CKD in Children

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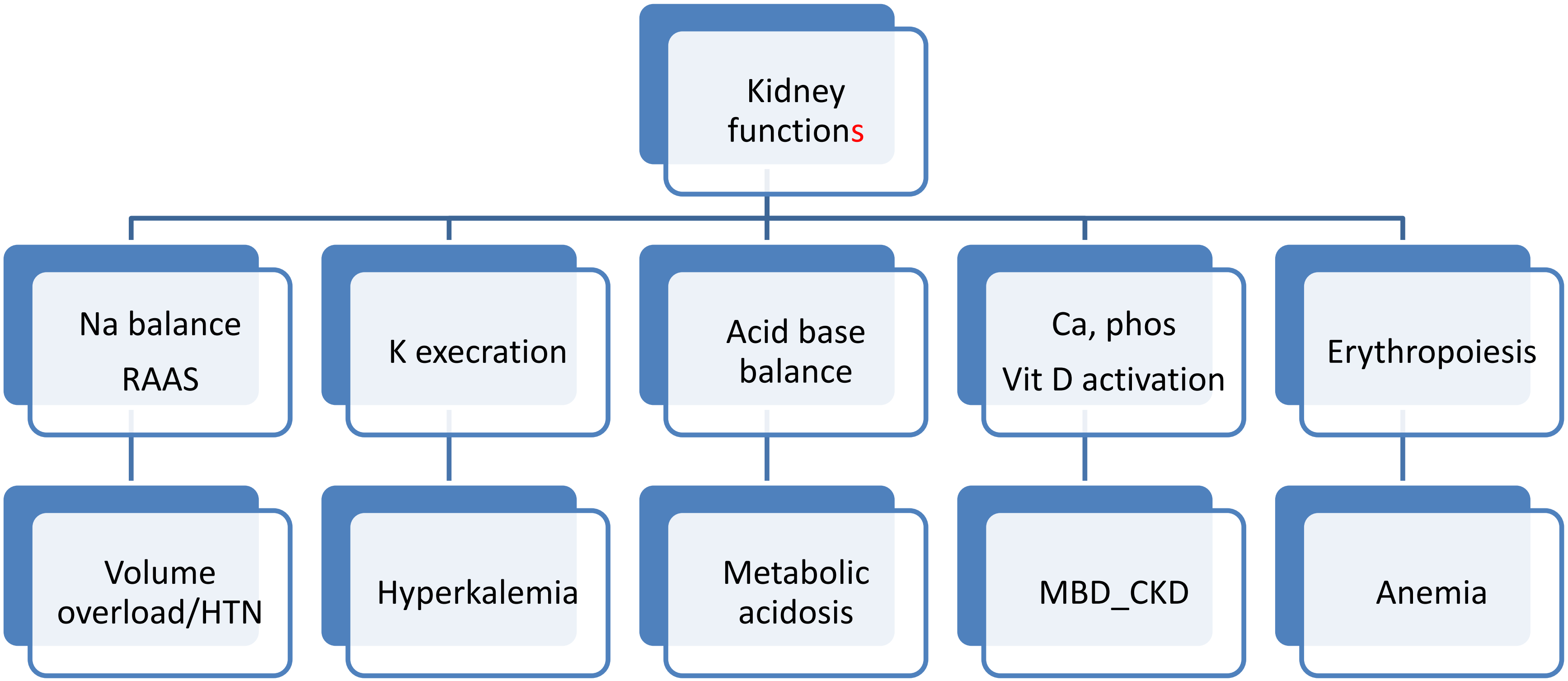
Introduction

- The many functions of kidney
- CKD
  - Definition
  - Stages
  - Etiology
  - Complications
- Practical pearls for taking care of Children with CKD

The many functions of kidney



Definition of CKD

- Abnormalities of kidney structure or function for >3 months with implications for health
- Stages of CKD

Table 4 K/DOQI stages of chronic kidney disease [8]

