Approach To Patient With Renal Disease

Prep. By :
Dr. Alaa Eldeen Elmassry
Consultant Internist
Head Of The Medical Department

We will discuss ….

- **Approach to patient with hematuria**
- **Approach to patient with proteinuria**
- **Approach to patient with impaired kidney function**

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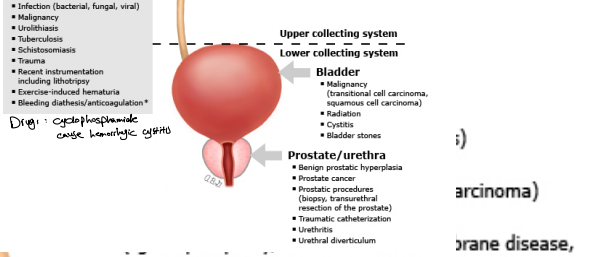
Hematuria

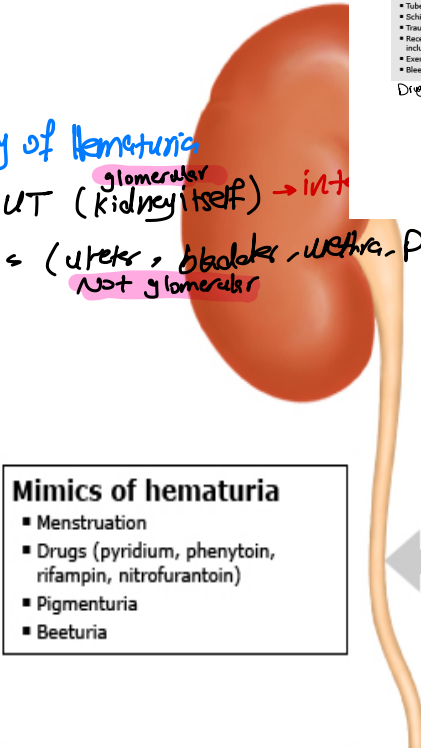
Macroscopic

- **Gross Hematuria / Microscopic Hematuria.**
- **Glomerular / Non-glomerular**

Etiology Of Hematuria

* According to Pathology of Hematuria
  - from upper part of UT (kidney itself) → glomerular → int
  - " lower " " " (ureter, bladder, urethra, prostate) → not glomerular
    - urologist





Alport syndrome)
- Structural disease (polycystic kidney disease, medullary sponge kidney)
- Pyelonephritis
- Hydronephrosis/distension
- Hypercalciuria/hyperuricosuria
- Malignant hypertension
- Renal vein thrombus/renal artery embolism
- Arteriovenous malformation
- Papillary necrosis (sickle cell disease)

infection TB

Mimics of hematuria

- Menstruation
- Drugs (pyridium, phenytoin, rifampin, nitrofurantoin)
- Pigmenturia
- Beeturia

Ureter

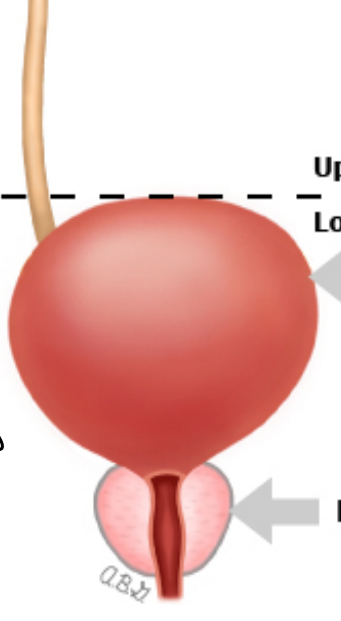
- Malignancy
- Stone — nephrolithiasis
- Stricture
- Fibroepithelial polyp
- Post-surgical conditions (ureteroiliac fistula)

- trauma

Renal and/or upper or lower collecting system:

