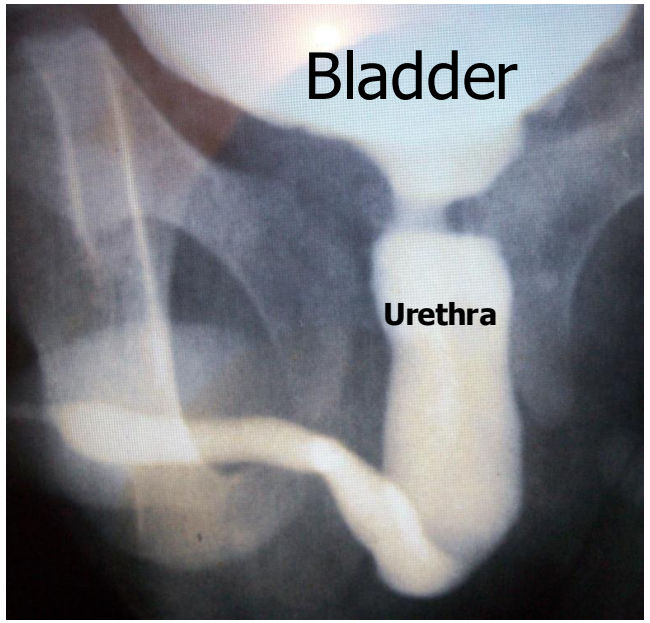
Back pressure effects

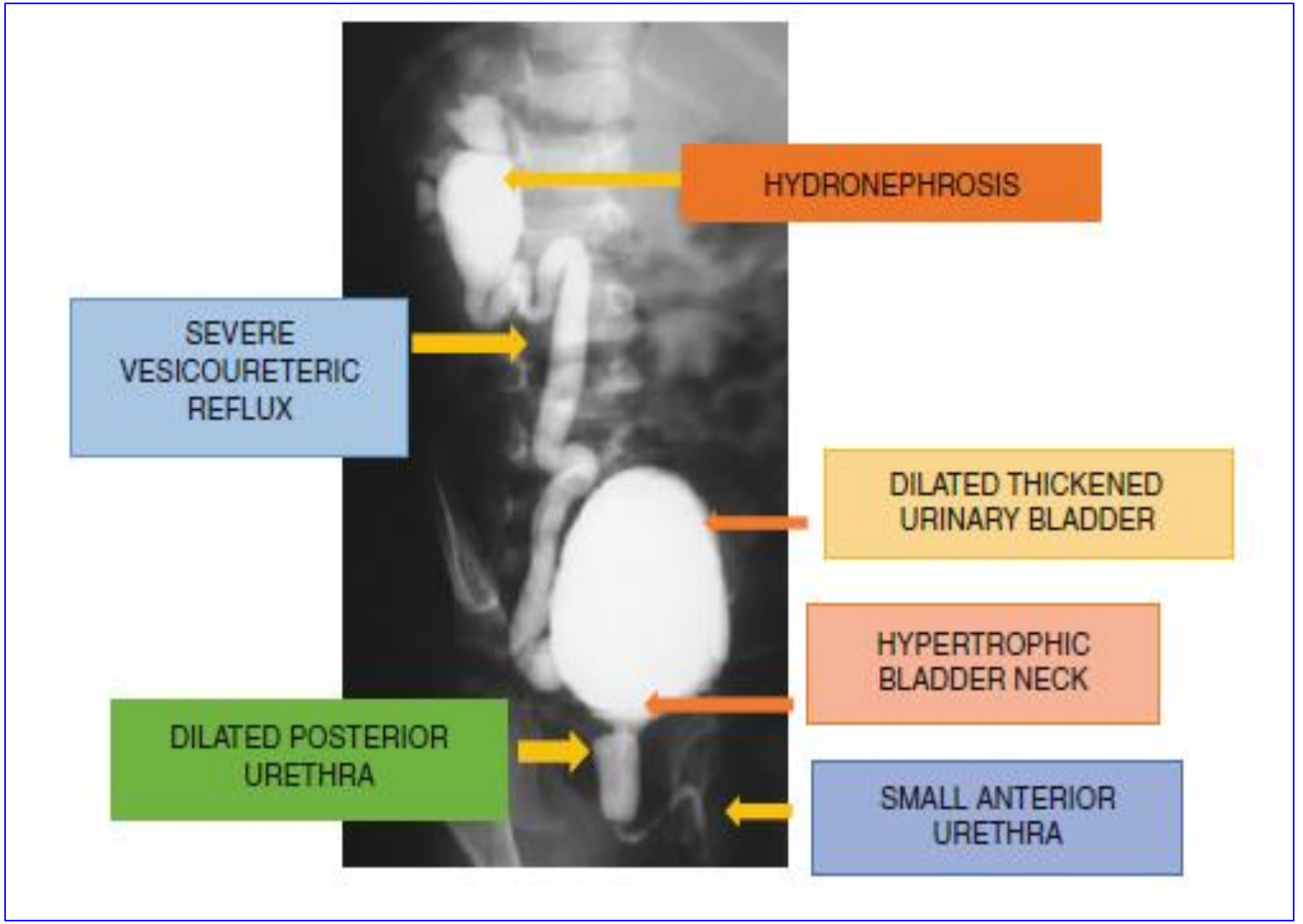
- Urethra
- Bladder neck
- Bladder wall
- Ureters
- Renal dysplasia



Back pressure effect

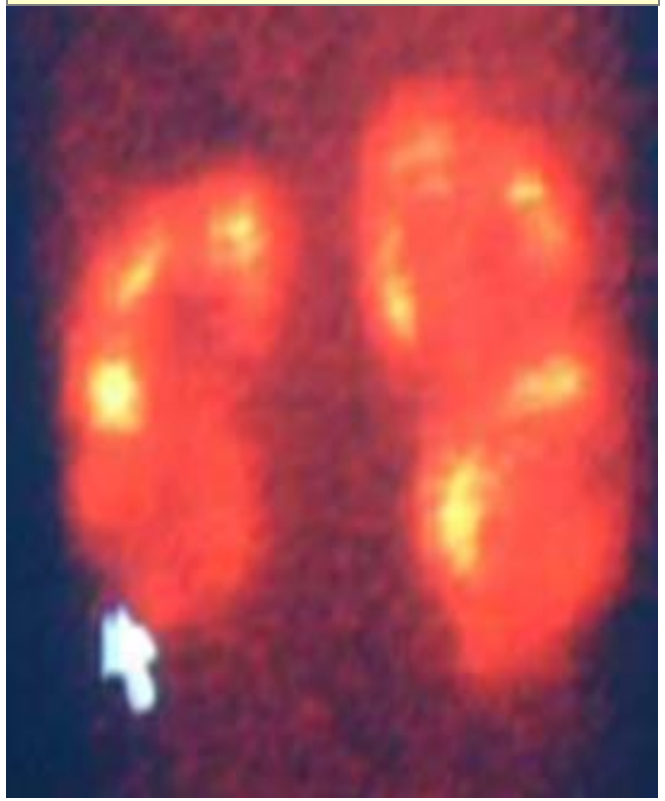
Bladder neck





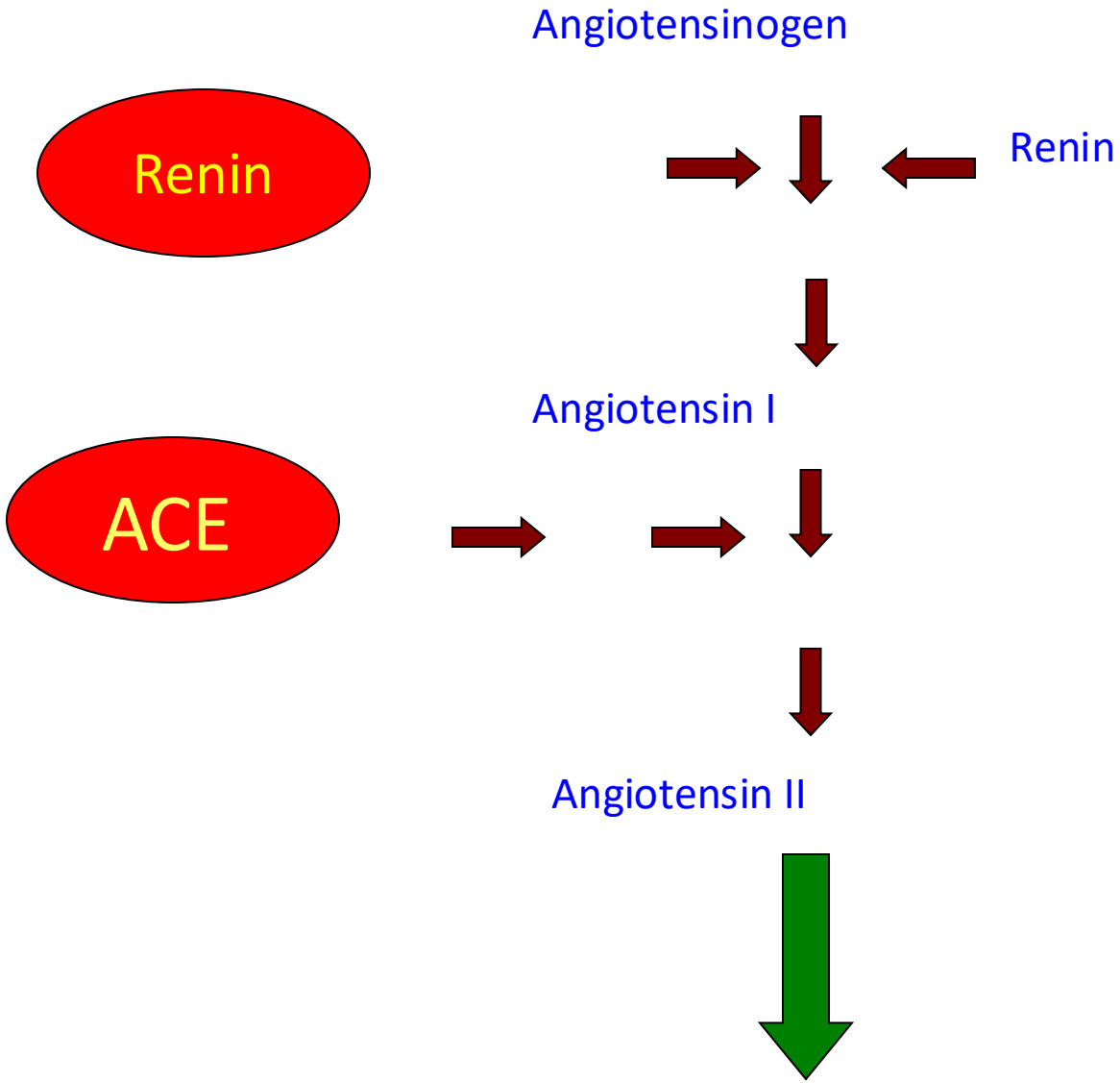
Post-ablation issues

Renal Scars (DMSA scan)



- Can we retard the pace of renal injury
  - RAS pathway
  - Genetic & Non-genetic molecular markers
  - Urinary cytokines & role of RAS blockade
  - Point of care test
  - Antenatal diagnosis & cordocentesis

The Renin Angiotensin System Pathway



Mediator for Apoptosis

Fig. 3. Those in whom PRA became normal after a period (mean duration 24.2 months) of follow up and remained normal till the last follow up (n:=12). No indication for upper tract deterioration (GFR) has been noted till last follow-up.

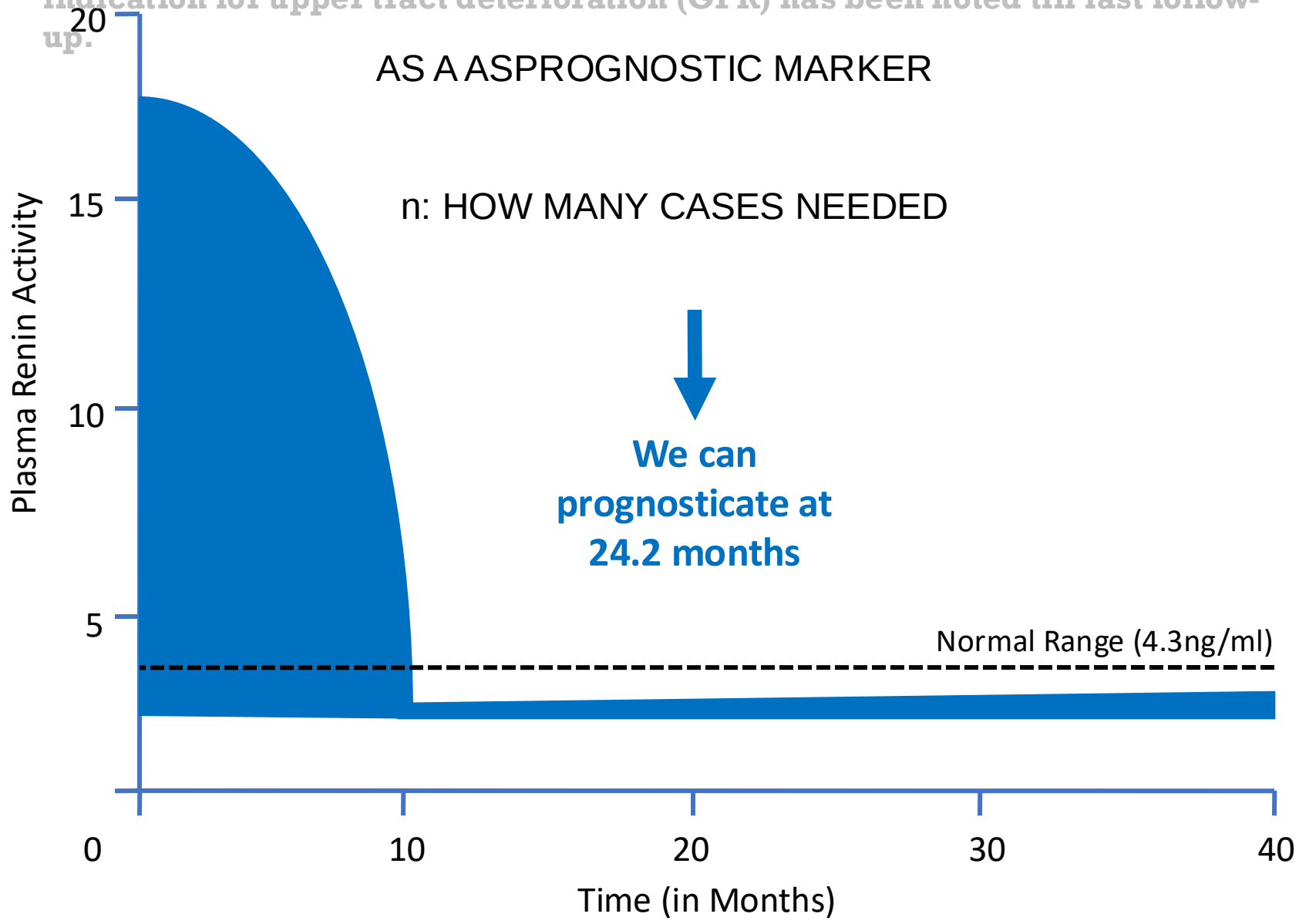
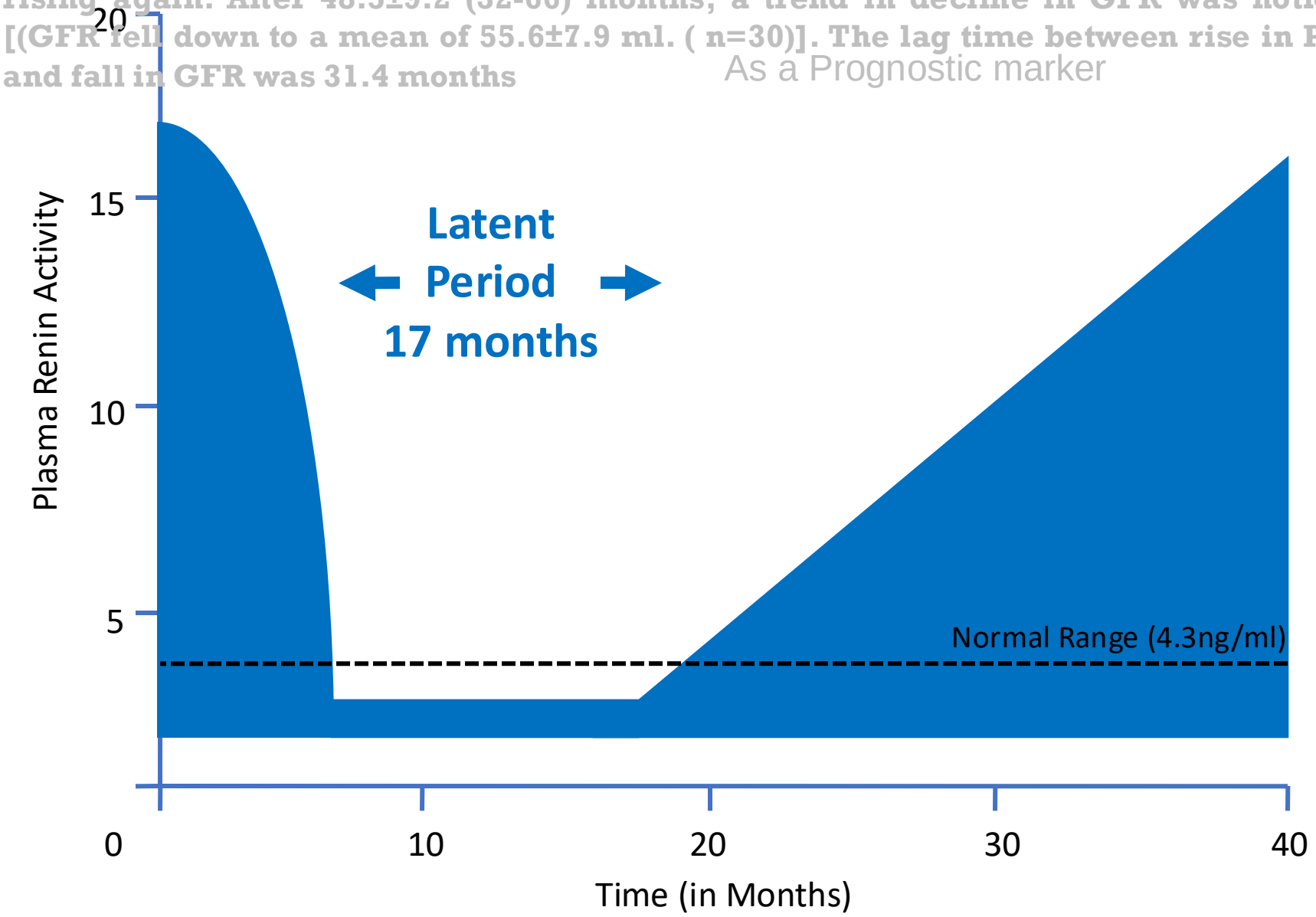
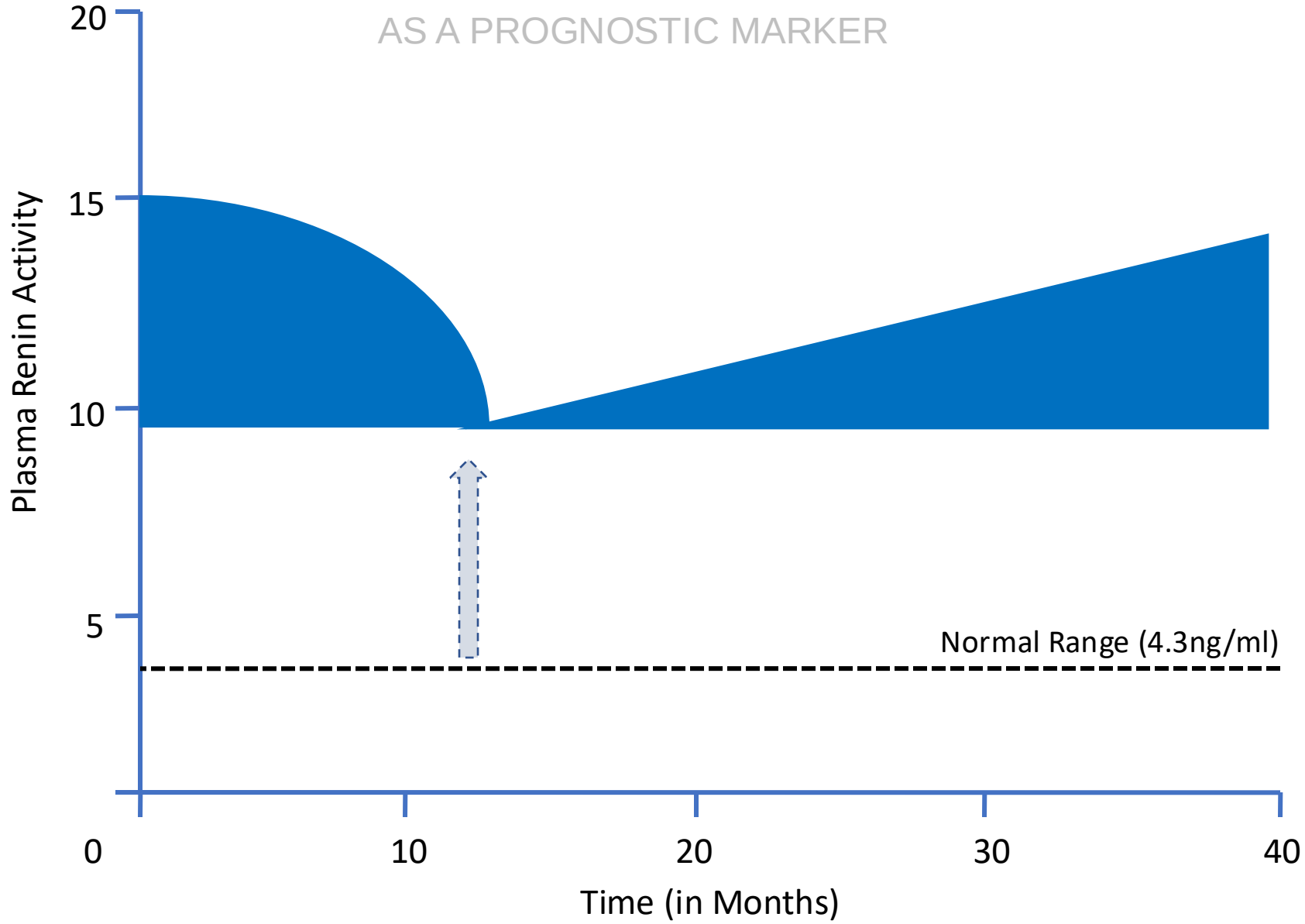


Fig. 2. In 30 out of 50 (60%) patients PRA became normal after valve ablation. It remained normal for a mean duration of 17.1±4.1 months(12-26 mo.) and then started rising again. After 48.5±9.2 (32-66) months, a trend in decline in GFR was noticed [(GFR fell down to a mean of 55.6±7.9 ml. (n=30)]. The lag time between rise in PRA and fall in GFR was 31.4 months

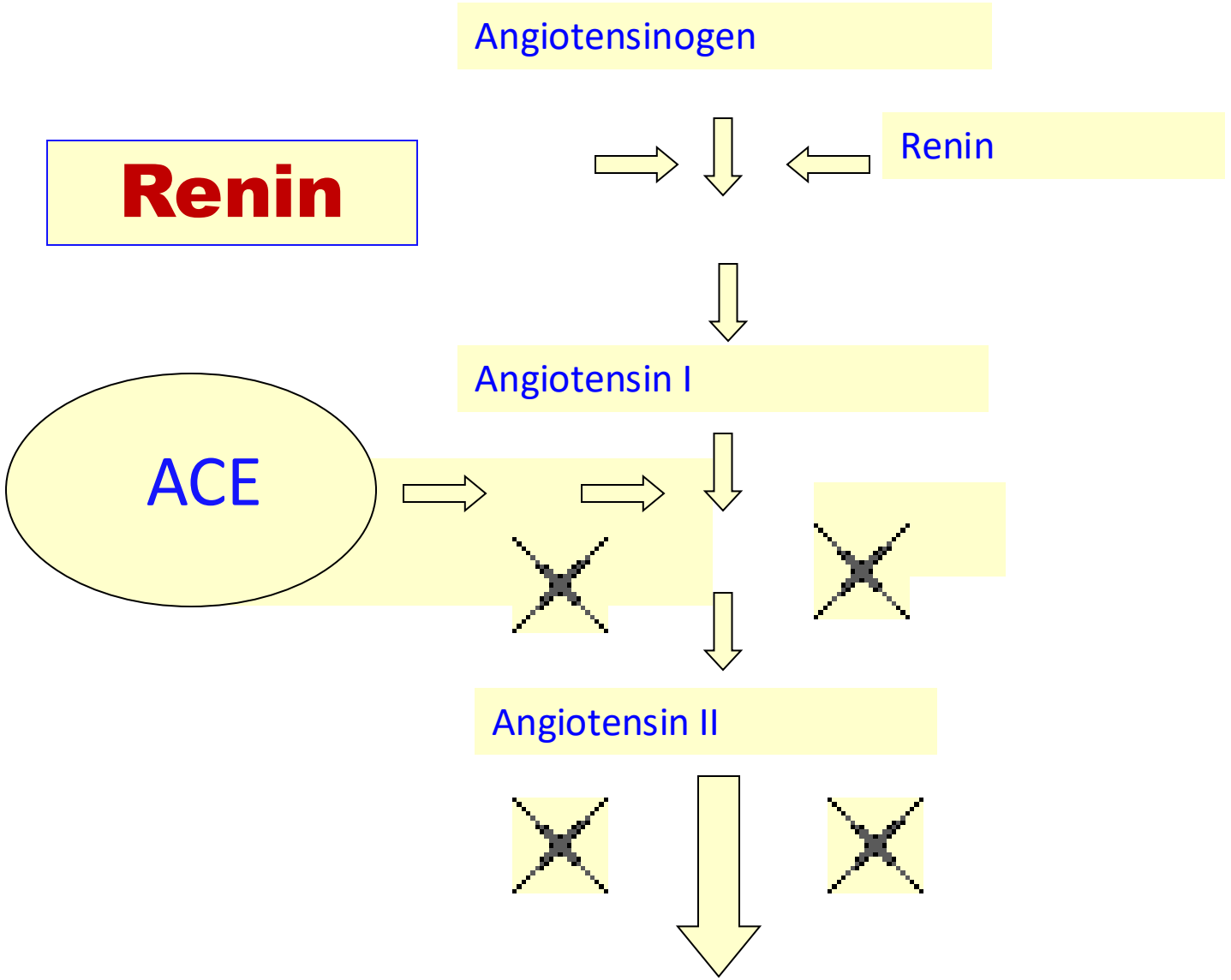
As a Prognostic marker



Those in whom PRA did not touch normal values and remained high even at the last follow up. During the follow up 26.7±4.4 (18-32) months their GFR had also started showing fall (n=8)



The Renin Angiotensin System Pathway



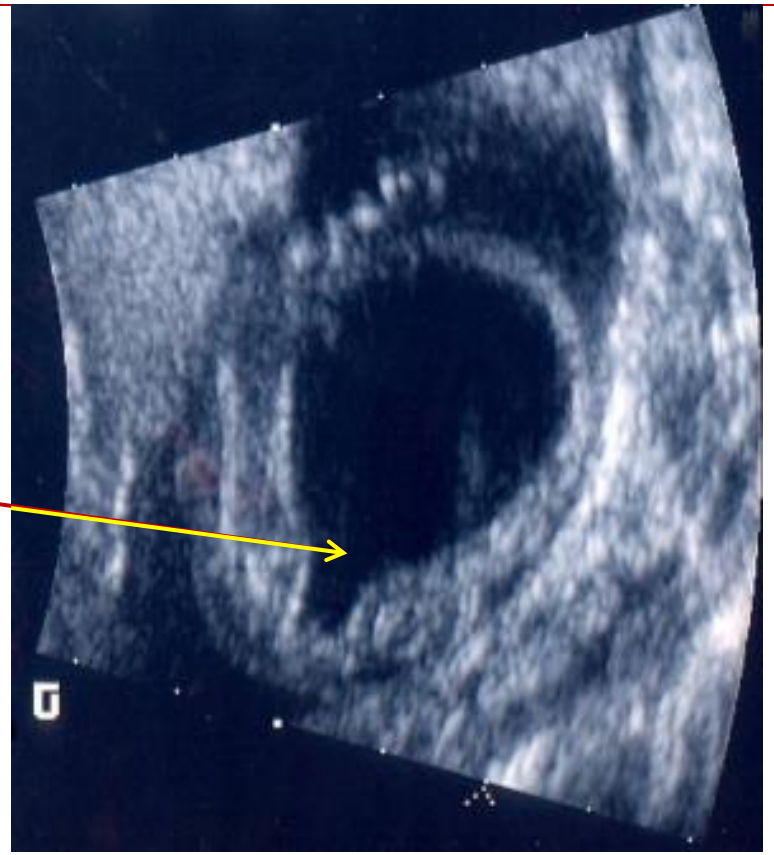
Mediator for Apoptosis

Antenatal diagnosis
Current status

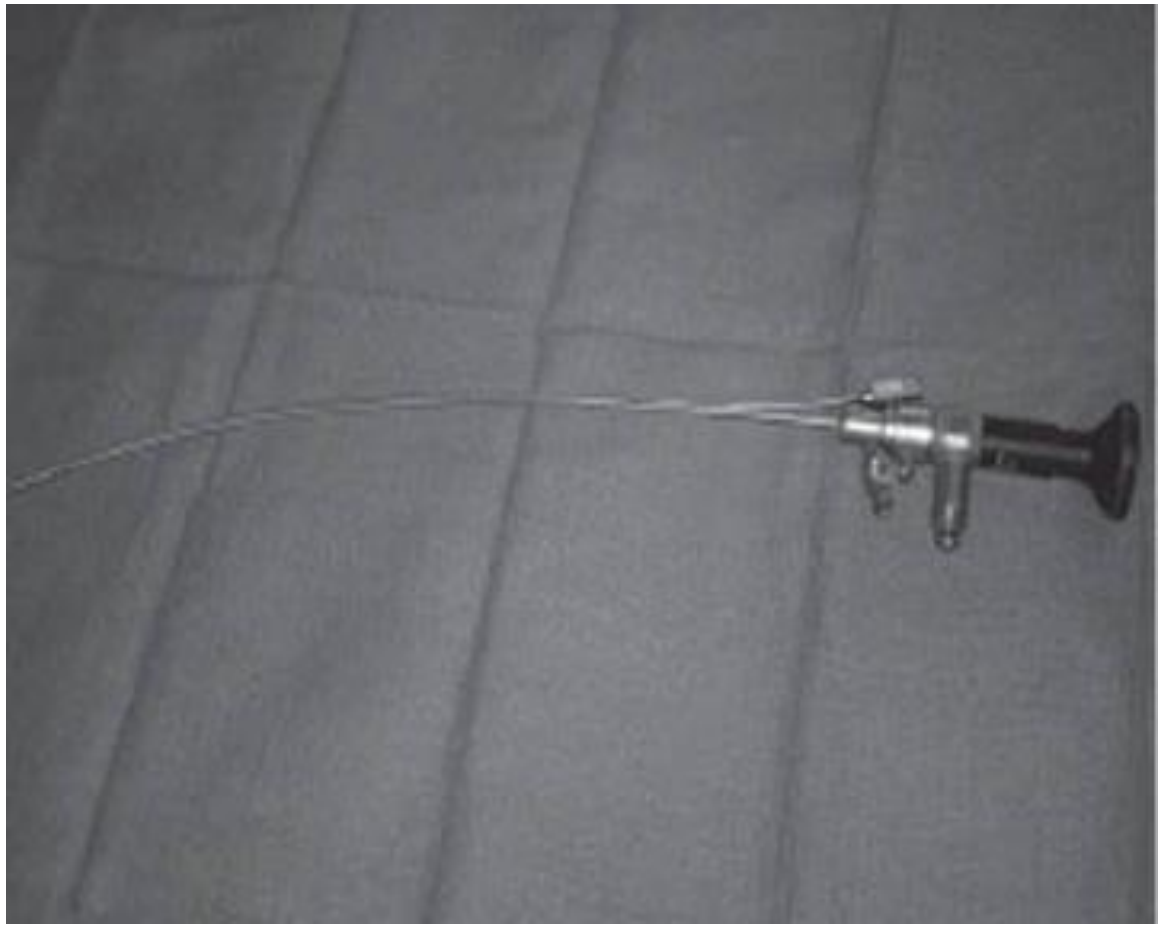
Sonography features

- B/L hydronephrosis
- Male sex-Karyotyping
- Amniotic fluid status
- Key- hole sign
- Failure of bladder emptying
- Cortico-medullary diff.
- Foetal ascites/urinoma