Stage	Description	GFR (ml/min/ 1.73 m^2)
1	Kidney damage with normal or increased GFR	$\geq$90
2	Kidney damage with mild decrease in GFR	60–89
3	Moderate decrease in GFR	30–59
4	Severe decrease in GFR	15–29
5	Kidney failure	<15 (or dialysis)

Serum creatinine-based bedside equation

Schwartz I equation
eGFR (ml/min/1.73 m2) =ka Ht (cm)/Scr

The constant k:
0.33 in premature infants <1 y/o
0.45 in term infants <1 y/o
0.55 in children and adolescent girls
0.7 in adolescent boys >13

Table 1 Normal GFR ranges by age measured by inulin clearance (Modified from Schwartz and Furth [2], p. 1840)

Age (gender)	Mean GFR ± SD (ml/min per 1.73 m^2)
Preterm babies	
1–3 days	14.0 ± 5
1–7 days	18.7 ± 5.5
4–8 days	44.3 ± 9.3
3–13 days	47.8 ± 10.7
8–14 days	35.4 ± 13.4
1.5–4 months	67.4 ± 16.6
Term babies	
1–3 days	20.8 ± 5.0
3–4 days	39.0 ± 15.1
4–14 days	36.8 ± 7.2
6–14 days	54.6 ± 7.6
15–19 days	46.9 ± 12.5
1–3 months	85.3 ± 35.1
0–3 months	60.4 ± 17.4
4–6 months	87.4 ± 22.3
7–12 months	96.2 ± 12.2
1–2 years	105.2 ± 17.3
Children	
3–4 years	111.2 ± 18.5
5–6 years	114.1 ± 18.6
7–8 years	111.3 ± 18.3
9–10 years	110.0 ± 21.6
11–12 years	116.4 ± 18.9
13–15 years	117.2 ± 16.1
2.7–11.6 years	127.1 ± 13.5
9–12 years	116.6 ± 18.1
Young adults	
16.2–34 years	112 ± 13

Prevalence

Table 5 Epidemiology of chronic kidney disease in European countries (Modified from Harambat et al. [31])

Country	Italy PMID: 12671156 [32]	Belgium PMID: 20148340 [33]	Spain PMID: 20613854 [34]	Sweden PMID: 9260241 [35]	France PMID: 7947040 [36]	Serbia PMID: 22058136 [37]	Turkey PMID: 18936979 [38]
Period	1990–2000	2001–2005	2007–2008	1986–1994	1975–1990	2000–2009	2005
Number of cases	1,197	143	605	118	127	336	282
Inclusion criteria	0–19 years GFR < 75	0–19 years CKD3-5	0–17 years CKD2-5	0.5–15 years GFR <30 or SCr >120 (>3 years) >150 (3–9 years), >180 (>10 years)	0–15 years SCr > 133 (<2 years) or 175 (>2 years)	0–18 years CKD 2–51.	0–18 years GFR <75
Pediatric population covered (millions)	16.8	2.4	11.3	1.7	0.5 (Lorraine)	1.7 (not including Kosovo)	24
Incidence (pmarp)	12.1	11.9	8.7	7.7	10.5	14.3	11.9
Prevalence (pmarp)	74.7	56	71.7	59	66	96.1	
Male/ female ratio	2.0	1.3	1.9	1.6	1.4	1.7	1.3
Age at diagnosis	6.9 mean	3.0 (median)	3.9 (mean)	3.3 and 11.3 in congenital and acquired disorders (median)	6.3 and 10.6 in congenital and acquired disorders (median)	5.2 (median)	8 (mean)

Etiology

Table 7 Causes of CKD in the CKiD cohort [49]