- Infection (bacterial, fungal, viral)
- Malignancy
- Urolithiasis
- Tuberculosis
- Schistosomiasis
- Trauma
- Recent instrumentation including lithotripsy
- Exercise-induced hematuria
- Bleeding diathesis/anticoagulation *

Drugs : cyclophosphamide cause hemorrhagic cystitis



Upper collecting system

Lower collecting system

Bladder

- Malignancy (transitional cell carcinoma, squamous cell carcinoma)
- Radiation
- Cystitis
- Bladder stones

Prostate/urethra

- Benign prostatic hyperplasia
- Prostate cancer
- Prostatic procedures (biopsy, transurethral resection of the prostate)
- Traumatic catheterization
- Urethritis
- Urethral diverticulum

1-Gross Hematuria(macroscopic hematuria)

- Gross hematuria is suspected because of the presence of red or brown urine.
- The color change does not necessarily reflect the degree of blood loss, since as little as 1 mL of blood per liter of urine can induce a visible color change.
- Intermittent excretion of red to brown urine can be seen in a variety of clinical conditions other than bleeding into the urinary tract (myoglobiuria, beeturia) passing red or pink urine after ingesting beetroot especially with iron deficiency anemia البيتي
- Gross hematuria with passage of clots usually indicates a lower urinary tract source but can be seen with some forms of intrarenal bleeding (eg, kidney cancer). prostate urinary bladder ureter

- As contamination with blood is a possibility in menstruating and postpartum women, urine for analysis is best obtained when the other cause of bleeding has ceased.
- If this is not possible, a tampon can be inserted, and urinalysis can be obtained after the perineum is cleansed.

* Myoglobinuria & Hemoglobinuria

↳ pigment from muscles → so injury & damage to muscles (rhabdomyolysis)

Hemoglobinuria Hb → inside RBCs
↳ free Hb normally is low but in hemolytic anemia especially intravascular hemolysis
↑ free Hb → Hemoglobinuria

*Pigment uria
- Beeturia
- Drugs

Significant Hematuria: → emergency
- Clot that obstruct the urethra & cause urine retension → need foley catheter
- Anemia & need transfusion
- obstruction in ureter → hyponephrosis & renal colic

* But mostly benign & limited & need only assurance of the patient

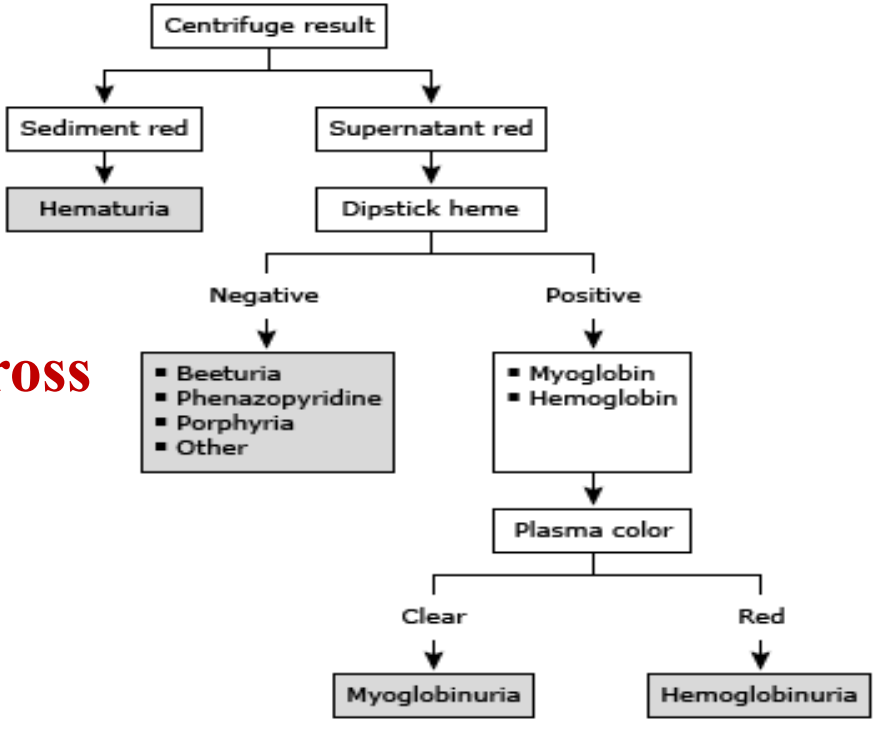
- **The initial step in the evaluation of patients with red urine is centrifugation of the specimen to see if the red or brown color is in the urine sediment or the supernatant.**
- **Hematuria is responsible if the red to brown color is seen only in the urine sediment, with the supernatant being clear. A rare exception is that lysis of red blood cells (RBCs) in patients with gross hematuria and very dilute urine can result in a red supernatant.**
- **If, on the other hand, it is the supernatant that is red to brown, then the supernatant should be tested for heme (hemoglobin or myoglobin) with a urine dipstick:**