Nijagal, et al. *In* Bajpai M., Gearhart JP(eds.) Progress in Paediatric Urology: Vol. 13

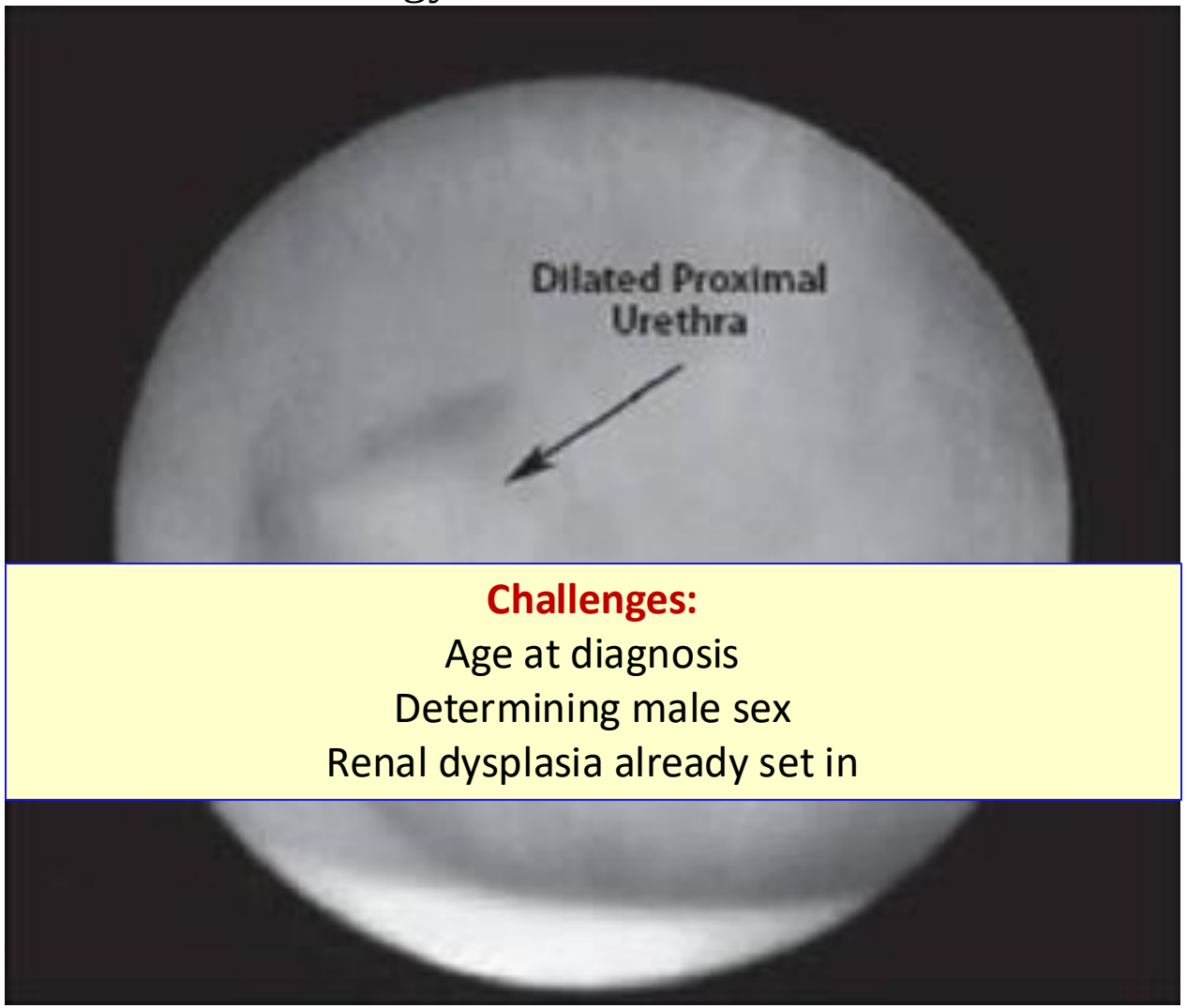


Nijagal, et al. *In* Bajpai M., Gearhart JP(eds.) Progress in Paediatric Urology: Vol. 13



3 mm foetoscope with working channel

Nijagal, et al. *In* Bajpai M., Gearhart JP(eds.) Progress in Paediatric Urology: Vol. 13



Challenges:

Age at diagnosis

Determining male sex

Renal dysplasia already set in

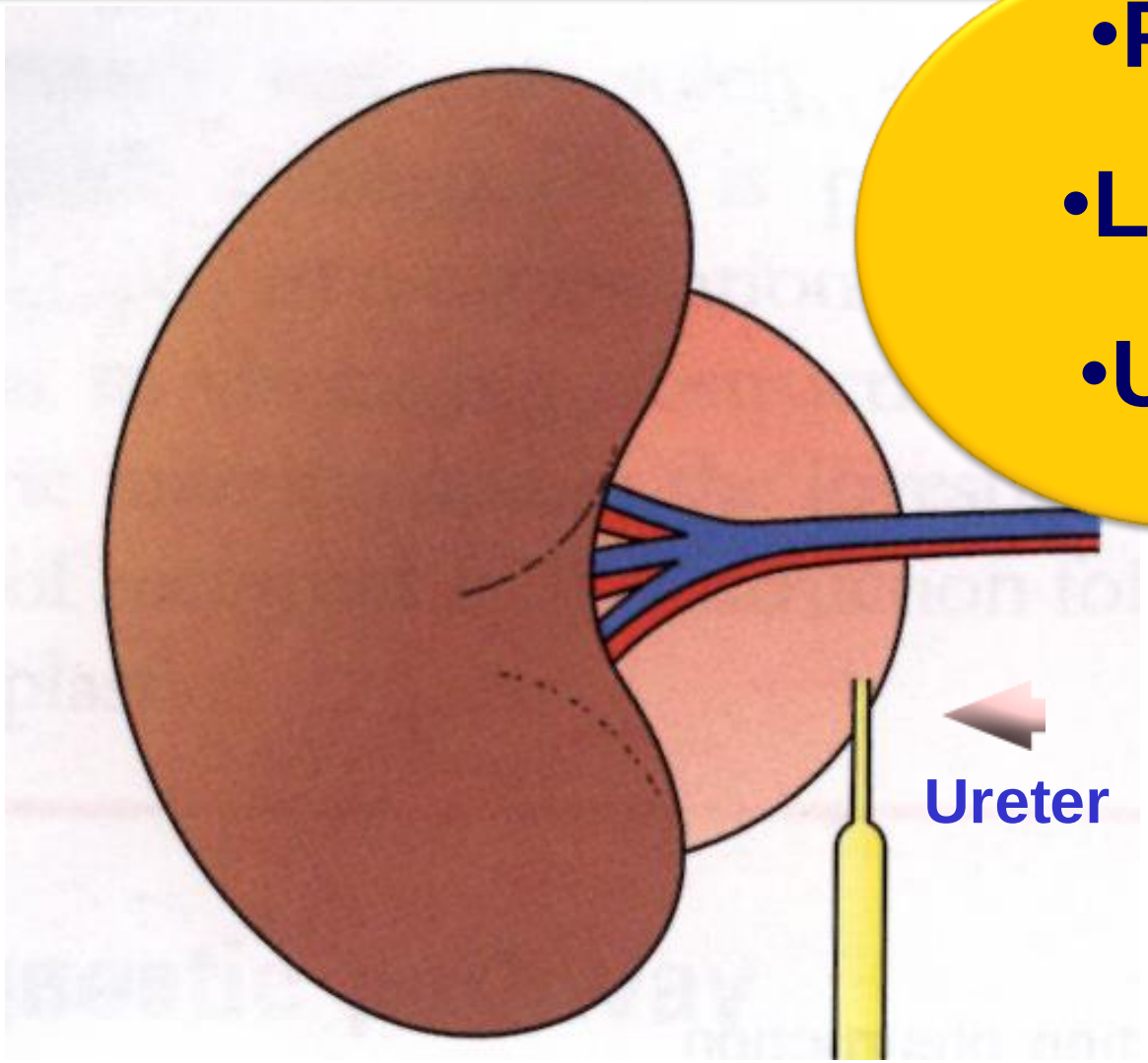
PUJO

Congenital Unilateral
Pelvi-Ureteric Junction Obstruction-

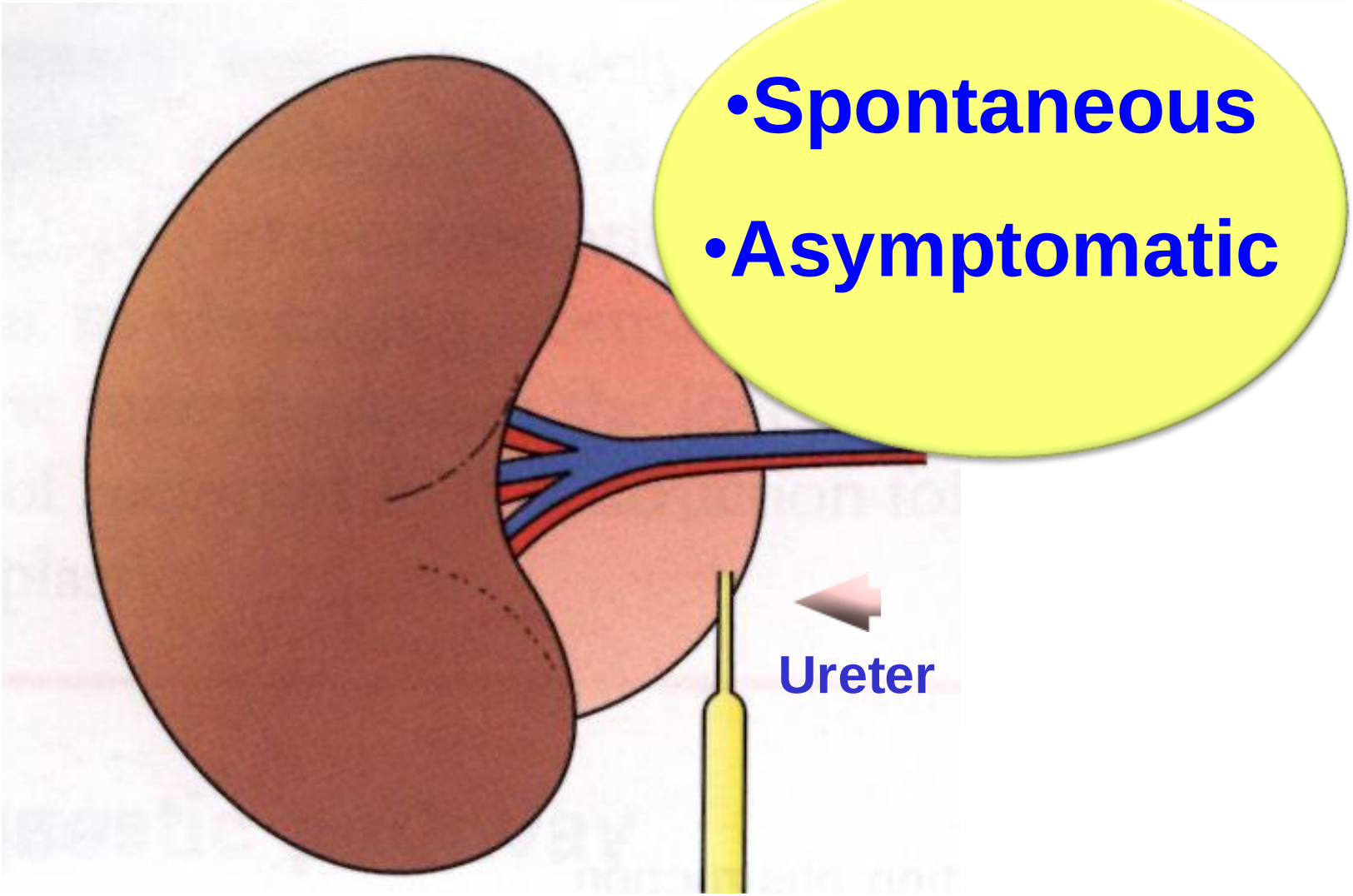
What is new:

- Diagnosis
- Surgical options
- How best to Follow Up
  - Post-pyeloplasty-

PUJO: Classical presentation



Postnatal



Postnatal follow-up of

antenatal hydronephrosis:

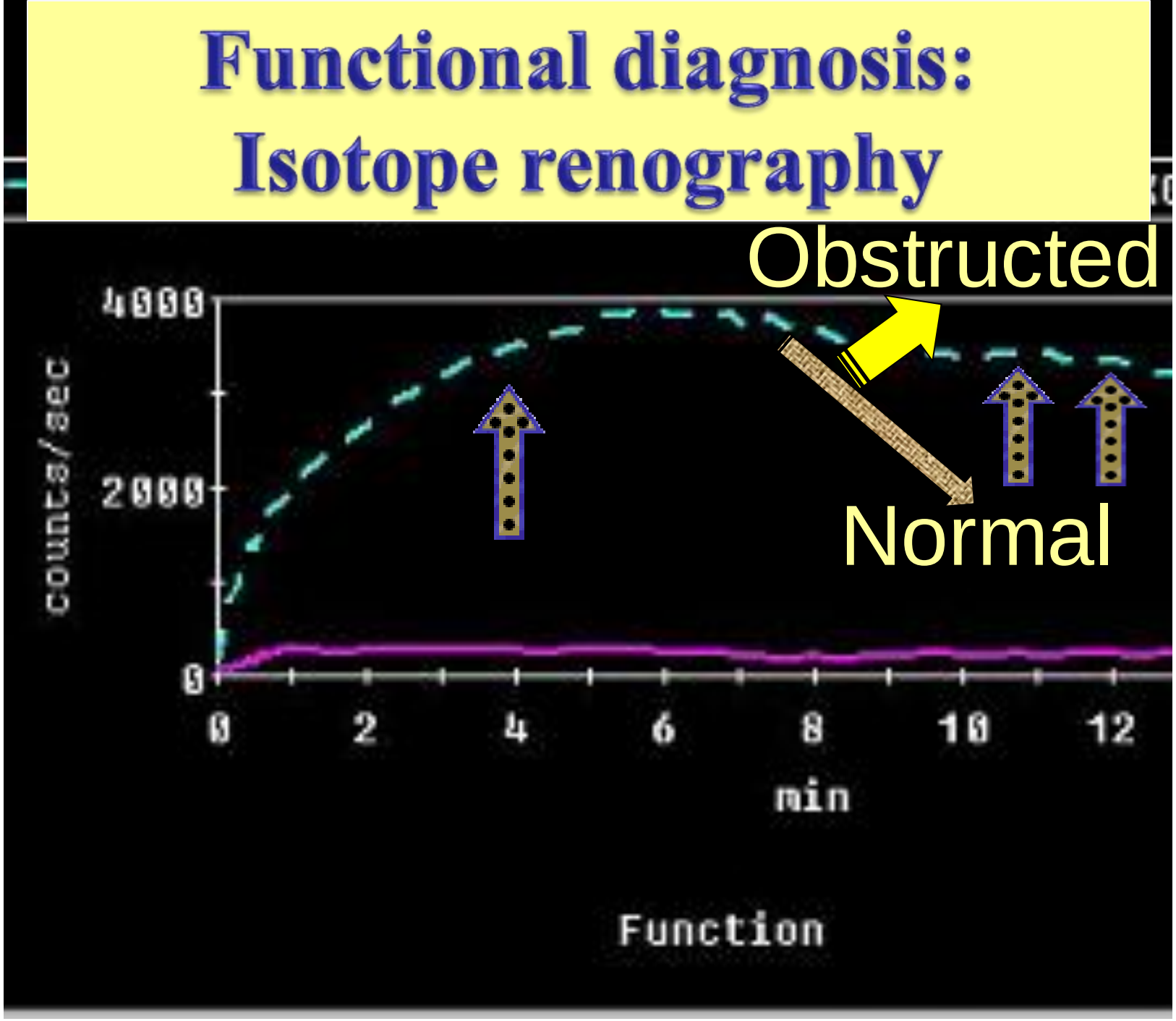
A health-care challenge!

J Perinatol. 2009 May;29(5):382-7. Epub 2009 Feb 5.
Cordero L, Nankervis CA, Oshaughnessy RW, Koff SA, Giannone PJ.

- n: 268 fetuses with ANH.
- 15 000 USG reports;
- 1/3 resolved; **2/3** required postnatal follow-up.
  - i.e., n= 180 with HN
    - **91 infants were lost to follow-up!!**
    - **Pitfall of conservative approach.**

IPNA

Functional diagnosis: Isotope renography



When to operate:
Redefined: non-operative F-U

- ❑ Retrospective diagnosis
- ❑ How long to F-U rest of cases?
  - ✓ Is there a better investigation?

When to operate:
Redefined: non-operative F-U

- Koff: By 18 mo. age= 75% - Surgery.

**Retrospective diagnosis

- How long to F-U rest of cases?

✓Is there a better investigation?

Present indications for surgery

At presentation:

- S.R.F.-<40%
- Lump
- Symptomatic

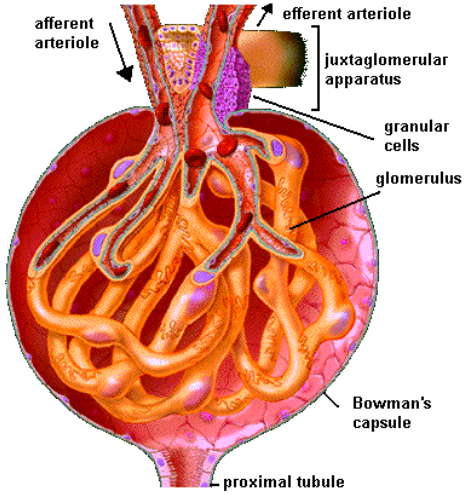
During F-U

- Fall in fn. > 10%

Direct Assay: Plasma Renin Activity

Angiotensinogen

Renin



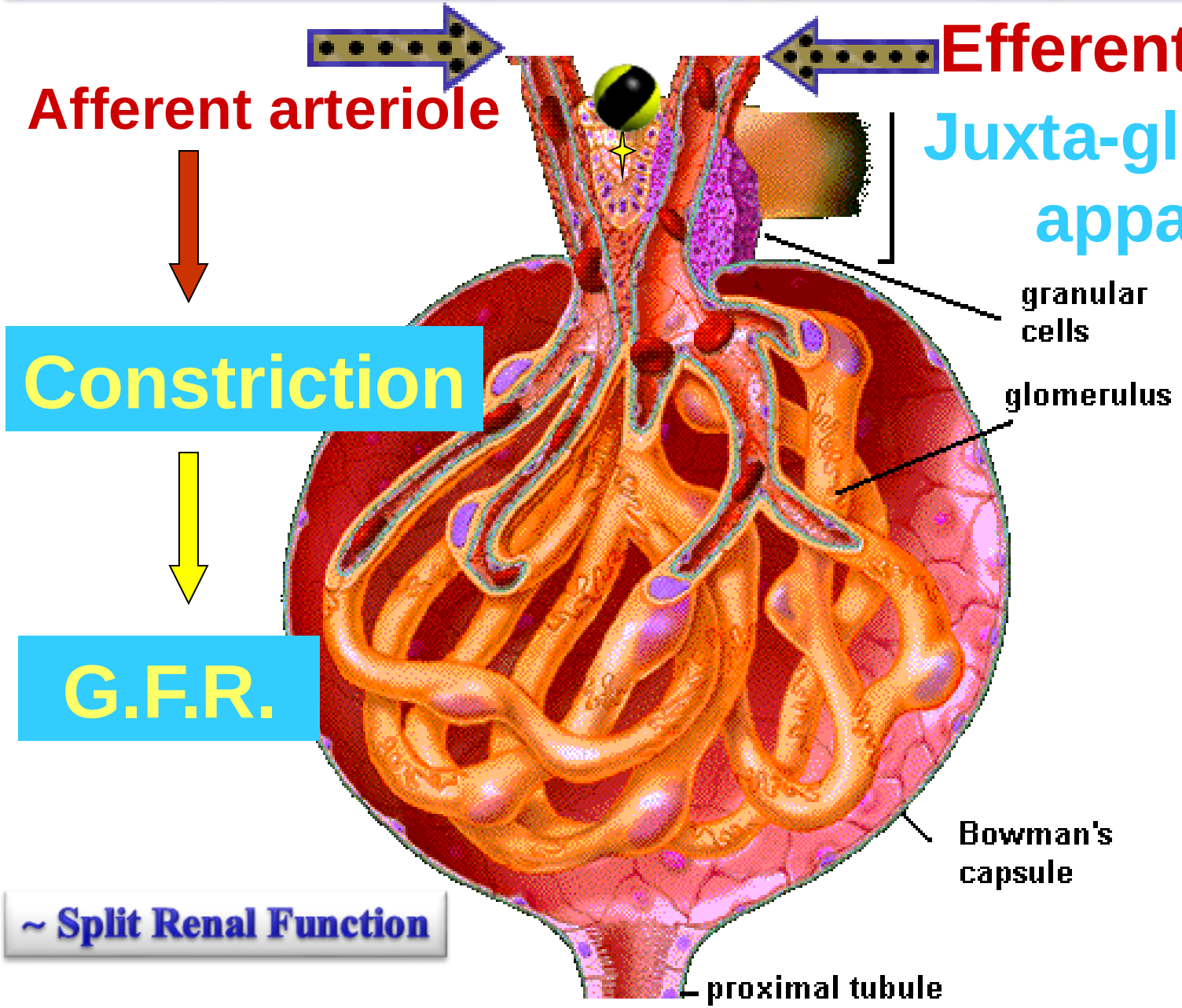
Angiotensin I

ACE

Angiotensin II

Apoptosis

G.F.R. / S.R.F. & Compensatory mechanism



Constriction

G.F.R.

~ Split Renal Function

Could PRA become a diagnostic test?

European journal of Obs.&Gyn.: n:11 foetuses

- RAS is activated even in Foetuses with hydronephrosis-

Direct assays:

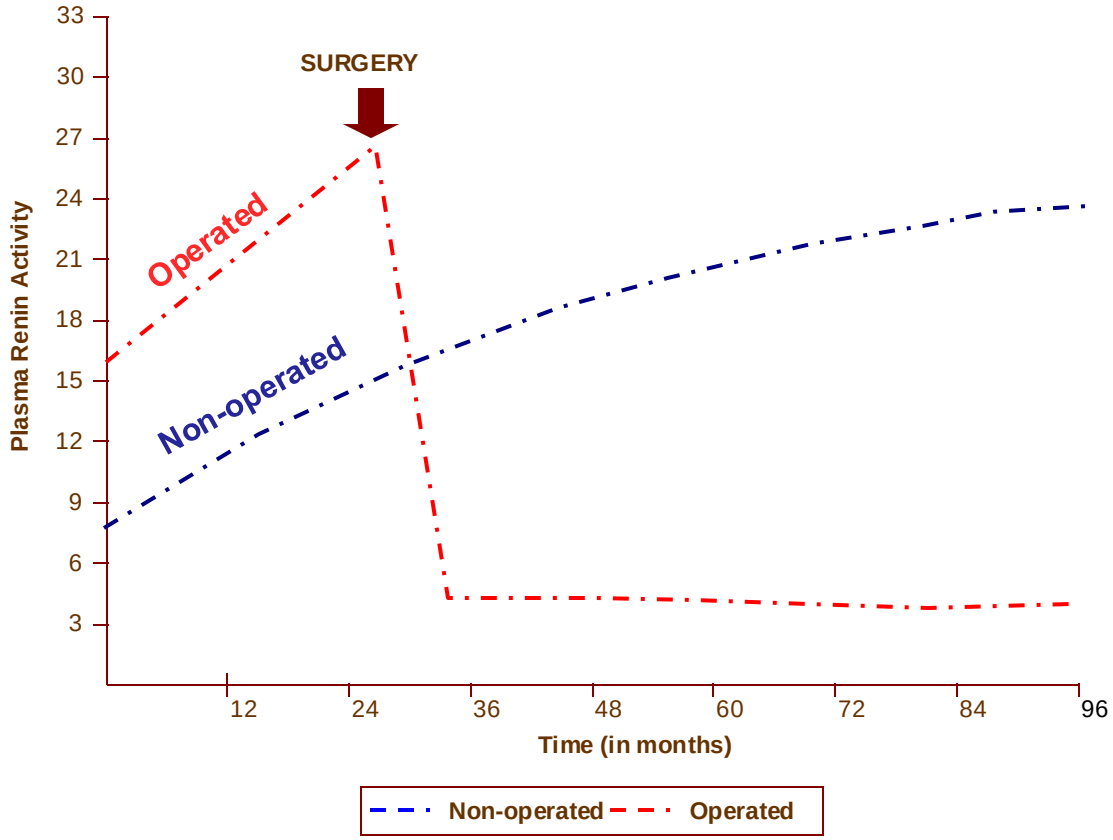
Plasma Renin Activity (PRA)

Surgery vs PRA

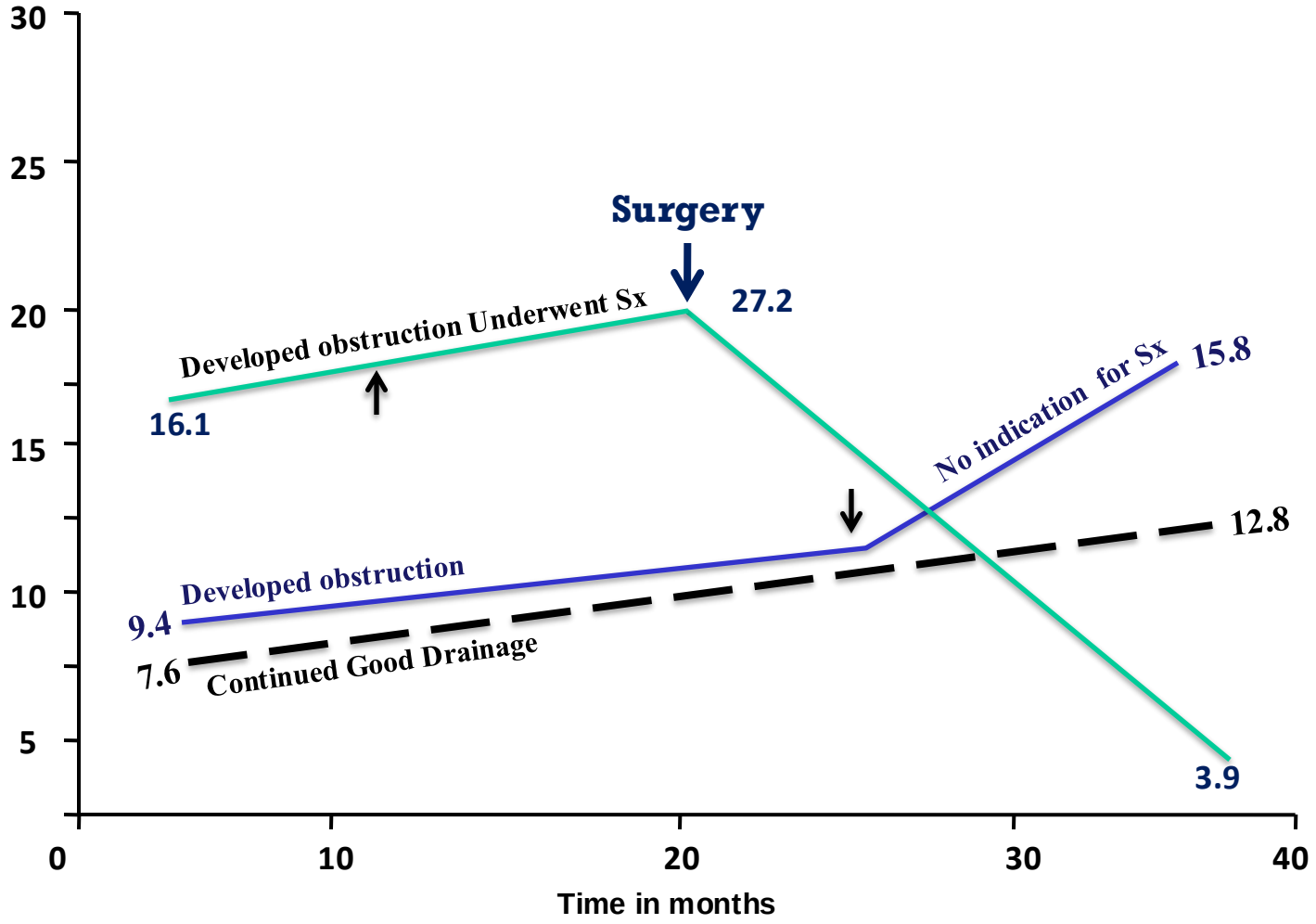
PRA: n=90

Post-pyeloplasty (n=50) vs Non- Op. (n=40)

Mean F-U= 33.0±17.1 (11-106 months)



Non-obstructed (?) Hydronephrosis vs RENIN



In the presence of pelvicalyceal dilatation and with drainage halftimes between 7 and 20 minutes or equivocal obstruction PRA can serve as a better marker for stratifying patients for surgery. As none of our patients had drainage halftimes below 7 minutes.