Glomerular diagnosis $n = 129$ (22 %)	% (n)	Nonglomerular diagnosis $n = 457$ (78 %)	% (n)
Focal and segmental glomerulosclerosis	33 % (42)	Obstructive uropathy	26 % (118)
Hemolytic uremic syndrome	22 % (28)	Aplastic/hypoplastic/dysplastic kidneys	23 % (105)
Systemic immunologic disease	9 % (12)	Reflux nephropathy	19 % (87)
Familial nephritis	7 % (9)	Autosomal recessive polycystic kidney	4 % (19)
IgA nephropathy	5 % (7)	Renal infarct	4 % (18)
Chronic glomerulonephritis	5 % (7)	Syndrome of agenesis of abdominal musculature	2 % (11)
Membranoproliferative glomerulonephritis type I	3 % (4)	Pyelo/interstitial nephritis	2 % (9)
Idiopathic crescentic glomerulonephritis	2 % (3)	Cystinosis	2 % (9)
Membranous nephropathy	2 % (3)	Oxalosis	2 % (7)
Henoch-Schonlein purpura	2 % (3)	Medullary cystic disease	1 % (6)
Congenital nephrotic syndrome	2 % (2)	Wilms' tumor	1 % (4)
Membranoproliferative	2 % (2)	Autosomal-dominant polycystic kidney disease	<1 % (2)
Other	5 % (7)	Other	14 % (62)

CKD chronic kidney disease, *CKiD* chronic kidney disease in children study

Complications of CKD

- Anemia
- Metabolic acidosis, electrolytes abnormalities
- Mineral Bone Disease
- HTN
- Growth and developmental delay

Anemia of CKD

Table 10 Common causes of anemia in chronic kidney disease

Erythropoietin deficiency
Iron deficiency Dietary iron deficiency Gastrointestinal loss, phlebotomy, menses Poor absorption of enteral iron Iron depletion from ESA use
Chronic inflammation Complement activation from dialysis Systemic inflammatory diseases (systemic lupus erythematosus, Wegener's granulomatosis, etc.) Surgical procedures
Bone marrow suppression Inhibitory factors Hyperparathyroidism Medications (immunosuppressive drugs)
Increased red cell turnover Carnitine deficiency Primary renal disease (hemolytic uremic syndrome)
Malnutrition B12 or folate deficiency Carnitine deficiency
Aluminum toxicity

Table 9 He… of anemia in children [87]

Age range	…concentration
0.5–5 years (	
5–12 years o	
12–15 years	
>15 years ol	…emales) …ales)

Management of Anemia in CKD

- ESA rHuEPO pre-dialysis 100 units/kg/week
- Goal Hgb ↑ 1–2 g/dL/mo
- target 11-12 not to exceed 13 g/l
- Iron 3-6 mg/kg/day
- Folate
- B 12
- Blood Transfusions
  - symptomatic anemia
  - significant ongoing hemolysis
  - unresponsiveness to ESA therapy
- improvements in:
  - apatite, exercice tolerance, oxygen consomption, intelligence testing scores, and quality of life

Mineral bone Disease in CKD
CKD-MBD

- Definition:
- Systemic disorder with abnormalities in Ca, Phos, PTH, fibroblast growth factor (FGF)-23 or vit D
- Abnormalities in bone histology, or extra-skeletal calcification
- Increase the risk for poor growth and fractures

CKD-MBD

- FGF-23
  - decreases circulating levels of 1,25-dihydroxy vitaminD3 (calcitriol) by:
    - decreasing synthesis through the suppression of renal 1-α hydroxylase
    - increasing catabolism by stimulating 24-hydroxylase.
- PTH
  - regulate circulating levels of serum calcium
- Calcitriol
  - regulate intestinal calcium absorption

