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Nephrology: Chronic Kidney Disease & Urinary Tract Infections

Eddie Needham, MD
Program Director and Academic Chairman
AdventHealth Winter Park
Family Medicine Residency Program
Professor, Loma Linda University School of Medicine
Eddie.Needham.MD@AdventHealth

Lecture Modules

- Chronic kidney disease
- Proteinuria
- Hematuria
- Urinary tract infections (UTI)
  - Pediatrics

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Chronic Kidney Disease

A 63 y.o. female with hypertension and diabetes has a Cr(creatinine) of 1.7 and a GFR(glomerular filtration rate) of 33. What stage CKD(chronic kidney disease) does she have?

A. Stage 1
B. Stage 2
C. Stage 3
D. Stage 4
E. Stage 5

Correct answer is C

- The answer is C. The stage of CKD helps determine therapy.
- More specifically, an eGFR 45-60 mL/min = CKD 3a
- eGFR 30-45 mL/min = CKD 3b
- CKD 3b is more suggestive of significant kidney disease

Chronic Renal Failure (CRF) or Chronic Kidney Disease (CKD)

- CKD is divided into five stages based upon estimated GFR
  - Stage 1 – GFR >90 mL/min
  - Stage 2 – GFR 60-90 mL/min
  - Stage 3 – GFR 30-60 mL/min
    - 3a – GFR 45-60 mL/min
    - 3b – GFR 30-45 mL/min
  - Stage 4 – GFR 15-30 mL/min
  - Stage 5 – GFR <15 mL/min

CKD Definition

A patient has CKD when GFR <60 ml/min/1.73 m^2 for >3 months

Glomerular Filtration Rate Calculations

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- Cockcroft-Gault equation

$$\frac{(140 - \text{age}) \times (\text{Wt in kg})}{\text{serum creatinine} \times 72} \quad (\times 0.8 \text{ in women})$$

- MDRD equation[1,2]
- Of note, the GFR is now routinely calculated for physicians on the BMP

Source: [1] Levey AS, Greene T, Kusek J, and Beck G. A simplified equation to predict glomerular filtration rate from serum creatinine (abstract). *J Am Soc Nephrol*. 2000. 11: p.155A.
[2] Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med*. 1999 Mar 16;130(6):461–70.

CKD – Stage Based Treatment

- Stage 1
  - Treat comorbid conditions, monitor high risk pts
- Stage 2
  - Estimate progression
- Stage 3
  - Evaluate and treat complications/comorbidities
- Stage 4
  - Refer to nephrology if not yet done
  - Prepare for renal replacement therapy (HD or PD)
- Stage 5
  - RRT, manage complications

A 64 y.o. female with diabetes is found to have an elevated microalbumin /creatinine ratio of 103 (normal <30). Which drug is most likely to slow the progression of this condition?

A. Chlorthalidone
B. Spironolactone
C. Ethacrynic acid
D. Lisinopril
E. Carvedilol

Correct answer is D

- Angiotensin converting enzyme inhibitors (ACEI) have been found to slow the progression of diabetic nephropathy. They should be instituted in all diabetic patients in whom the microalbumin/creatinine ratio is > 30.

Interventions That Have Been Proven to Be Effective in Slowing the Progression of CKD Include

- Strict glucose control in diabetes
- Strict blood pressure control
  - <125/75 in diabetic nephropathy
  - <135/85 in nondiabetic nephropathy
- Use of Angiotensin-converting enzyme inhibition or angiotensin-2 receptor blockade

Source: National Kidney Foundation. *K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification. Am J Kidney Dis 39:S1-S266,* 2002 (suppl 1)

Chronic kidney disease
Key Points

- Know the CKD stages
  - Stage 4 and 5 → nephrology c/s to prepare for RRT
- Use ACEI to prevent the progression of diabetic nephropathy when microalbumin/ creatinine ratio > 30
- Aggressively manage co-morbidities to slow progression of CKD

Proteinuria

Proteinuria

- Nephrotic range proteinuria = 3–3.5gm protein/24 hour collection
- The urinary albumin:creatinine ratio is a marker of nephropathy
  - A ratio >30 suggests the implementation of preventive measures, e.g., ACEI as appropriate, more aggressive BP control
- In general, significant proteinuria signals more severe CKD and a worse prognosis

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Hematuria

A 64 y.o. male presents with 2 episodes of asymptomatic gross hematuria in the past week. He has smoked 2-3 ppd for 40 years. He does not have HTN(hypertension) or DM(diabetes mellitus). What is the most likely etiology of the hematuria?

A. Bladder cancer

B. Lung cancer

C. BPH (benign prostatic hyperplasia)

D. Polycystic kidney disease

Correct answer is A

- Bladder cancer is the most likely answer given this patient's tobacco exposure. Gross hematuria is associated with a 20-25% chance of urinary tract malignancy and the patient should be thoroughly evaluated.

Hematuria Introduction

- Up to 9%-18% of otherwise healthy individuals have some degree of hematuria
- Hematuria can serve as a marker for infection, stone disease, or cancer
- Most frequently, the cause of hematuria is not found
- Hematuria may be transient, occurring on a single instance in 39% of soldiers over 12 years, and occurring in 16% on more than one instance over the same period[1]

Source: [1]Froom P, Ribak J, Benbassat J. Significance of microhaematuria in young adults. Br Med J (Clin Res Ed) 1984;288:20-2.

