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Nephrology: Acute Kidney Injury Pathophysiology and Clinical Manifestations

Eddie Needham, MD, FAAFP

Program Director and Academic Chairman,

AdventHealth Winter Park Family Medicine Residency Program

Clinical Professor, UCF-COM

Clinical Professor, LLU-COM

Lecture Modules

- Definition and Pathophysiology
- Risk Factors
- Common Drugs That Cause AKI
- Clinical Manifestations

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Definition and Pathophysiology

Question: A 64 year old male presents with lower abdominal pain and decreased urination x 2 days. The BUN and creatinine are 34 and 3.0. He has no chronic medical problems. What is the most likely cause of his AKI?

A. Prerenal azotemia

B. Renal artery stenosis

C. Retroperitoneal fibrosis

D. Benign prostatic hypertrophy

Answer Explanations

Correct answer is D

- The BUN/Cr ratio suggests an intrarenal or postrenal etiology. In an older male with no chronic medical conditions, benign prostatic hyperplasia (BPH) is obstruction is the most likely cause. In some cases, the bladder can be palpated or percussed on examination. An ultrasound would readily confirm the diagnosis without exposure to contrast agents

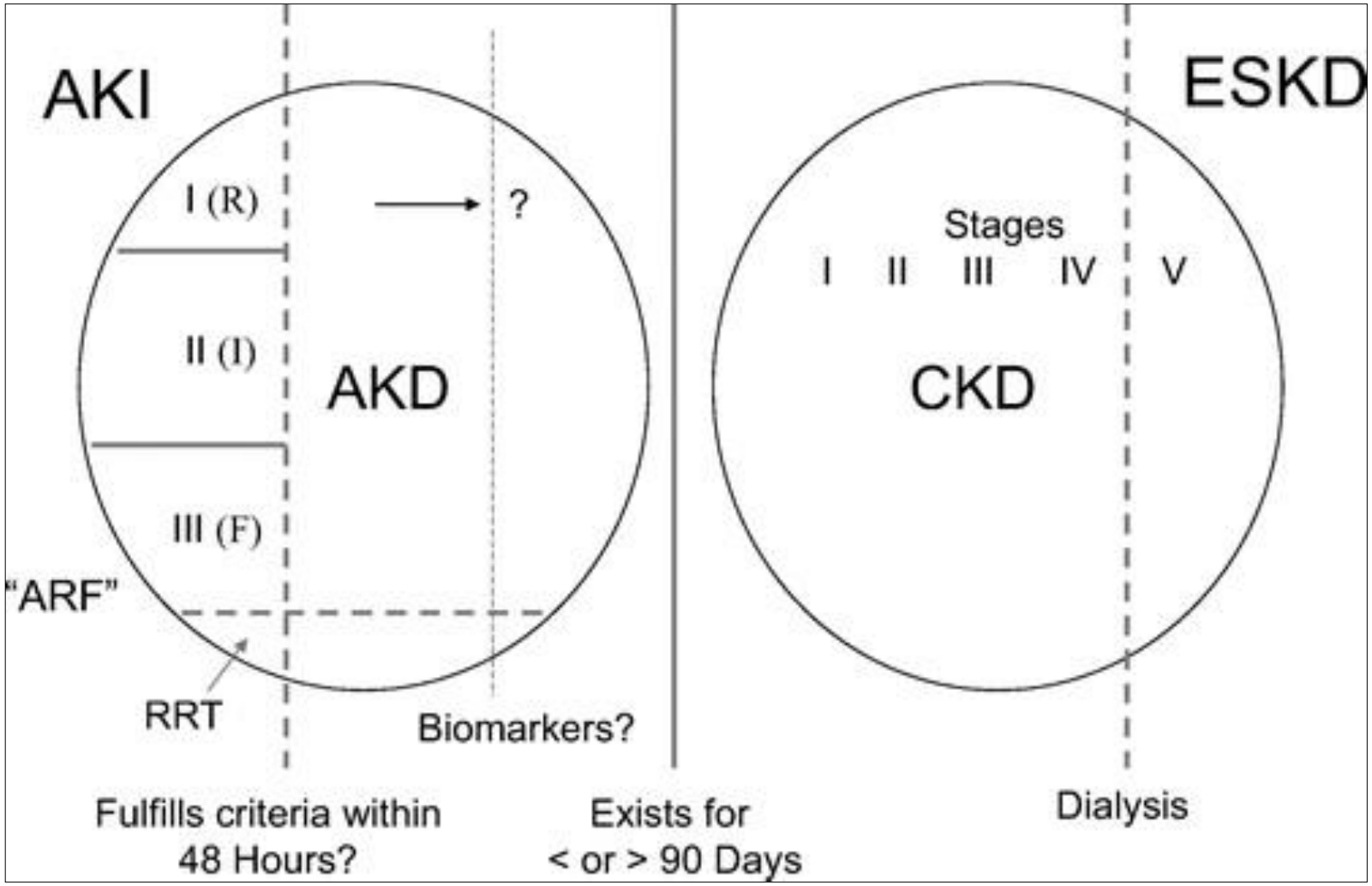
