Pediatric Nephrology Pearls for the Advanced Practice Provider

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Attestation

No disclosures or conflicts of interests

Objectives

1

Recognize the impact of kidney disease on the patient/family unit and the healthcare system

2

Identify and contrast causes of pediatric kidney disease with the adult population

3

Review basic kidney function and how presence of dysfunction may appear in a child with kidney injury or disease

4

Describe first line evaluation and when to refer to nephrology

Why Early Diagnosis Matters

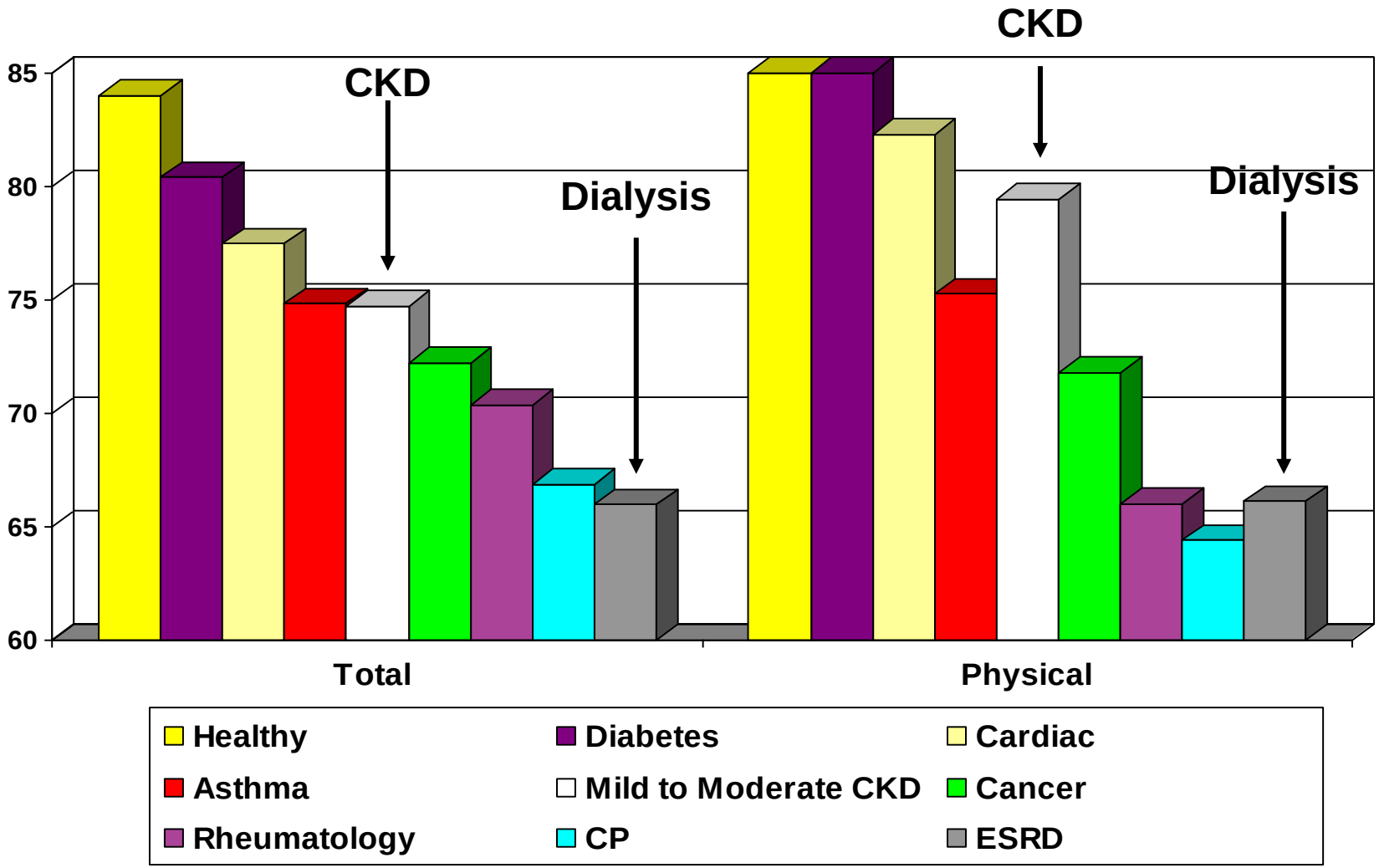
CKD is a progressive and costly disease

Children with CKD become adults with CKD

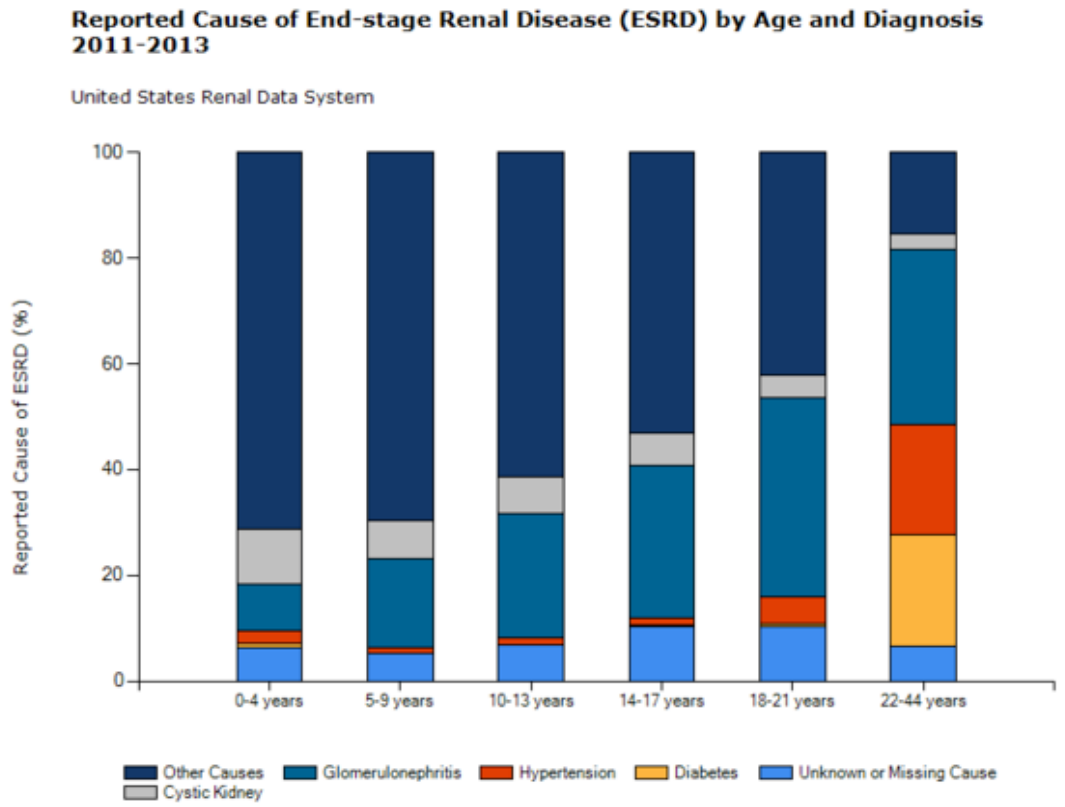
Children with CKD reported poorer overall Health Related Quality of Life (HRQoL) scores compared to healthy children

Comparison of HRQOL Across Chronic Illness Groups

(PedsQL youth self-report data)



USRDS Data on Causes of ESKD

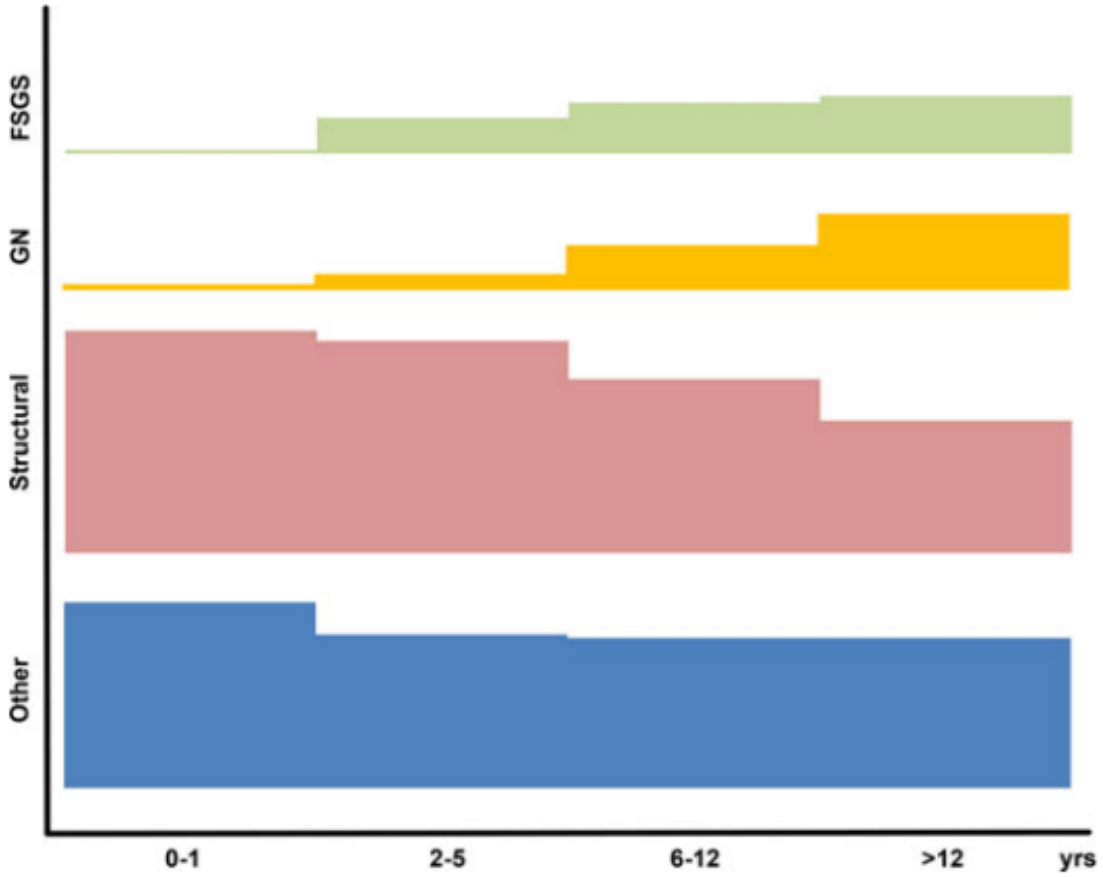


Centers for Disease Control and Prevention. Chronic Kidney Disease Surveillance System—United States. website. http://nccd.cdc.gov/CKD.