Continued good drainage: Drainage at last follow up: t ½ less than 20 minutes; n=17; Mean follow-up in months: 58.1±7.8 (43-68)

Developed obstruction: Drainage at last followup t ½ more than 20 minutes; n=13; Mean follow-up in months: 35.2±19.6 (16-67)

Underwent pyeloplasty: n=8, Mean duration before Sx 27.5±9.5 (14-42 months) after Sx 20.8±4.9 (16-30 months)

Prenatally Diagnosed Unilateral Hydronephrosis: Prognostic Significance of Plasma Renin Activity

Minu Bajpai,* C. S. Bal, M. Tripathi, M. Kalaivani and Arun K. Gupta

From the Departments of Pediatric Surgery (MB), Nuclear Medicine (CSB, MT), Biostatistics (MK) ar Institute of Medical Sciences, New Delhi, India

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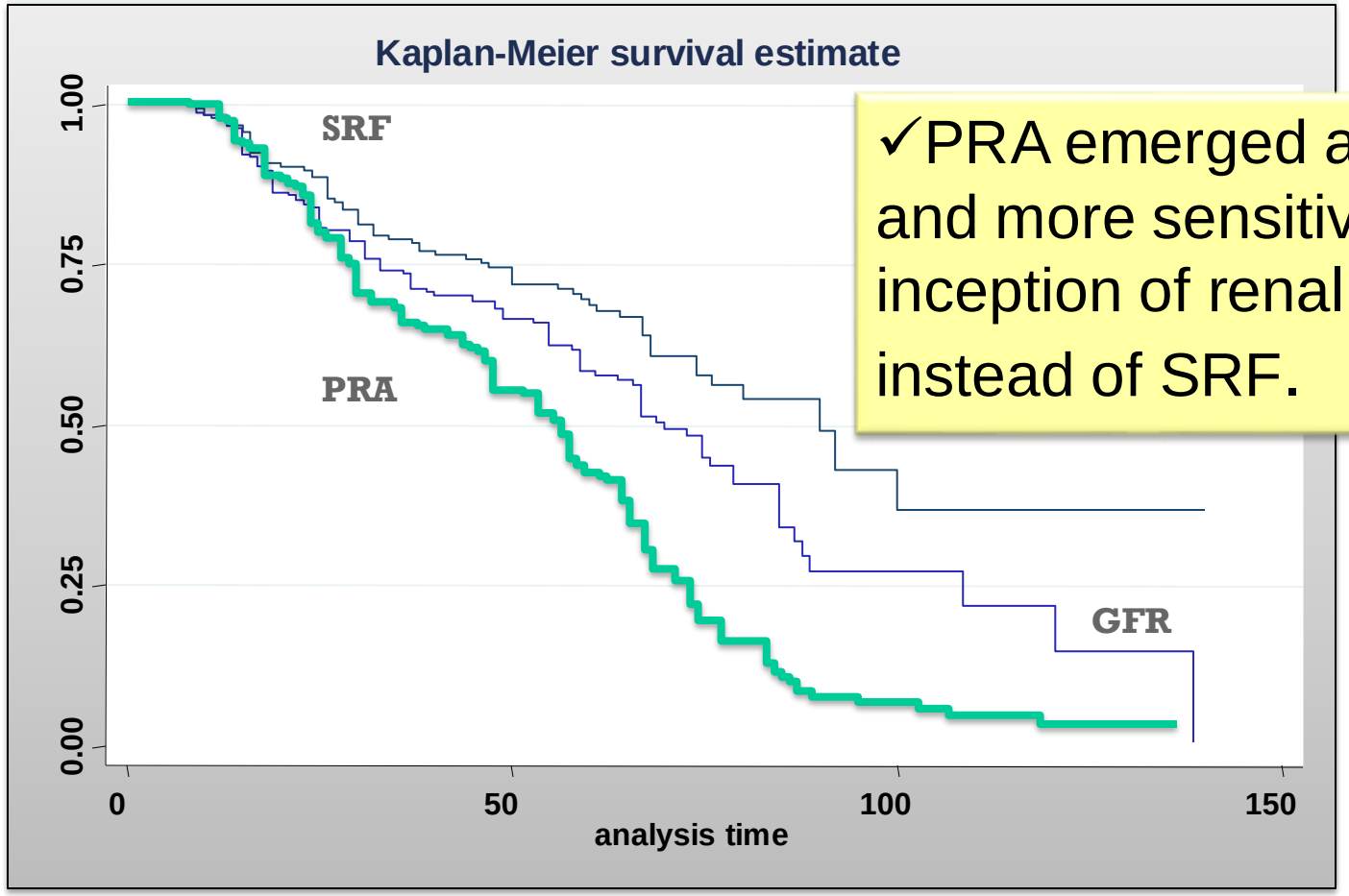
Dochead: Pediatric Urology

Vol. 178, 000-000, December 2007
Printed in U.S.A.
DOI:10.1016/j.juro.2007.08.058

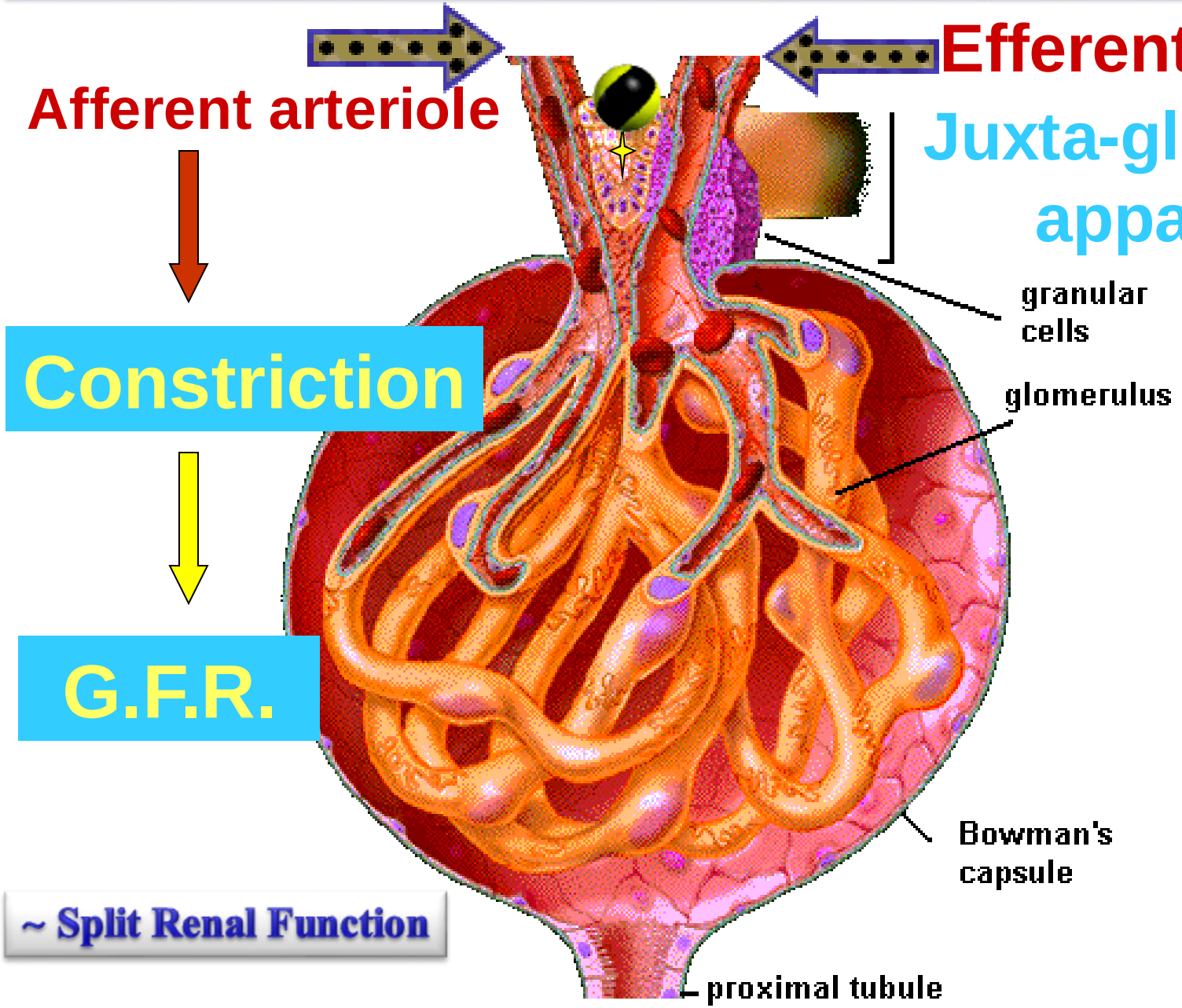
Kaplan-Meier Survival Estimation on the basis of S.R.F., G.F.R., P.R.A.
n: 307; Non-operative= 151; Pyeloplasty= 119



✓PRA emerged as the earliest and more sensitive marker of inception of renal damage instead of SRF.

- **SRF** — By **98 months 37% patients** still did not develop any indication for surgery
- **GFR** — By **98 months 26% patients** still did not develop any indication for surgery
- **PRA** — **By 86 months no patients** remained without indication for surgery

G.F.R. / S.R.F. & Compensatory mechanism

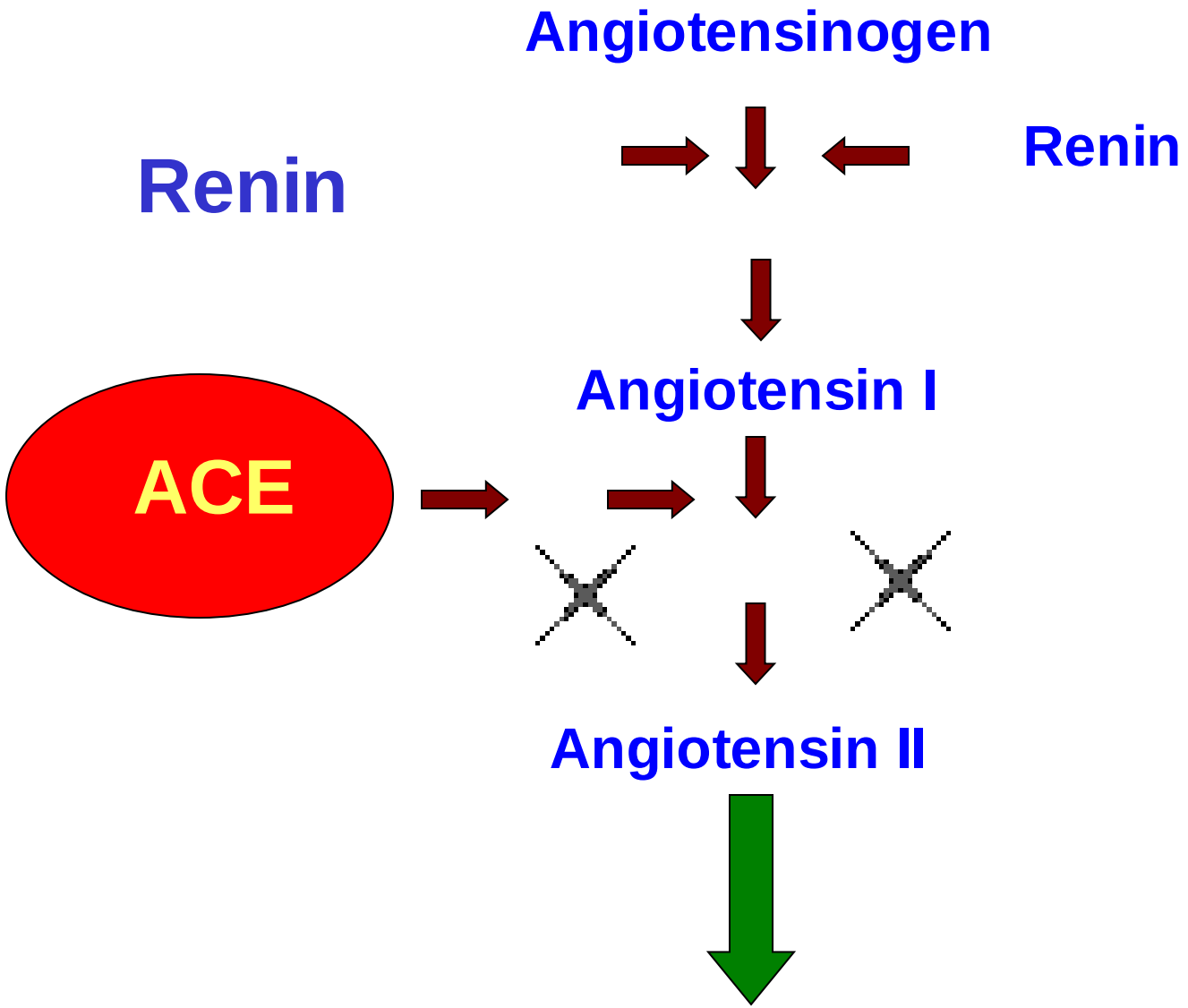


Constriction

G.F.R.

~ Split Renal Function

The Renin Angiotensin System Pathway



Mediator for Apoptosis

‘Captopril challenge Test’

- N= 25 patients; U/L HN
- Age= 1 mo. To 144 months
- F-U= 6-72 months
- Activation seen in 32%
  - **Surgery in 75%**
  - **All grades: II, III, IV**

Captopril renography determines
End point of Non-op. mng.

0022-5347/02/1685-2158/0
THE JOURNAL OF UROLOGY®

Vol. 168, 2158–2161, November 2002
Printed in U.S.A.
DOI: 10.1097/01.ju.0000034367.40739.6f

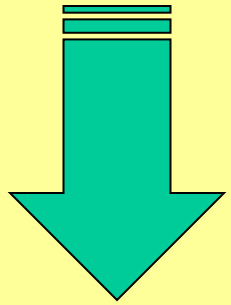
PROGNOSTIC SIGNIFICANCE OF CAPTOPRIL RENOGRAPHY FOR MANAGING CONGENITAL UNILATERAL HYDRONEPHROSIS

MINU BAJPAI,* A. PURI, M. TRIPATHI AND A. MAINI

From the Departments of Paediatric Surgery and Nuclear Medicine, All India Institute of Medical Sciences, New Delhi, India

- **Surgical options-**
  - -Open surgery
  - -Laparoscopy
  - -Robotic surgery
  - -Lumbotomy
  - -Lumboscopy

Less & less ports



Results-

Robotic vs Laparoscopic vs Open surgery

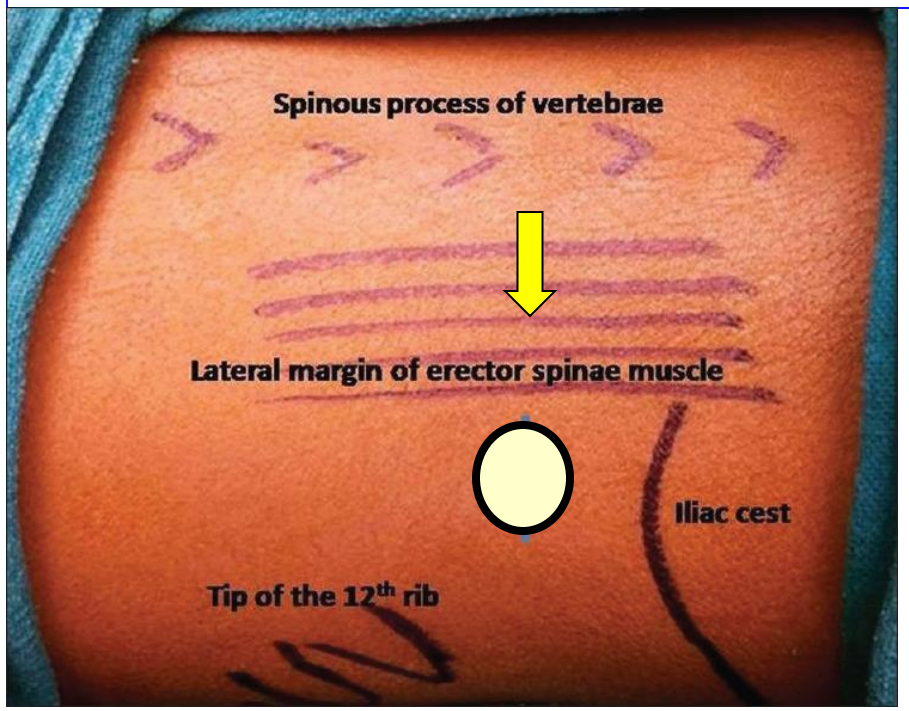
Primary outcomes: no significant differences between Robotic & 3-port Laparoscopy or Open surgery

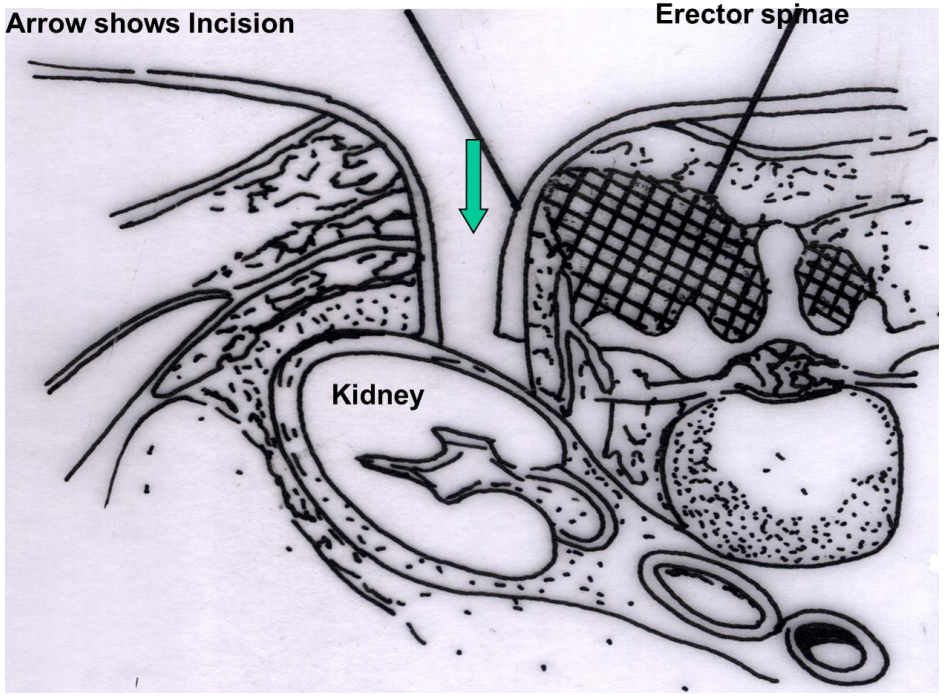
Secondary outcomes:

- Robotic: Short hospital stay, lower blood loss; less opiate requirement

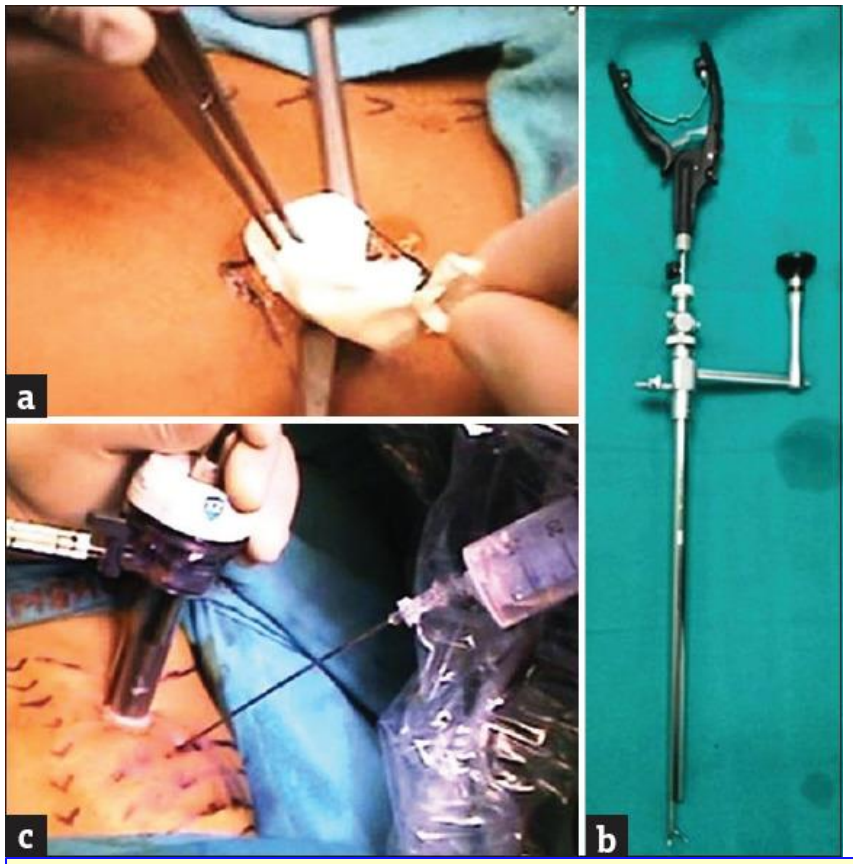
–OT time & cost is more

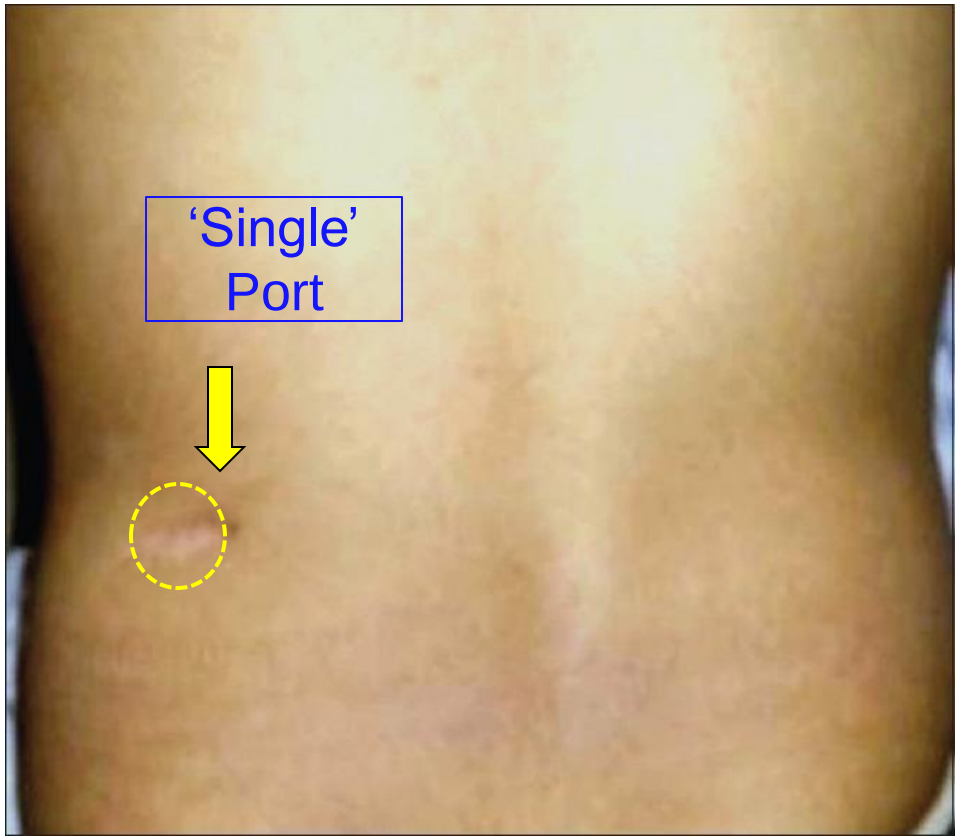
‘Single’ Port Lumboscopy Pyeloplasty





Lumboscopy Pyeloplasty





J Indian Assoc Pediatr Surg. 2020 May-Jun; 25(3): 163–168.
Published online 2020 Apr 11. doi: 10.4103/jiaps.JIAPS_5_19

Lumboscopic-Assisted Pyeloplasty: A Single-Port, Retroperitoneoscopic Approach for Children with Pelvi-Ureteric Junction Obstruction

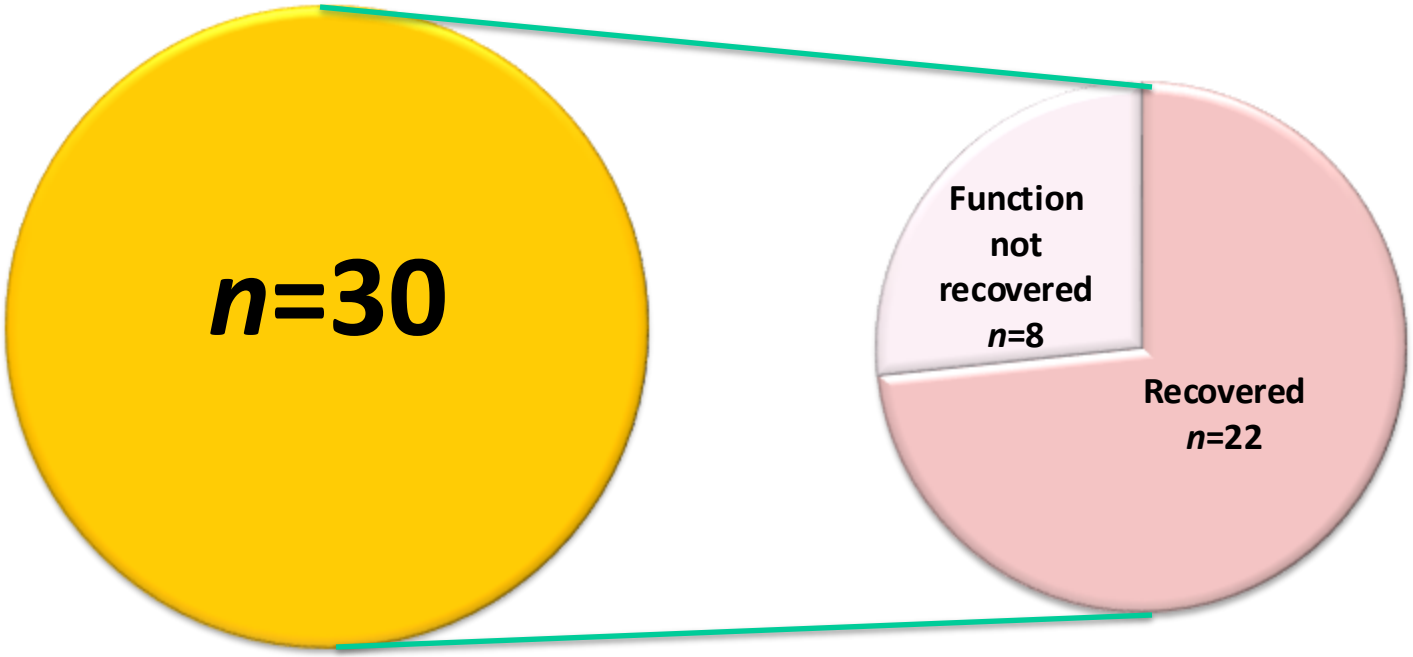
Minu Bajpai, Kashish Khanna, Vikram Khanna, Prabudh Goel, and Dalim Kumar Baidya[1]

IPNA

PUJO-
Other issues..