CKD-MBD

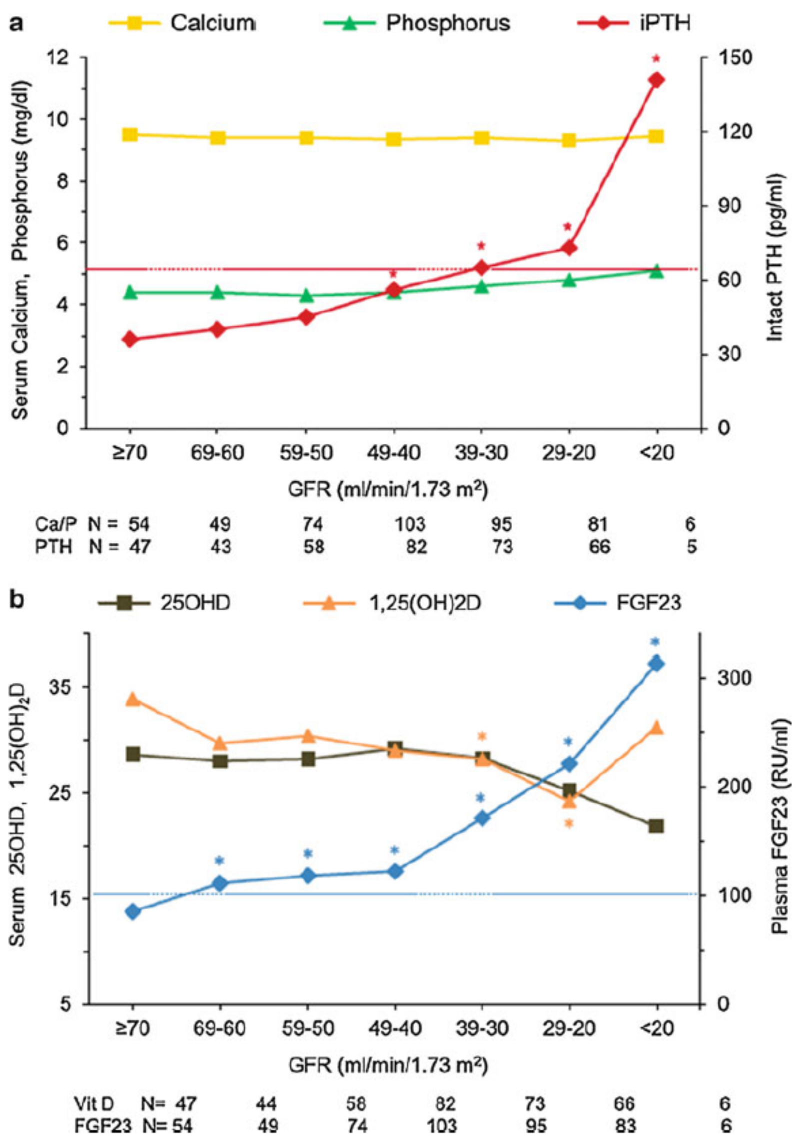
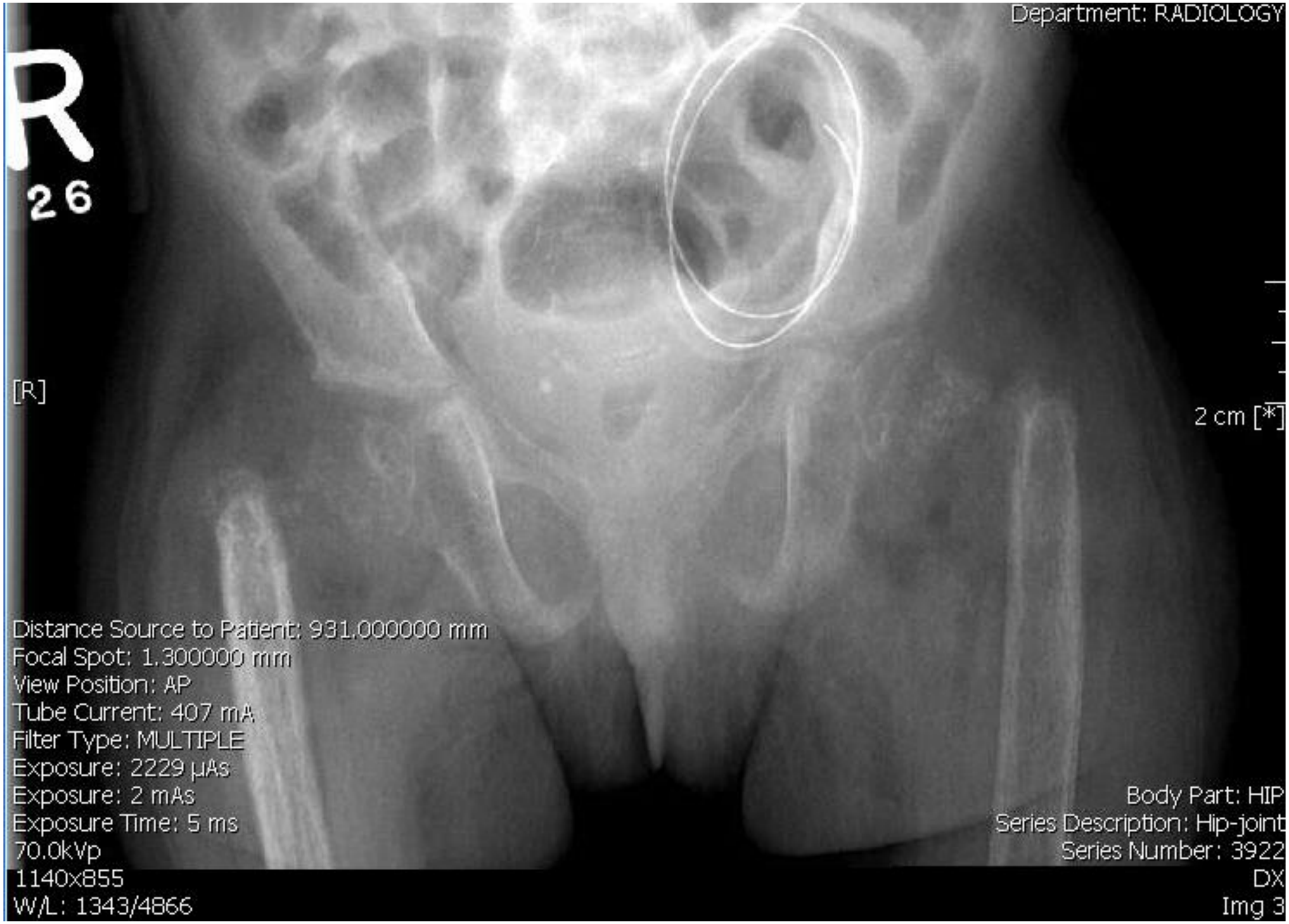


