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Thanks to our Speaker!

- Poyyapakkam R. Srivaths, MD, MS
  - Medical Director of Pheresis Services
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Chronic Kidney Disease in Children

Poyyapakkam Srivaths MD, MS

Texas Children's Hospital

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What is Chronic Kidney Disease?

- Chronic Kidney Disease (CKD) is defined as abnormalities of kidney structure or function, present for more than 3 months.
  - Lasting damage to the kidneys that can get worse over time
- Main signs of kidney damage:
  - Decreased glomerular filtration rate (GFR)
  - The GFR test shows how well your kidneys are working. Shows how much blood is filtered through glomeruli (kidney filters) in 60 seconds.
    - **Less than 60 ml/min/1.73m^2 could mean kidney damage**
  - Albuminuria – too much protein in your urine

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Glomerular Filtration Rate in Children

- The most common measure of kidney function is estimated GFR (eGFR)
- Recently updated formula:
  - eGFR – 0.412*ht/serum creatinine (mg/dL)

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Chronic Kidney Disease Stages

- CKD stages were introduced to help define the progression of the disease and how to treat it.
- There are certain changes in the body or complications that happen more often at certain GFR levels regardless of CKD cause.

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Chronic Kidney Disease Staging (KDIGO 2012)

Stage	Description	Glomerular Filtration Rate (GFR) (mL/min/1.73 m^2)
1	Kidney damage with normal or increased GFR	Greater than 90
2	Kidney damage with mild decrease GFR	60-89
3a	Mild to moderate decrease GFR	45-59
3b	Moderate to severe decrease GFR	30-44
4	Severe decrease GFR	15-24
5	Kidney failure	Less than 15 (or dialysis)

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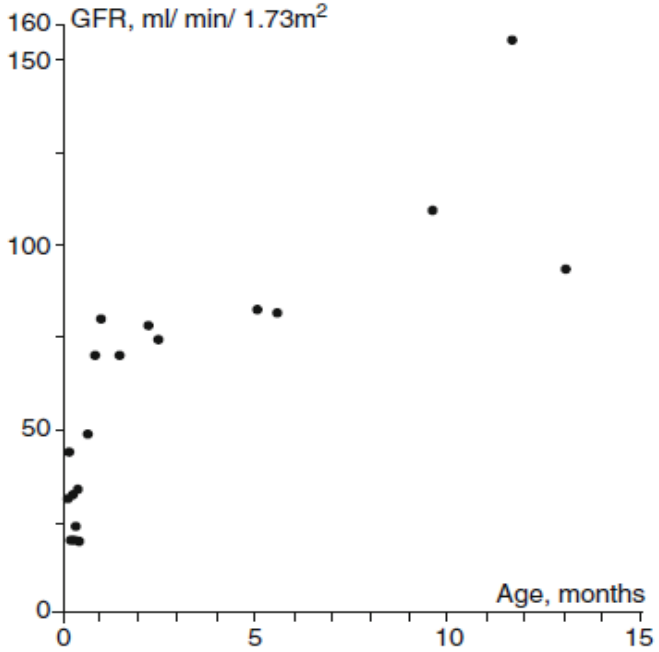
GFR and Age

- GFR becomes normal by 2 years of age
- A healthy newborn can have a GFR which is between 40-60 ml/min/1.73m^2



Aperia, A. Acta ped Scandinavia, 1975

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Differences in CKD Staging for Children

1. Staging of Chronic Kidney Disease does not include patients younger than 2 years old.
2. Duration of more than 3 months to define Chronic Kidney Disease does not apply to newborns and infants less than 3 months of age.
3. Urine protein can be used instead of urine albumin excretion in children.

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Proteinuria (protein in urine) Categories

Category	Protein excretion rate (mg/24 hours)	Protein creatinine ratio (mg/G)		Terms
A1	Less than 30	Less than 30		Normal to mildly increased
A2	30-300	30-300		Moderately increased
A3	Greater than 300	Greater than 300		Severely increased