- Aberrant vessels
- Approach to:
  - Bilateral PUJO
  - Non-functioning kidneys
    - ✓**Can we improve lost function?**

Non-functioning kidneys
Function recovery after PCN



Twenty two out of 30 (73.3%) successfully recovered their function after PCN

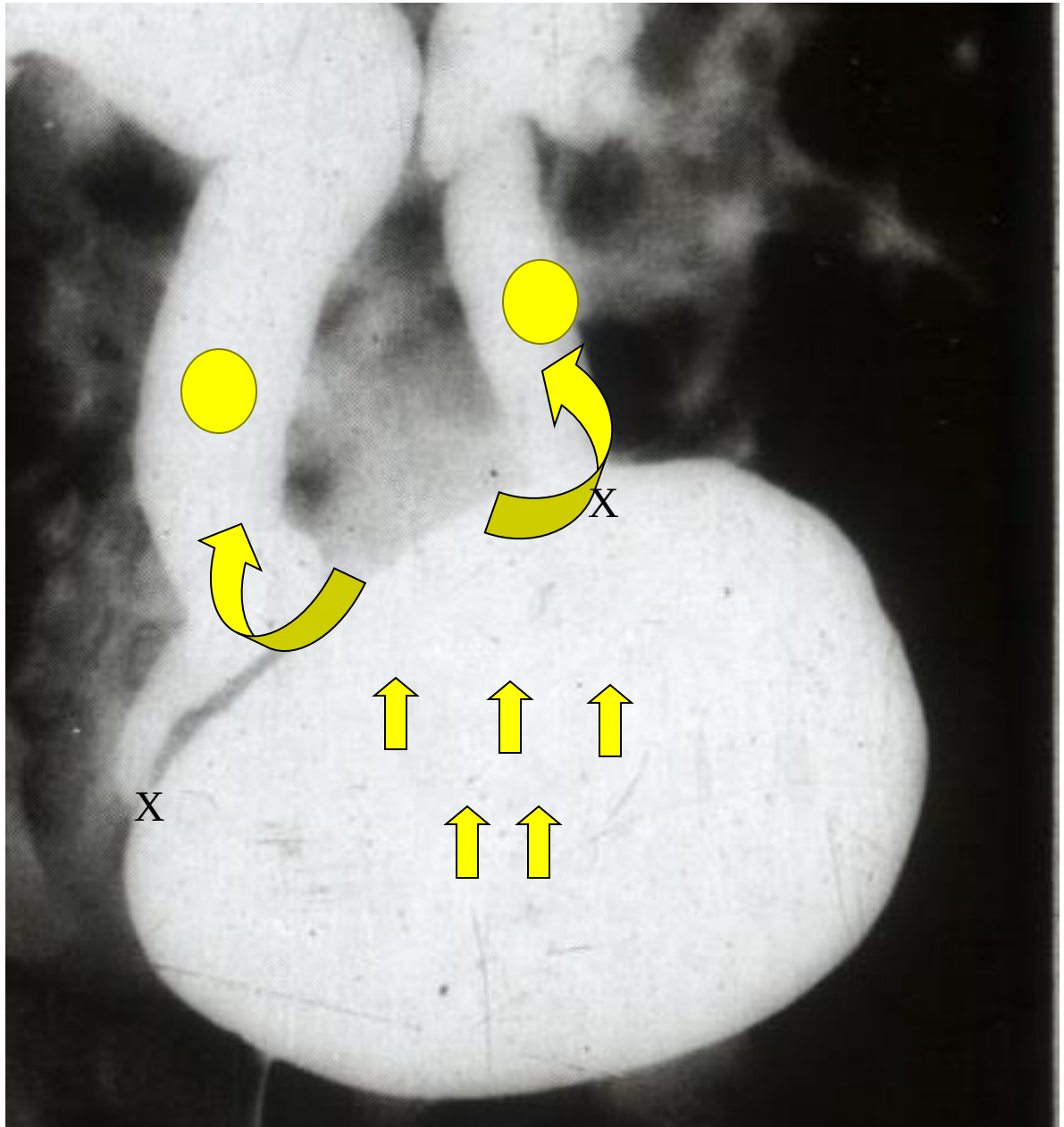
Follow up imaging

Hsi RS[1], Holt SK[2], Gore JL[2], Lendvay TS[2], Harper JD[2].
National Trends in Followup Imaging after Pyeloplasty in Children in the United States. J Urol. 2015 Sep;194(3):777-82. doi: 10.1016/j.juro.2015.03.123. Epub 2015 Apr 11

- First imaging is Renography: 6 mo
- Second ultrasonography: 6-12 mo
- After one year: No imaging in 1/3 ; Rest- ultrasound only

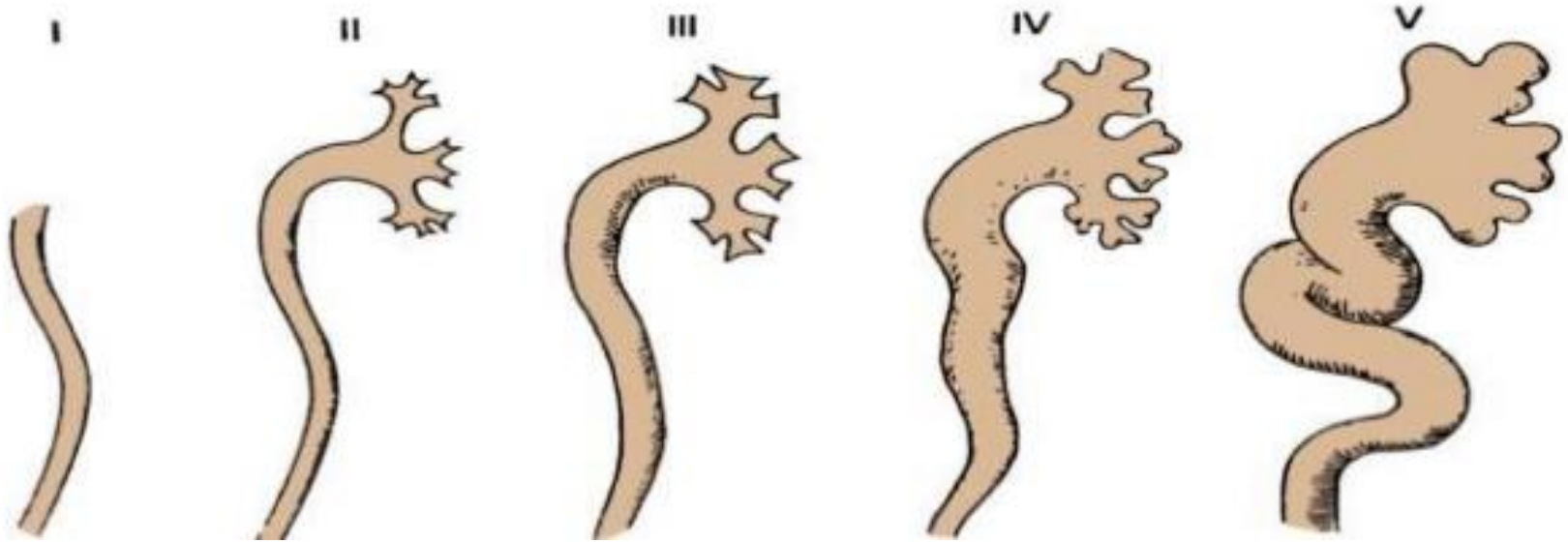
Modern Management of VUR: Intention to Cure or Intention to Treat Reflux

Primary Vesicoureteric Reflux



International classification(VCUG)

Grade	Description
I	Into a nondilated ureter
II	Into the pelvis and calyces without dilatation
III	Mild to moderate dilatation of the ureter, renal pelvis, and calyces with minimal blunting of the fornices
IV	Moderate ureteral tortuosity and dilatation of the pelvis and calyces
V	Gross dilatation of the ureter, pelvis, and calyces; loss of papillary impressions; and ureteral tortuosity

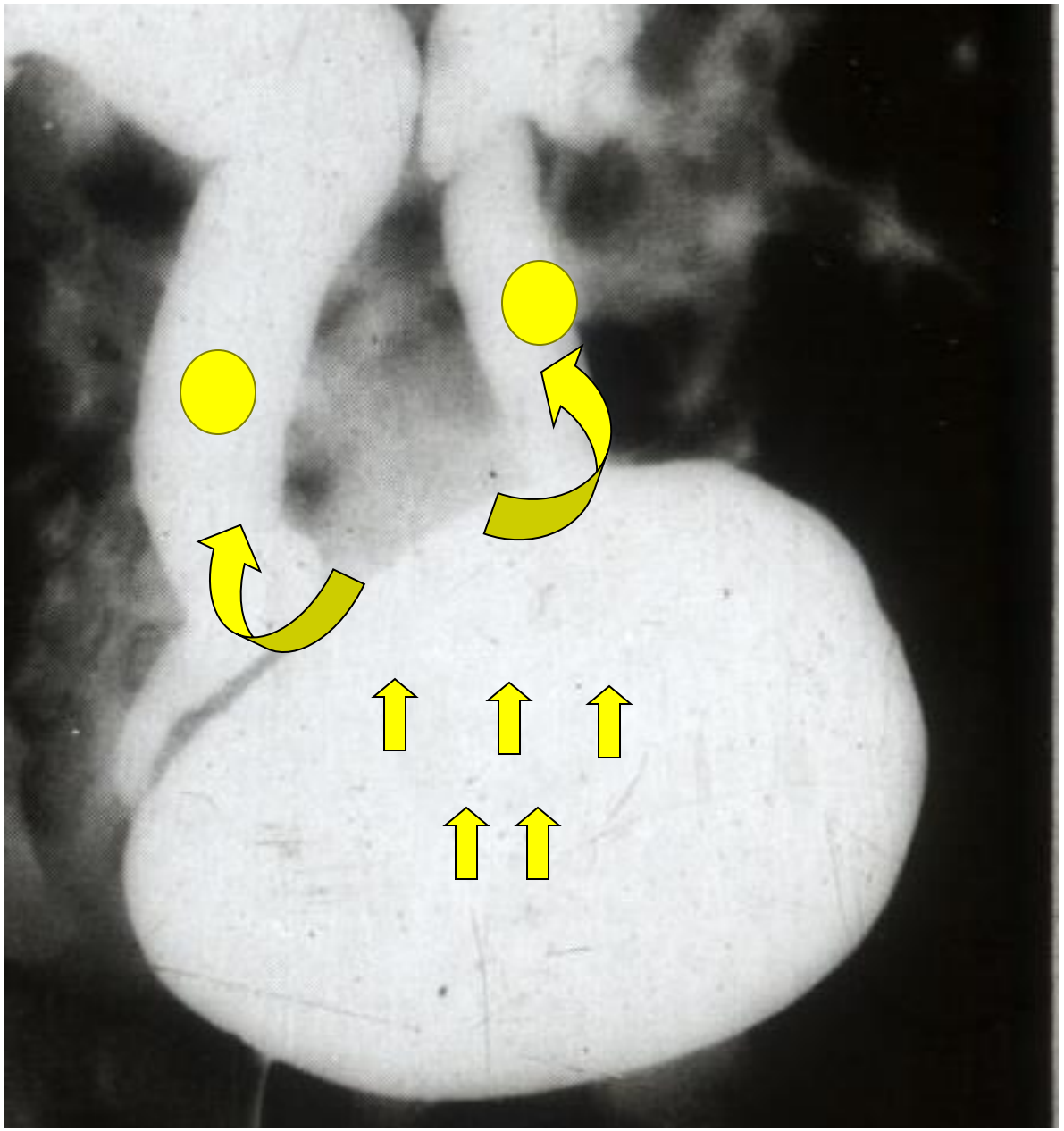


Vesicoureteric Reflux (V.U.R.)

Incidence

- 1% of all children
- 37% – 49% patients with U.T.I.
- Renal failure requiring Renal Transplant
  - ✓ in 3 – 25% children &
  - ✓ in 10 – 15% adults

Vesicoureteric Reflux



Pyelonephritis

↓

Renal scarring

↓

Decreased function

↓

CKD(ESRD)

↓

Hypertension

↓

Somatic growth

Goal of treatment

Prevention of:

- Renal injury
- Symptomatic pyelonephritis
- Other complications of reflux

Modalities

- Medical
- Interventional: Surgical / Endoscopic

*Outcome of 10 years of severe VUR

managed medically:

Report of

International Reflux Study in Children.

Jean Smellie, et al. The Journal of Pediatrics 2001, 139: 656-63

Follow-up	VUR with dilatation	VUR without dilatation	No reflux
5 years	**48%**	**37%**	**15%**
10 years	**23%**	**25%**	**52%**

Chochrane review-

June 15, 2011

- Medical tt.
  - 40% children develop scars despite antibiotics
- Surgical tt.
  - After surgery postop. resolution rate after 4-5 yrs.= 93-99%

❖ **It reduces incidence of pyelonephritis**

Antibiotics

- Pyelonephritis occurs **despi**
- Long-term use have side ef
  - Nausea, vomiting, resistance
- **NICE guidelines:** P*rophyl*
  REDUCE renal scarring in
  months of age who have gr
  vesicoureteric reflux.

*Infants have **non-specific sym**
UTI & greater risk of morb
related to infection.

* **RIVUR trial:** Antibiotics- be
placebo if given for short perio
effects with prolonged use.

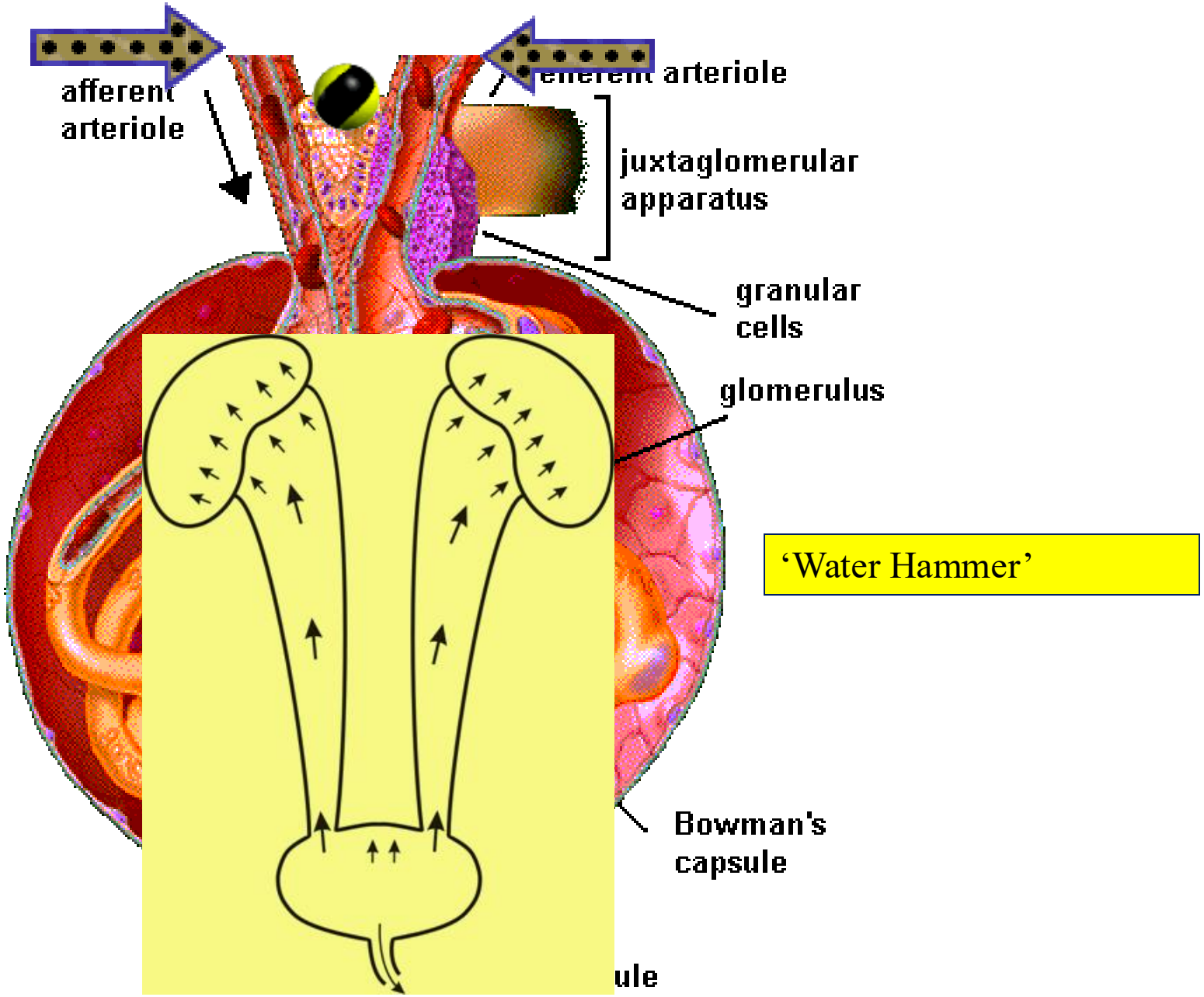
Current indications of Surgery

- Progression of **scars**
- Appearance of new **scars**
- More than **2 UTIs** in last 6 months
- Progression of grades of VUR

Facts

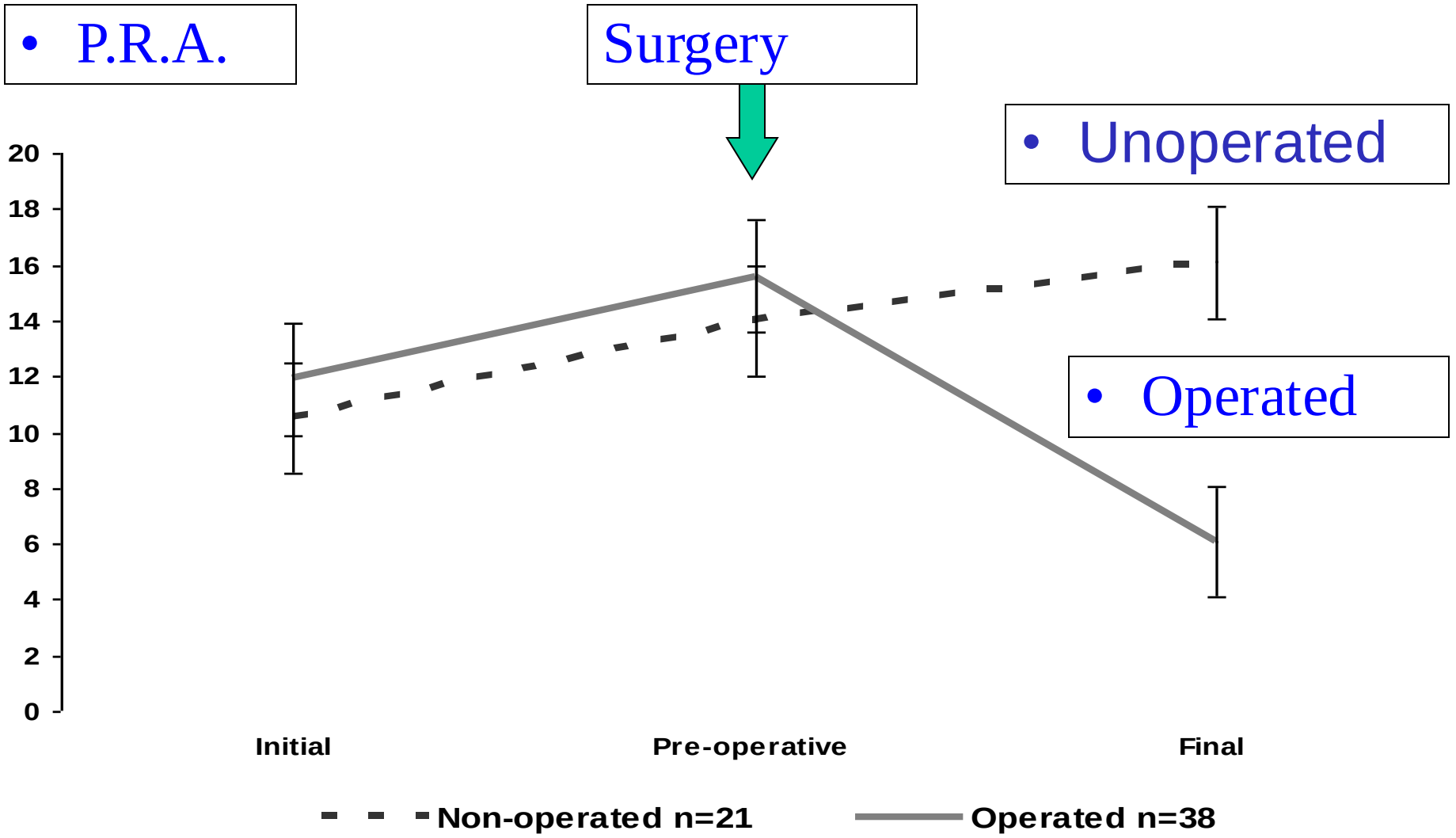
With current indications of intervention:

- Irreversible loss of function
- Pregnancy related complications
- ESRD & Hypertension



‘Water Hammer’

Plasma Renin Activity (n: 59)



•Bajpai M, Kidney International, 2003, 64(5): 1643-7.
•Bajpai M, Journal of Paediatric Urology, 2008, Pages 60-64.

Kidney International, Vol. 64 (2003), pp. 1643–1647

Role of plasma renin activity in the management of primary vesicoureteric reflux: A preliminary report

MINU BAJPAI, KAMLESH PAL, CHANDRASHEKHAR S. BAL, ARUN K. GUPTA, and RAVINDER M. PANDEY

ELSEVIER

Journal of Pediatric urology

Plasma renin activity for monitoring vesicoureteric reflux therapy: Mid-term observations

Minu Bajpai [a,*], C.S. Bal [b], M. Kalaivani [c], Arun K. Gupta [d]

New techniques
Dextranomer/hyaluronic acid copolymer
Paradigm shift

- Non-immunogenic, biodegradable, biocompatible
- Injection therapy may be a simple way of eradicating reflux

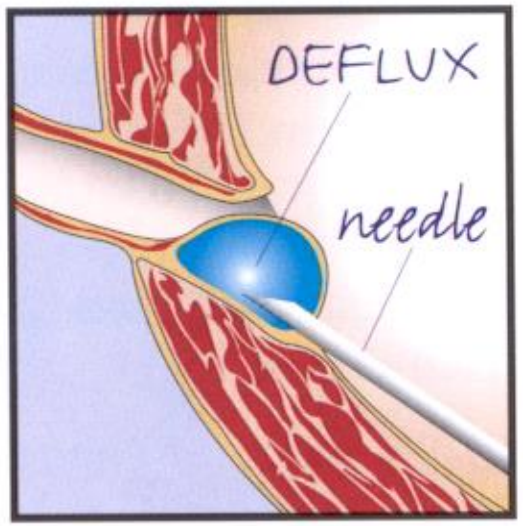


Fig. 4. A little bulge is formed which makes it harder for the urine to flow backwards.

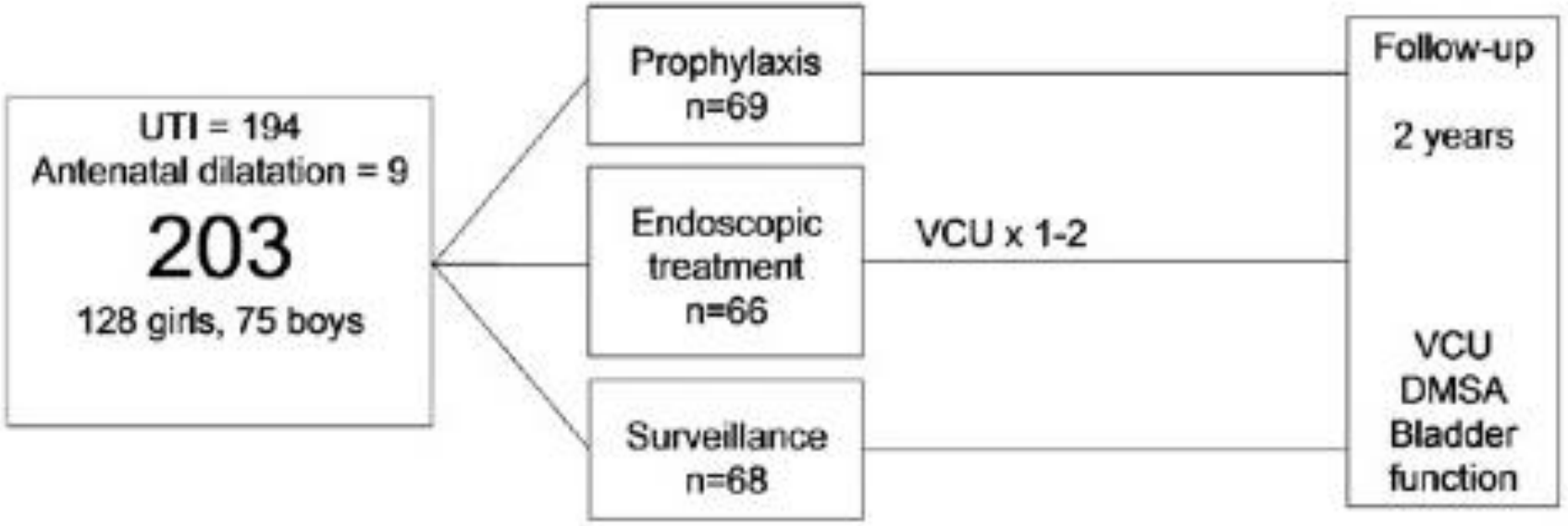
So what to do….

newly diagnosed grade III reflux???

- Surveillance?
- Prophylactic antibiotics?
- Injection therapy?

Swedish reflux study

- Randomized trial of children 1 - 2 years of age with grade III – IV reflux



Deflux *vs* Prophylaxis vs Surveillance:

Swedish study

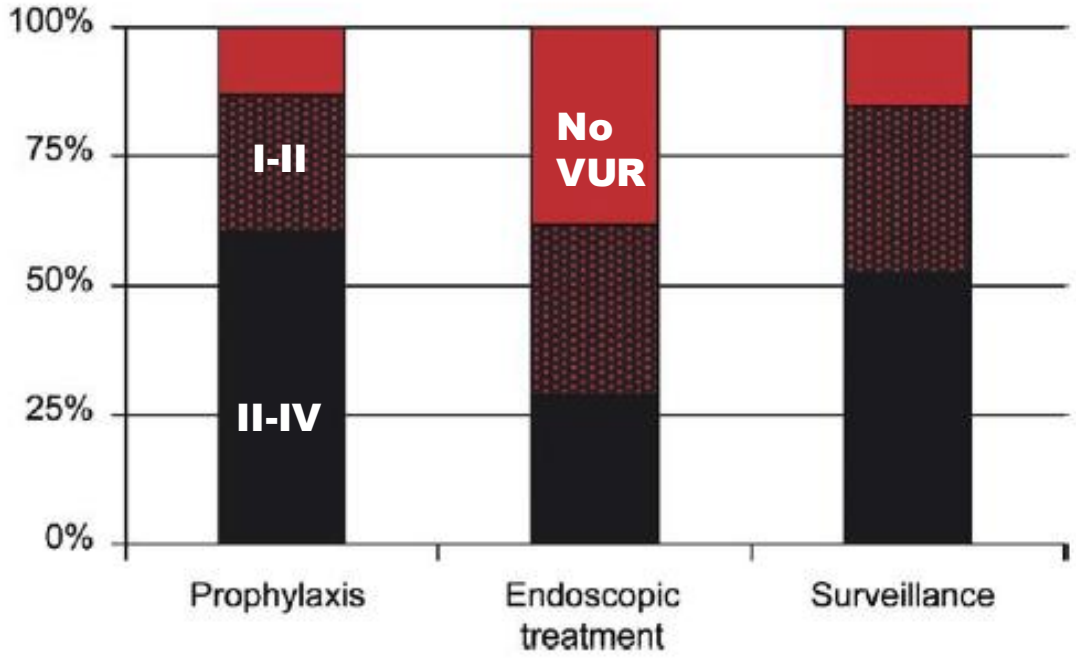
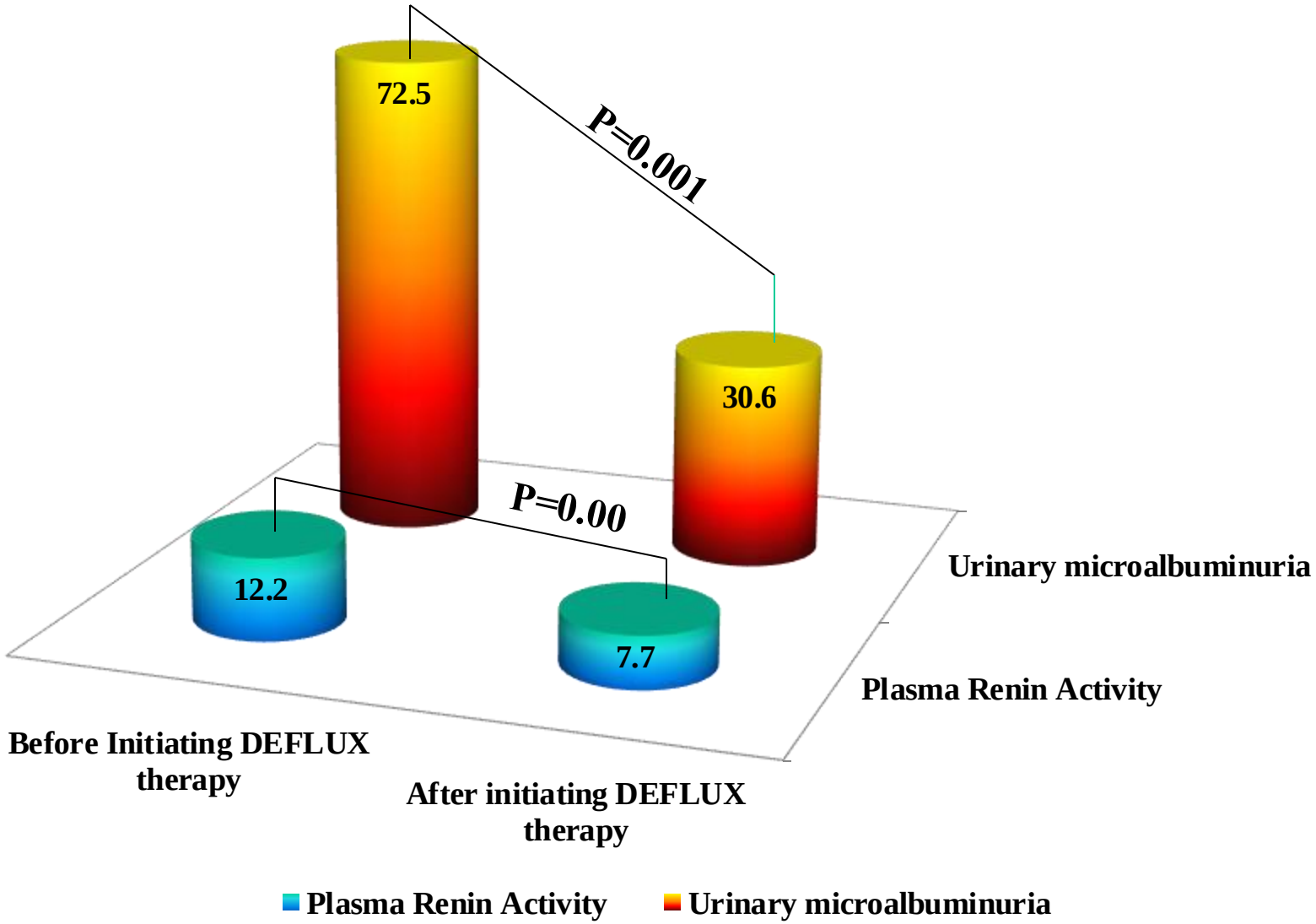
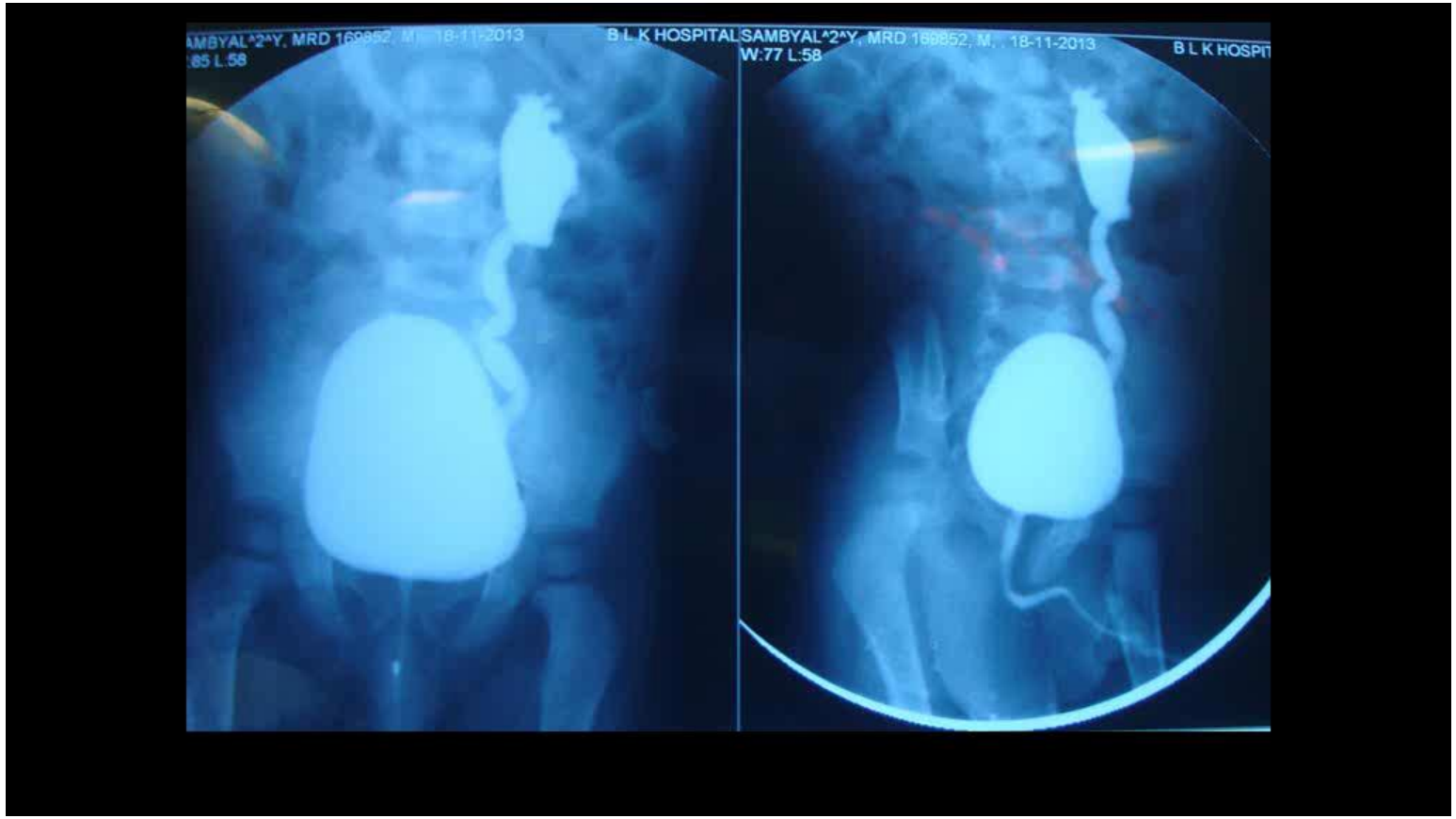


Figure 1. VUR status after 2 years in treatment groups. Red bars indicate no VUR. Red and black bars indicate grade I–II VUR. Black bars indicate grade II–IV VUR.