or pigment uria (beeturia)

- **A red to brown supernatant that is negative for heme (hemoglobin or myoglobin) is a rare finding that can be seen in several conditions, including porphyria, the use of the bladder analgesic phenazopyridine, and the ingestion of beets in susceptible subjects.**
- **A red to brown supernatant that is positive for heme is due to myoglobinuria or hemoglobinuria.**

(+) Heme test ⇒ Myoglobin or hemoglobin
(−) Heme test ⇒ Pigment uria , prophyria

Evaluation Of Gross Hematuria



Usually accidently discovered

2-Microscopic Hematuria

- **Microscopic hematuria refers to blood detectable only on examination of the urine sediment by microscopy.**
- **Microscopic hematuria may be discovered incidentally when blood (either RBCs or hemoglobin) is found on a urinalysis or dipstick done for other purposes.**
- **Although abnormal hematuria is commonly defined as the presence of three (or 5) or more RBCs per high-power field in urine sediment, there is no "safe" lower limit below which significant disease can be excluded**

In general → benign condition But proteinuria → urgent → end stage renal disease / cardiovascular disease

Glomerulonephritis ⇒ Autoimmune mediated disorder

Glomerular versus non- glomerular

- The identification of the glomeruli as the source of hematuria can optimize the subsequent evaluation.
- In particular, patients with clear evidence of glomerular hematuria may not need to be evaluated for potentially serious urologic disease unless there is some other reason to do so.
- Glomerular hematuria may result from immune-mediated injury to the glomerular capillary wall or, in noninflammatory glomerulopathies such as thin basement membrane nephropathy, from localized gaps in the glomerular capillary wall

→ serious causes
- glomerulonephritis
- IgA nephropathy
- poststrepto GN
- vasculitis
- lupus nephritis

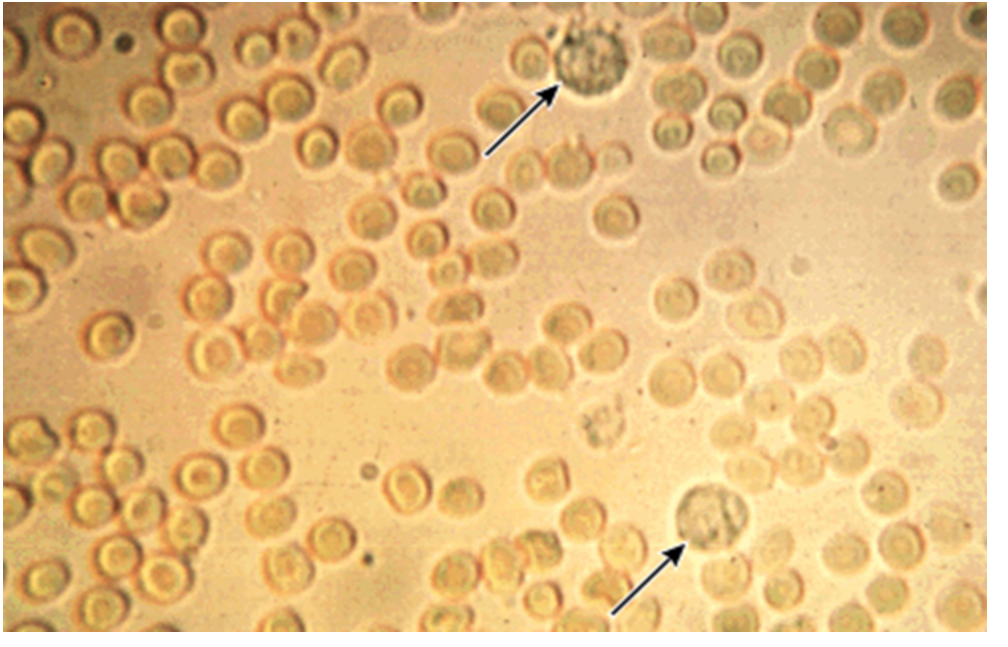
Cast ⇒ means the pathology related to kidney because the cast formed by passing through kidney tubules