Hematuria Definition

- According to the American Urological Association, hematuria is defined as 3 or more RBCs/HPF on urine microscopy on two of three urinalyses
- Other references have used 5 or more RBCs/HPF as abnormal
- It is important to partner with local laboratory resources to determine local standards

Source: Grossfeld GD, Litwin MS, Wolf JS, Hricak H, Shuler CL, Agerter DC, et al. Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy—part I: definition, detection, prevalence, and etiology. *Urology*. 2001;57:599–603.

AUA Risk Factors for Significant Disease in Patients With Microscopic Hematuria

Smoking history
Occupational exposure to chemicals or dyes (e.g., benzenes, aromatic amines)
Age older than 40 years
History of urologic disorder or disease
History of irritative voiding symptoms
History of urinary tract infection
Analgesic abuse
History of pelvic irradiation

Source: Grossfeld GD, Wolf JS, Litwin MS, et al: Evaluation of asymptomatic microscopic hematuria in adults: The American Urological Association best practice policy recommendations. Urology 2001;57:599-610.

Hematuria – Severity

- “Macroscopic hematuria” describes urine that is visibly stained red or brown. This is also called gross hematuria
- “Microscopic hematuria” describes urine that is not tinged red or brown eye but dips positive for blood
- Additionally, microscopic hematuria will have ≥3 RBCs/HPF on urine microscopy

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Gross hematuria

Urine visibly stained red or brown

Signs and Symptoms Associated With Hematuria

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- Symptoms of cystitis include
  - Dysuria
  - Suprapubic pain
  - Urgency
  - Frequency
- Dysuria can be present in prostatitis and urethritis

Hematuria Key Points

- Common causes include:
  - UTI
  - BPH
  - Nephrolithiasis
  - Bladder cancer
- Definition is 3 or more RBCs/HPF on 2 or more occasions

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Urinary Tract Infections (UTI)

A 31 y.o. female at 36 weeks gestation presents with dysuria, right CVAT, nausea with vomiting, and fever. Which of the following drugs is the best choice to treat her condition?

A. IV doxycycline

B. IV ceftriaxone

C. IV trimethoprim/sulfamethoxazole

D. IV ciprofloxacin

E. Oral nitrofurantoin

Correct answer is B

- A third generation cephalosporin is safe and effective during pregnancy for most causes of pyelonephritis. Tetracyclines can cause staining of the teeth. Sulfa drugs are associated with kernicterus in the third trimester and are contraindicated. Fluoroquinolones have a concern about cartilage development in utero. Nitrofurantoin in not an effective drug for pyelonephritis: therapy should initially be parenteral, not oral.

Culture Negative “UTI”

- The urethral syndrome is noted when a patient has symptoms of urethritis but the urine culture is negative
- Consider bacterial organisms other than E. coli and gram negative rods
  - Chlamydia trachomatis
  - Ureaplasma urealyticum
  - Mycoplasma hominis
- These are urinary “atypicals” and respond to tetracyclines and macrolides

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Urinary Tract Infections: Pediatrics

A 3 m.o. male infant presents with irritability. The exam is notable to a mildly tender suprapubic mass. The mother volunteers that the circumcision healed fine but the child dribbles when he urinates. He has previously had a UTI. The most likely cause of this is:

A. Wilm's tumor

B. Posterior urethral valves

C. Horseshoe kidney

D. Duplication of the urinary tracts

E. Spina bifida occulta

A 2 y.o. girl presents with fever of 102.7 and dysuria. She is found to have >50 WBCs/HPF on UA micro. She is started on appropriate antibiotics. Which subsequent studies should be performed?

A. Intravenous pyelography (IVP)
B. Ultrasound of the bladder and kidneys
C. Nuclear renal scan
D. Voiding cystourethrogram (VCUG) and renal ultrasound

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Pediatric UTIs

- In male infants, consider posterior urethral valves
- In female infants, consider vesicoureteral reflux
- Indications for a pediatric UTI workup
  - Children 2 – 24 months: Renal/bladder ultrasound
  - Only get VCUG if second or higher UTI, or if the RBUS is abnl
- Voiding cystourethrogram (VCUG) to evaluate for vesiculoureteral reflux and renal ultrasonography to evaluate the kidneys and bladder

Signs and Symptoms Associated With Hematuria

- Pain radiating from the flank to the groin can be found in several conditions
  - Renal colic/ureteral distention from nephrolithiasis (stones)
  - Blood clots
  - Papillary necrosis
- Costovertebral angle tenderness is common with pyelonephritis, trauma/hematoma, and bleeding or infection in a renal cyst

UTI
Key Points

- E. coli is the most common etiology
- The urine dipstick is effective in diagnosing uncomplicated UTIs
- Most patients only need 3 day therapy
- Children
    - Boys – consider posterior urethral valves
    - Girls – consider vesicoureteral reflux
- Pyelonephritis is associated with an ill pt