Plasma Renin Activity & Urinary microalbuminuria before and after initiaing DEFLUX therapy



Endoscopic injection ‘Deflux’



IPNA

Thanks

Case based Discussion

Moderator- Dr Shobha Sharma

Panelists – Dr OP Mishra, Dr Aditi Sinha, Dr Neha Bhandari, Dr Kanika Kapoor

Case Scenario

- 4 years boy with bow leg deformity & poor wt and Ht gain.
- Adequate food/calorie intake(prefers salty/savory foods).
- No H/O chronic diarrhea, jaundice, recurrent febrile illness, recurrent dehydration episodes , chronic drug intake.
- Passes urine multiple times in a day and night
- Based on X Ray(Rickets), received weekly 60K(~10).
- No improvement in repeat X Ray picture.

- On examination- wt and Ht below 2 SD.
- Was same 3 months back also
- No pallor, icterus
- BP between 50-90th centile.
- Wrist widening and genu varus deformity of lower limbs.
- 24 hr UO=8 ml/kg/hr and FBS of 82mg/dl

Dr Kanika

- Is this child having Polyuria?
- What other problems/clues can we get from given history and examination?

Polyuria is defined as Urine output more than 4 ml/kg/hr in children and more than 6 ml/kg/hr in neonates

Urine output more than 2 L/m²/day in children is Polyuria

Clinical Features

- ✓ Deformity of legs
- ✓ Polyuria, ? Polydipsia
- ✓ Failure to thrive
- ✓ Preference for savory food
- ✓ Signs of Rickets
- ✓ Refractory Rickets
- ✓ Stunting and wasting
- ✓ Normal Blood Sugar

Refractory Rickets- Lack of response to adequate dose of vitamin D(2000-3000IU/day for 12 weeks or 60K sachets every 2 weeks for 5 doses) after 12 weeks.

Dr Neha

Considering above case scenario which differentials will you keep?

- Polydipsia
- Polyuria
- FTT
- Refractory Rickets

Differentials…

Polydipsia, Polyuria, FTT — **DM**, **DI**, **RTA**, **CKD**

FTT, Refractory Rickets — **CLD**, **Malabsorption syndromes(CF), CD**, **RTA**, **CKD**

Polydipsia, Polyuria, FTT, Refractory Rickets - **CKD**, **RTA**

Dr Aditi

- What initial investigations will you do in this case?

Investigations

- Assess nutritional status
  - 24-hr dietary recall
  - Examination for micronutrient deficiencies
  - Celiac serology, TSH/FT3/FT4 (consider other etiologies..)
- Evaluation for failure to thrive, bony deformities
  - Blood urea, serum creatinine

  Rule out chronic kidney disease, e.g., nephronophthisis, reflux nephropathy
  - Venous blood gas, serum electrolytes

  Rule out metabolic acidosis (renal tubular acidosis), metabolic alkalosis (Bartter syndrome), hypernatremia (diabetes insipidus)
  - Complete blood counts, peripheral smear

  Rule out concomitant anemia, evaluate type of anemia
- In view of history of rickets, bony deformities
  - Calcium, phosphorus, serum alkaline phosphatase
  - 25-hydroxyvitamin D, parathormone
  - X ray knees AP view

  Confirm/rule out active rickets, nutritional deficiency, CKD mineral bone disease

Case scenario

- **Hb-**11.5g/dl, TLC and platelets-N
- **KFT - N** (U=26mg/dl; Cr=0.4mg/dl)
- **Sbil**=0.5mg/dl
- **ALT/AST**=20/22IU/L
- **S ALP**= 840IU/L
- **Celiac serology**- Neg
- **S Ca/P-** 9/ 4.5 mg/dl
- **25(OH)D3** – 52 ng/dl,
- **X- Ray**

- VBG- pH- 7.32, HC03- 16, Pco2- 30mmHg
- serum Na- 139, k- 3.0, cl- 112 mmol/L
- **SAG=11(12-16)(Na – HCO3+Cl)**
- **Hyperchloremic Metabolic Acidosis or NAGMA**

Dr Kanika

- What are the causes of Normal AG metabolic acidosis?
- How to differentiate between non-renal and renal cause?

Normal Anion Gap Metabolic Acidosis (NAGMA)

- ✓ Extra Renal – GI losses
  - ✓ Diarrhea,
  - ✓ Removal of Bile and Pancreatic Secretions through tube drainage
- ✓ Uretro-sigmoidostomy
- ✓ Drugs - Cholestyramine
- ✓ Renal- Renal tubular Acidosis

Step 2- Estimate urine anion gap (UAG)

- $Na^+ + K^+ + NH_4^+ +$ Unmeasured Cations = $Cl^- +$ Unmeasured Anions
- Urine Anion Gap + NH_4^+ = Unmeasured Anions- Unmeasured Cations
- **UAG = 80 – NH_4^+**
- Positive UAG- Distal RTA;
  Decreased NH_4^+ excretion
- Negative UAG- GI losses with normal renal function
  Increased NH_4^+ excretion

Step 2- urine osmolal Gap

Urine Osmolal Gap- where UAG poorly estimates NH excretion- AKI, CKD, proximal RTA on alkali therapy, ketoacidosis

Urine Osmolal Gap= Measured urine Osmolality- Calculated Urine Osmolality

UOG= Uosm- [(2 Na^+ +K^+)+ BUN/2.8 + Glucose/18 + **NH_4^+**

UOG is **10-100 mosm/kg** normally**;**

> 100 mosm/Kg suggests increased NH_4^+ excretion

Step 3- urine pH

Integrity of distal urinary acidification

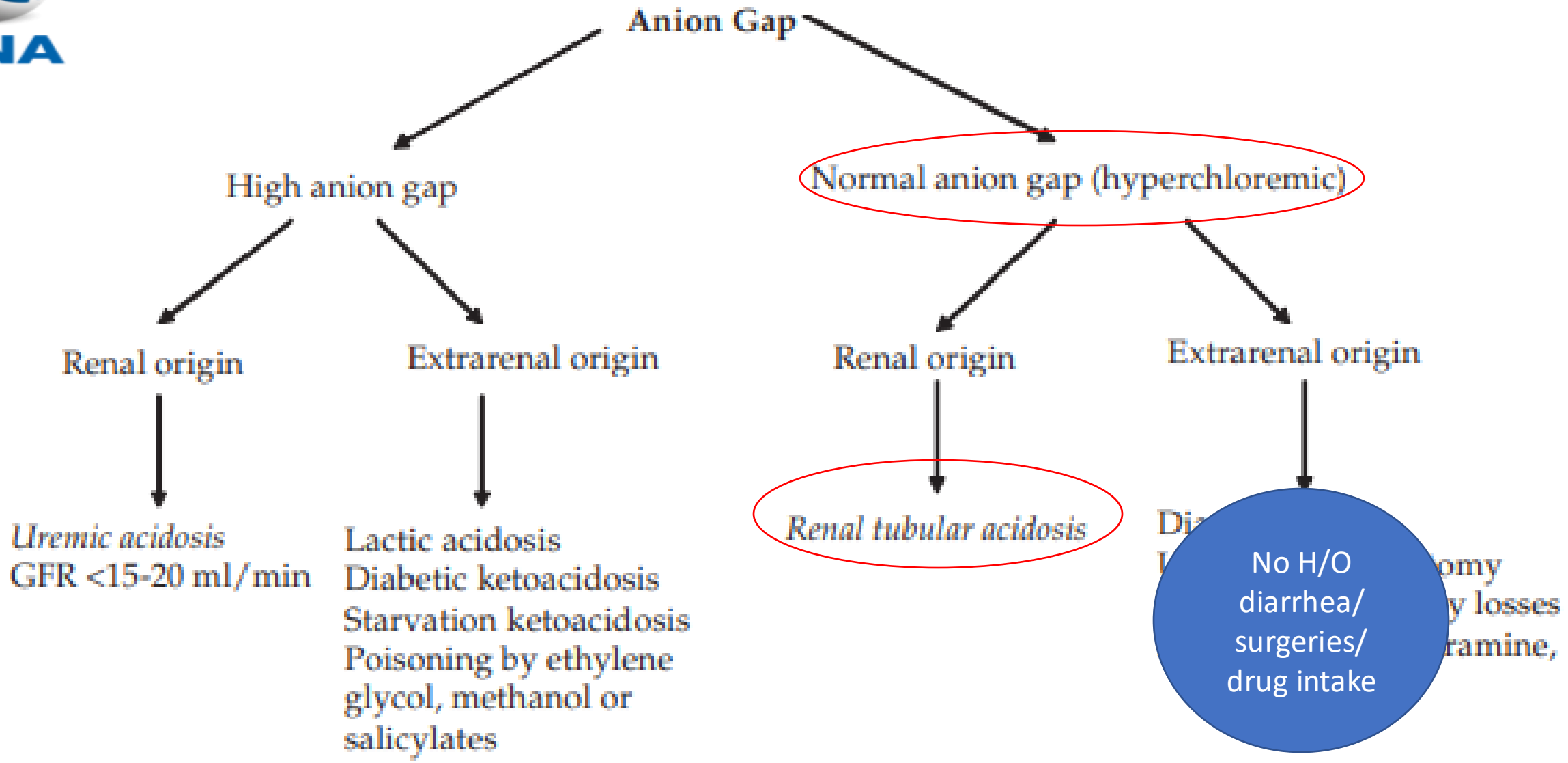
In the presence of systemic acidosis,

urine pH is normally <5.3.

pH > 5.5 Distal RTA

pH < 5.5 - Proximal RTA

Urine pH should be measured electrometrically on fresh voided early morning urine sample



Evaluation of Renal Tubular Acidosis Indian Journal of Pediatrics, Volume 74—July, 2007

Case Scenario

- Urine pH= 6.5,
- Urine Na=60mEq/L , K=30mEq/L, Urine Cl=25mEq/L
- Urine Anion Gap = positive
- Measured Urine Osm=250, Calculated Urine Osm= 180
- UOG<100

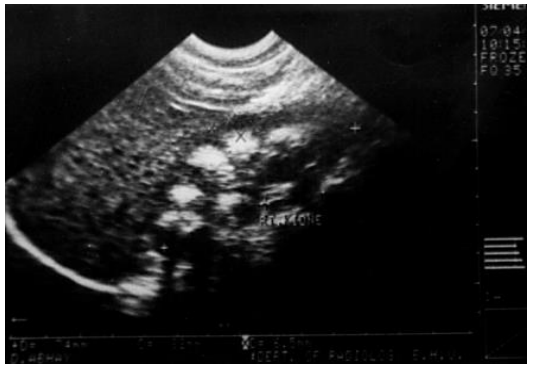
- **High Urine pH in presence of MA**
- **Positive UAG with low UOG** – Evidence of Decreased NH4 secretion

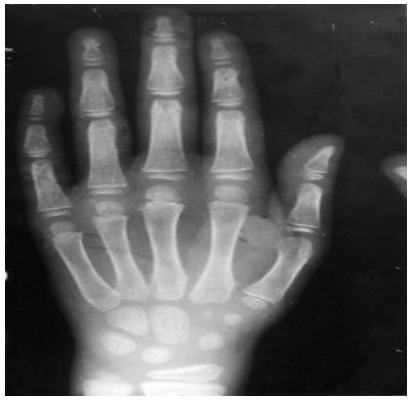
RTA with ?Distal acidification Defect

Dr Neha

- When should we suspect RTA?
- What are different types of RTA? Which is most common?

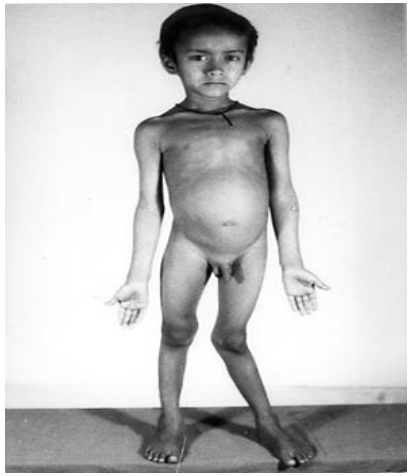
Initial Presentation: RTA





- **Infancy** – FTT, Vomiting & dehydration, urinary tract infection, diarrhea or constipation

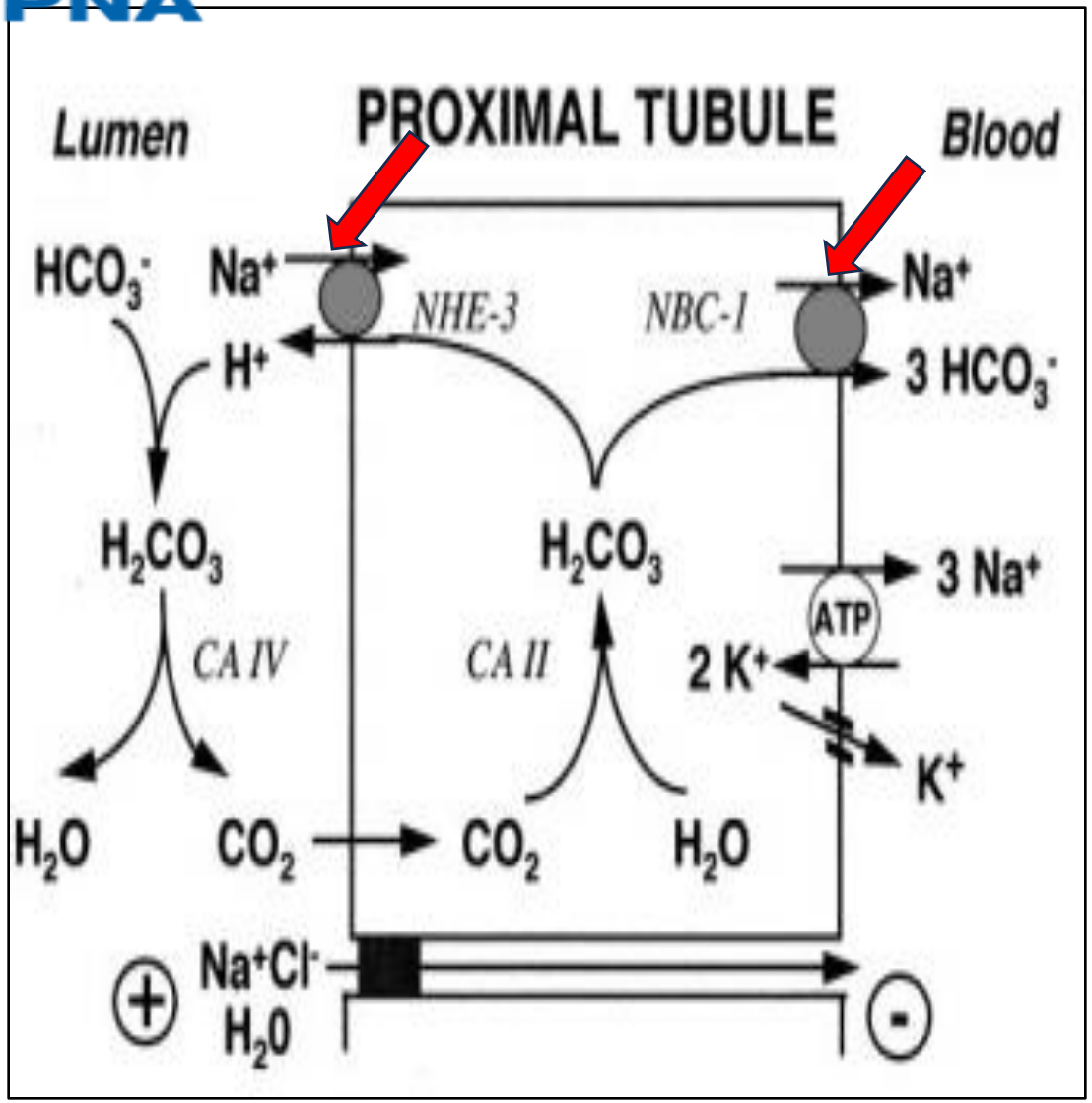
- **Childhood** – Short stature, FTT, Polyuria & Polydipsia, Rickets & delayed walking, bowing of legs, frontal bossing, urolithiasis

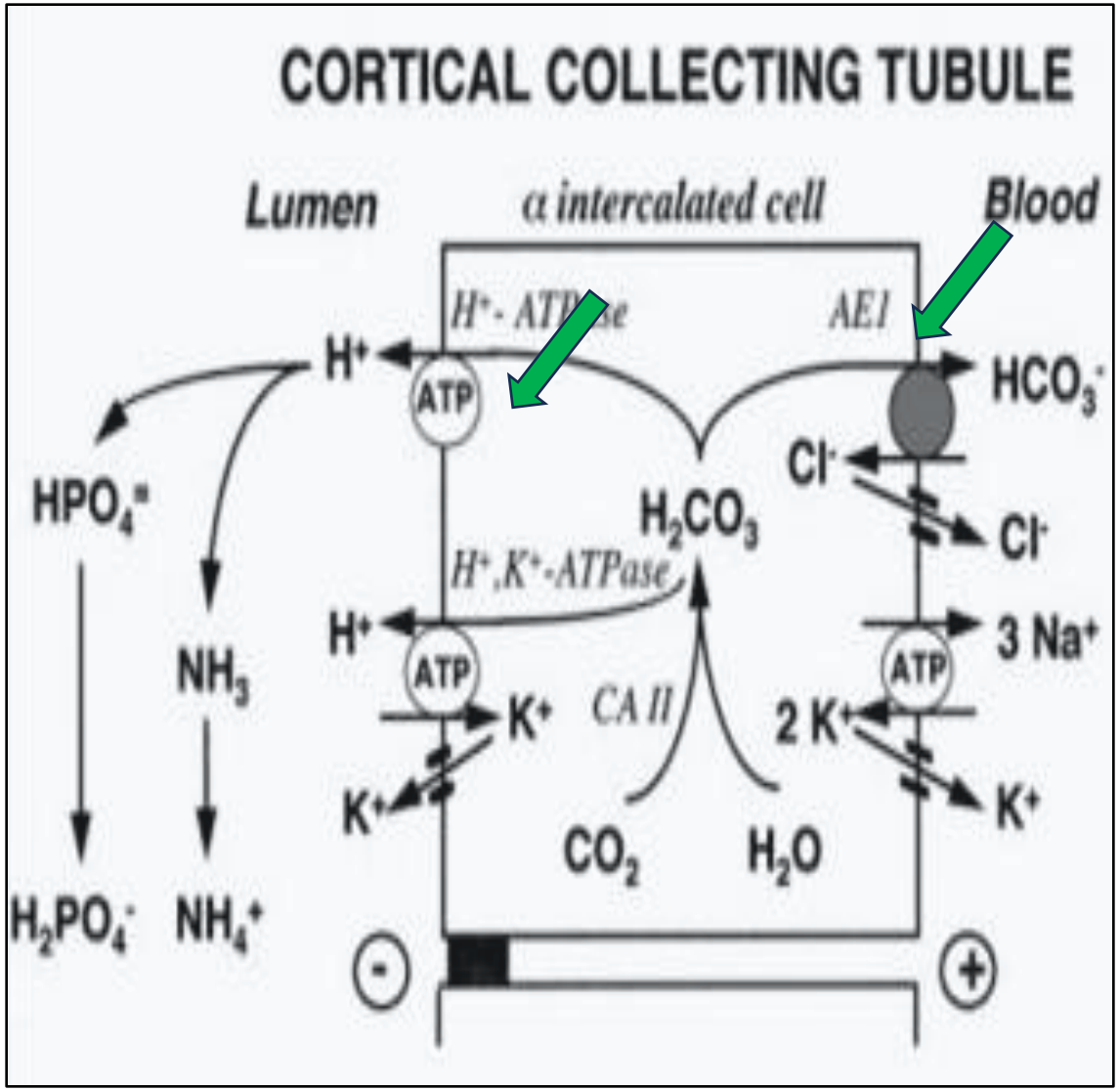


- **Adolescence** – Urolithiasis

What are different types of RTA? Which is most common?

- **Type 1 or Distal RTA**—due to impaired distal H ion secretion (Most common)
- **Type 2 or Proximal RTA-** due to impaired HCO3 Reabsorption
- **Type 3 or mixed RTA**– Distal RTA with bicarbonate wasting
- **Type 4 RTA** or hypoaldosteronism-reduced aldosterone or resistance


Lumen
PROXIMAL TUBULE
Blood
HCO3-
Na+
NHE-3
NBC-1
Na+
H+
3 HCO3-
H2CO3
H2CO3
3 Na+
CA IV
CA II
ATP
2 K+
K+
H2O
CO2
CO2
H2O
Na+Cl-
H2O


CORTICAL COLLECTING TUBULE
Lumen
α intercalated cell
Blood
H+- ATPase
AE1
H+
ATP
HCO3-
Cl-
HPO4=
H2CO3
Cl-
H+,K+-ATPase
H+
ATP
3 Na+
NH3
ATP
K+
CA II
2 K+
K+
K+
CO2
H2O
H2PO4-
NH4+

Dr Aditi

- What is Bicarbonate loading test?
- How can we differentiate between proximal and distal RTA after Bicarbonate loading test?

Bicarbonate loading test

Allows biochemical confirmation between proximal and distal RTA

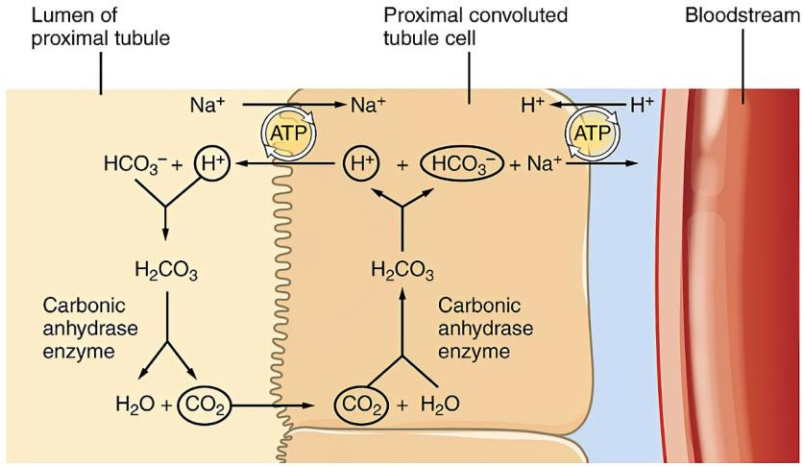
Fractional excretion of bicarbonate(>10-15%)
Proximal tubular dysfunction - pRTA

Urine - blood CO2 (<20mmHg)
Distal renal tubule dysfunction - dRTA

Procedure

- Sodium bicarbonate is given as IV infusion till serum HCO3 levels reach the normal range (22-24 mEq/L)
- Urine pH is measured every 30-60 min and test is terminated when consecutive samples show urine pH > 7.4

Role of the bicarbonate loading test



Hyperchloremic metabolic acidosis (normal anion gap)

Urine anion gap

Negative → Diarrheal loss; Sodium chloride infusion

Positive

Consider renal tubular acidosis

Urine pH
Serum potassium
Bicarbonate loading

Urine pH <5.3 Serum K^+ low or normal U–B CO_2 >20 mm Hg $FEHCO_3^-$ >10-15%	Urine pH >5.3 Serum K^+ low, normal U–B CO_2 <20 mm Hg $FEHCO_3^-$ <5%	Urine pH >5.3 Serum K^+ high, normal U–B CO_2 <20 mm Hg $FEHCO_3^-$ <5%	Urine pH <5.3 Serum K^+ high or normal U–B CO_2 >20 mmHg $FEHCO_3^-$ <5%
Proximal RTA	**Classic type 1 RTA**	**Hyperkalemic type 1 RTA** (voltage defect)	**Type 4 RTA**
Screen for other proximal tubular defects	Screen for hypercalciuria & nephrocalcinosis; furosemide test; evaluate hearing, dentition & peripheral smear		Look for kidney disease; TTKG; plasma renin & aldosterone

Case scenario

- After Hco3 loading which was done by IV route till serum HCO3 was 24mEq/L:
- Fe HCO3 approx. 5% (Normal)
- Urine-Blood CO2 **<20mmHg**(urine PCo2=40; Blood PCo2=30 mmHg)

Distal acidification Defect

Additional investigations

- **Fanconi Syndrome(eg Cystinosis) –** Glucosuria, phosphaturia, LMWP(ß2 microglobinuria), proteinuria

- **Distal RTA –** Urine Ca : Cr(hypercalciuria), US(KUB) for Nephrocalcinosis(medullary) – (comb of hypercalciuria, hypocitraturia and high urine pH)

- **Hyperkalemic RTA(Type IV) –** Transtubular potassium gradient(aldosterone response)

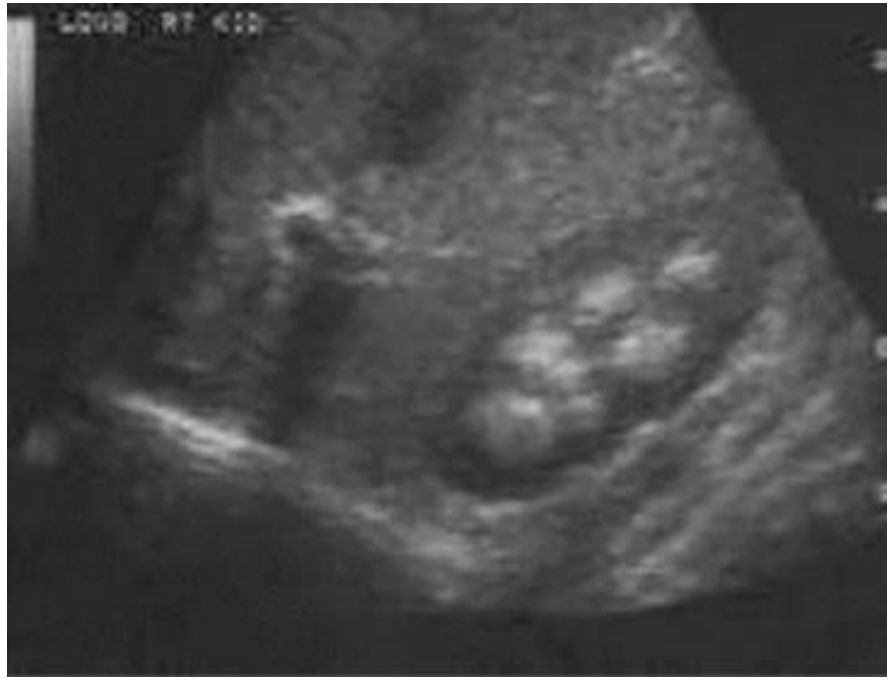
$$TTK^{+}G = \frac{K^{+}(U) \times Osm\ (S)}{K^{+}(S) \times Osm\ (U)}$$

- **Incomplete dRTA -** Furosemide-fludrocortisone test(FF test)

- Confirmation of diagnosis by genetic analysis as there may be overlap among clinical and biochemical picture, important for genetic counselling

Case scenario

- No need for F-F test
- US(KUB) **bilateral medullary NC**
- Urine Calcium: Cr=**2(hypercalciuria)**
- Urine for glucose and protein negative
- Genetic analysis- Not done



Distal RTA

How do we treat Case of RTA(distal) - Sir

Management of RTA

- Mainstay - Alkali therapy
- Helps in restoration of growth as well as improvement in rickets
- In dRTA, improvement in hypokalemia, hypercalciuria with stabilization or even reversal of NC and hence preventing long term kidney dysfunction
- **Potassium citrate formulation** preferred for dRTA@ 3-4 upto 10 mEq/Kg/d in 3-4 divided doses
- Alternatively Sodium salt of bicarbonate can be used with equal efficacy
- In pRTA – Alkali dose starting from 10mEq/kg/d to higher
- In Fanconi Syndrome vitamin D , phosphate supplement in addition
- **Dose requirement of alkali decreases with age**

Management of RTA

- **Syp Polycitra** (supplies 2mEq/ml base and 1 mEq/ml K+ and Na+)
- **Syp Uriliser** (potassium citrate 1 mEq/ml)
- **Nodosis** (Sodium bicarbonate Syp1 ml = 0.8 meq base, Tab 500 mg tablet = 6meq base), 1000 mg= 12 mEq

Goal of Therapy - serum bicarbonate concentration of 22 to 24 mEq/L in dRTA and low normal in pRTA (continuous bicarbonaturia)

Take Home Message…

- RTA is rare but should be suspected in poorly growing child with normal kidney function and metabolic acidosis
- Biochemical investigations are helpful in not only diagnosing but also identifying type of RTA
- Genetic confirmation is recommended for all cases – overlap in phenotype, genetic counselling
- Mainstay of management is Alkali therapy

THANKS….