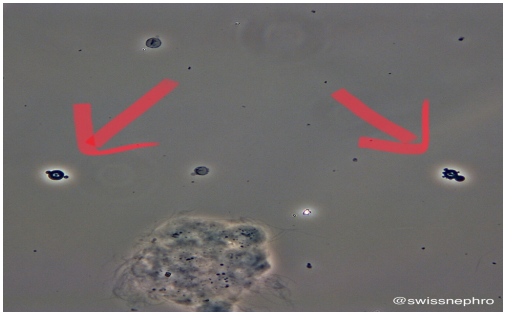
- **Signs of glomerular bleeding (best identified by a nephrologist or other experienced examiner) include :**

1. **RBC casts** due to passing through tubules
   * WBC cast ↳ pyelonephritis
2. **A dysmorphic appearance of some RBCs**
   * granular cast ↳ Acute interstitial nephritis
3. **Acanthocyte** (protrusion or angular projection) ↳ due to passing through glomerular basement membrane
4. **In patients with gross hematuria, a brown, cola-colored urine** → Mostly present at distal part (Non-glomerular)
5. **Proteinuria exceeding 500 mg/day that is temporally related to the onset of hematuria.**

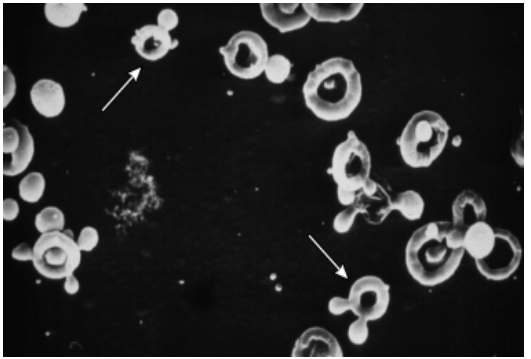
- **Blood clots, if present, are almost always due to nonglomerular bleeding** from lower UT

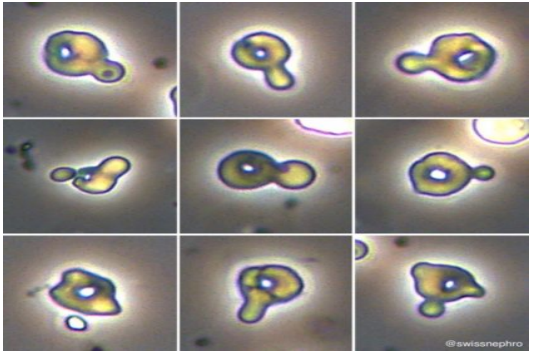
Acanthocyte





Phase-contrast micrograph showing dysmorphic RBCs in urine sediment(RED ARROW)