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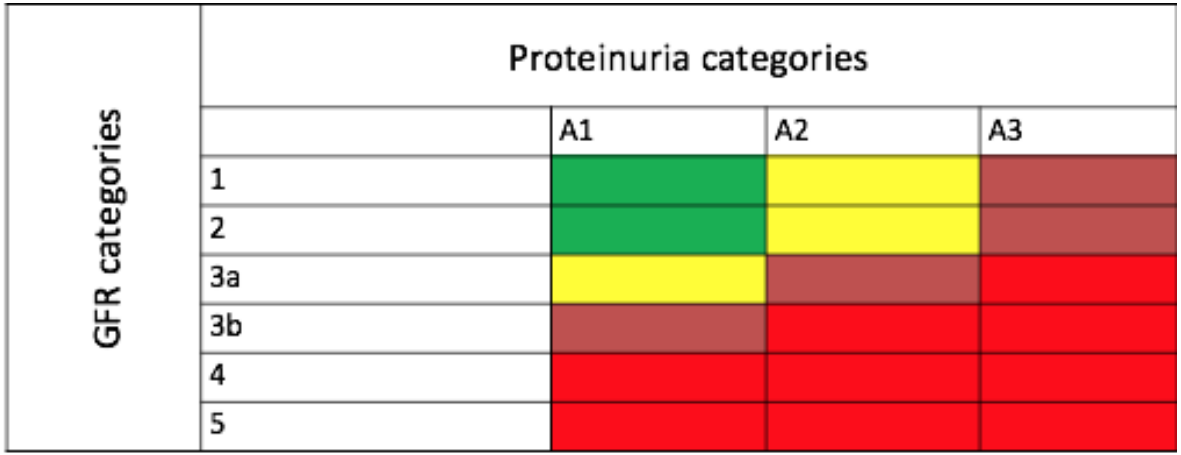
Why Have Proteinuria in Classification?

Risk of progression

- Green : Low risk for progression and complications
- Yellow : Moderately increased risk
- Orange : High risk
- Red : Very high risk



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Two Important Study Cohorts in Pediatric CKD Pts

- **CKiD**- Ongoing study observing and following initially moderate and then mild to moderate pediatric chronic kidney disease patients from US and Canada.

Furth SL, Cole SR, Moxey-Mims M, Kaskel F, Mak R, Schwartz G, et al. Design and methods of the Chronic Kidney Disease in Children (CKiD) prospective cohort study. Clin J Am Soc Nephrol. 2006 Sep;1(5):1006–15)

- **ESCAPE** – Interventional study of children with moderate chronic kidney disease from Europe where one group of had standard control of BP and other group had intensified treatment.

Strict blood-pressure control and progression of renal failure in children, N Engl J Med, 361 (2009), pp. 1639-1650

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Proteinuria categories for Children and risk stratification

			Baseline UPCR		
			<0.5	[0.5, 2.0]	>2.0
Baseline GFR Stage	I	≥90	n=44 CKID: 100% ESCAPE: 0% glomerular dx: 48% events=3 p-y=132.79 *IR=2.3 (0.73, 7.00)* *per 100 p-y*	n=12 CKID: 100% ESCAPE: 0% glomerular dx: 67% events=1 p-y=45.82	n=4 CKID: 100% ESCAPE: 0% glomerular dx: 100% events=1 p-y=11.40
	II	[60, 90)	n=200 CKID: 95% ESCAPE: 5% glomerular dx: 29% events=12 p-y=814.40 *IR=1.5 (0.84, 2.6)* *per 100 p-y*	n=48 CKID: 94% ESCAPE: 6% glomerular dx: 58% events=14 p-y=171.93 *IR=8.1 (4.8, 13.8)* *per 100 p-y*	n=17 CKID: 100% ESCAPE: 0% glomerular dx: 88% events=6 p-y=42.26 *IR=14.2 (6.4, 31.6)* *per 100 p-y*
	IIIa	[45, 60)	n=190 CKID: 73% ESCAPE: 7% glomerular dx: 18% events=34 p-y=956.79 *IR=3.6 (2.5, 5.0)* *per 100 p-y*	n=100 CKID: 78% ESCAPE: 22% glomerular dx: 25% events=30 p-y=469.27 *IR=6.4 (4.5, 9.1)* *per 100 p-y*	n=23 CKID: 91% ESCAPE: 9% glomerular dx: 57% events=15 p-y=65.91 *IR=22.8 (13.7, 37.8)* *per 100 p-y*
	IIIb	[30, 45)	n=153 CKID: 54% ESCAPE: 46% glomerular dx: 8% events=47 p-y=797.97 *IR=5.9 (4.4, 7.8)* *per 100 p-y*	n=101 CKID: 75% ESCAPE: 25% glomerular dx: 21% events=51 p-y=476.89 *IR=10.7 (8.1, 14.1)* *per 100 p-y*	n=52 CKID: 69% ESCAPE: 31% glomerular dx: 46% events=40 p-y=125.12 *IR=32.0 (23.5, 43.6)* *per 100 p-y*
	IV	[15-30)	n=69 CKID: 48% ESCAPE: 52% glomerular dx: 7% events=41 p-y=236.31 *IR=17.4 (12.8, 23.6)* *per 100 p-y*	n=97 CKID: 46% ESCAPE: 54% glomerular dx: 8% events=65 p-y=262.01 *IR=24.8 (19.5, 31.6)* *per 100 p-y*	n=59 CKID: 59% ESCAPE: 41% glomerular dx: 36% events=52 p-y=89.05 *IR=58.4 (44.5, 76.6)* *per 100 p-y*

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CKiD Study & Escape Combined