Case based Discussion

Moderator- Dr Shobha Sharma

Panelists – Dr OP Mishra, Dr Aditi Sinha, Dr Neha Bhandari, Dr Kanika Kapoor

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Considering above case scenario which differentials will you keep?

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FTT, Refractory Rickets — **CLD**, **Malabsorption syndromes(CF), CD**, **RTA**, **CKD**

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Investigations

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- What are the causes of Normal AG metabolic acidosis?
- How to differentiate between non-renal and renal cause?

Normal Anion Gap Metabolic Acidosis (NAGMA)

- ✓ Extra Renal – GI losses
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- ✓ Uretro-sigmoidostomy
- ✓ Drugs - Cholestyramine
- ✓ Renal- Renal tubular Acidosis

Step 2- Estimate urine anion gap (UAG)

- $Na^+ + K^+ + NH_4^+ +$ Unmeasured Cations = $Cl^- +$ Unmeasured Anions
- Urine Anion Gap + NH_4^+ = Unmeasured Anions- Unmeasured Cations
- **UAG = 80 – NH_4^+**
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- Negative UAG- GI losses with normal renal function
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Urine Osmolal Gap- where UAG poorly estimates NH excretion- AKI, CKD, proximal RTA on alkali therapy, ketoacidosis

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Step 3- urine pH

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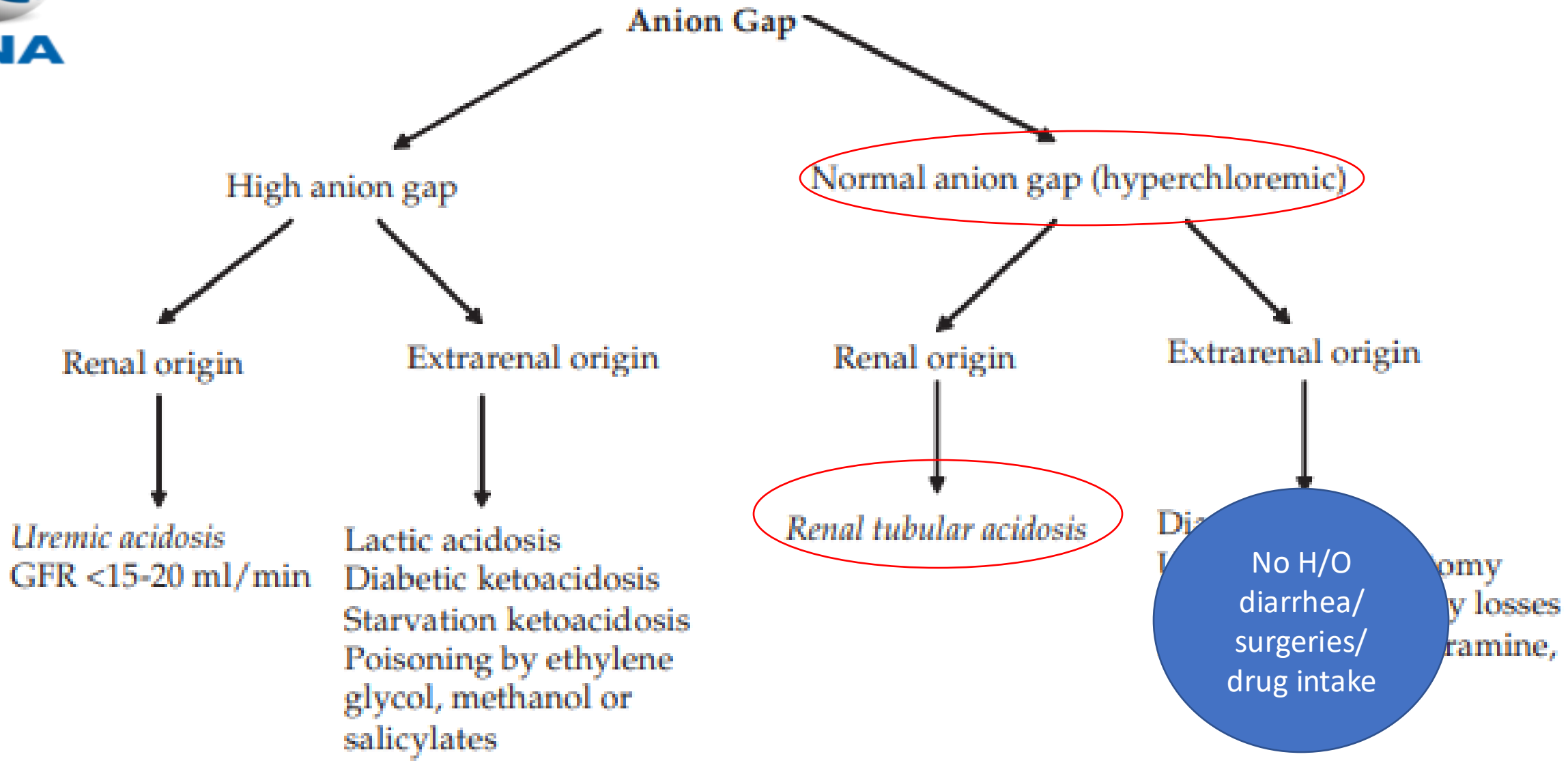
pH > 5.5 Distal RTA

pH < 5.5 - Proximal RTA

Urine pH should be measured electrometrically on fresh voided early morning urine sample



Evaluation of Renal Tubular Acidosis Indian Journal of Pediatrics, Volume 74—July, 2007

Case Scenario

- Urine pH= 6.5,
- Urine Na=60mEq/L , K=30mEq/L, Urine Cl=25mEq/L
- Urine Anion Gap = positive
- Measured Urine Osm=250, Calculated Urine Osm= 180
- UOG<100

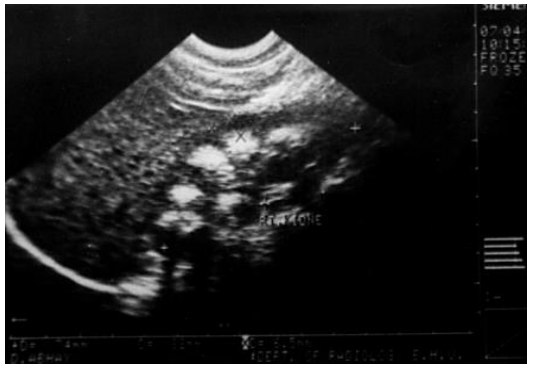
- **High Urine pH in presence of MA**
- **Positive UAG with low UOG** – Evidence of Decreased NH4 secretion

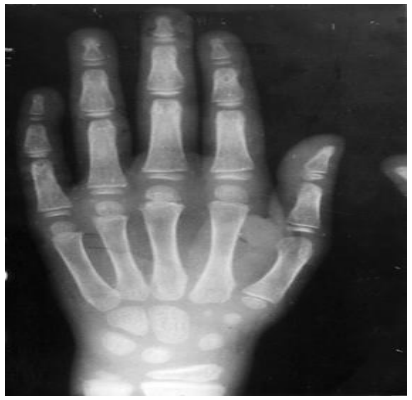
RTA with ?Distal acidification Defect

Dr Neha

- When should we suspect RTA?
- What are different types of RTA? Which is most common?

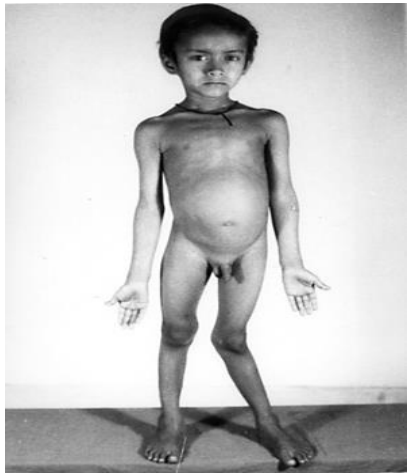
Initial Presentation: RTA





- **Infancy** – FTT, Vomiting & dehydration, urinary tract infection, diarrhea or constipation

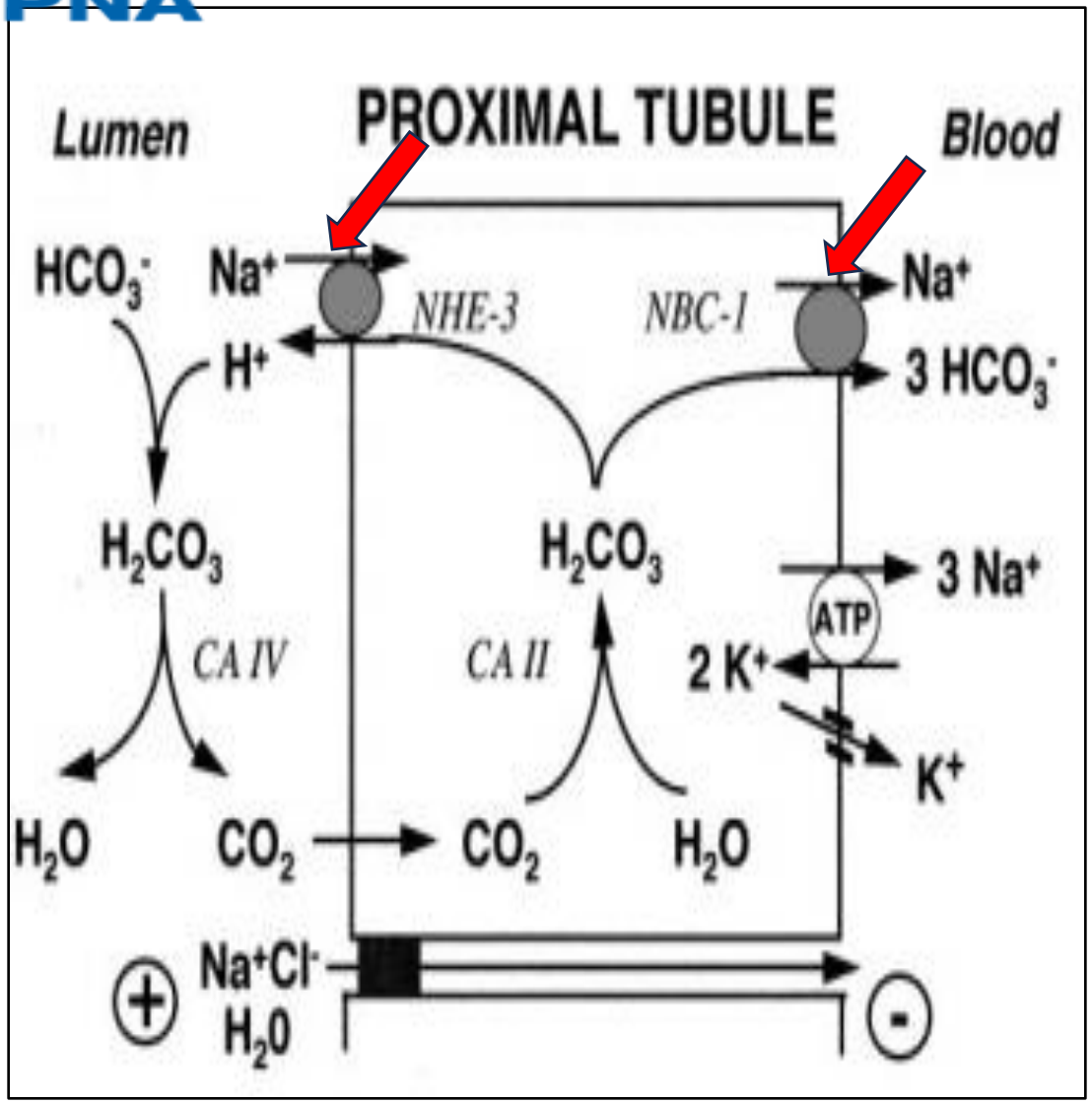
- **Childhood** – Short stature, FTT, Polyuria & Polydipsia, Rickets & delayed walking, bowing of legs, frontal bossing, urolithiasis

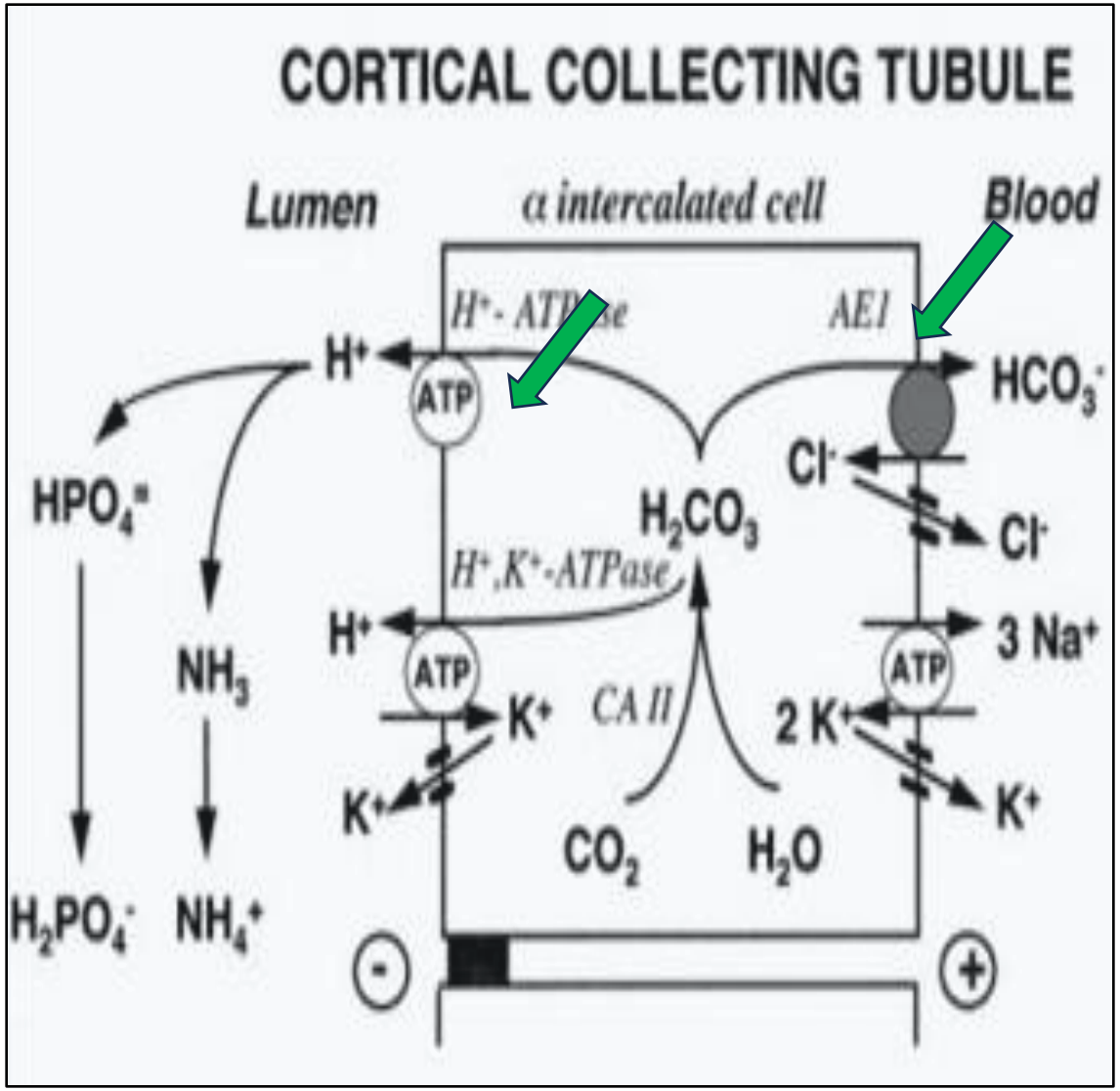


- **Adolescence** – Urolithiasis

What are different types of RTA? Which is most common?

- **Type 1 or Distal RTA**—due to impaired distal H ion secretion (Most common)
- **Type 2 or Proximal RTA-** due to impaired HCO3 Reabsorption
- **Type 3 or mixed RTA**– Distal RTA with bicarbonate wasting
- **Type 4 RTA** or hypoaldosteronism-reduced aldosterone or resistance


Lumen
PROXIMAL TUBULE
Blood
HCO3-
Na+
NHE-3
NBC-1
Na+
H+
3 HCO3-
H2CO3
H2CO3
3 Na+
CA IV
CA II
ATP
2 K+
K+
H2O
CO2
CO2
H2O
Na+Cl-
H2O


CORTICAL COLLECTING TUBULE
Lumen
α intercalated cell
Blood
H+- ATPase
AE1
H+
ATP
HCO3-
Cl-
HPO4=
H2CO3
Cl-
H+,K+-ATPase
H+
ATP
3 Na+
NH3
ATP
K+
CA II
2 K+
K+
K+
CO2
H2O
H2PO4-
NH4+

Dr Aditi

- What is Bicarbonate loading test?
- How can we differentiate between proximal and distal RTA after Bicarbonate loading test?

Bicarbonate loading test

Allows biochemical confirmation between proximal and distal RTA

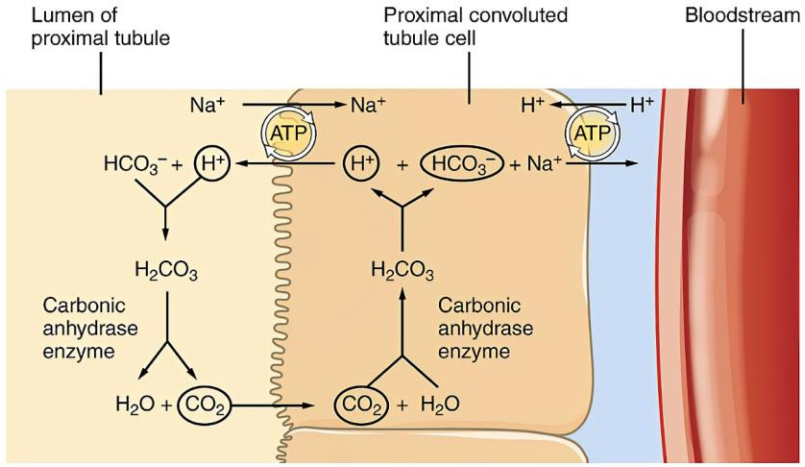
Fractional excretion of bicarbonate(>10-15%)
Proximal tubular dysfunction - pRTA

Urine - blood CO2 (<20mmHg)
Distal renal tubule dysfunction - dRTA

Procedure

- Sodium bicarbonate is given as IV infusion till serum HCO3 levels reach the normal range (22-24 mEq/L)
- Urine pH is measured every 30-60 min and test is terminated when consecutive samples show urine pH > 7.4

Role of the bicarbonate loading test



Hyperchloremic metabolic acidosis (normal anion gap)

Urine anion gap

Negative → Diarrheal loss; Sodium chloride infusion

Positive

Consider renal tubular acidosis

Urine pH
Serum potassium
Bicarbonate loading

Urine pH <5.3 Serum K^+ low or normal U–B CO_2 >20 mm Hg $FEHCO_3^-$ >10-15%	Urine pH >5.3 Serum K^+ low, normal U–B CO_2 <20 mm Hg $FEHCO_3^-$ <5%	Urine pH >5.3 Serum K^+ high, normal U–B CO_2 <20 mm Hg $FEHCO_3^-$ <5%	Urine pH <5.3 Serum K^+ high or normal U–B CO_2 >20 mmHg $FEHCO_3^-$ <5%
Proximal RTA	**Classic type 1 RTA**	**Hyperkalemic type 1 RTA** (voltage defect)	**Type 4 RTA**
Screen for other proximal tubular defects	Screen for hypercalciuria & nephrocalcinosis; furosemide test; evaluate hearing, dentition & peripheral smear		Look for kidney disease; TTKG; plasma renin & aldosterone

Case scenario

- After Hco3 loading which was done by IV route till serum HCO3 was 24mEq/L:
- Fe HCO3 approx. 5% (Normal)
- Urine-Blood CO2 **<20mmHg**(urine PCo2=40; Blood PCo2=30 mmHg)

Distal acidification Defect

Additional investigations

- **Fanconi Syndrome(eg Cystinosis) –** Glucosuria, phosphaturia, LMWP(ß2 microglobinuria), proteinuria

- **Distal RTA –** Urine Ca : Cr(hypercalciuria), US(KUB) for Nephrocalcinosis(medullary) – (comb of hypercalciuria, hypocitraturia and high urine pH)

- **Hyperkalemic RTA(Type IV) –** Transtubular potassium gradient(aldosterone response)

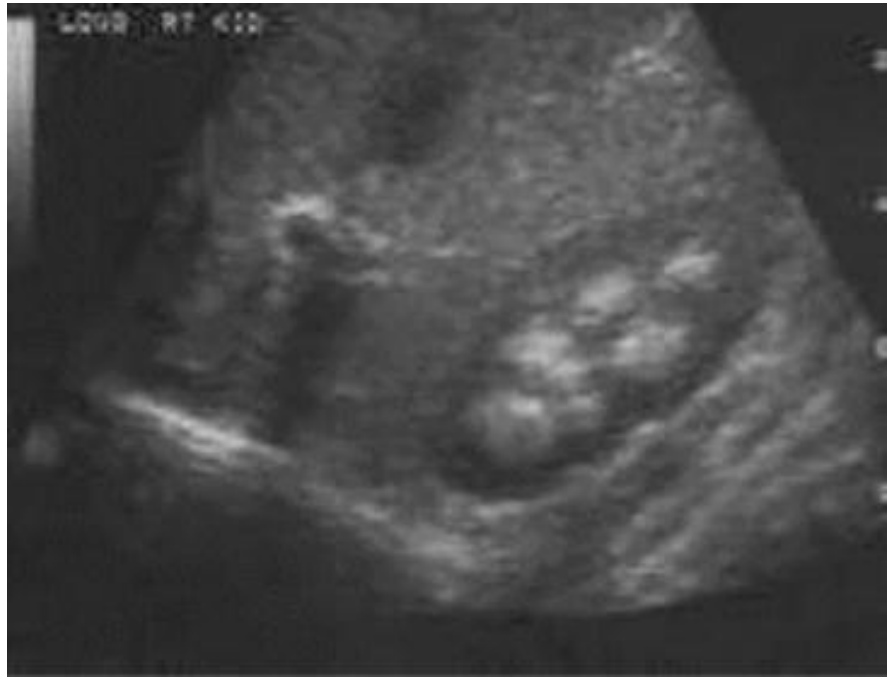
$$TTK^{+}G = \frac{K^{+}(U) \times Osm\ (S)}{K^{+}(S) \times Osm\ (U)}$$

- **Incomplete dRTA -** Furosemide-fludrocortisone test(FF test)

- Confirmation of diagnosis by genetic analysis as there may be overlap among clinical and biochemical picture, important for genetic counselling

Case scenario

- No need for F-F test
- US(KUB) **bilateral medullary NC**
- Urine Calcium: Cr=**2(hypercalciuria)**
- Urine for glucose and protein negative
- Genetic analysis- Not done



Distal RTA

How do we treat Case of RTA(distal) - Sir

Management of RTA

- Mainstay - Alkali therapy
- Helps in restoration of growth as well as improvement in rickets
- In dRTA, improvement in hypokalemia, hypercalciuria with stabilization or even reversal of NC and hence preventing long term kidney dysfunction
- **Potassium citrate formulation** preferred for dRTA@ 3-4 upto 10 mEq/Kg/d in 3-4 divided doses
- Alternatively Sodium salt of bicarbonate can be used with equal efficacy
- In pRTA – Alkali dose starting from 10mEq/kg/d to higher
- In Fanconi Syndrome vitamin D , phosphate supplement in addition
- **Dose requirement of alkali decreases with age**

Management of RTA

- **Syp Polycitra** (supplies 2mEq/ml base and 1 mEq/ml K+ and Na+)
- **Syp Uriliser** (potassium citrate 1 mEq/ml)
- **Nodosis** (Sodium bicarbonate Syp1 ml = 0.8 meq base, Tab 500 mg tablet = 6meq base), 1000 mg= 12 mEq

Goal of Therapy - serum bicarbonate concentration of 22 to 24 mEq/L in dRTA and low normal in pRTA (continuous bicarbonaturia)

Take Home Message…

- RTA is rare but should be suspected in poorly growing child with normal kidney function and metabolic acidosis
- Biochemical investigations are helpful in not only diagnosing but also identifying type of RTA
- Genetic confirmation is recommended for all cases – overlap in phenotype, genetic counselling
- Mainstay of management is Alkali therapy

THANKS….

IPNA

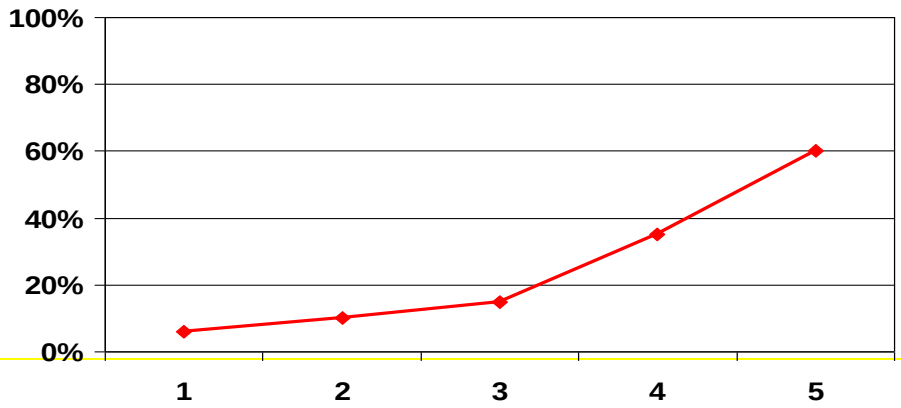
International Pediatric Nephrology Association

Web of UTI—Common mistakes

Why is it important to treat UTI

- UTI is more common in female except in extreme of age
- Risk : Scarring, may cause permanent damage
- Younger child, Delay in Rx → Renal Scarring
- Aim …. Treat promptly … ent Scarring

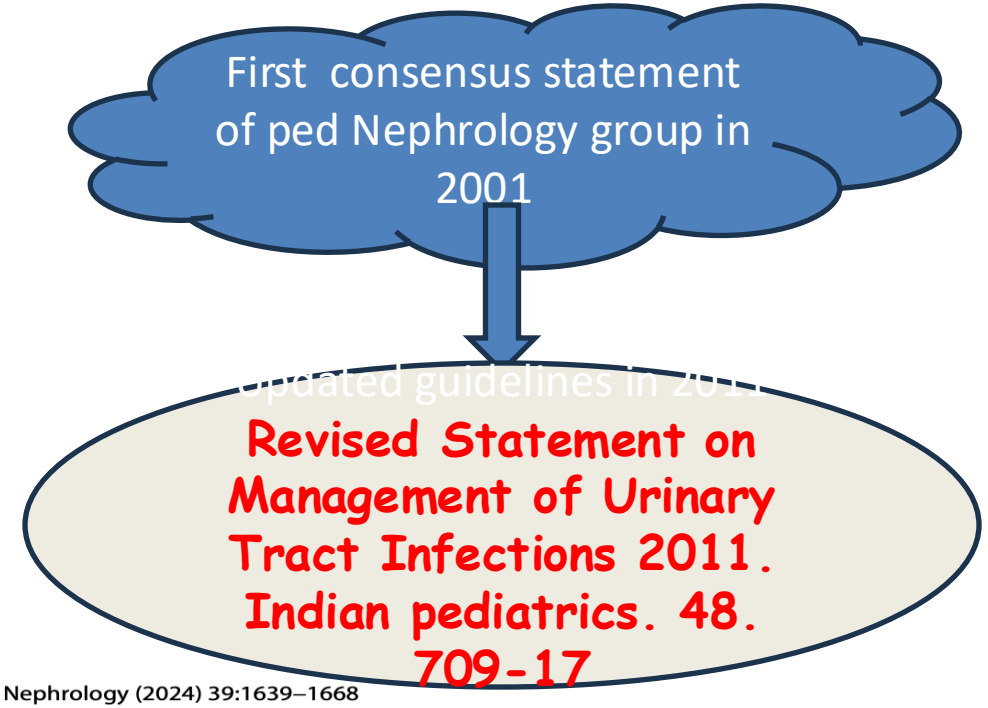
Risk of Renal Scarring by Number of UTIs



Infect Dis Clin North Am. 1987;1(4):713–729

Various guidelines on UTI in children

- Sweden 1999
- NICE 2007
- AUA 2010
- AAP 2011
- ISPN (Indian) 2011
- EAU 2012
- ISPN (Italian) 2019
- ISPN (Indian) 2023



Pediatric Nephrology (2024) 39:1639–1668
https://doi.org/10.1007/s00467-023-06173-9

GUIDELINES

Check for updates

Evidence-based clinical practice guideline for management of urinary tract infection and primary vesicoureteric reflux

Pankaj Hari[1] · Jitendra Meena[1] · Manish Kumar[2] · Aditi Sinha[1] · Ranjeet W. Thergaonkar[3] · Arpana Iyengar[4] · Priyanka Khandelwal[1] · Sudha Ekambaram[5] · Priya Pais[4] · Jyoti Sharma[6] · Madhuri Kanitkar[7] · Arvind Bagga[1] · on behalf of Indian Society of Pediatric Nephrology

Received: 25 June 2023 / Revised: 27 August 2023 / Accepted: 17 September 2023 / Published online: 28 October 2023

Issues related to UTI in children

- Clinical features and Diagnosis
- Choices and duration of therapy
- Protocol for follow up – MCU, DMSA
- Antibiotic Prophylaxis

Incidence
Boys—2%
Girls—6%
Experience atleast 1 episode of UTI

17 recommendations

18 clinical practice points

Case 1.

- 8 month old male infant presented with
  - Excessive crying
  - Vomiting
  - Refusal to feed for 3 days
  - No stream issues

On oral Antibiotics (Cefixime) for 1 day

Antenatal scan : Bilateral minimal calyceal dilatation

Is it UTI?

Features of UTI in **infants** are **nonspecific**: thus a high degree of suspicion is necessary.

1) Infant or child with "unexplained fever" beyond 3 days.
   – Fever generally will not break with conservative measures.
2) Neonates – usually part of septicemia and presents with fever, vomiting, lethargy, jaundice and seizures.
3) Infants & young children – may present with fever, diarrhea, vomiting, abd. pain, and poor weight gain.
4) Older child – dysuria, hematuria, urgency, frequency, flank pain, foul smelling urine, or onset of wetting.