Saran R, Li Y, Robinson B, et al. US Renal Data System 2015 Annual Data Report: epidemiology of kidney disease in the United States . *Am J Kidney Dis* . 2016;67(3)(suppl 1):S1-S434.

Another perspective

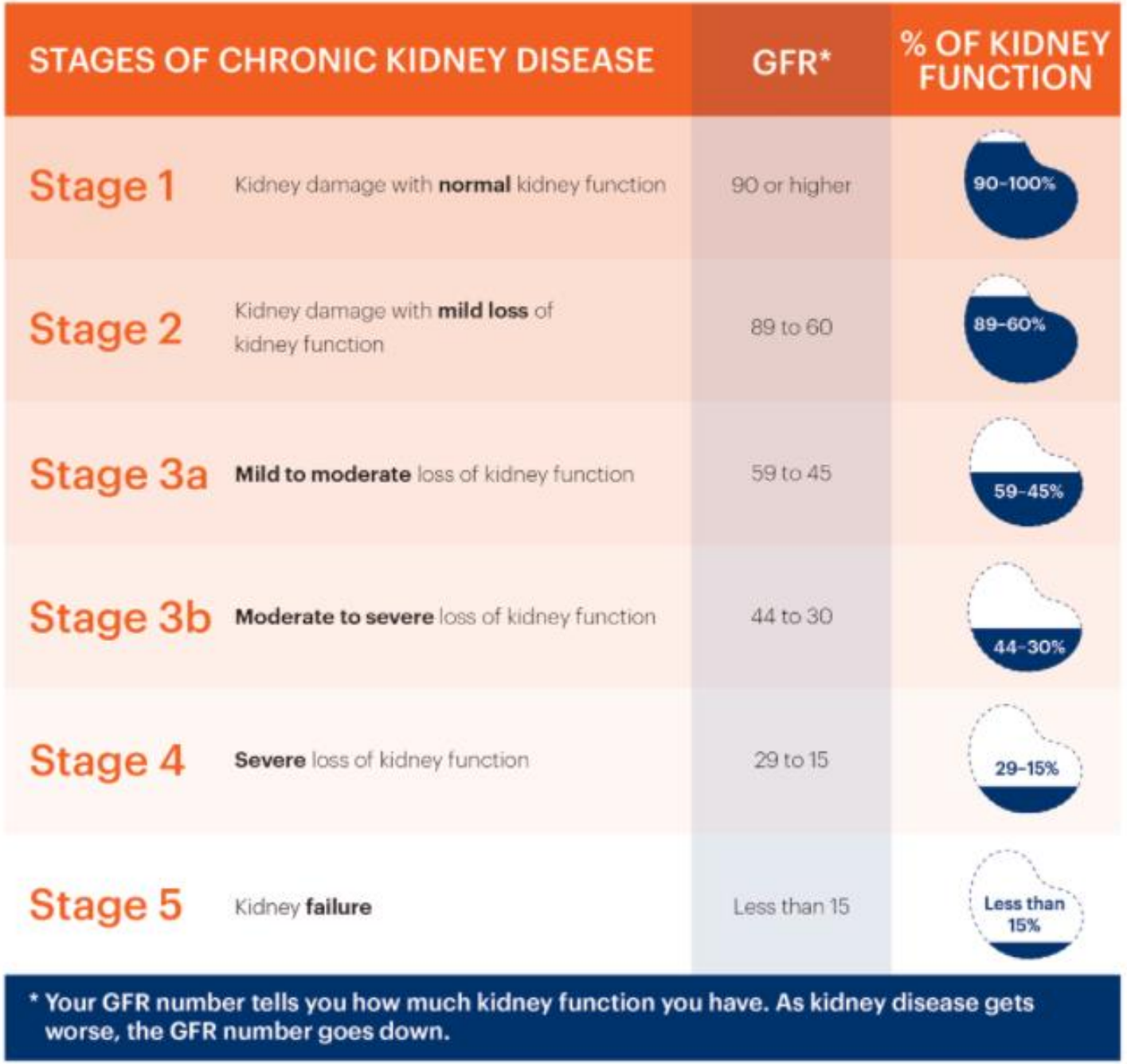
Fig. 2. Impact of different causes of CKD in children among age groups. The graph shows the variation of the impact of different diagnostic groups in determining CKD over time, highlighting how glomerular diseases significantly increase in older children, while structural disorders are more common as causes of CKD in infants and younger children. CKD, chronic kidney disease; FSGS, focal segmental glomerulosclerosis; GN, glomerulonephritis; yrs, years.