Table 12 Frequency of measurement of bone and mineral factors and target ranges of serum PTH by stage of CKD [183]

CKD stage	Frequency of calcium, phosphorus, and CO2	Frequency of PTH and alkaline phosphatase	Target serum PTH (pg/ml)
2	Annually	Annually	35–70[a]
3	Every 6 months	Every 6 months	35–70[a]
4	Every 3 months	Every 3 months	70–110[a]
5	Every month	Every 3 months	200–300

[a]Based on expert opinion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Series Number: 3922
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Management of CKD-MBD

- Maintain serum calcium and phosphorus close to the normal range for age
  - phosphate binder
  - Reduced dietary intake
- Maintain serum PTH level appropriate for CKD stage
  - Vitamin D
  - Active form of vitamin D, calcitriol
  - Calcimimetics, increase its sensitivity to ionized calcium. Cinacalcet
  - parathyroidectomy with autotransplantation to the forearm or abdomen

CKD-MBD

Table 14 Recommended supplementation for vitamin D deficiency in patients with CKD [183]

Serum 25 (OH) D (ng/ml)	Definition	Ergocalciferol (vitamin D2) dose	Therapy duration (months)
<5	Severe vitamin D deficiency	8,000 IU/day orally (or 50,000 IU per week) × 4 weeks and then 4,000 IU/day (or 50,000 IU twice per month) × 2 months	3 months and then remeasure 25 (OH) D levels
5–15	Mild vitamin D deficiency	4,000 IU/day orally (or 50,000 IU every other week) × 12 weeks	3 months and then remeasure 25 (OH) D levels
16–30	Vitamin D insufficiency	2,000 IU/day (or 50,000 IU every 4 weeks)	3 months and then remeasure 25 (OH) D levels