Clinical features

- Depends upon age of child—infant & Young children

- Level of infection

Acute Pyelonephritis

High fever, flank pain(abdomen), pain tenderness & UTI

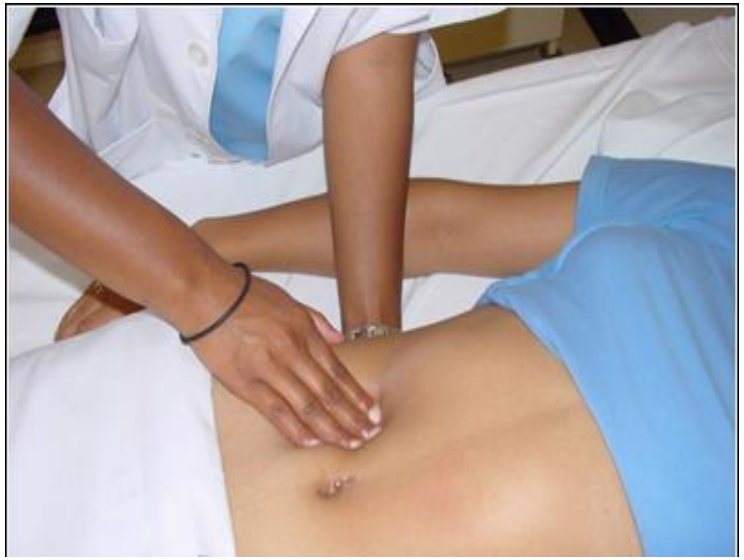
Cystitis

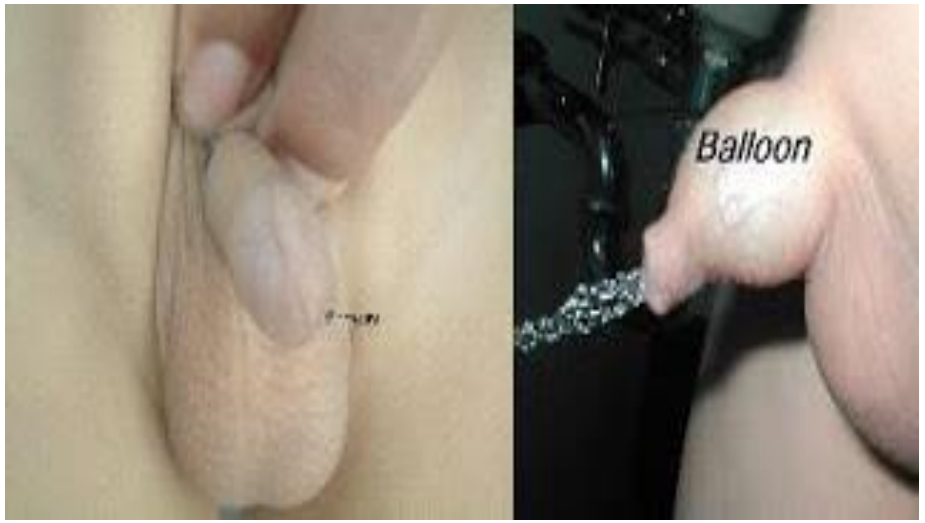
No or low-grade fever, dysuria, urgency, frequency, hematuria(fresh blood or clots),No systemic features

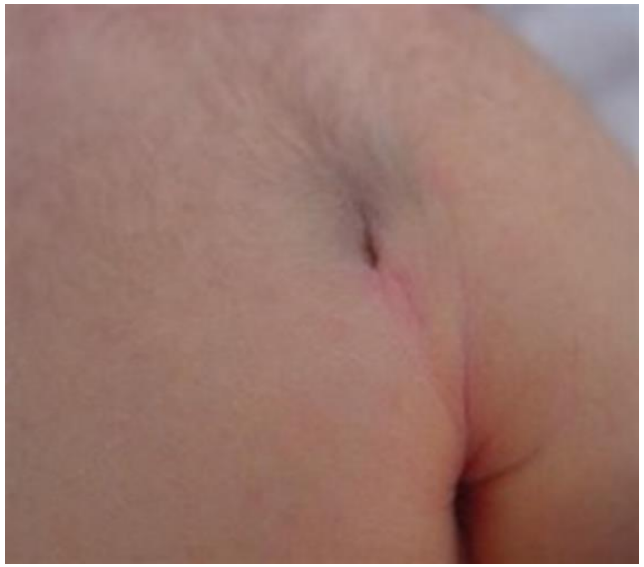
Specific points in history & examination

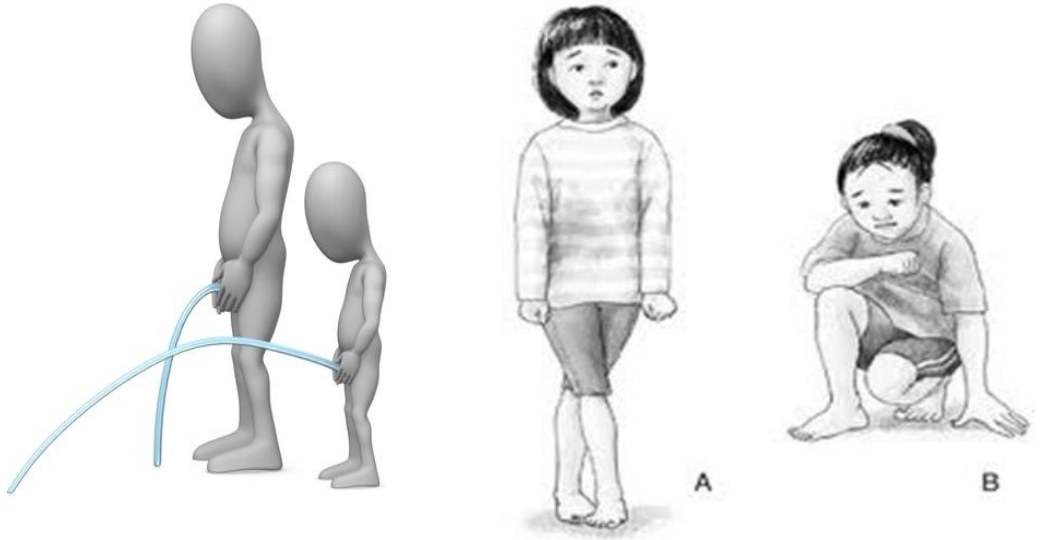
- Antenatally diagnosed renal anomaly
- Look for palpable bladder
- History of Poor urine flow
- Recurrent fever of uncertain origin
- Abdominal mass/genital examination
- Look for urinary stream to r/o lower tract obstruction
- Look for Spinal lesions
- Constipation/voiding dysfunction
- Measure BP

Dr Mukta Mantan




Balloon

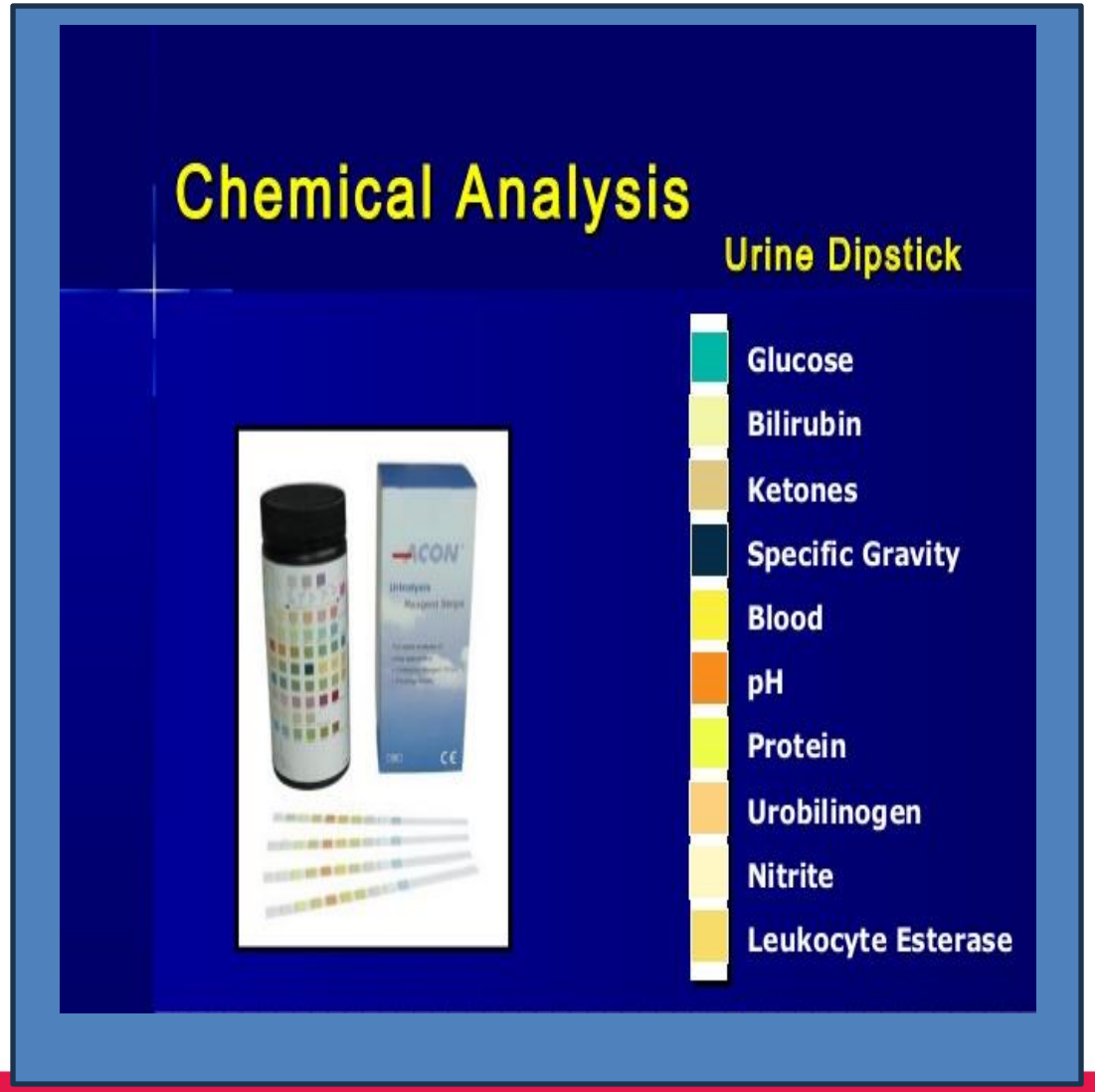



A
B

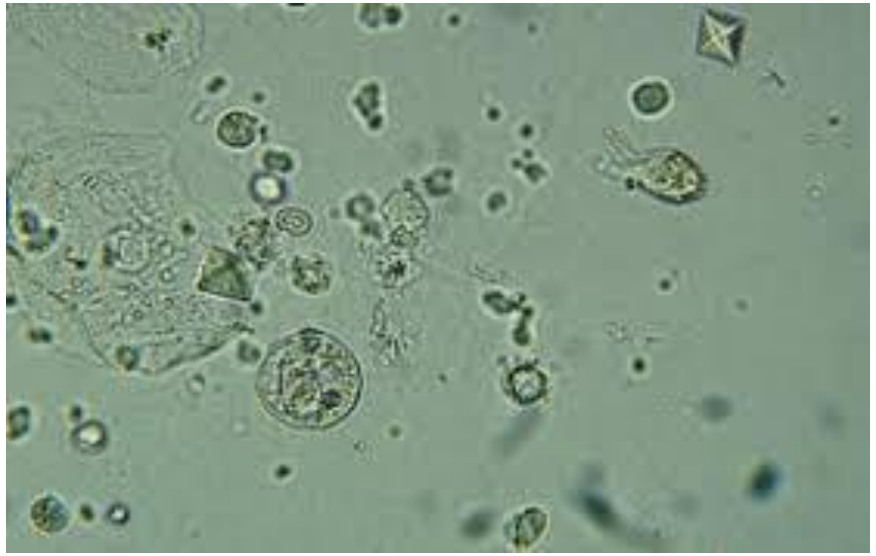
How will you diagnose UTI

- Urine routine / microscopy
- Urine culture

Test	Sensitivity (%)	Specificity (%)
Leucocyte esterase	83	78
Nitrite	53	98
LE or Nitrite	**94**	72
Microscopy WBC	73	81
LE, Nitrite or Microscopy	**99.8**	70



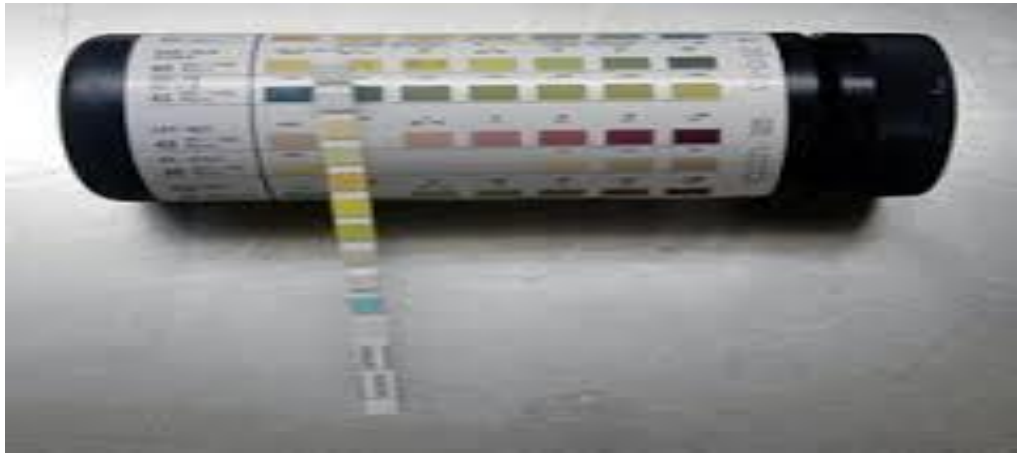
Urinalysis may help to initiate antibioitics prior to urine C/S report



Presence of Leukocyturia: ***>5 leukocytes/ hpf*** in a centrifuged or >10 leukocytes/mm3 in an uncentrifuged sample

Bacteriuria : 1 or more bacteria present on an unspun gram-stained specimen ***per/hpf***

- ***Presence of leukocyte esterase & nitrites on dipstick*** has combined sensitivity 68% & specificity of 98% for detection of UTI



Urine collection methods

- Non-invasive methods (clean- catch, adhesive bags, and nappy pads) are easy to use
- Invasive methods (suprapubic aspiration and catheterization)
- Quick wee methods

Dr Upasana

Questions???

1. Is Urinalysis sufficient ?

2. Should both urine culture and Urinalysis be positive ?

3. What if urine culture sent after 1 dose of antibiotic

4.How to store urine samples?

Methods of urine collection

- Methods of urine collection
- Suprapubic aspiration: Gold standard
- Bag sample
- Catheterization vs suprapubic aspiration:
  - Sensitivity = 95%
  - Specificity = 99%

Bag Sample is Not suitable for culture.

- Negative culture rules out UTI
- Positive culture likely to be false-positive
  - 88% false-positive overall
  - 95% in boys

Urine specimen

- Urine specimen should be plated within 1-2 hour of collection
- If delay is anticipated, store safely at 4 degree for 12-24 hours

Diagnosis of UTI

- significant growth of single uropathogens in urine culture
- The presence of leukocyturia is not necessary.

- Suprapubic aspiration→>10*3 (CFU/mL)
- Catheterization-- >10*4 (CFU/mL)
- Clean-catch→ >10*5(CFU/mL)
- The previous threshold of ≥ 10*5 CFU/ml has been lowered

Diagnosis of UTI

- Pyuria/bacteriuria

  +

- Urine culture

What is your next step? ....Select anyone!!

- Send a urine analysis & Rx UTI as outpatient
- Bag the child for Urine inv & then start antibiotics, adjust as per sensitivity
- Catheterize child for urine culture and begin oral antibiotics
- Admit and catheterize for UC and start iv antibiotics

Dr Manish

Case 1--Inv done

- Urine R/M : PC- 30-40/hpf, RBC- 3-4/hpf, Albumin- trace
- Urine c/s : E.coli (>100000/mL)
- USG KUB : Prominence of Rt renal pelvis, Bladder wall thickened (3mm) ? Cystitis, pre void- 20ml

Potential Management of the case

- Hospitalization
- IV antibiotics
- VCUG
- Clinical follow up
- ???

Oral Vs IV Antibiotics

1. Infants less than 2 months of age
2. Severely ill patients
3. Patients who are unable to ingest oral antibiotic

RX of UTI

1. Age
2. Severity of illness
3. Site of infection
4. Presence of structural abnormality
5. Local antimicrobial susceptibility pattern

Recommendation

We suggest using 3rd-generation cephalosporins or co-amoxiclav as initial empirical antibiotic therapy in children with suspected febrile UTI (2⊕◯◯◯).

We suggest first-generation cephalosporin (cephalexin, cefadroxil) or co-amoxiclav as initial empirical therapy in adolescents with cystitis (2⊕◯◯◯).

Recommendation

We suggest preference of oral over intravenous antibiotic therapy for treatment of acute febrile UTI in all children except: (i) infants less than 2 months of age, (ii) severely ill patients, and (iii) patients who are unable to ingest oral antibiotics (2⊕◯◯◯).

When intravenous antibiotic therapy is initiated, it may be switched over to oral therapy after 3–4 days (1⊕⊕◯◯).

Pediatric Nephrology (2024) 39:1639–1668

Clinical practice point

We suggest changing initial antibiotic therapy only in patients with clinical treatment failure regardless of antibiotic sensitivity patterns.

Clinical practice point

We suggest 7–10 days of therapy with the antibiotic in children with acute symptomatic UTI.

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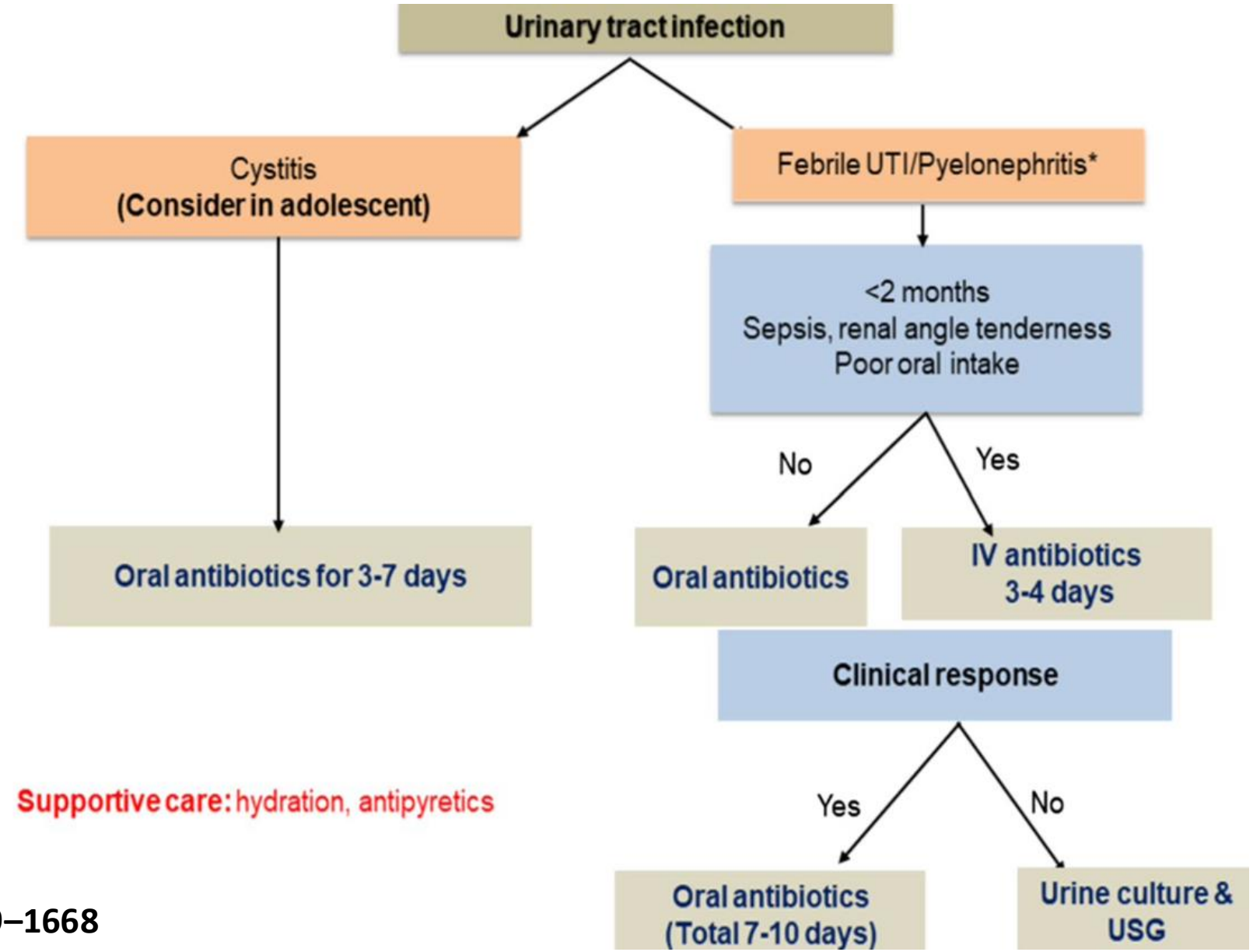
Treatment of UTI

IF No response in 2-3 days then risk factors present & non sensitivity of uropathogens—repeat urine culture & USG KUB

Urine culture no need to repeat, if clinical response+



Supportive care: hydration, antipyretics

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Antibiotics for T/t & Prophylaxis

Antibiotics	Route	Dose (mg/kg/day)
Treatment		
Amoxicillin-clavulanic acid	Oral	30–40 of amoxicillin, in 3 divided doses
	Intravenous	60–100 of amoxicillin, in 3 divided doses
Cefixime	Oral	8–10, in 2 divided doses
Cefuroxime axetil	Oral	20–30, in 2 divided doses
Cephalexin	Oral	40–60, in 2–3 divided doses
Cefpodoxime	Oral	10, in 2 divided doses
Ceftriaxone	Intravenous	75–100, in 1–2 divided doses
Cefotaxime	Intravenous	100–150, in 2–3 divided doses
Ciprofloxacin	Oral	10–20, in 2 divided doses
Ofloxacin	Oral	15–20, in 2 divided doses
Amikacin	Intravenous or intramuscular	10–15, single dose
Gentamicin	Intravenous or intramuscular	5–6, single dose
Prophylaxis		
Co-trimoxazole[1]	Oral	2 of trimethoprim single dose
Nitrofurantoin[2]	Oral	1–2, single dose
Cephalexin[3]	Oral	10–12.5, single dose
Cefadroxil	Oral	5, single dose
Amoxicillin[4]	Oral	15, single dose

25% of daily dose given HS

Ideal drug for prophylaxis

- Urinary concentration above MIC & cause minimal alteration of the bowel flora
- Desired drug level sustained for the greater part of day
- Few side effects; not induce development of bacterial resistance
- Dose is 25% of normal -given HS

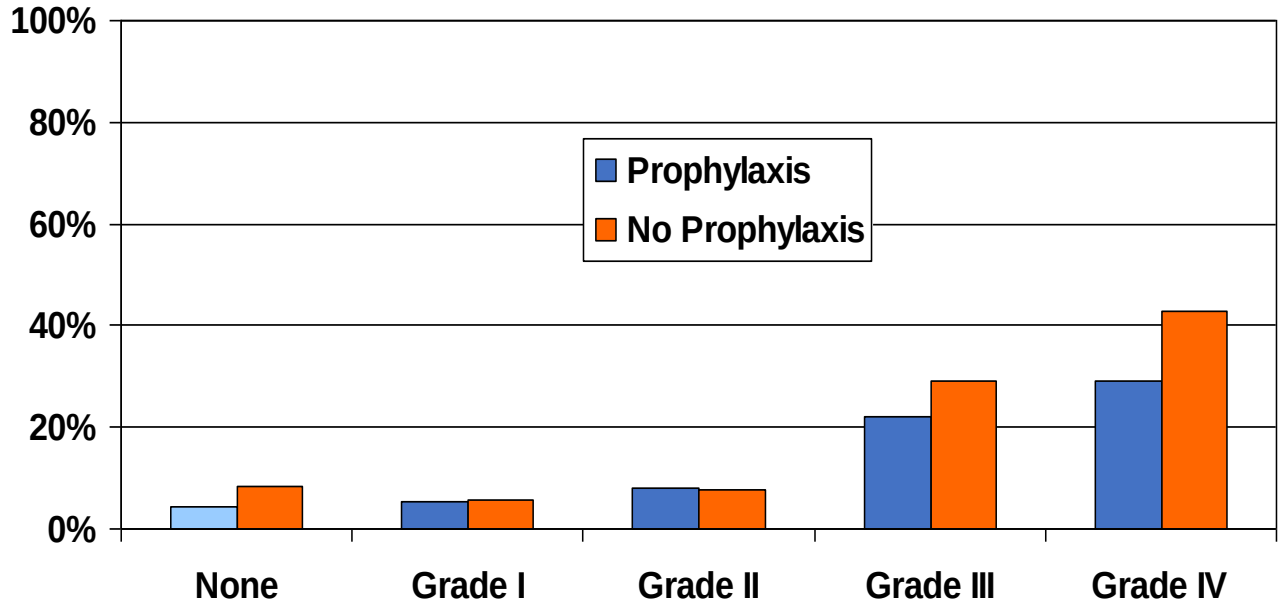
Pediatric Infect Dis J 1996

Antibiotic Prophylaxis

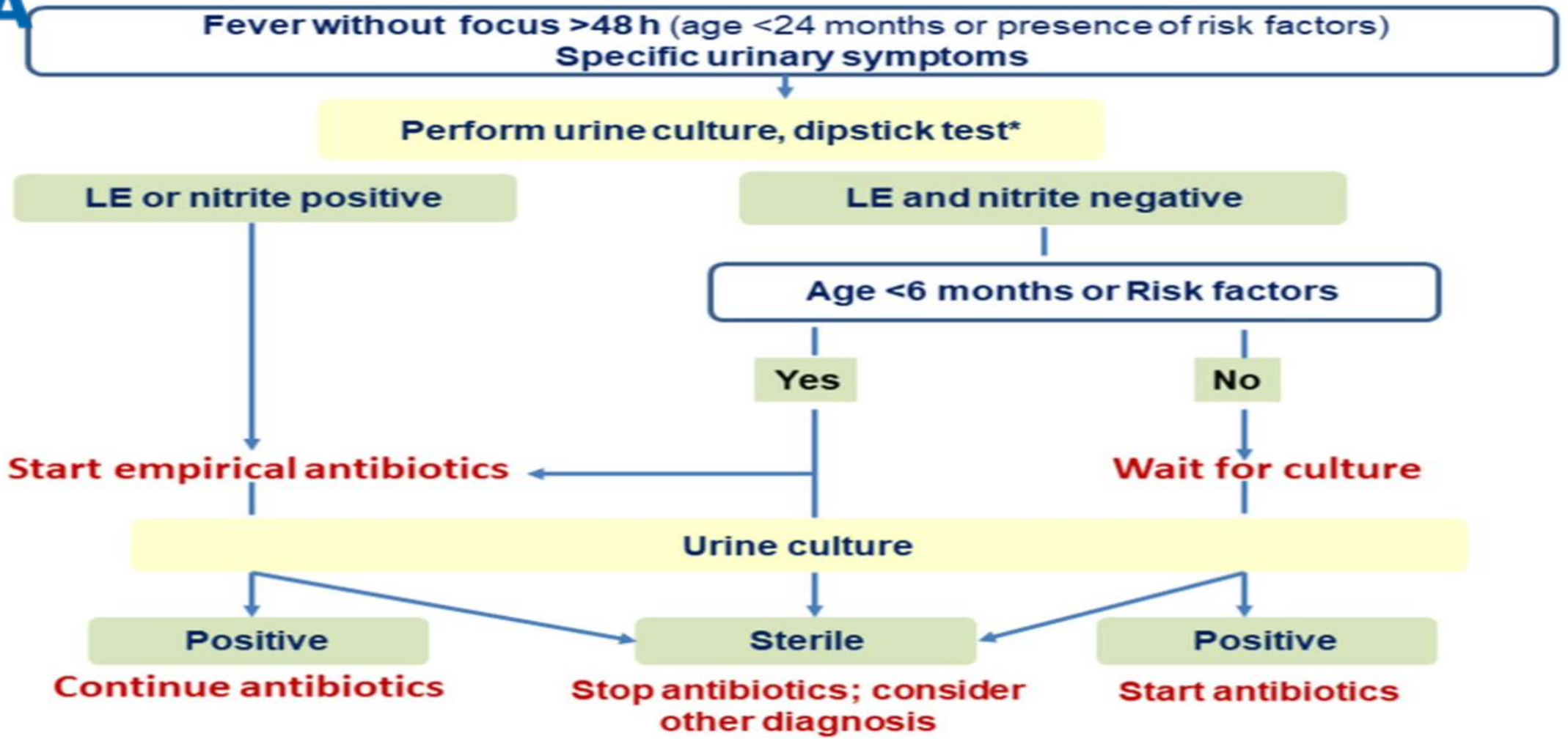
- Pooled evidence from 5 trials (664 participants) suggests that antibiotic prophylaxis, as compared to placebo or no therapy, has little or no effect on the recurrence of symptomatic UTI
- Primary VUR and bladder bowel dysfunction (BBD) are important risk factors for recurrence
- High-grade (grades 3–5) primary VUR
- AP with recurrent febrile UTI and low-grade primary VUR,
- Risk of recurrent UTI with resistant uropathogens was threefold higher in patients receiving antibiotic prophylaxis.
- **Common determinants for discontinuation of antibiotic prophylaxis across all observation studies have been the absence of BBD, toilet training, and lack of recurrence of UTI in the last 12 months**

Recurrence Rate of Febrile UTI

By Reflux Grade, 1,091 Infants 2-24 Months



Approach to diagnosis of UTI



Journal of International Pediatric Nephrology Association(2024) 39:1639–1668

Case 2

- A 6yr girl Recurrent UTI
- 3 episodes, 1st UTI symptomatic
- Urine R/M – WBCs+
- Urine Culture sensitivity- E.coli
- Next 2 episode asymptomatic (parent's cautious)
- No pyuria, urine culture- E.coli (10^4--10^5 cfu /ml)
- USG KUB normal
- Diagnosis???

Dr Manish

Diagnosis of UTI (Interpretation of results)

Asymptomatic Bacteriuria

- Presence of significant bacteria with no symptoms or pyuria
- Incidence 1-2% girls ,0.03% boys
- Healthy children with ABU should not be treated with an antibiotic

Clinical practice point

We do not suggest the use of antibiotics for the treatment of asymptomatic bacteriuria. We suggest that routine urine cultures should not be performed in asymptomatic children.