Becherucci, F., Roperto, R. M., Materassi, M., & Romagnani, P. (2016). Chronic kidney disease in children. *Clinical kidney journal*, *9*(4), 583–591. https://doi.org/10.1093/ckj/sfw047

Stages of kidney function

- Glomerular Filtration Rate (GFR) is estimated using serum creatinine
- Labs use different assays for creatinine including Jaffe (rhymes with “the old way”) and enzymatic (this one should be “automatic” at every lab but it’s not).
- eGFR calculator for patients 1-25 years now validated and ready to use!



Kidney Development and Physiology

Nephron – functional "filtration" unit of the kidney

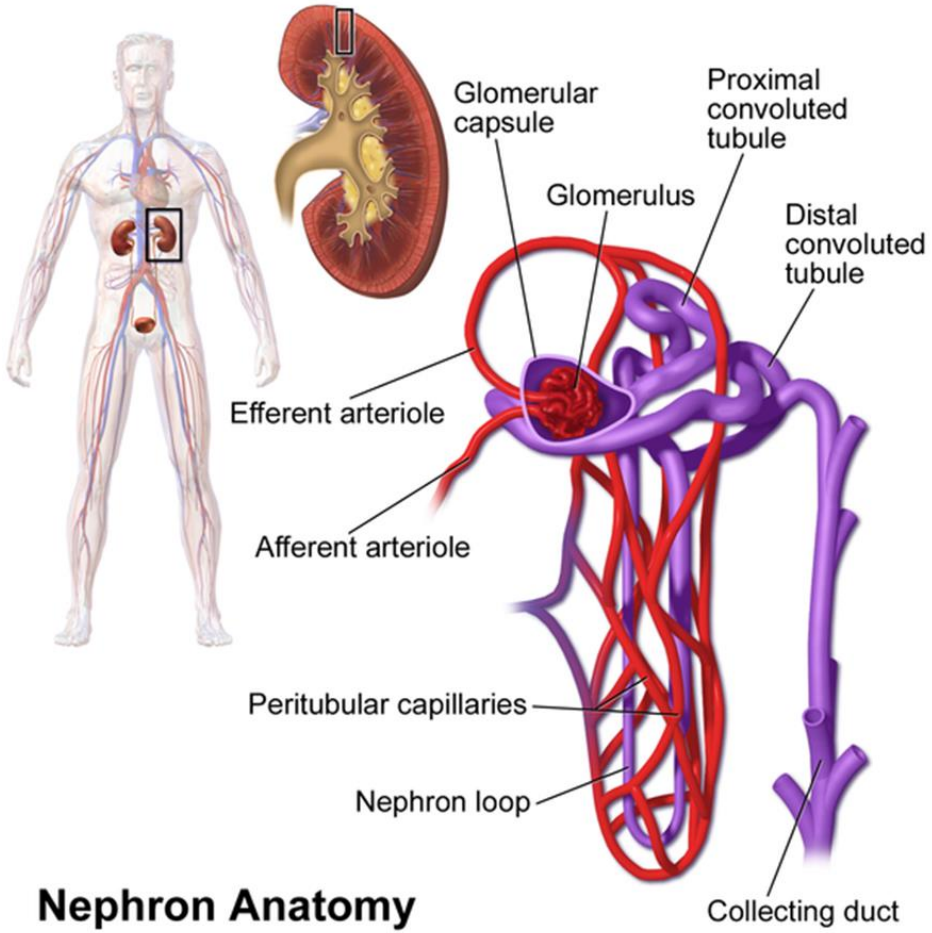
Includes glomerulus + tubulocapillary system

Functioning begins @ approx. 6-10 weeks gestation

Nephron development continues until around 36 weeks gestation

Each **healthy** kidney has approximately 1 million nephrons

Post-natal function takes about 18-24 months to reach maturity



Nephron Anatomy

Bruce Blaus Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014". WikiJournal of Medicine 1 (2). DOI:10.15347/wjm/2014.010. ISSN 2002-4436.

Prenatal and birth history matters

Teratogens can cause absent or abnormal formation of kidneys	Major contribution of urine production occurs around 19-20 weeks gestation	Prenatal work up	Premature birth
• Alcohol • Cocaine • ACEI/ARBs • Immunosuppressive meds • Epilepsy meds • Glucocorticoids • Vitamin A deficiency	• Remember fetuses “drink their pee” but this impacts lung development too • Prenatal history of oligohydramnios can be a major clue	• Perhaps only ~30% of kidney abnormalities are found on prenatal ultrasound • Often in the third trimester	• Limited number of nephrons created • Exposure to nephrotoxic meds in NICU • Low-birth weight has been suggested as a risk factor for CKD

What Do My Kidneys Do?

- Clean your blood
- Help control blood pressure
- Help make red blood cells
- Help keep your bones healthy
- Help you grow
- Control how much fluid stays in your body and how much leaves

Children's Mercy
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What Happens To My Body If My Kidneys Stop Working?