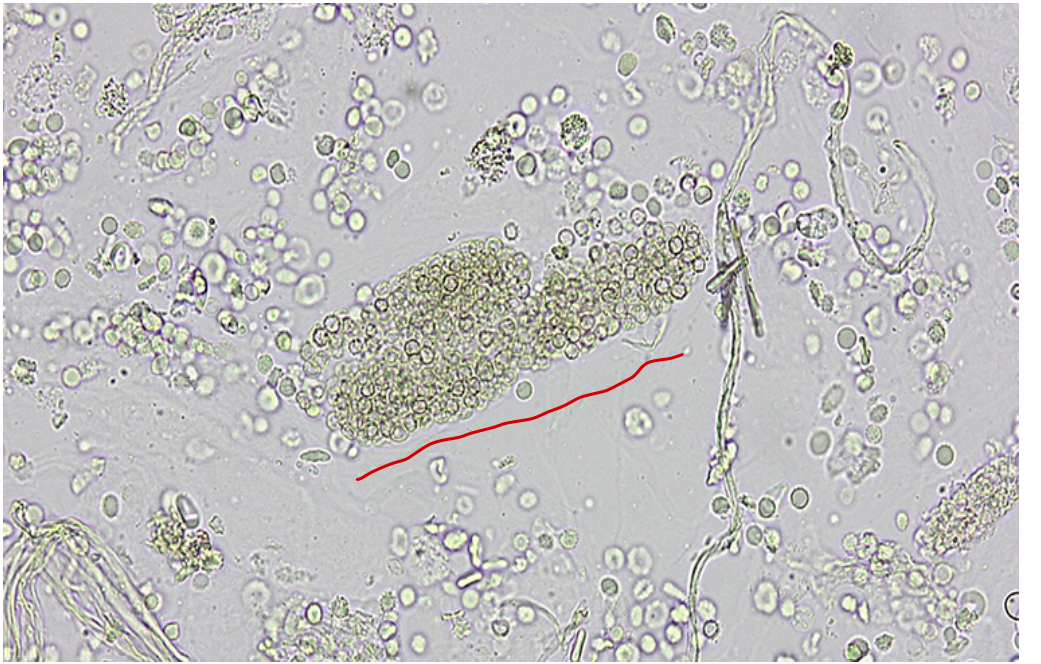




Acanthocytes (White arrows) can be recognized as ring forms with vesicle-shaped protrusions.

angular shape

Cast
Glomerular
Casts



Photomicrograph of urine sediment with a red cell cast

Initial Evaluation

- **As a general principle, hematuria itself is not imminently dangerous unless non-glomerular bleeding is so brisk that it causes clots that**

1. **Obstruct the ureter(s),** hydronephrosis & renal colic
2. **Clots that obstruct the bladder outlet causing urinary retention, or**
3. **Blood loss that results in anemia.**

- **Hematuria is common and frequently benign in young patients, and a cause is often not identified**

History

- History of menstrual cycle.
- History of vigorous exercise.
- Patients who have findings suggestive of urinary tract infection (eg, fever, dysuria, presence of white blood cells [WBCs] in the urine, positive dipstick for nitrite) should undergo urine culture to evaluate for urinary tract infection.
- In patients with urinary tract infection, the infection should be treated and the urinalysis should be repeated approximately six weeks after completion of antibiotic therapy in order to determine if the hematuria is persistent.

- **A recent upper respiratory infection or symptoms of upper respiratory disease raise the possibility of postinfectious or infection-related glomerulonephritis, immunoglobulin A (IgA) nephropathy, vasculitis, anti-glomerular basement membrane (GBM) disease, or sometimes hereditary nephritis.**
- **A positive family history of kidney disease, as in hereditary nephritis, polycystic kidney disease, or sickle cell disease.** → Cause papillary necrosis & hematuria
- **Unilateral flank pain, which may radiate to the groin, usually suggests ureteral obstruction due to a calculus or blood clot but can occasionally be seen with malignancy or IgA nephropathy.**
- **Symptoms of prostatic obstruction in older men such as hesitancy and dribbling.**
- **History of a bleeding disorder or bleeding from multiple sites due to excessive anticoagulant therapy. However, it should not be assumed that hematuria alone can be explained by chronic anticoagulation.**