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Dr Manish

Adjunctive Therapy --role

- Adjunctive corticosteroids
- Vitamin A
- In preventing scarring in children with febrile UTI

Meta-analysis of three randomized controlled trials (RCTs) (529 children) showed that adjunctive corticosteroids in addition to oral antibiotic therapy significantly reduced the risk of kidney scarring in comparison to those who received placebo (RR 0.57; 95% CI 0.36–0.90)

Based on the current evidence, the guideline panel concluded that it is difficult to decide for or against the additional use of corticosteroids or vitamin A in children with febrile UTI

Pediatric Nephrology (2024) 39:1639–1668

Dr Manish

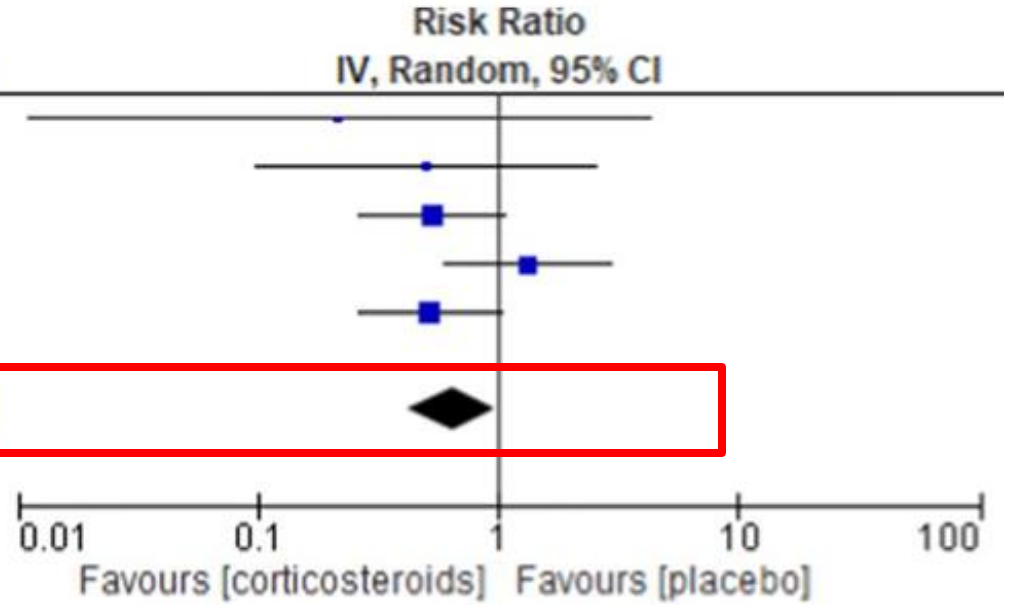
The efficacy and safety of corticosteroids in pediatric kidney scar prevention after urinary tract infection: a systematic review and meta-analysis of randomized clinical trials

Nikolaos Gkiourtzis[1] · Agni Glava[1] · Maria Moutafi[1] · Theopisti Vasileiadou[1] · Theodora Delaporta[1] · Panagiota Michou[2] · Nikoleta Printza[3] · Kali Makedou[4] · Despoina Tramma[1]

Study or Subgroup	Corticosteroids Events	Total	Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Da Dalt 2021	0	23	2	25	2.0%	0.22 [0.01, 4.29]
Ghaffari 2019	2	30	4	30	6.6%	0.50 [0.10, 2.53]
Huang 2011	6	19	39	65	32.5%	0.53 [0.26, 1.05]
Rius-Gordillo 2021	11	56	9	60	25.0%	1.31 [0.59, 2.92]
Shaikh 2020	12	197	22	188	33.9%	0.52 [0.27, 1.02]
Total (95% CI)		**325**		**368**	**100.0%**	**0.64 [0.42, 0.98]**
Total events	31		76			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 4.32$, $df = 4$ ($P = 0.36$); $I^2 = 7\%$

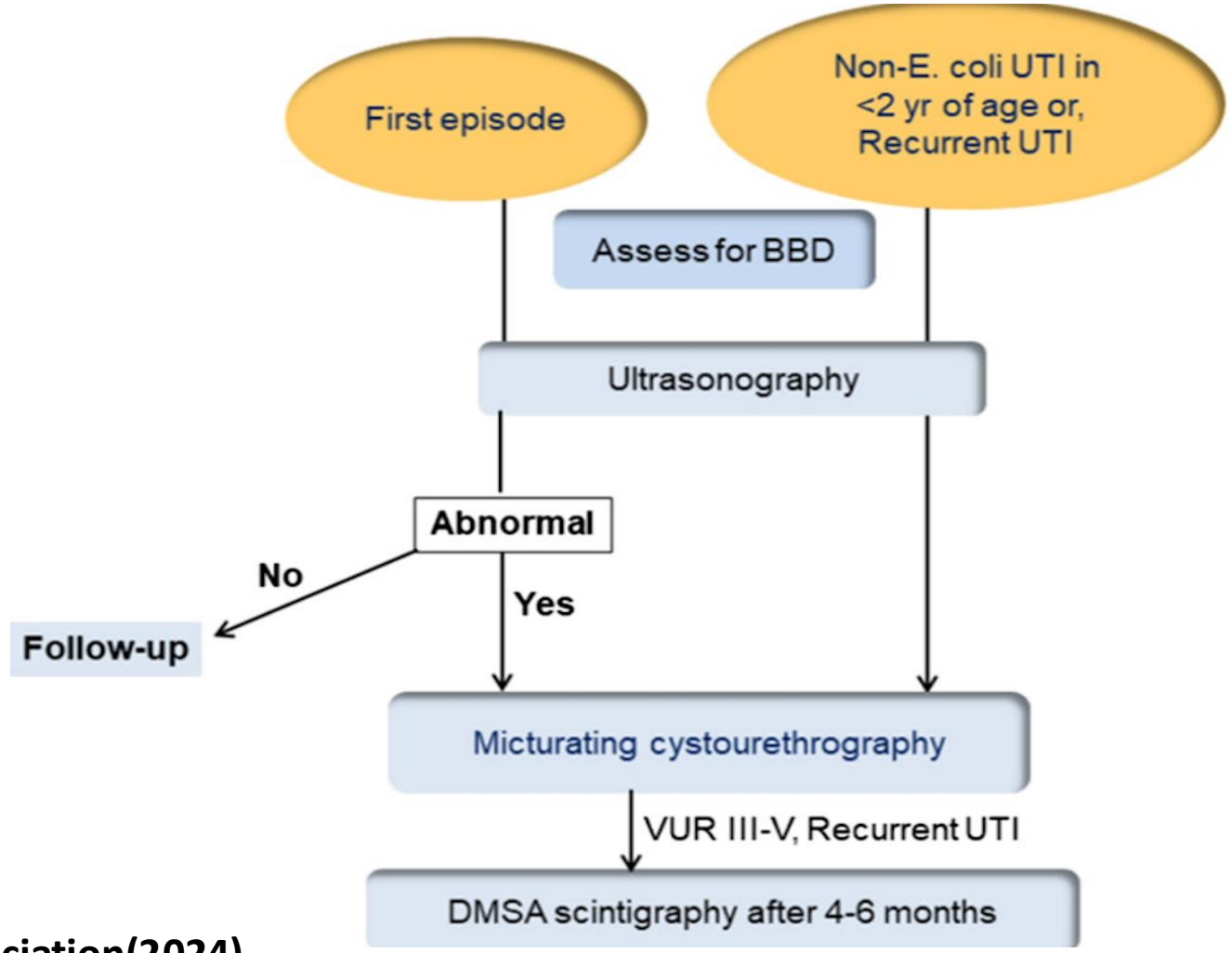
Test for overall effect: $Z = 2.04$ ($P = 0.04$)



Pediatric Nephrology (2023) 38:3937–3945

Imaging after first episode of UTI

Abnormal ultrasound is indicated by
Small kidneys,
Abnormal renal echogenicity,
Pelvi-caliceal dilatation,
Ureteral dilatation,
Uro-epithelial thickening of the renal pelvis,
Bladder wall thickness,
Bladder diverticulum.
bladder bowel dysfunction;



Journal of International Pediatric Nephrology Association(2024)

In whom should MCUG be done?

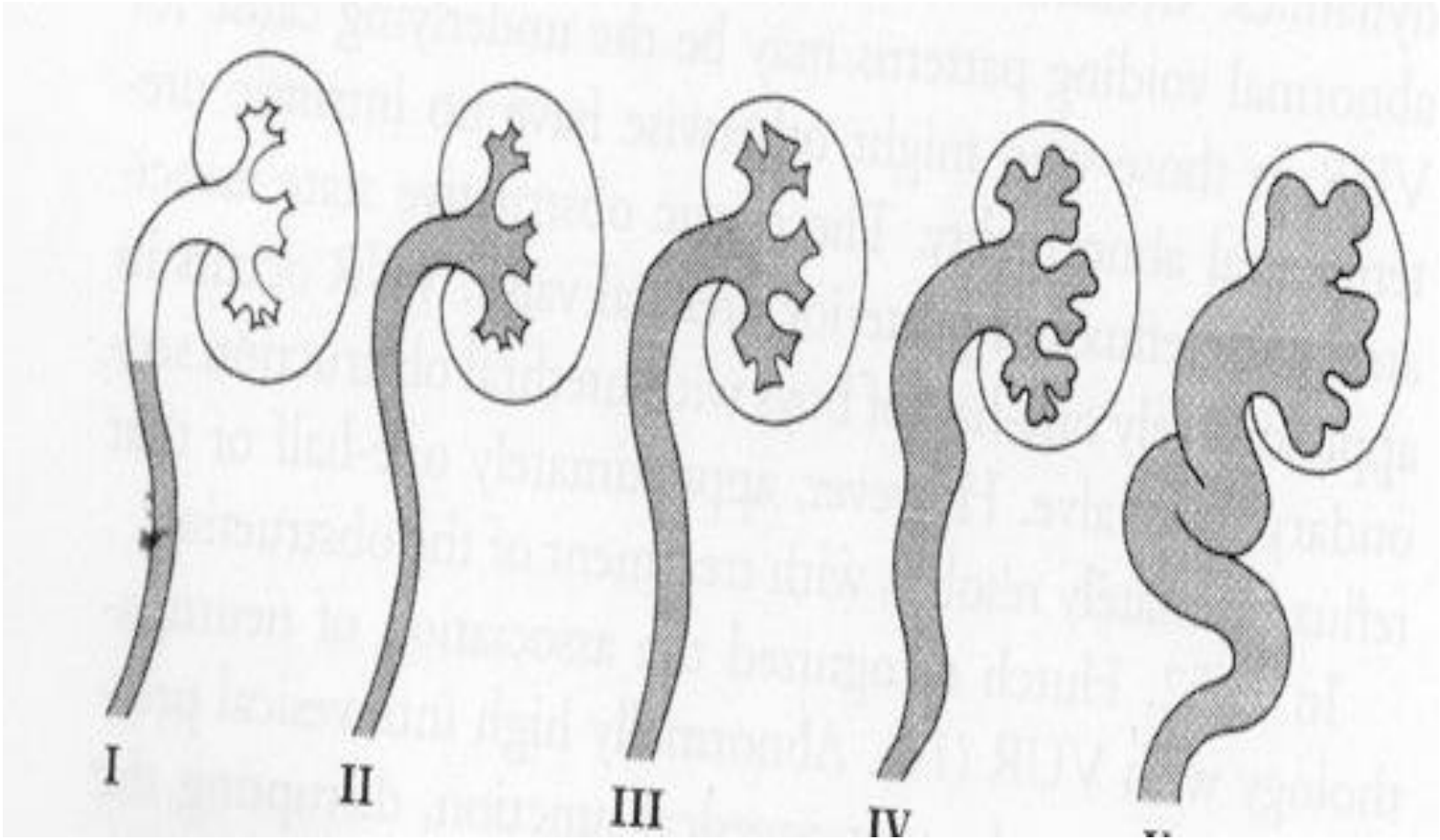
ISPN guidelines suggest performing MCUG in children with one of the following

- UTI caused by non-E.coli uropathogens in children less than 2 years
- Abnormal ultrasound scan

  or
- History of recurrent UTI

Dr Mukta Mantan

Grading of VUR on MCUG



Bowel Bladder Dysfunction

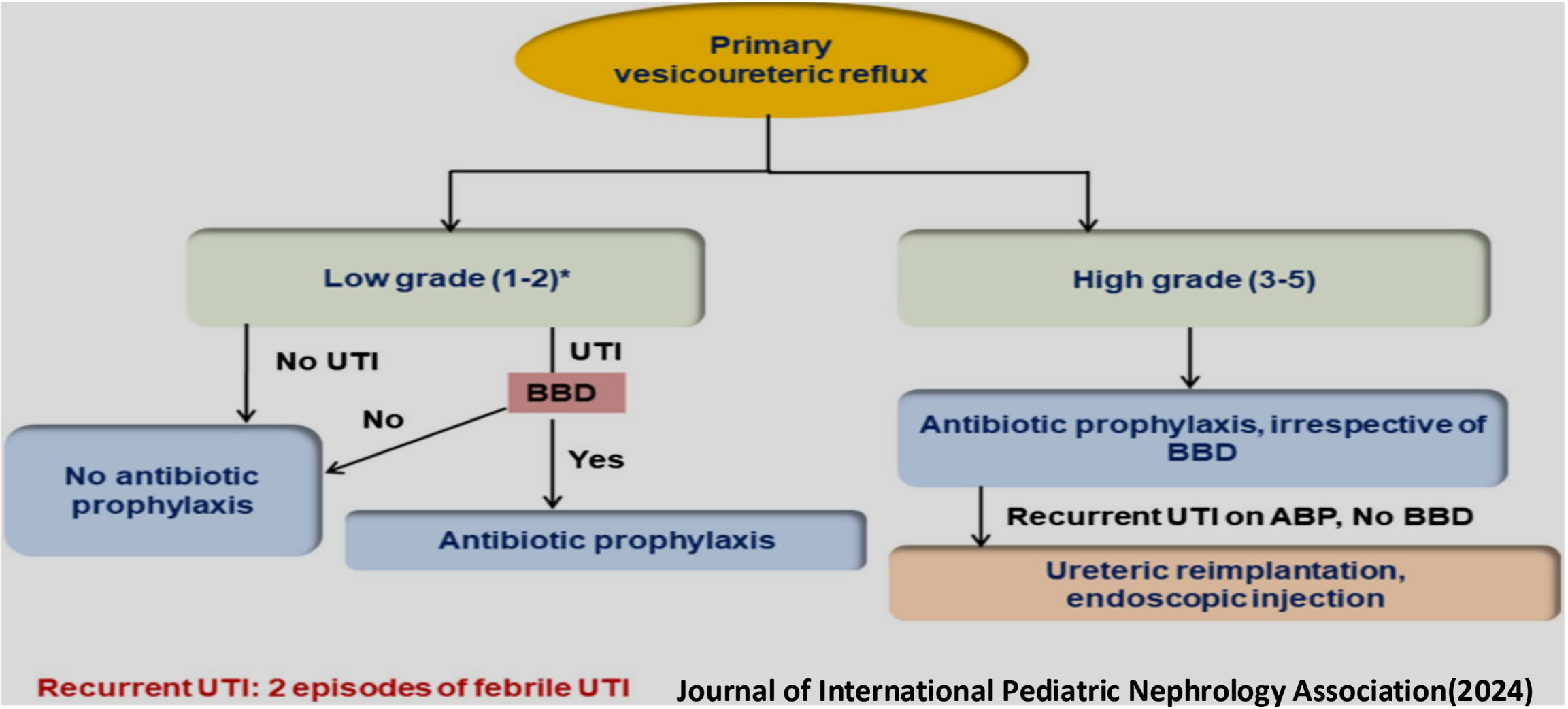


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Table 4 Treatment of bladder-bowel dysfunction

	Therapy	Description	Remarks
First line	Urotherapy	Voiding diary Increase fluid intake (6–8 cup/day) Reduce intake of caffeine, chocolate Frequent (2–4 hourly); double voiding Adequate posture; support both feet on stool/flat surface	Ensure compliance to urotherapy Should be continued for at least 6 months
	Bowel regimen	Hydration, increase intake of fibre, bowel training Polyethylene glycol: 1–1.5 g/kg/d for 3 days followed by 0.25–0.5 g/kg/d	
Second line	Overactive bladder	Oxybutynin: 0.2 mg/kg/dose 2–3 times daily Tolterodine: 2–4 mg/day Mirabegron: 12.5–25 mg/day or Neuromodulation	Side effects of oxybutynin includes constipation, dry mouth blurred vision, headache, drowsiness
	Dysfunctional voiding	Tamsulosin: 0.2–0.4 mg/day Doxazosin: 1 mg/day Biofeedback therapy	Hypotension, CHF
	Underactive bladder	Clean intermittent catheterization Biofeedback therapy	No specific pharmacotherapy for underactive bladder
Third line	Botulinum toxin	50–100 IU injected For overactive bladder: intra-detrusor injection of botulinum toxin For refractory dysfunctional voiding: injection into the bladder neck	Used as last option in refractory patients

Prevention of Recurrence of UTI

Table III Strategies for Prevention of Recurrence of UTI in Children

Strategy	*Indications*
Antibiotic prophylaxis	High-grade VUR, recurrent UTI in patients with BBD, Infants with low-grade VUR
Surgical re-implantation	Recurrent febrile UTI despite antibiotic prophylaxis and adequate management of BBD
Cranberry products	Patients with recurrent UTI and normal urinary tract. No data to support its use in patients with VUR
Urotherapy*	All patients with BBD
Circumcision	Can be suggested as an option in patients at-risk of recurrence of UTI

**Urotherapy includes behavioral modifications (regular bladder and bowel habits, adequate fluid intake, optimal posture during voiding etc.) information and demystification related to lower urinary tract symptoms, adequate intervals between urinations, documentations of voiding symptoms and systematic follow-up. BBD: Bladder-bowel dysfunction; VUR: Vesicoureteral reflux*

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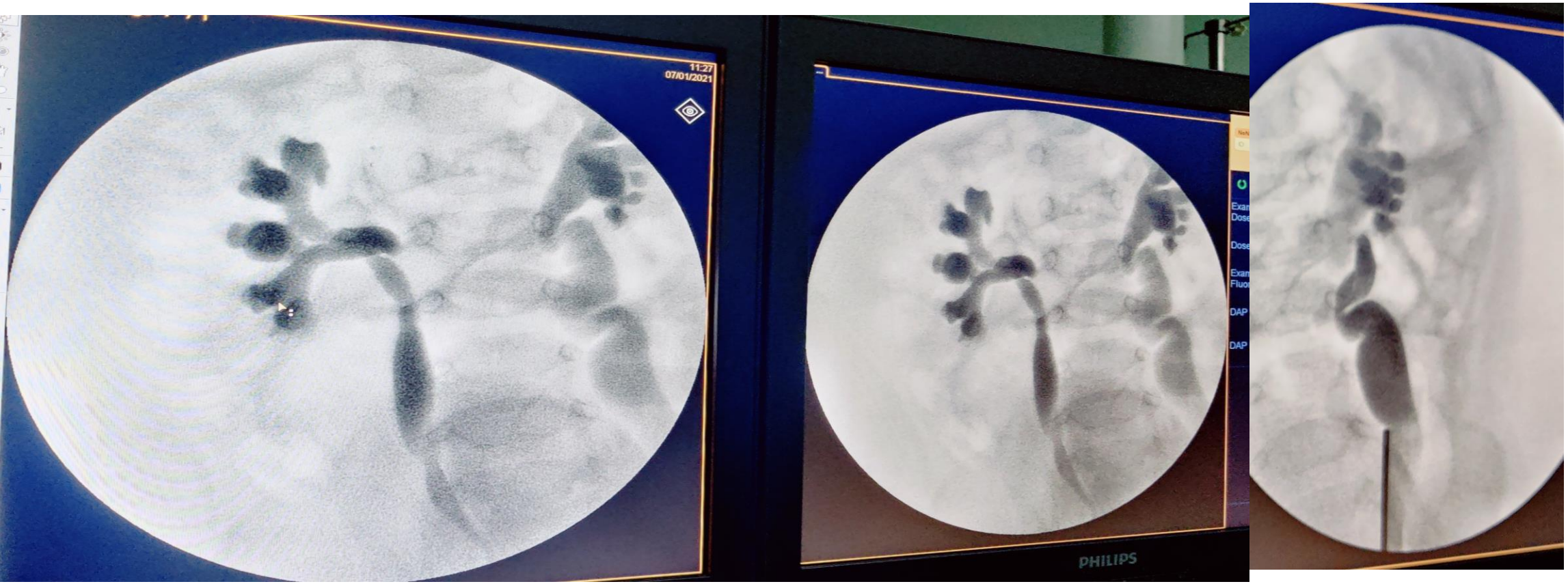
Case 3

- 5month boy with history of UTI at 4 month of age, urine routine pus cells++, urine culture E.coli 10x5 CFU/ml
- Received cefixime for 2 weeks. Rpt. urine pus cell 2-4
- USG(KUB): RT 7.6X2.6mm, Lt 4.8x 2.0mm(small dysplastic)
- Hypertension: BP 105/78mmhg

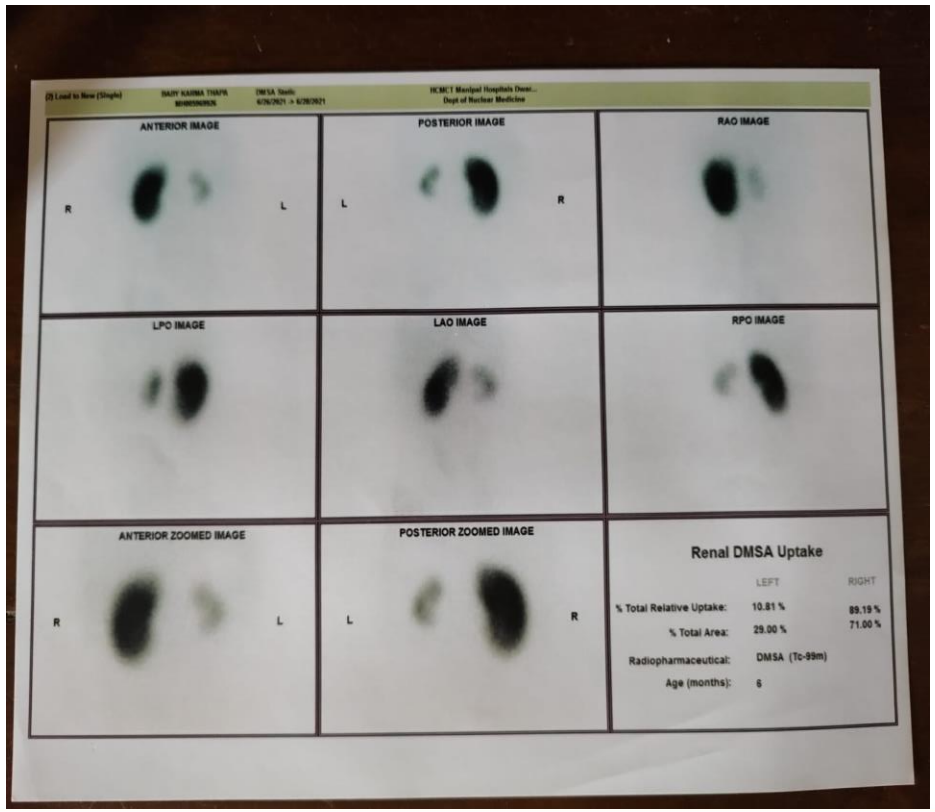
MCU



MCU: B/L Reflux grade 5 VUR Rt >left

Function of kidney

- DMSA: Left small dysplastic ,Rt normal in size & CMD maintained, small scar+,Left10.8%,Rt 89%
-



What do u advise

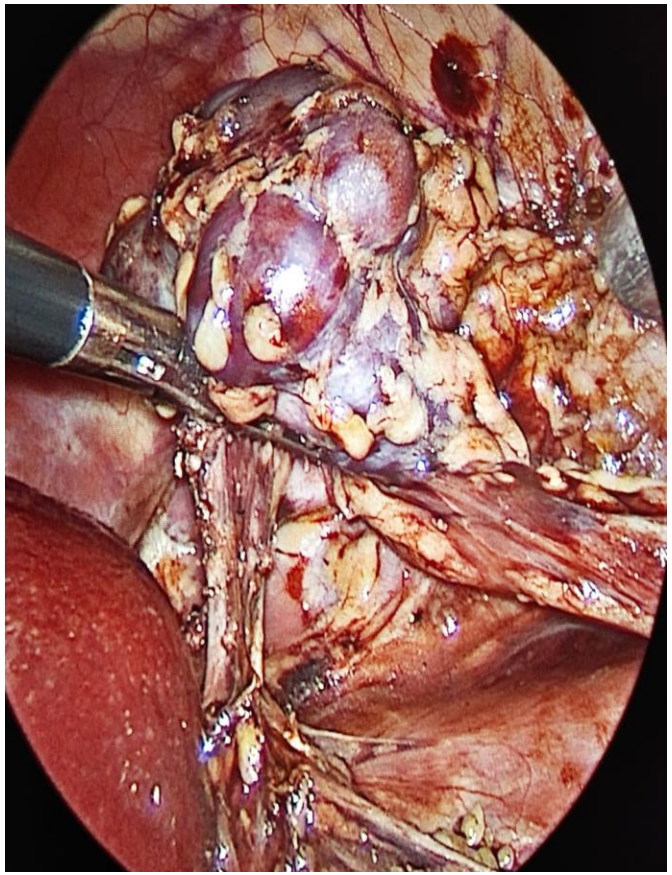
- Nephroureterectomy
- Ureteric Reimplantation or ureterostomy
- Combined Ureteric reimplant with nephroureterectomy
- Medical therapy
- Any other evaluation before proceeding

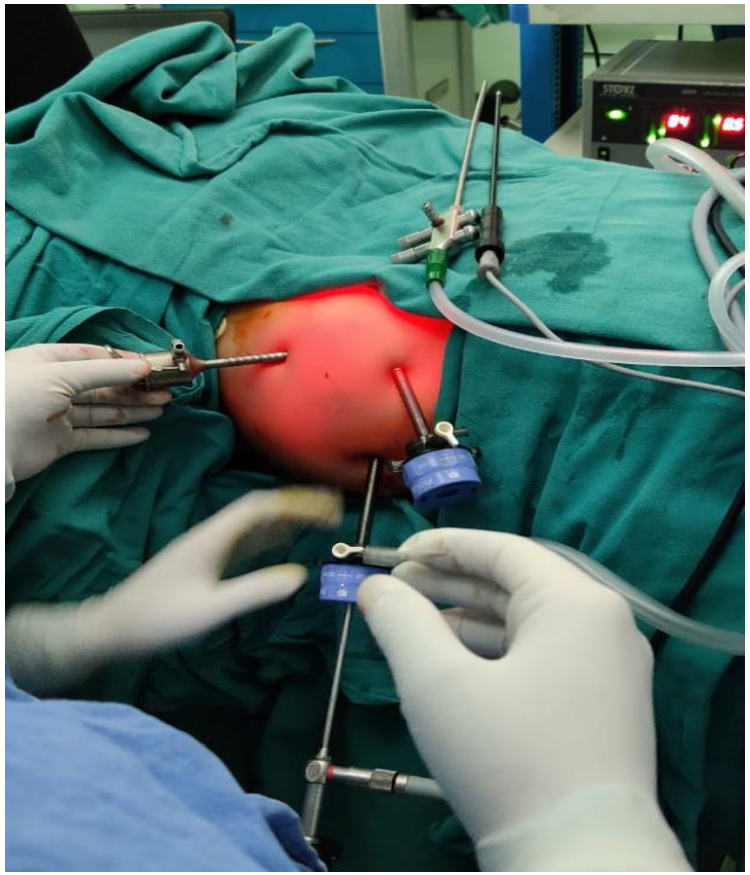
Next Laparoscopic or Open

Bladder evaluation

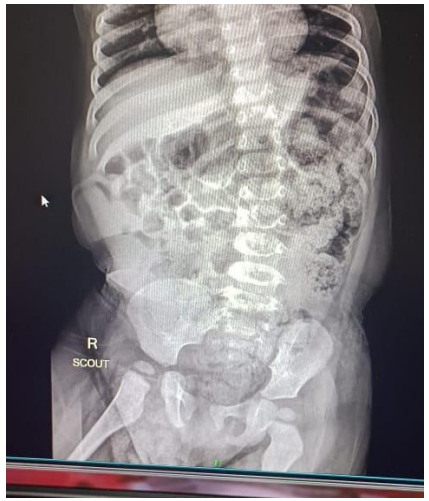
- Uroflowmetry
- Visual voiding video

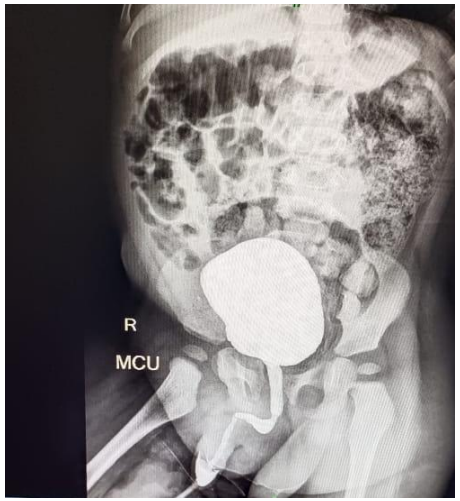
Left Lap Nephroureterectomy with right Ureteric reimplant in same sitting





6months post surgery MCU and follow up





Take Home Message

- Any child with fever without focus rule out UTI
- ABU & cystitis are often misdiagnosed as pyelonephritis
- Urine collection method is a key to correct diagnosis
- Older children with VUR, recurrent symptomatic UTI and VUR with concomitant BBD, are risk factors for the development of reflux nephropathy
- USG Kidney should be repeated periodically to monitor kidney growth in high grade VUR
- DMSA Scan should be repeated during follow-up only in children with recurrence of UTI.

STOOL CHART

BRISTOL STOOL CHART

TYPE 1		**Separate hard lumps** VERY CONSTIPATED
TYPE 2		**Lumpy and sausage like** SLIGHTLY CONSTIPATED
TYPE 3		**A sausage shape with cracks in the surface** NORMAL
TYPE 4		**Like a smooth, soft sausage or snake** NORMAL
TYPE 5		**Soft blobs with clear-cut edges** LACKING FIBER
TYPE 6		**Mushy consistency with ragged edges** INFLAMMATION
TYPE 7		**Liquid consistency with no solid pieces** INFLAMMATION AND DIARRHEA

MEDICALNEWSTODAY

IPNA