Acute Kidney Injury

- Define acute kidney injury (AKI)
- Calculate glomerular filtration rates
- Identify risk factors and prevention strategies for AKI
- Classify AKI into its' three categories
- Identify treatment options in AKI

ARF, AKI, or AKD?

- Acute kidney injury (AKI) is the preferred term that describes the normal rise in BUN and creatinine that occurs in acute dehydration while kidney function is preserved
  - The kidney stills concentrates urine
  - If corrected, the kidney function returns to normal
- Acute tubular necrosis (ATN) describes a decline or failure in kidney function itself

The Spectrum of Acute Kidney Injury



Source: Kellum JA, Acute Kidney Injury. Crit Care Med 2008; 36: ppS141-45.

AKI – Definitions

- Strict definition is lacking
- Increase of serum creatinine of 0.5 mg/dL above baseline
- Increase of serum creatinine of 50% above baseline
- Decrease in glomerular filtration rate (GFR) of 50% from baseline
- Oliguria = urine output <400 cc per 24 hours
- Anuria = urine output <100 cc per 24 hours

AKI – Epidemiology

- AKI occurs in 1%–5% of hospitalized patients
- AKI affects 15%–20% of patients in the ICU
  - ICU mortality in patients with AKI is reported as 50%–70%
- Infection and cardiovascular complications are the most common causes of death