Risk Group	Study	N=	Person-years	Events	Expected time to event (95% CI), years*		
					10th Percentile	25th Percentile	50th Percentile
A	Non-Glomerular	321	1537.68	36	5.1 (4.2, 6.1)	>10	>10
	Glomerular	113	366.30	13	2.9 (2.3, 3.6)	5.8 (4.5, 7.1)	>10
B	Non-Glomerular	236	1205.46	66	2.8 (2.3, 3.3)	5.5 (4.7, 6.4)	>10
	Glomerular	65	233.71	25	1.6 (1.3, 2.0)	3.2 (2.5, 3.8)	6.2 (4.9, 7.5)
C	Non-Glomerular	82	397.47	43	1.9 (1.5, 2.3)	3.7 (2.9, 4.6)	7.4 (5.8, 9.0)
	Glomerular	36	121.69	14	1.1 (0.8, 1.4)	2.1 (1.6, 2.7)	4.2 (3.2, 5.2)
D	Non-Glomerular	74	254.58	44	1.0 (0.8, 1.3)	2.0 (1.6, 2.5)	4.0 (3.1, 4.8)
	Glomerular	18	47.63	12	0.6 (0.4, 0.7)	1.1 (0.8, 1.5)	2.3 (1.7, 2.8)
E	Non-Glomerular	117	337.50	76	0.7 (0.6, 0.9)	1.4 (1.1, 1.7)	2.7 (2.3, 3.2)
	Glomerular	32	49.63	29	0.4 (0.3, 0.5)	0.8 (0.6, 1.0)	1.6 (1.2, 1.9)
F	Non-Glomerular	38	72.49	33	0.3 (0.2, 0.4)	0.7 (0.5, 0.9)	1.3 (1.0, 1.7)
	Glomerular	21	16.56	19	0.2 (0.1, 0.3)	0.4 (0.3, 0.5)	0.8 (0.5, 1.0)

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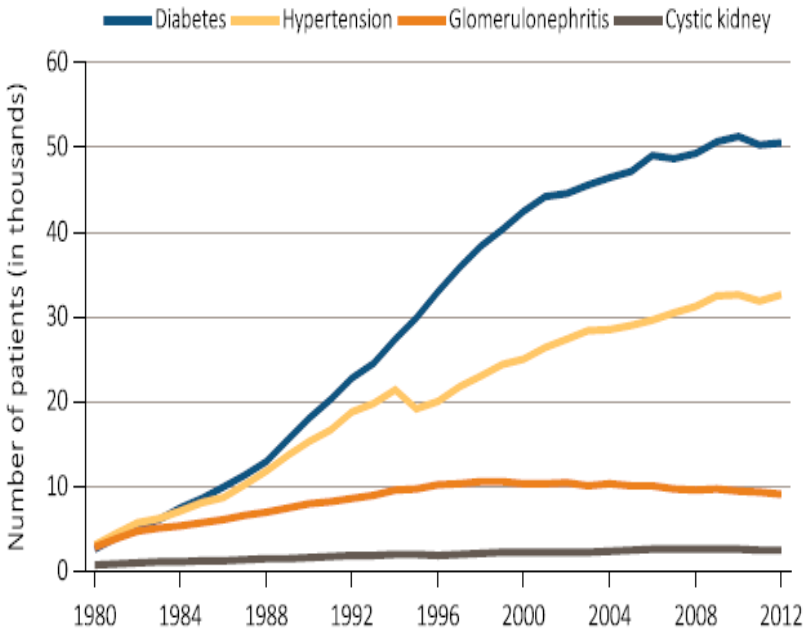
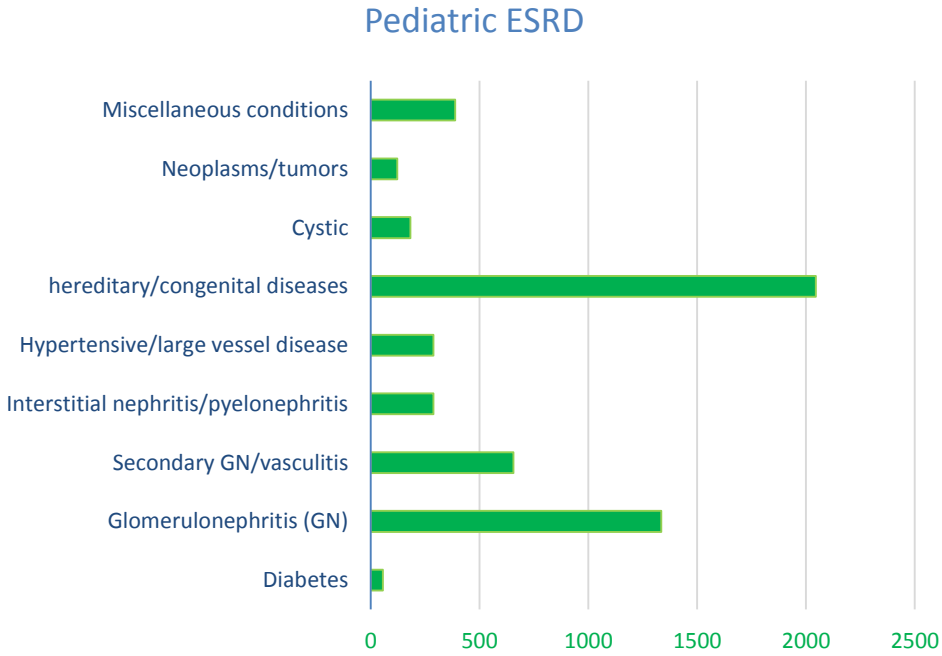
Causes of ESRD (USRDS)