Cardiovascular Complications in CKD

- **HTN**
- ESCAPE trial:
  - CKD progression slowed by targeting a mean BP below the **50th** percentile.
- Fourth Report on Blood Pressure in Children
  - The target blood pressure in untreated children with CKD should be auscultated readings less than the **90th** percentile for age, gender, and height or **120/80** mmHg
- KDIGO guidelines suggest that blood pressure should be lowered to less than the **50th** percentile in those with proteinuria

Management of CVS in CKD

- The preferred antihypertensive in CKD ACE inhibitors or ARBs
  - decrease proteinuria
  - slow CKD progression
- thiazide diuretics in earlier stages of CKD not effective when the GFR falls below 30 ml/min/1.73 m2

Management of CVS in CKD

- **Lipids:**
- K/DOQI guidelines:
  - All adolescents evaluated for dyslipidemia
  - Fasting lipid profile for total cholesterol, LDL, HDL, and triglycerides

- Therapeutic lifestyle (TLSC)
  - Six months of therapy for children with CKD and a fasting LDL >100 mg/dl
  - Reduced dietary saturated fat and cholesterol intake
  - Moderate exercise

- Lipid-lowering drugs restricted:
  - >10 yrs
  - Fasting LDL >190 mg/dl or >160 mg/dl and two other risk factors
  - If target LDL levels (<100 mg/dl) are not reached after 6 mo of TLSC

Metabolic Acidosis and Electrolyte Imbalance

- Metabolic acidosis:
  - GFR <50 %
  - Affect bone
  - Replace with sodium bicarbonate
- Na and water:
  - CKD from obstructive uropathy or renal dysplasia
  - defective urinary concentrating abilities from a decreased tubular responsiveness to vasopressin
  - polyuric with substantial urinary sodium losses
- Potassium:
  - <15 ml/min/1.73 m2

Nutrition in CKD

- Which food a child with CKD should eat and/or avoid?

- Energy
  - compromised growth is seen when caloric intake is less than 80 % of requirements
  - High calorie renal formula
  - Tube feeding

- Protein

Nutrition in CKD

Daily Protein Needs for Children with CKD

Age Range		Grams of Protein Needed per Pound of Body Weight			
		Pre-dialysis	Hemodialysis		Peritoneal Dialysis
Infant	0–6 months	1	1.2		1.3–1.4
	7–12 months	0.73	1.1		1.0–1.1
Toddler	1–3 years	0.5	0.7		0.9
Child	4–6 years	0.5	0.7		0.9
	7–10 years	0.45	0.6		0.8
Adolescents	11–14 years	0.45	0.6		0.8
	15–18 years	0.4	Girls	Boys	0.6–0.7
			0.5	0.6	

Nutrition in CKD

Protein Content of Foods	
Food	**Serving Size**
Turkey breast	41 grams/cup
Large hamburger with vegetables and condiments	34 grams/8-ounce (oz) sandwich
Tuna sub	30 grams/6-inch sub
Cottage cheese	25 grams/cup
Chili con carne	24 grams/cup
Cold-cut sub	21 grams/6-inch sub
Fast-food taco	20 grams/6-oz taco
Fish sandwich with tartar sauce and cheese	20 grams/6.5-oz sandwich
Baked beans	17 grams/cup
Chicken nuggets	16 grams/6 nuggets
Yogurt	13 grams/8-oz container
Beef stew	11 grams/cup
Fast-food burrito with meat and beans	11 grams/4-oz burrito
Cooked peas	8 grams/cup
Chicken noodle soup	6 grams/cup

Nutrition in CKD

- Potassium-rich foods
  - Alternate food preparation methods
  - Soaking vegetables before cooking

- Phosphate:
  - Decrease intake of high phosphate food
  - Phosphate binder

- In infants
  - Low-solute formulas
  - sodium polystyrene sulfonate (Kayexalate) resin
    - decrease the potassium content of the formula