If your kidneys stop working, you might…

- May pee less or not at all
- Feel tired
- Not feel hungry as often
- Have higher blood pressure
- Grow slower than other kids
- Have itchy skin
- Have puffy hands, feet, or face
- Sometimes feel like you have to throw up

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HPI and Physical Exam

- Well-child exams are one of the best opportunities to gather info at ANY age
- Urogenital exam should appear as expected
- Abdomen should not be unusually swollen or distended: do NOT palpate vigorously if you see or question distention (Wilm's tumor)
- Frequent UTIs in girls and any UTI in a male should be followed closely
- Respiratory issues may co-exist
- Look for syndromic features
  - Eye and ear abnormalities may also mean kidney disease

HPI and Physical Exam

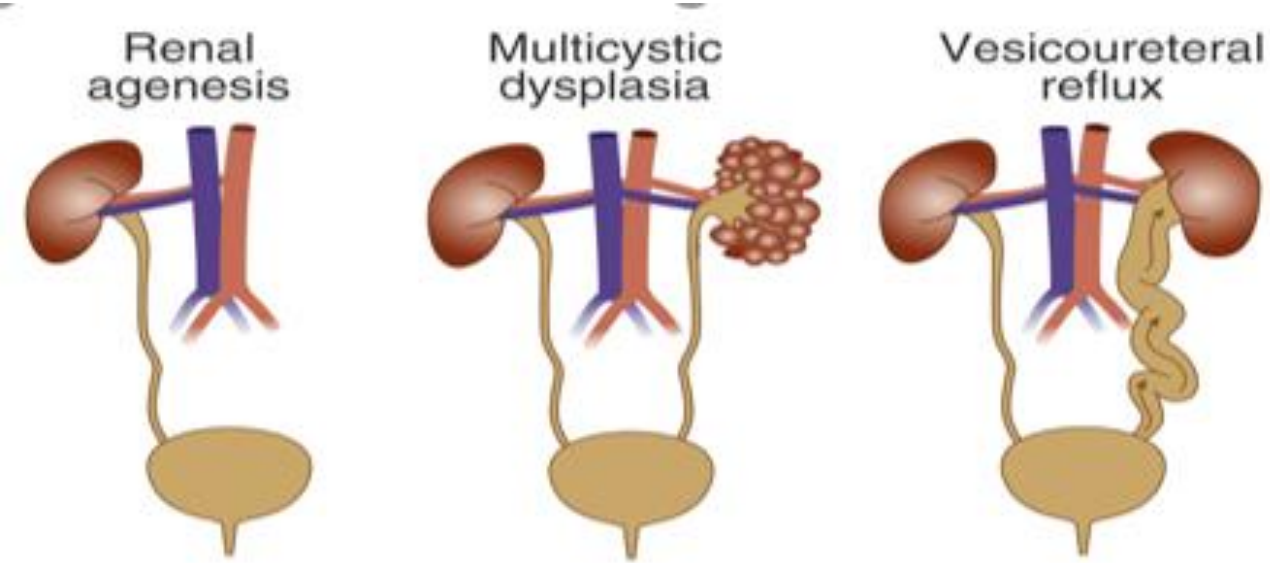
- Proper measurement of length/height, head circumference, weight and blood pressure is imperative for accurate trending
  - Failure to meet major milestones in growth and development could indicate kidney dysfunction
  - Use AAP 2017 Clinical Practice Guideline for BP monitoring and management
    - AAP still suggests annual BP starting at age 3 years
    - BP should be taken **earlier than 3 years and/or at every visit** for those with known renal disease, diabetes, coarctation of the aorta, or on meds known to increase BP