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Chronic Kidney Disease

- In younger children, the most common causes are congenital abnormalities of the kidney and urinary tract (CAKUT), or birth defects, such as renal hypo dysplasia and/or obstructive uropathy.
- The most common obstructive lesions are posterior urethral valves and prune belly syndrome, both of which only occur in boys.
  - Therefore boys have higher prevalence of CKD than girls
- Much higher contribution from CAKUT as cause of Chronic Kidney Disease when compared to ESRD as glomerulonephritis (acute inflammation of the kidney) will progress rapidly to ESRD.

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CAKUT- RENAL Hypodysplasia

- Renal hypoplasia: Small kidney with reduced number of nephrons (filters) but has a normal structure.
- Renal dysplasia: Malformed kidney tissue. Dysplastic kidneys can have cysts – Cystic Renal Dysplasia
- For all practical purposes when a patient presents a small kidney without macroscopic cysts they are often referred to as hypoplastic/dysplastic kidney.

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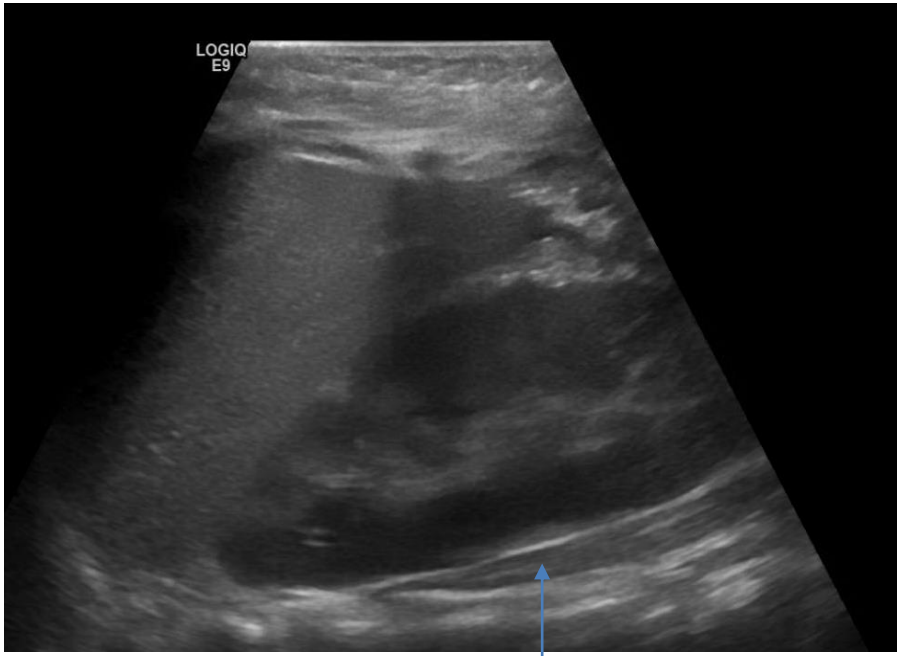
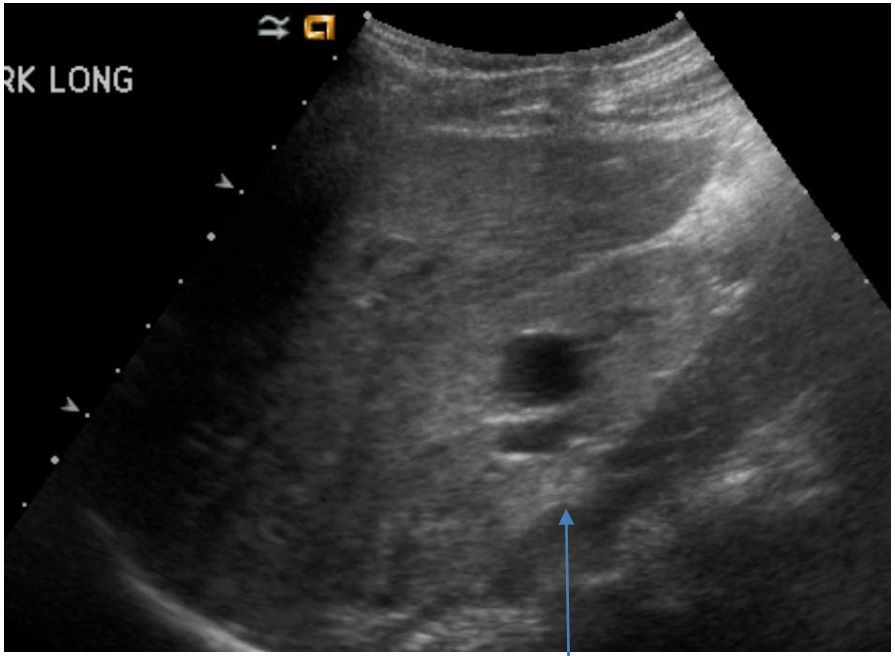
Images