Nutrition in CKD

High- and Low-potassium Foods	
High-potassium Foods	**Low-potassium Alternatives**
Oranges and orange juice	Apples and apple juice
Melons	Cranberries and cranberry juice
Apricots	Canned fruit
Bananas	Strawberries, blueberries, raspberries
Potatoes	Pineapple
Tomatoes	Cabbage
Sweet potatoes	Boiled cauliflower
Cooked spinach	Mustard greens
Cooked broccoli	Frozen or raw broccoli
Beans (baked, kidney, lima, pinto)	Frozen peas

Nutrition in CKD

Table 13 Recommended maximum oral and/or enteral phosphorus intake for children with CKD [183]

Age in years	Phosphorus dietary reference intake (mg/day)
Under 0.5	100
0.5–1.0	275
1–3	460
3–8	500
9–18	1,250

Nutrition in CKD

High- and Low-phosphorus Foods	
High-phosphorus Foods	**Low-phosphorus Alternatives**
Dairy foods (milk, cheese, yogurt)	Liquid nondairy creamer
Beans (baked, kidney, lima, pinto)	Green beans
Nuts and peanut butter	Popcorn
Nuts and peanut butter	Unprocessed meats from a butcher
Processed meats (hot dogs, canned meat)	Lemon-lime soda, root beer
Cola	Powdered iced tea and lemonade mixes
Canned iced teas and lemonade	Rice and corn cereals
Bran cereals	Egg whites
Egg yolks	Sorbet
Ice cream	

Nutrition in CKD

- https://www.niddk.nih.gov/health-information/kidney-disease/children/caring-child-kidney-disease/nutrition-chronic-kidney-disease
- https://www.kidney.org/atoz/content/nutrichild

Growth in CKD

- NAPRTCS CKD registry data:
- Ht CKD is 1.5 SD < age and gender-specific norms
- Malnutrition marked effect in infants and young children
- European Study
  - compromised growth if caloric intake <80 % of reqs
  - modest reduction in dietary protein to the minimum acceptable amount (0.8–1.1 g/kg/day)
  - No relationship noted between the dietary protein intake and growth

Growth in CKD

- K/DOQI Pediatric:
- Correct nutritional deficiencies and metabolic abnormalities prior to rhGH
- **Consider GH therapy in patients with:**
  - GFR < 75 mL/min/1.73 m2 and
  - Height SDS <–1.88 (3rd percentile), ***or*** height velocity SDS <–2
- rhGH therapy early to maximize growth potential

Cognitive and Psychosocial Development

- Neurocognitive development and psychosocial adjustment affected
- Etiology:
  - Direct effect of uremia on growing brain
  - Lost educational opportunities from school absenteeism
- Lower short-term verbal and visual memory
- Impairment of new learning capacity deficits in selective higher-order executive functioning of the brain related to attention
- Early participation of experts in behavioral and developmental pediatrics
  - assess the cognitive ability and emotional well-being
  - individualized education plans and counseling
  - educational emotional, and functional potential may be optimized

Practical points in the care of child with CKD

- Medication dose adjustment

- When to transfer care to pediatric nephrologist?
  - Stage IV and V
  - Uncontrolled HTN, acidosis or electrolyte despite medical treatment.

Table 1 Drug dosing of commonly used pediatric antibiotics. *MW* molecular weight, *h* hour