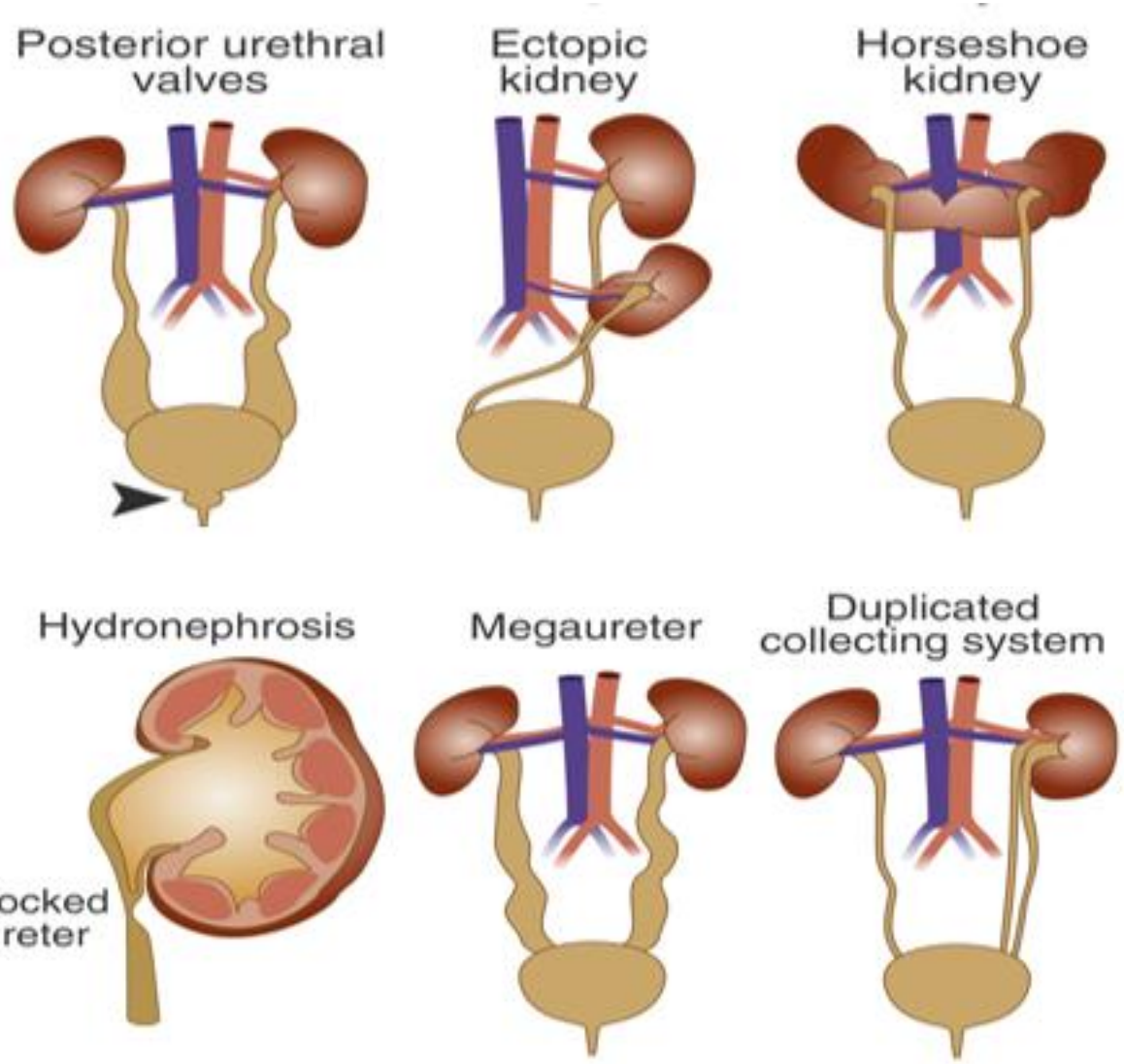
CAKUT

Congenital Anomalies of the Kidney and Urinary Tract

- Umbrella term for several more specific diagnoses that are caused by abnormal embryonic or fetal development
  - Parenchymal malformation
  - Renal migration
  - Collecting system
- Commonly diagnosed in infants and younger children depending on the abnormality
- Usually good prognosis, but some conditions progress to ESKD or will at least have complications into adulthood

CAKUT in pictures





Not pictured = renal dysplasia/hypoplasia

Knoers NVAM, Renkema KY. The genomic landscape of CAKUT; you gain some, you lose some. Kidney Int. 2019;96(2):267-269. doi:10.1016/j.kint.2019.03.017

One kidney is all you need

Some abnormalities go undiagnosed for a period of time (or forever!) because one kidney compensates for the other.

Bilateral abnormalities are going to have more significant symptoms and present earlier in life.

Only needing one kidney benefits a kidney transplant patient and allows for living donation!

Practice Pearls

- Renal dysplasia often co-exists with a collecting system anomaly
- Watch for CAKUT in the infant to elementary school age child
- Symptom presentation may include
  - UTI
  - Fever
  - Hematuria
  - Abdominal pain
- Obtain BMP, urinalysis and renal ultrasound
  - eGFR can be calculated from the serum creatinine
- Refer to nephrology (call us if you're unsure!)
  - We partner closely with urology and will consult them when indicated
- Need annual BP and urinalysis

Glomerular Diseases

- Also an umbrella term for several more specific diagnoses that cause injury to the glomerulus
  - Primary: kidney alone
  - Secondary: autoimmune disorder, infection, vasculitis
- Commonly diagnosed in older children and adolescents/young adults
- These diagnoses can progress through the kidney stages quickly because they affect the glomeruli directly
- ***Hematuria and proteinuria*** are the two MOST important initial findings to make you think of a glomerular diagnosis

Key Point

Children who have evidence of glomerular bleeding may have nephritic syndrome secondary to glomerulonephritis.

Those with heavy proteinuria are likely to have nephrotic syndrome.

Nephritis or Nephrosis? Both?

Key labs to obtain: microscopic urinalysis, urine protein/creatinine ratio, BMP, lipid level (non-fasting)

Nephritis

- Inflammation triggered by an immune response
- Hematuria
- Red cell casts
  - (aka sediment)
- Dysmorphic red cells
- Will require further workup (refer to nephrology)

Nephrosis

- Heavy proteinuria (4+ on a dipstick)
- First AM spot urine sample for protein/creatinine ratio
- Low serum albumin, high level of lipidemia
- Few or no cells or casts
- Will require further workup (refer to nephrology)

Proteinuria

Transient

- Occurs with fever, exercise, stress, seizures
- Most common
- As implied, it resolves with no treatment

Orthostatic

- Mostly in teens
- Protein present when up and about, absent after laying (why it's important to get follow up first morning urine samples when in doubt)

Persistent

- Occurs in about 0.1% of children with proteinuria
- Persists despite ruling out transient or orthostatic causes
- Definitely requires Nephrology evaluation

Causes of glomerulonephritis in children

Primary glomerulonephritis
Membranous glomerulonephritis
Immune complex-mediated membranoproliferative glomerulonephritis
C3 glomerulopathies (Dense deposit disease, C3 glomerulonephritis)
IgA nephropathy
Anti-glomerular basement membrane disease
Idiopathic crescentic glomerulonephritis
Secondary glomerulonephritis
Post-streptococcal glomerulonephritis
Other post-infectious glomerulonephritis
Infective endocarditis
IgA vasculitis (Henoch-Schönlein purpura nephritis)
Systemic lupus erythematosus nephritis
Granulomatosis with polyangiitis (formerly called Wegener's granulomatosis)

IgA: immunoglobulin A.