Normal



Small dysplastic kidney with cyst

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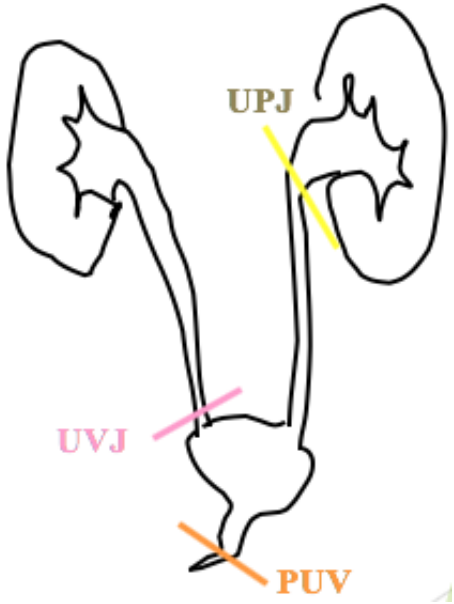
Obstructive Uropathy in Children

- Posterior urethral valves **(PUV)**
  - persistent tissue in posterior prostatic urethra of male
  - bilateral hydronephrosis ± VU reflux
- Ureteropelvic junction **(UPJ)** obstruction
  - At the level kidney and ureter
- Ureterovesical junction **(UVJ)** obstruction
  - At the level of ureter and bladder



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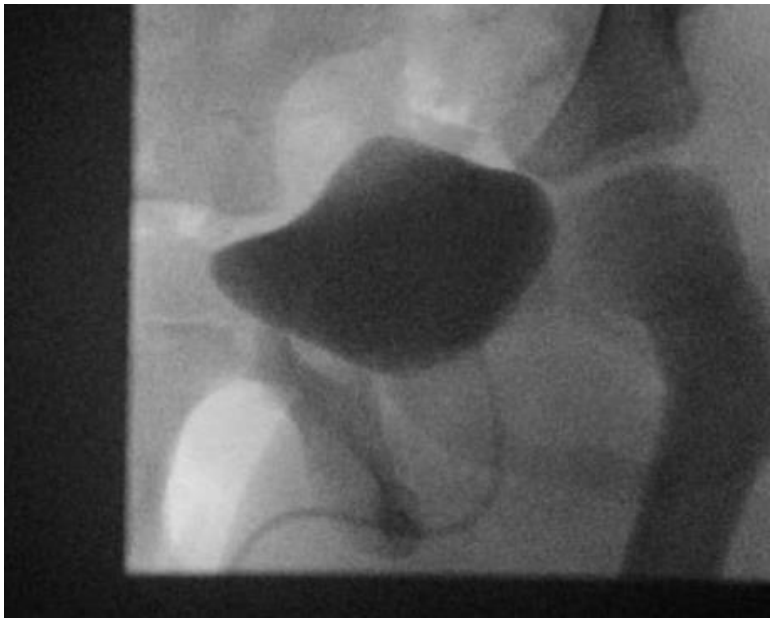
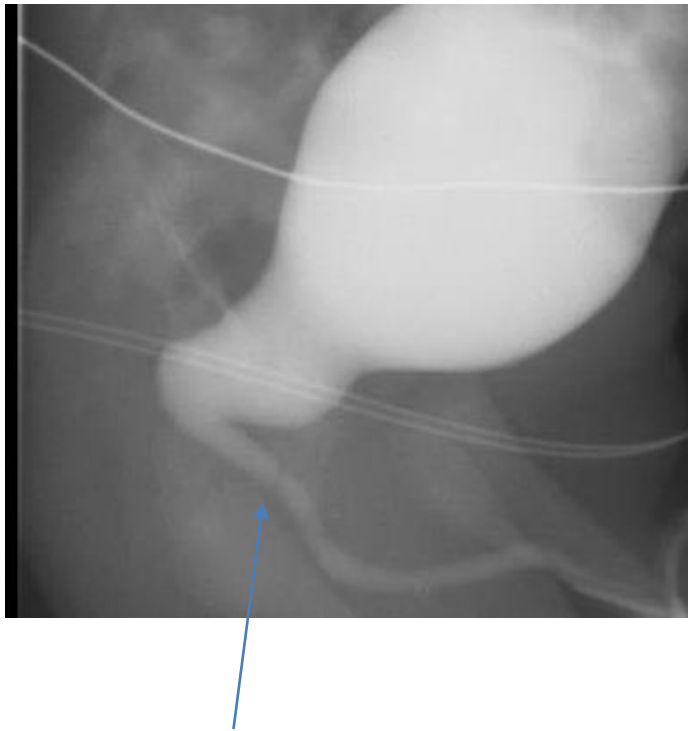
Posterior Urethral Valves