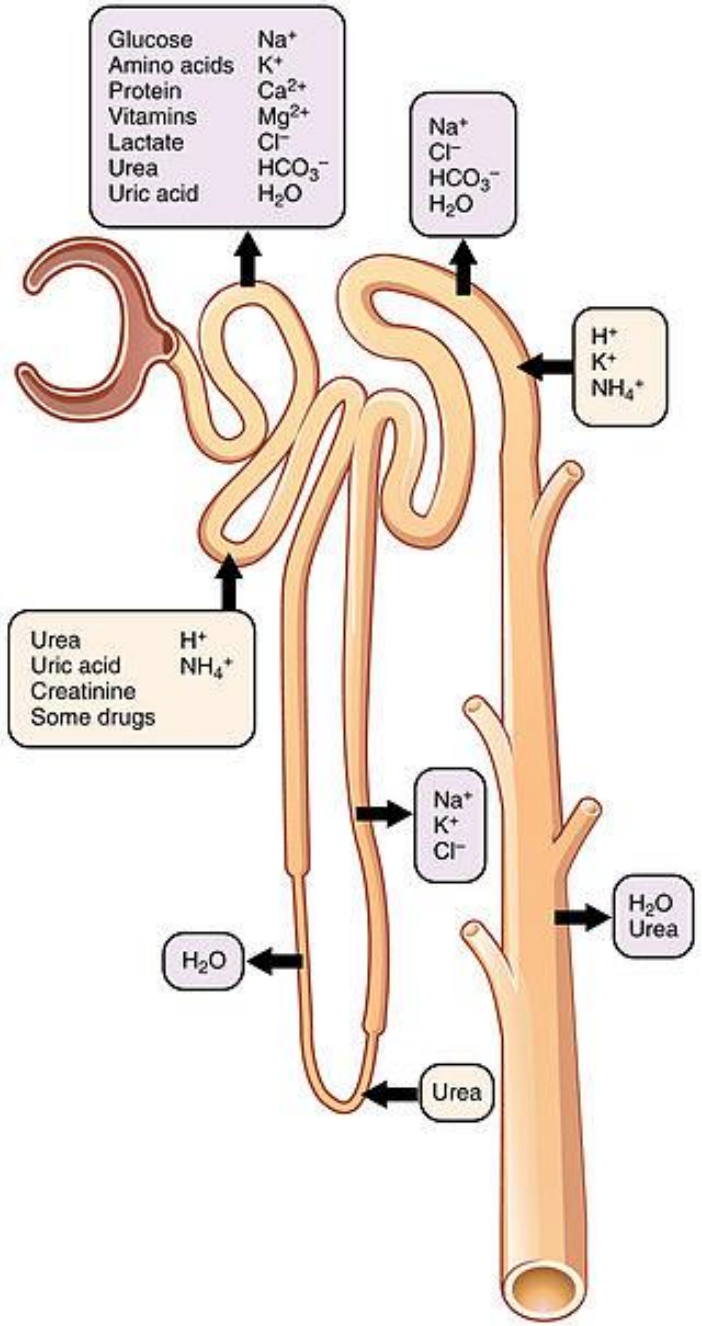
Source: Thadhani, R et al. Acute renal failure. N Engl J Med 1996; 334: 1448-60.
Singri, N et al. Acute renal failure. JAMA 2003; 289: 747-51.