Original figure modified for this publication. Reproduced with permission from: Niaudet P. Nephritic Syndrome. In: Comprehensive Pediatric Nephrology, Geary DF, Schaefer F (Eds), Mosby, Philadelphia 2008.

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- Primary
  - Proteinuria
  - Edema ranging from mild to anasarca
  - Low serum albumin in more severe cases
  - Hypertension
  - Hematuria (usually dark colored)
  - Elevated serum creatinine
- Secondary
  - Any of the above plus
  - Fever
  - Rash
  - Arthralgias
  - Pulmonary hemorrhage
  - Anemia

Presentation

Common triggers

- GAS is the most common trigger for post-infectious glomerulonephritis
  - Males>females
  - GAS throat = 1-3 weeks later
  - GAS skin = 3-6 weeks later
- IgA nephropathy = hematuria 1-2 days after upper respiratory infection

Bacterial and viral agents associated with post-infectious glomerulonephritis

Bacterial infections
Skin or throat (Streptococcus group A)
Endocarditis (Staphylococcus aureus, Streptococcus viridans)
Visceral abcess (Staphylococcus aureus, E. coli, Pseudomonas, Proteus mirabilis)
Shunt nephritis (Staphylococcus aureus, Staphylococcus albus, Streptococcus viridans)
Pneumonia (Diplococcus pneumoniae, Mycoplasma)
Typhoid fever (Salmonella typhi)
Viral infections
Epstein Barr virus
Parvovirus B19
Varicella
Cytomegalovirus infection
Coxsackie
Rubella
Mumps
Hepatitis B
Parasitic infections
Schistosoma mansoni
Plasmodium falciparum
Toxoplasma gondii
Filaria