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Role of the Kidneys in the Body

The kidneys are vital organs. They help to:

- Regulate water and electrolyte balance
- Get rid of wastes in the body
- Get rid of harmful substances (hormones and drugs) that affect body function
- Regulate blood pressure
- Regulate red blood cell production
- Balance minerals in the body

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Chronic Kidney Disease consult

- Regulation of water and electrolyte balance: Fluid overload , electrolyte (potassium) and acidosis
- Get rid of wastes in the body: eGFR
- Get rid of harmful substances (hormones and drugs) that affect body function: Dosing for eGFR and avoiding nephrotoxic meds, nutrition and growth
- Regulate blood pressure: HTN management
- Regulate red blood cell production: Anemia
- Balance minerals in the body : Chronic kidney disease- mineral bone disorder

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Nutrition

- Extremely important in infants and young children: Protein energy malnutrition needs to be addressed aggressively
- Multiple Contributing factors
- Assessment: Anthropometry (measurement of ht/wt etc.), lab values such as albumin, cholesterol
- Nutritional support from a specialized dietitian is necessary
- It may be necessary to provide enteral nutrition (nasogastric or gastrostomy) or parenteral nutrition
- It is also important to have child life and psychologist involved, if difficulty in compliance with the required restricted diet is seen

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Growth Impairment

- Impaired growth is a common complication of chronic kidney disease; it can have a huge psychologic impact on a child and negatively affect his or her quality of life - About one-third of all children with CKD have a height below the third percentile for age.
- Causes - include malnutrition/protein-energy wasting, chronic acidosis, severe renal osteodystrophy, sodium depletion, and growth hormone (GH) resistance.
- Get bone age X ray; consult renal dietitian
- Growth hormone is not low in children with chronic kidney disease.
- CKD can be thought of as a condition associated with partial GH resistance which can be overcome by GH treatment.
- Complications of GH not very common
- Current consensus recommendations are that children with growth impairment and CKD, for whom no other cause is apparent, be treated with GH. Despite this recommendation, only about one in four of eligible children with a height less than the fifth percentile are prescribed GH.

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Chronic Kidney Disease: Mineral and Bone Disorder

- Phosphate retention: Keeping phosphate in the body
- Low levels of active vitamin D
- Both these elevate parathyroid hormone (PTH)
- Phosphate retention also causes increased Fibroblast Growth Factor 23 (FGF23)

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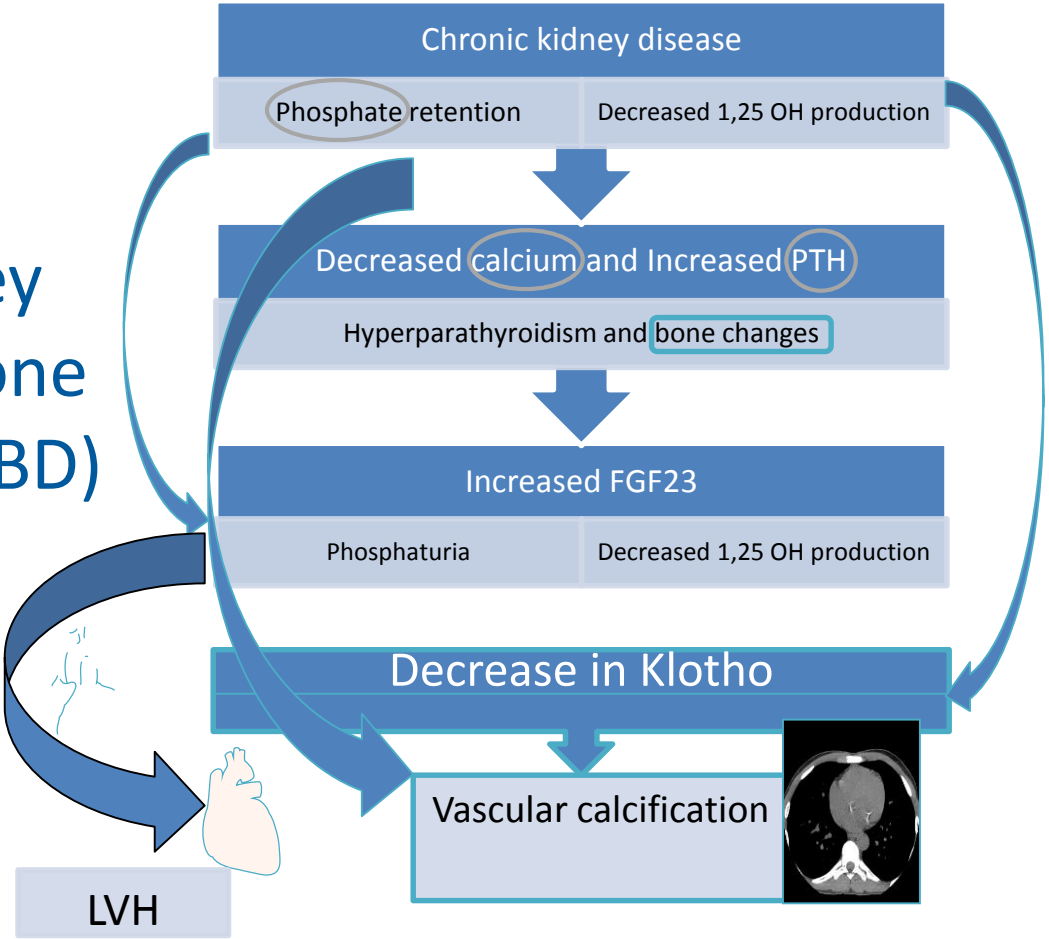
Chronic Kidney Mineral and Bone Disorder (CK MBD)