AKI – Pathophysiology

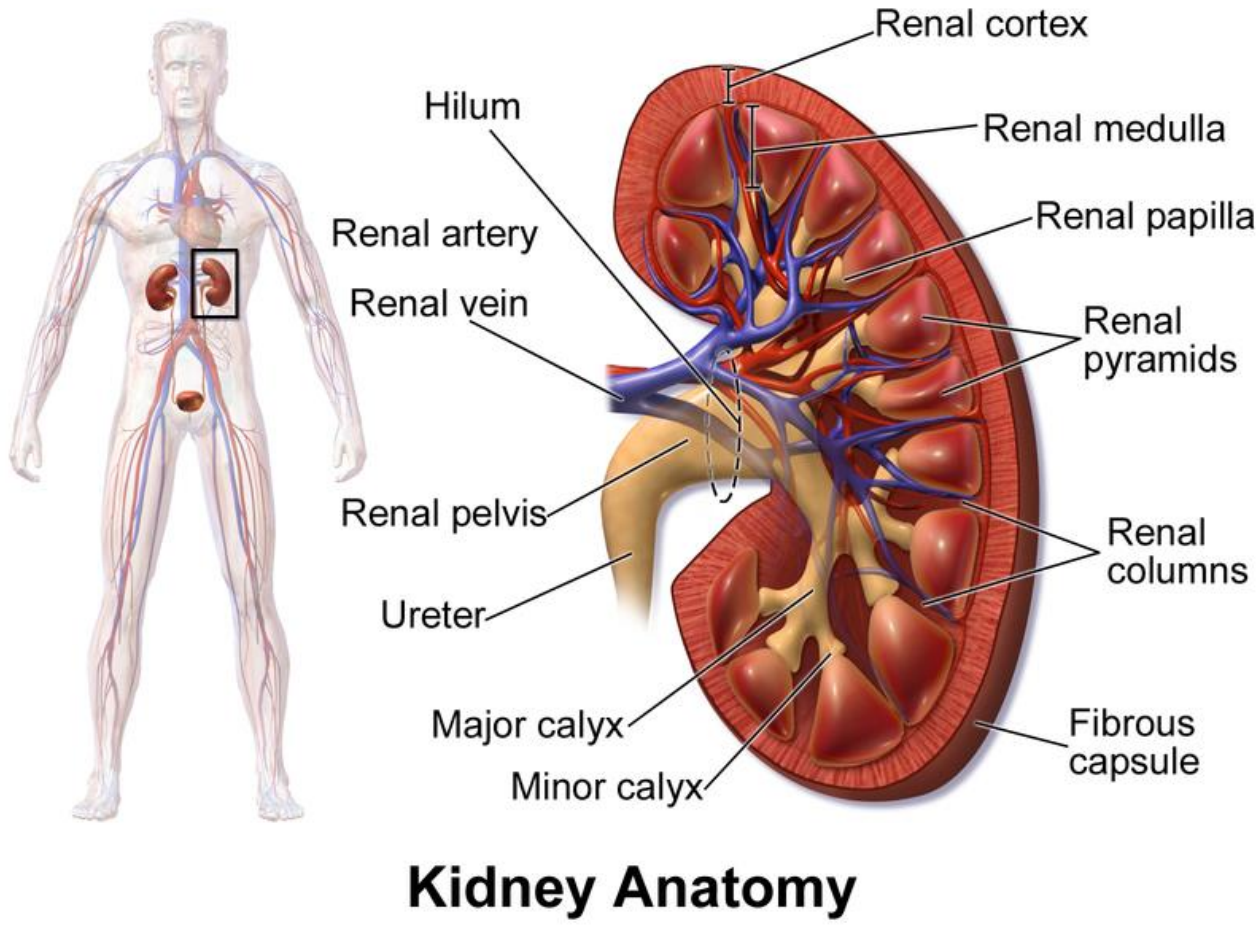
- The kidneys are microscopically arranged into nephrons
- They remove the body's nitrogenous wastes and creatinine
- Additionally, they maintain fluid and electrolyte homeostasis
- Quick example – kidneys don't work
  - → Fluid overload (edema) and hyperkalemia

The Nephron

- Capable of forming urine
- Has two major components
  - Glomerulus
  - Tubule
    - Proximal
    - Loop of Henle
    - Distal
    - Collecting



The Kidney Is Quite Vascular



Kidney Anatomy

20% of cardiac output goes to the kidneys

Definition and Pathophysiology Key Points

- AKI is generally defined with
  - Creatinine increase of 0.5
  - Creatinine increase by 50%
  - Decrease in GFR by 50%
- Use the BUN/Cr ratio to help localize the pathophysiology
  - BUN/Cr > 20 suggests a prerenal state

Risk Factors

Question: Which of the following is not a common risk factor for AKI?

A. Endometriosis

B. Diabetes mellitus (DM)

C. Heart failure

D. Advanced age

Answer Explanations

Correct answer is A

- Endometriosis is not a common risk factor for AKI. The other conditions are.

AKI – Risk Factors

- Medical risk factors include
  - Diabetes mellitus
  - Chronic renal insufficiency
  - Heart failure
  - Advanced age
- Situational risk factors include
  - Potential volume depletion (eg, acute gastroenteritis)
  - Medications (eg, diuretics)
  - Technologies – dye studies ? (CT, angiography, etc…)

GFR in AKI

- In AKI, the GFR is changing over 12-24 hours. As such, the calculated GFR is an extremely rough estimate of the actual kidney function
- For example, if both renal arteries are temporarily ligated, the creatinine will rise approximately 1 mg/dL per day

AKI – History and Physical

- Both of these clinical elements are often unrevealing
- The diagnosis is frequently based on lab findings alone
- Historical findings
  - Attached table
- Physical exam findings
  - Attached table

Source: Needham E, Management of Acute Renal Failure. Am Fam Physician 2005; 72: 1739-46.