Drugs	Normal Dose/day Not to exceed adult dose	Dose at GFR 50–30	Dose at GFR 30–10	Dose at GFR < 10	MW	Plasma protein binding	%eliminated by kidney	Elimination t½ with normal GFR
Aminoglycosides								
Amikacin	15–22.5 mg/kg div Q8h	Q12–18 h	Q18–24 h	Q48–72 h	585.6	<11 %	>95	2–3 h
Gentamicin	6–7.5 mg/kg div Q8h	Q12–18 h	Q18–24 h	Q48–72 h	477.6	<30 %	>95	5–>100 h
Tobramycin	6–7.5 mg/kg div Q8h	Q12–18 h	Q18–24 h	Q48–72 h	467.5	<30 %	>95	2–3 h
Carbapenems								
Imipenem + cilastin	60–100 mg/kg div Q6h	7–13 mg/kg/ dose Q8h	7.5–12.5 mg/kg/dose Q12h	7.5–12.5 mg/kg/ dose Q24h	Imipenem: 299.3	Imipenem 13–21 % cilastin 40 %	70	1 h
meropenem	30–100 mg/kg div Q8h	20–40 mg/kg/ dose Q12h	10–20 mg/kg/ dose Q12h	10–20 mg/kg/dose Q24h	383.5	2 %	70	1 h
Cephalosporins								
Cefaclor	20–40 mg/kg div Q8–12 h	Normal	Normal	50 % dose	367.8	25 %	80	40 min
Cephalexin	25–100 mg/kg div Q6–8 h	Normal	Q8–12H	Q12–24H	347.4	10.60 %	~100	1–1.5 h
cefazolin	50–150 mg/kg div Q8h	60 %, Q12h	25 %, Q12h	10 %, Q24h	454.5	74–86 %	80–100	2 h
Cefixime	8 mg/kg div Q12–24 h	75 %	75 %	50 %	453.4	76–91 %	20–35	3–4 h
Cefotaxime	100–200 mg/kg div Q6–8 h	35–70 mg/kg, Q8–12 h	35–70 mg/kg, Q12h	35–70 mg/kg, Q24h	619.6	31–50 %	80	1.4–1.9 h
Cefotiam	50–100 mg/kg				525.6	76–91 %	80	0.9–1.2 h
Ceftazidime	100–150 mg/kg div Q8h	50 mg/kg q12h	50 mg/kg q24h	50 mg/kg q48h	546.6	17 %	80–90	1.8–2.2 h
Ceftriaxone	50–100 mg/kg Q24h	Normal	Normal	Normal	554.6	85–95 %	67	6–9 h
Cefuroxime	75–150 mg/kg div Q8h	Normal	Normal dose Q8–12 h	Normal, Q24h	424.4	33–50 %	95	1–1.5 h

Case Scenario 1

- 11 y/o boy CKD 2nd to PUV
- BP 134/96
- Growth parameters Ht 131 cm Wt 26 Kg below normal
- Labs:
- Hgb 9.3 MCV 85
- Creat 2 mg/dl (176) Urea 42 mg/dl (15), K 4, Ca 2.3mmol Phos 3.4mmol PTH 78pmol

eGFR=131*0.55/2= 36 ml/min/1.73

Problem List

- CKD III
- HTN
- Growth delay
- Anemia of CKD
- Elevated phos and PTH

Plan

- Start Antihypertenisve
- Optimize nutrition
- Treat anemia
- Phos Dietary restriction/binder
- Vitamin D level

Case Scenario 2

- 3 y/o girl hypoplastic kidney
- BP 98/60
- Ht 88 cm Wt 12.6 kg WNL
- Creatinine 0.7 (62), Hgb 11.4
- HCO_3 14

eGFR=88*0.55/0.7=69

Problem List

- CKD II
- Metabolic acidosis

Plan

- Start Sodium bicarbonate

Case Scenario 3

- 6 y/o boy CKD secondary to reflux nephropathy
- Vomiting and diarrhea for 3 days
- Ht 107 cm Wt 17 kg WNL
- BP 96/64 HR 140
- Home meds enalapril, NaHCO3
- Dry mucous membrane
- Labs: Creat 1.27(112) ((base line0.79 (70)), urea 12, CH2 13

eGFR=107*0.55/1.27=46

Problem List

- CKD III
- Dehydration
- Worsening kidney function
- (acute on chronic renal failure)
- Metabolic acidosis

Plan

- HOLD enalapril
- IVF with sodium bicarbonate

Question?

Thank You