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How do we treat Chronic Kidney Mineral and Bone Disorder

- Phosphorous restriction and/or phosphate binders
- If PTH sufficiently high – hyperparathyroidism and may need active vitamin D
- If 25 D level low, treatment with calciferol
- Avoid hypercalcemia (too much calcium in blood) since this has been associated with vascular calcification even in children
- Correct metabolic acidosis

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Metabolic Acidosis

- Retention of phosphate or sulfate as acids may lead to metabolic acidosis.
- Treatment consists primarily of supplemental bicarbonate or citrate solutions.
- Treatment of metabolic acidosis in children is important for ensuring growth and bone health.

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Anemia of CKD

Age (years)	Hemoglobin concentration (g/dl)
0.5-5	Less than 11
5-12	Less than 11.5
12-15	Less than 12
Older than 15 males	Less than 13
Older than 15 female	Less than 12

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Anemia of CKD

- Anemia is very common in later stages of CKD
- Healthy kidneys make a hormone called erythropoietin (EPO).
  - EPO sends a signal to the body to make more red blood cells.
  - If your kidneys are not working as well as they should, they can't make enough EPO. Without enough EPO, your body doesn't know to make enough red blood cells.
  - This means fewer red blood cells are available for carrying oxygen through your body.
- Iron is a mineral found in many foods, such as meats and leafy greens. Your body uses iron to make red blood cells. A common cause of anemia in people with CKD is iron deficiency.
  - Iron deficiency means you do not have enough iron in your body. It can be caused by not getting enough iron in your diet or by losing blood, either through blood tests or during dialysis.
  - If you don't take in enough iron through your diet, you can get anemia.
  - Around half of people with CKD stages 2 to 5 have some kind of iron deficiency.

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Treatment of Anemia

- EPO can be administered either subcutaneously (under the skin) or intravenously (particularly in patients receiving hemodialysis).
- Iron therapy is required for almost all children with chronic kidney disease to prevent and treat anemia.
- Since intestinal absorption is hampered (due to elevated hepcidin levels) in CKD, intravenous iron has been used in patients with CKD.

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High Blood Pressure

- Strict blood pressure control is the only intervention which has been shown to slow the progression of Chronic Kidney Disease in children.
- Agents such as ACE-I or Angiotensin Receptor Blockade (ARB) are to be used as preferred agents in children with CKD and hypertension.
- Side effects from these medications in children with CKD include hyperkalemia (high potassium) and worsening of renal function due to less plasma in the blood.

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Developmental Delay and Quality of Life

- Developmental issues occur most when kidney failure happens in infancy.
- The CKiD study has shown about a third of patients even with mild to moderate chronic kidney disease have impairment in measures of IQ, academic achievement and attention regulation, with elevated blood pressure and lower GFR associated with lower scores.
- Multiple studies have evaluated quality of life and social behavior in children with chronic kidney disease, and shown lower health related quality of life scores when compared to healthy controls as well as more sleep and fatigue related symptoms.

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Progression

- The natural course of CKD is that after the first damage to the kidneys, there is slow decline of kidney function.
- This decline does not occur the same way for every patient.
- In the beginning, the decline is somewhat slow, while later stages of CKD are associated with faster decline.