Probable Causes of AKI Based on the History

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History Review of systems		Probable causes
Pulmonary system	- Sinus, upper respiratory, or pulmonary symptoms	- Pulmonary-renal syndrome, vasculitis
Cardiac system	- Symptoms of heart failure - Intravenous drug abuse; prosthetic valve or valvular disease	- Decreased renal perfusion - Endocarditis
Gastrointestinal system	- Diarrhea, vomiting, poor intake - Colicky abdominal pain radiating flank to groin	- Hypovolemia - Urolithiasis
Genitourinary system	- Symptoms of benign prostatic hypertrophy	- Obstruction
Musculoskeletal system	- Bone pain in older patient - Trauma, prolonged immobilization	- Multiple myeloma, prostate cancer - Rhabdomyolysis (pigment nephropathy)
Skin	-Rash	-Allergic interstitial nephritis, atheroemboli, systemic lupus erythematosus, thrombotic thrombocytopenic purpura, vasculitis
Constitutional symptoms	- Anorexia, fatigue, fever, weight loss	- Malignancy, vasculitis

Probable Causes of AKI Based on the History

History		Probable causes
Medical history	Diabetes mellitus, multiple sclerosis, stroke	Neurogenic bladder
Surgical history	Recent surgery or Recent procedure	Atheroemboli, ischemia, endocarditis Contrast agent
Medication history	Acyclovir (Zovirax), angiotensin converting enzyme inhibitors, antibiotics, nonsteroidal antiinflammatory drugs	Acute tubular necrosis, allergic interstitial nephritis, decreased renal perfusion

Probable Causes of AKI Based on Physical Exam Findings

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Physical examination	Possible causes
Vital signs - Elevated temperature - Blood pressure	Possible infection Hypertension: nephrotic syndrome, malignant hypertension, Hypotension: volume depletion, sepsis
Weight loss or gain	Hypovolemia, hypervolemia
Mouth	Dehydration
Jugular veins and axillae hypovolemia, hypervolemia (perspiration)	Hypovolemia, hypervolemia
Pulmonary system	Signs of heart failure
Heart	New murmur of endocarditis, signs of heart failure
Abdomen	Bladder distention suggesting urethral obstruction
Pelvis	Pelvic mass
Rectum	Enlarged prostate
Skin	Rash of interstitial nephritis, purpura of microvascular disease, livedo reticularis suggestive of atheroembolic disease, splinter hemorrhages or Osler's nodes of endocarditis

Risk Factors Key Points

- Be aware of common risk factors for AKI
  - Chronic kidney disease (CKD), DM, HTN, increased age, heart failure
- AKI is often asymptomatic
  - Have a high index of suspicion
  - Practically speaking, many Emergency Department (ED) patients get a Chem7/ basic metabolic panel (BMP) for this reason

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Common Drugs That Cause AKI

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Question: Of the following drugs, which is not a common cause of AKI?

A. Diuretics
B. Non-steroidal anti-inflammatory drugs (NSAIDS)
C. Aminoglycosides
D. Insulin

Answer Explanations

Correct answer is D

- Diuretics cause AKI through volume contraction leading to prerenal azotemia. NSAIDs affect vascular tone leading to vasoconstriction. Aminoglycosides are a direct toxin. Insulin does no appreciable damage to the kidney. It is used in diabetes who are, however, at increased risk of AKI

Common Drugs That Cause AKI Key Points

- The most common drugs associated with AKI are
  - NSAIDs
  - Angiotensin-converting-enzyme inhibitors (ACEIs)
  - Aminoglycosides
- CT contrast was previously listed as a common cause of AKI
- Recent data suggests CT contrast dye is a neutral factor
- eGFR< 30 → consider preprocedural IV saline

Clinical Manifestations

Question: This patient presents with hematuria and a BUN/Cr = 27/2.4. The most likely cause is:

A. Systemic Lupus Erythematosus (SLE)
B. Dermatomyositis
C. Wegener's granulomatosis
D. Seborrheic dermatitis

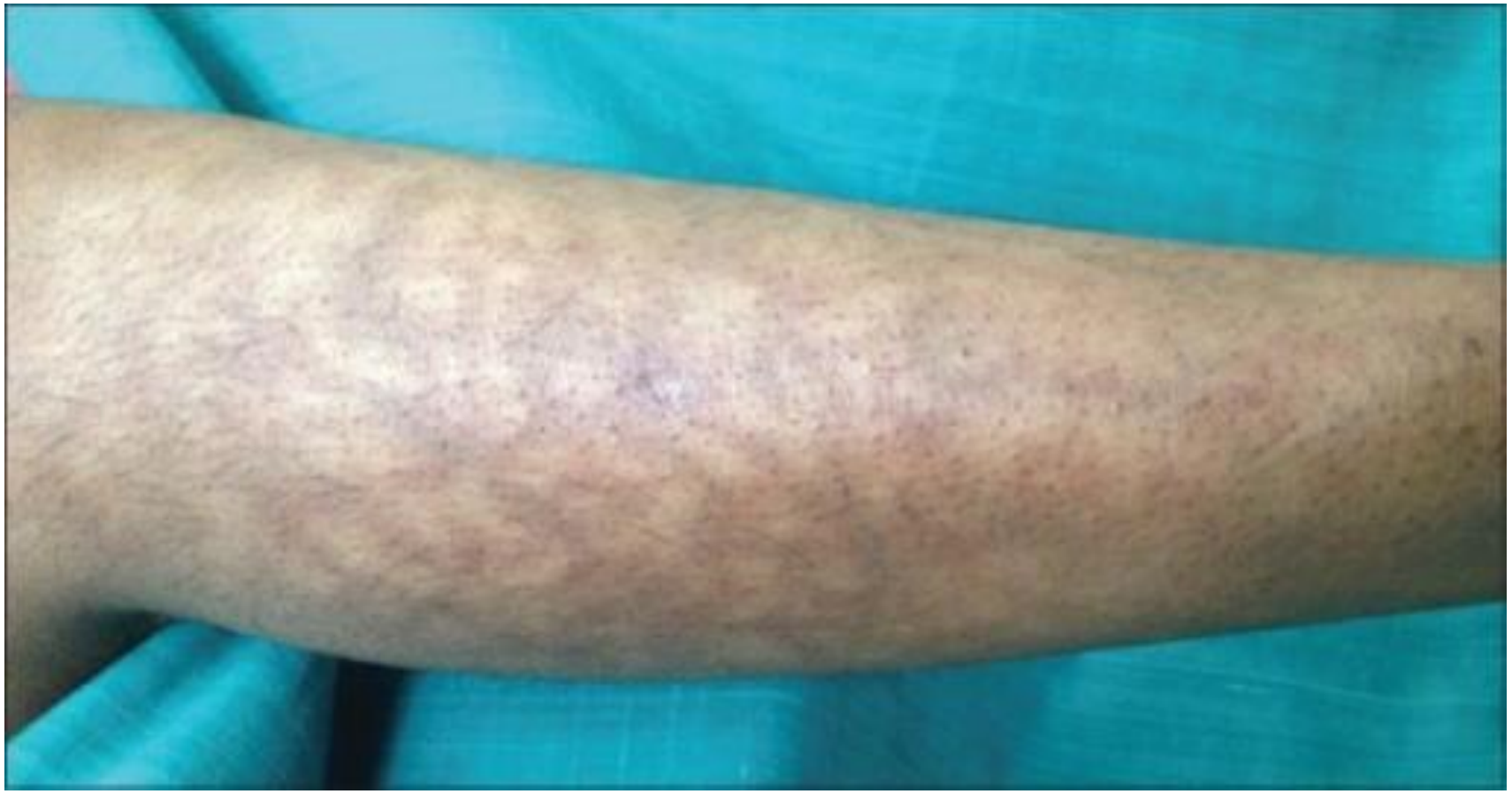
Answer Explanation

Correct answer is A

- This patient has the classic malar rash of lupus. The hematuria and BUN/Cr suggest systemic involvement, and SLE commonly has these manifestations. Dermatomyositis can cause a heliotrope rash on the upper eyelids but does not generally affect the kidneys. Wegener's granulomatosis is a pulmonary renal syndrome and is not associated with a malar rash. Seborrheic dermatitis has not renal involvement