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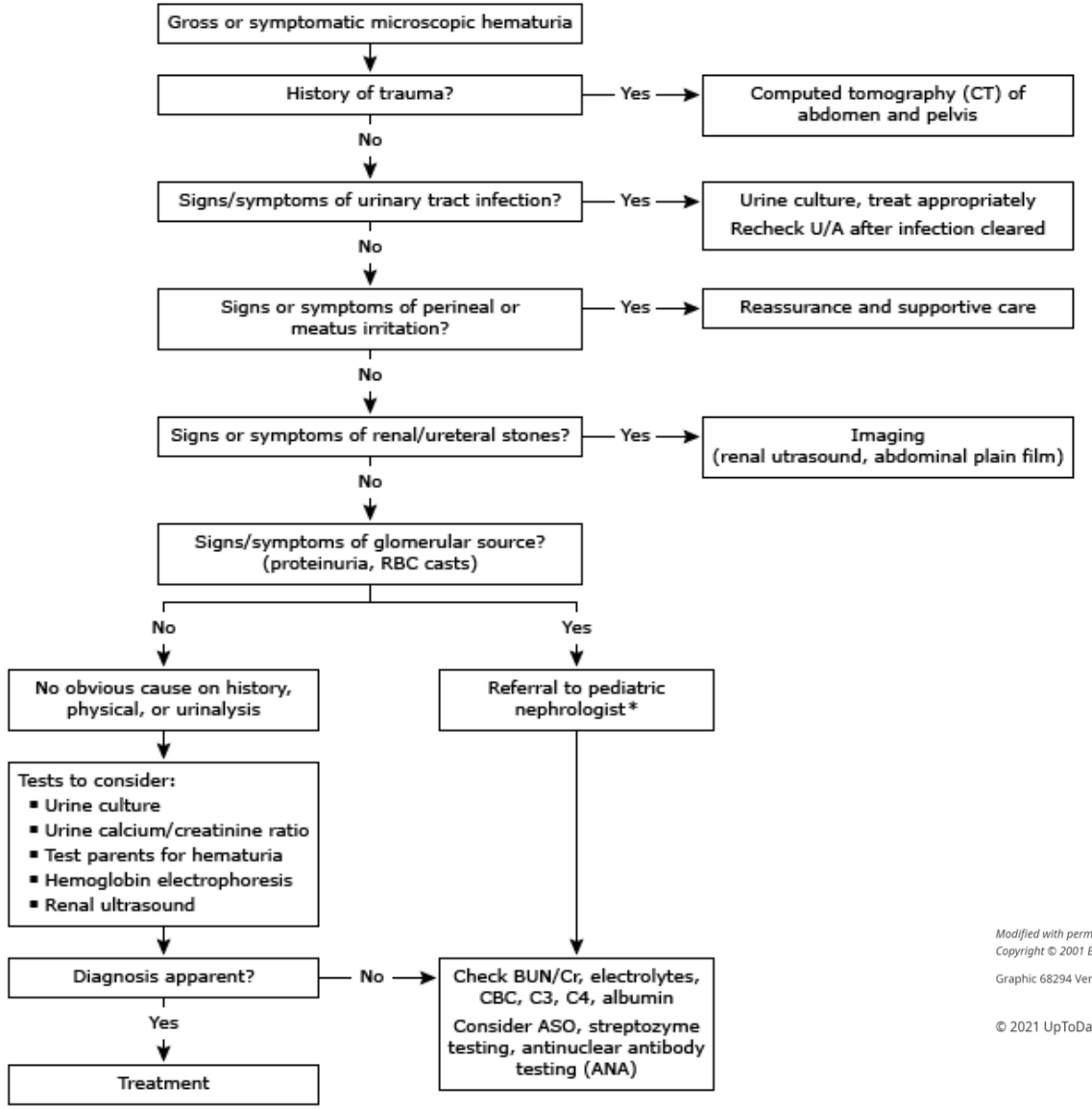
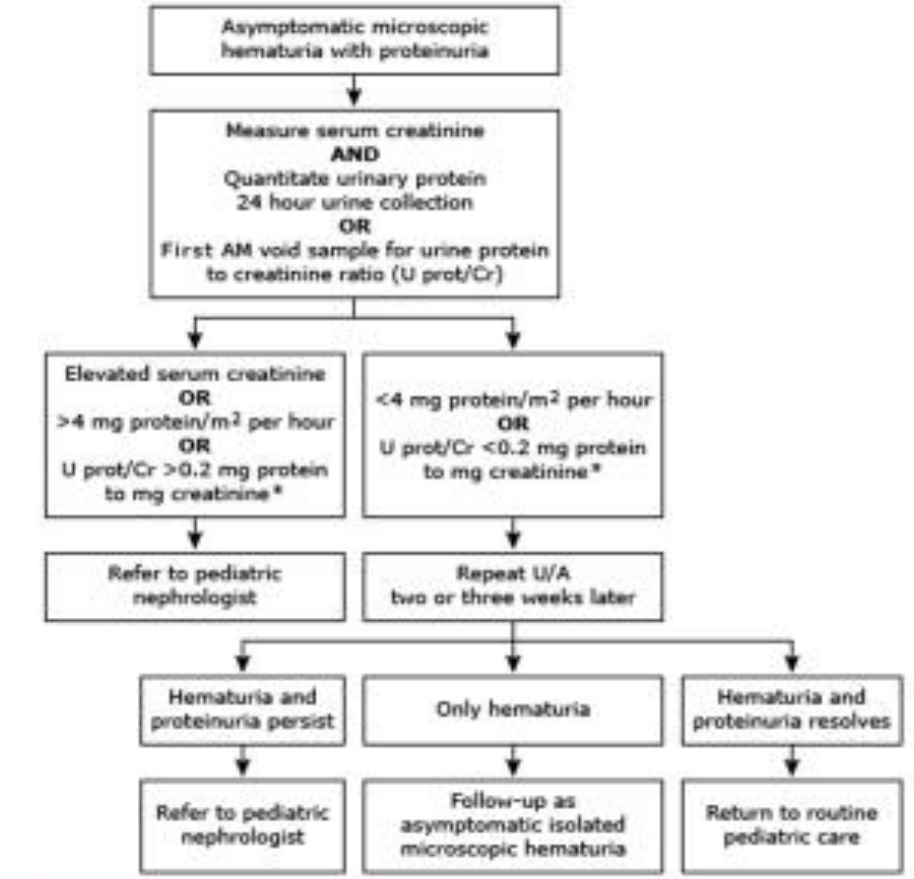
Algorithm for gross or symptomatic microscopic hematuria in children



Modified with permission from: Patel HP, Bissler JJ. Hematuria in children. Pediatr Clin North Am 2001; 48:1519. Copyright © 2001 Elsevier.

Graphic 68294 Version 5.0

Diagnostic algorithm for asymptomatic microscopic hematuria with proteinuria in children



U/A: urinalysis.

* For children between 6 and 24 months, the threshold value is 0.5 mg protein to mg creatinine.

Modified from: Diven SC, Travis LB. A practical primary care approach to hematuria in children. Pediatr Nephrol 2000; 14:65.

Common things are common

- Hematuria could indicate
  - Kidney stones
  - UTI
  - Nutcracker syndrome
    - May have orthostatic proteinuria
    - Compression of left renal vein
    - Left flank pain may be present
    - Hematuria is usually asymptomatic

Practice Pearls

Glomerular bleeding = inflammation related to an immune response

- within the kidney
- outside source such as lupus

Nephritis and nephrosis can be separate scenarios or overlap

Red cell casts = glomerular source of hematuria

- Absence doesn't mean you can check a glomerular source off your list

Watch for glomerular signs primarily in the adolescent/young adult

Symptom presentation may include

- Edema
- Hypertension
- Hematuria
- Proteinuria
- Recent infection

Obtain BMP, serum albumin, lipid panel, microscopic urinalysis and AM spot urine protein/creatinine ratio

Refer to nephrology (call us if you're unsure!)

- We partner closely with Rheumatology and Infectious Disease and will consult them when indicated

Thank you!

References

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