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Risk factors Associated with Progression

- Underlying disease- Glomerular cause of Chronic Kidney Disease is associated with greater risk of progression
- Genetic predisposition
  - Example- APLO1 is allele associated with greater risk of progression
- Severity of CKD at the time of diagnosis, as reflected by presenting glomerular filtration rate (GFR)
- Degree of baseline proteinuria (protein in urine) both in glomerular and in non-glomerular causes of CKD
  - Graded increase in risk for progression which starts even with less severe degree of proteinuria
- Growth- The Italikid study has shown worsening of renal function with growth spurt which occurs during puberty.
- Episodes of acute kidney injury also accelerates progression of CKD.
- Urinary tract infections- More frequent UTI's may be associated with an increased rate of worsening in kidney function.
- Hypertension- ESCAPE study showed that strict control of blood pressure resulted in slower decline of kidney function.
- Other factors such as uric acid and bone mineral metabolism factors such as FGF 23, serum phosphorus and parathyroid hormone

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Special Considerations

- Hyponatremia- May occur as a reflection of urinary sodium wasting, which is common with congenital high-output causes of CKD associated with CAKUT, and treatment may require salt supplementation.
- It is **not recommended** to restrict protein intake in pediatric patients with chronic kidney disease (CKD) unless evaluation of an individual's diet or laboratory values suggests that their protein intake is clearly excessive.
- In children whose flow of urine is blocked, particularly those with incomplete control of bladder emptying or those who require catheters, extra fluid can start building up in the kidney. This should be dealt with promptly by a urologist.
- For those with repeated urinary tract infections, efforts should be focused on prevention either by assuring appropriate bladder drainage or by using prophylactic antibiotics.

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Preparation for Kidney Failure

- Beyond stage 3b start considering renal replacement therapy (dialysis or transplant)
- Preemptive Transplantation- Getting a transplant before dialysis is needed. It is the preferred treatment for many children with progressive CKD. There is a longer graft function and longer life observed with preemptive transplantation when compared to children who have received chronic dialysis before transplantation.
- For patients in whom hemodialysis is the anticipated treatment for end-stage renal disease, and have a long wait time on dialysis, consideration should be given to placement of arteriovenous fistula a few months before it is expected that end-stage renal disease will develop.
- For peritoneal dialysis patients, explore suitability of home; catheter should be inserted approximately 2 weeks prior to its anticipated use.

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Renal Replacement Therapy

- Get help from child life providers about conversations at an age appropriate level for the child regarding CKD
- Be engaged with your health care team
- Conversations about renal replacement therapy should start at 40-45% of kidney function
- Talk about renal transplantation as the first option
- Also remember that renal transplant is not a cure. It also involves taking medications with strict adherence
- However graft survival is getting better- nearly 82% of living donor kidneys transplanted in 2006 were still functioning in 2016

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Living with CKD as a Child

- Generally no restriction in activity if BP are well controlled – encourage exercise
- A kidney friendly diet may be the best thing for the whole family
- School is the best environment for learning and social interactions – so encourage children to be in school- may need dietician/child life/school liaisons for accommodations
- Have conversations at age appropriate level regarding the child's disease so that they understand the "why"
- Be an advocate for your child's kidneys- ask about medication side effect, dosing etc.

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Tips and Tricks

- Children are not small adults – so seek help from a pediatric nephrologist if a child has CKD.
- CKD management needs a team approach – Dietician, often a social worker or child life focus on development and school needs.
- Pay attention to blood pressure and treat it well with the right medications.
- Talk to children about their disease at their age level discuss ways to live with CKD.
- We should remember that CKD does not define that child; every child deserves to realize their fullest potential.

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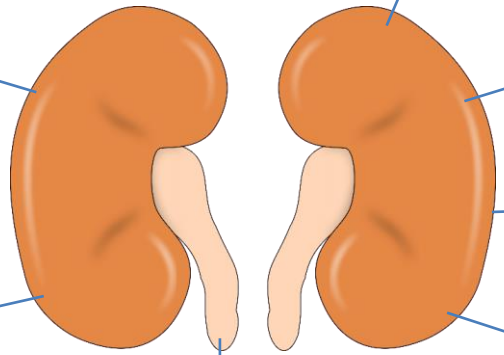
Kidney Report Card

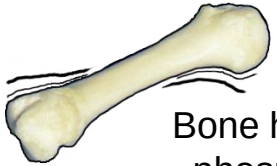
Heart
BP, Fluid control

Anemia

Nutrition and Growth



Renal transplantation



Bone health – calcium , phosphorus, PTH

eGFR

Electrolytes

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Thank you!

Questions?

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Next Month's Webinars

Slowing down kidney disease

Thursday, September 20th, 2018 | 2-3 p.m. (EST)

- The major causes and stages of chronic kidney disease
- Preventing chronic kidney disease
- The myths and facts about how to slow kidney disease

Randy Chen, MD

Practicing Nephrologist

San Mateo county

Tips for talking with your doctor

Tuesday, September 25th, 2018 | 1-2 p.m. (EST)

- Tips for talking with your doctor
- Questions you should ask at every visit
- Ways to talk with your doctor about your medicines, procedures, and surgery

Sagar Nigwekar, MD

Assistant Professor of Medicine

Harvard Medical School

Visit KidneyFund.org/webinars to register