Livedo Reticularis

Livedo Reticularis



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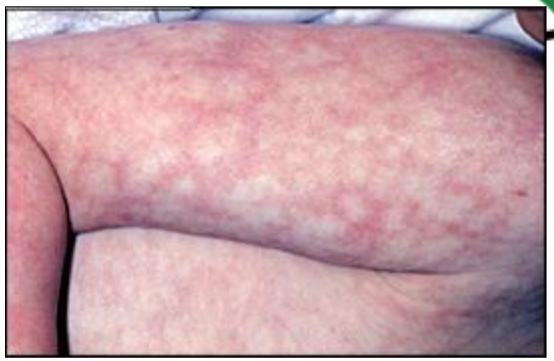
https://openi.nlm.nih.gov/detailedresult.php?img=PMC4594389_IDOJ-6-315-g005&query=livedo+reticularis&it=xg&req=4&npos=66

Cutis Marmorata a Normal Neonatal Finding



Source: O'Connor N, McLaughlin M, Ham P, Am Fam Physician. 2008;77(1):47-52.

Splinter Hemorrhages

Media from government website in public domain:
https://openi.nlm.nih.gov/detailedresult.php?img=PMC4375768_IDOJ-6-67-g016&query=splinter+hemorrhages&it=xg&req=4&npos=16

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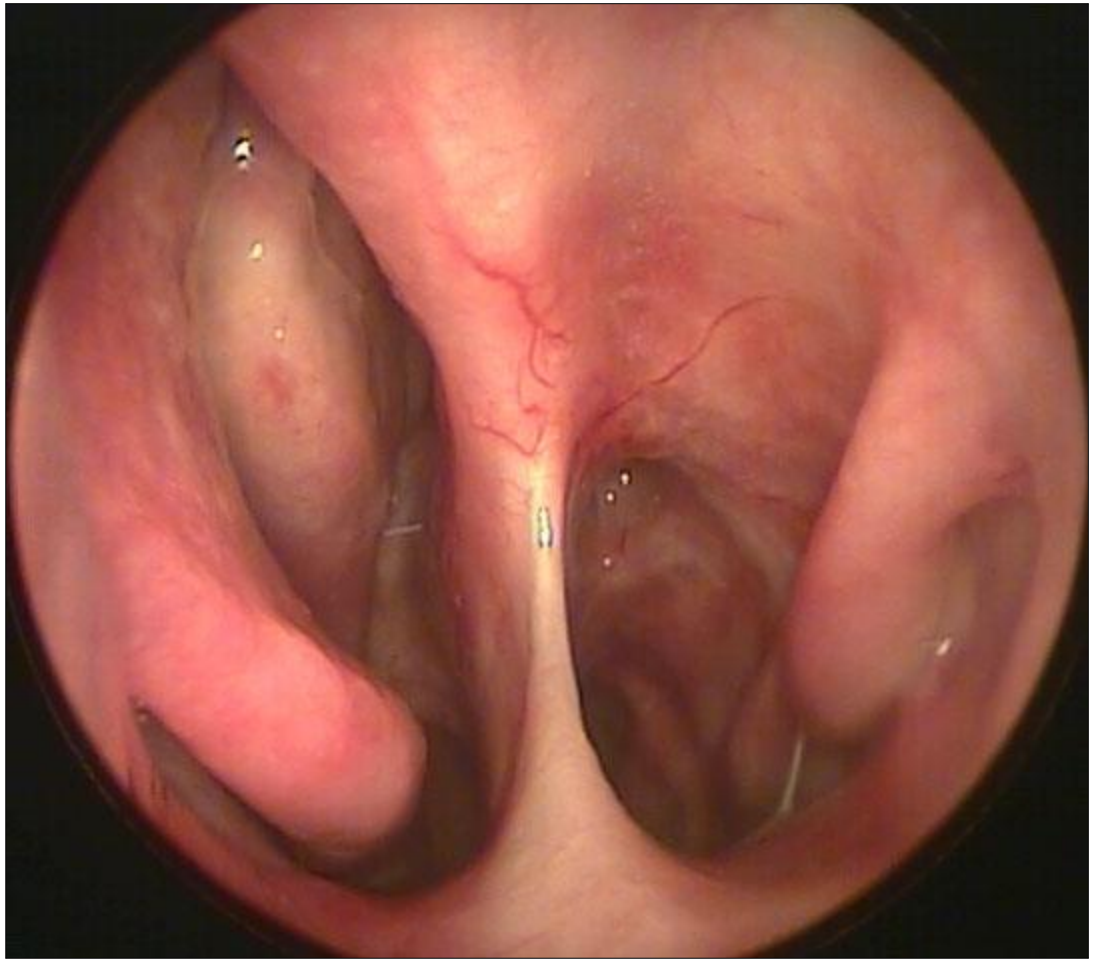
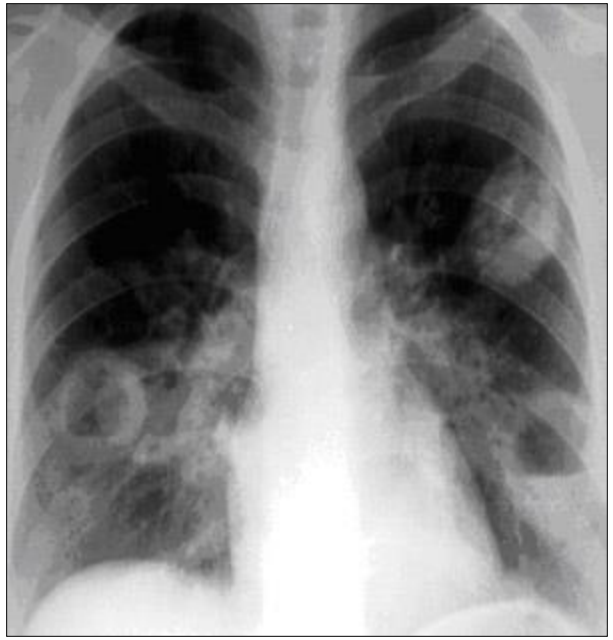
Splinter Hemorrhages
Conjunctival Petechiae
Osler's Nodes
Janeway Lesions

Slides from the American College of Rheumatology clinical slide Set 1995-1999

Wegener's Granulomatosis





Slides from the American College of Rheumatology clinical slide Set 1995-1999

Pulmonary renal syndromes

- Wegener's granulomatosis
  - c-ANCA
- Goodpasture's syndrome
  - Antiglomerular basement membrane Ab
- Both have distinctive lab values that help confirm the Dx

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Nephrotic Syndrome

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AKI – Tests to Order/Perform

- Basic metabolic panel for BUN, creatinine, and electrolytes
- Consider comprehensive metabolic panel (CMP) for calcium, magnesium, phosphorus
- Consider CBC if ARF on chronic renal failure (CRF) – may diagnose anemia in end stage renal disease (ESRD)
- Urinalysis
- Urine electrolytes to calculate the fractional excretion of sodium (FENa) (urine Na and Cr)

Clinical Manifestations Key Points

- Several conditions with physical exam findings have a propensity to affect the kidney
  - Connective Tissue Diseases like SLE
  - Pulmonary renal syndromes
- Generalized edema and anasarca suggest a renal disorder
- Most patients with AKI have no physical exam findings