Hemophilia

Even though the patient has bleeding tendency, there is maybe a local cause of mass or infection and should do investigations

warfarin

infection local mass ∈ hematuria

Upper respiratory tract inf $\xrightarrow{\text{10 days or weeks}}$ hematuria → Post-streptococcal glomerulonephritis

" $\xrightarrow{\text{2-3 days}}$ hematuria → IgA nephropathy

* Patient present with sudden pain at renal angle, vomiting, renal colic (severe)
  No fever, No trauma, hematuria ⇒ nephrolithiasis
* old patient, retension of urine, hesitancy ⇒ Benign prostatic hyperplasia (→ commonly) or prostatic cancer
* younge, sexually active patient ⇒ prostatitis

Catamenia hematuria, Catamenia hemoptesis

- **Cyclic hematuria in women** that is most prominent during and shortly after menstruation, suggesting **endometriosis** of the urinary tract

↳ ectopic endometrial tissue outside the uterus

Ask about medications cause bleeding as warfarin or drugs affect kidneys or urinary bladder (cyclophosphamide)cause cystitis or drugs cause red urine as rifampin, phenazopyridine

- **Medications** that might cause **nephritis** (usually with other findings, typically with kidney function impairment).
- **Black patients** should be screened for **sickle cell trait** or disease, which can lead to **papillary necrosis** and **hematuria.**

P in Brazil, South American

- Travel or residence in areas endemic for ***Schistosoma haematobium*** or tuberculosis. Schistosoma mansoni in Egypt & Saudan
- **Sterile pyuria with hematuria**, which may occur with renal tuberculosis, analgesic nephropathy, toxic nephropathy, and other interstitial diseases.

Physical Examination

pyelonephritis

- Fever , costophrenic angle tenderness may suggest infection.
- Palpable mass may suggest tumor or polycystic kidney or tumour.
- LL edema may suggest impaired kidney function nor concomitant proteinuria. → with buffy eyelids — nephrotic or nephritic syndrome → glomerular cause
- High blood pressure in CKD , AKI , ADPKD, malignant hypertension → severe elevation in B.P — ↳ cause palpable mass with secondary hypertension (renal causes)
- Per rectum exam : prostate enlargement. — & hard or firm → prostatic hyperplasia

Lab Investigation

- **Urine analysis and urine sediment**
- **look for proteinuria: if temporally related to the hematuria is suggestive of glomerular disease.**
- **Microhematuria alone does not typically lead to a significant increase in protein excretion.**
- **A dipstick test for protein that is greater than 1+ is rarely observed with nonglomerular bleeding, even with gross hematuria, unless the amount of gross blood is very large.**

don't differentiate between hemoglobinuria - myoglobinuria, hematuria

Most cases of hematuria → benign & No changes in KFT

- **KFT : urea , creatinine**(Patients with acute kidney injury or findings suggestive of glomerular bleeding should be referred to nephrologist)
- **Urine culture**
- **Urine cytology : is no longer recommended to assess for malignancy due to variable sensitivity and specificity.**
- **Coagulation profile : PT , PTT , INR**
- **kidney biopsy**

Bleeding tendency

Von willebrand disease (VWD)
↑ PT time ↑ Bleeding time
-Because it affects factor (VIII) & aggregation of platlets

→ rarely done on hematuria investigations

CTU or MRU ⇒ in nephrolithiasis

Imaging

- **Us abdomen for both kidneys and urinary bladder** - prostate
- **Computed tomography (CT) of the abdomen and pelvis without and with intravenous contrast for urography, also called CT urography (CTU).**
- **Intravenous pyelography**
- **Magnetic resonance urography**
- **Cystoscopy** → hemorrhagic cystitis - urinary bladder cancer
  urethral cancer

- **Attention**
- **Macroscopic hematuria should prompt urology referral even if self-limited, with further evaluation of nephrologic disease and malignancy as indicated.**

Risk Factors For Malignancy

- **Male gender**
- **Age >35 years**
- **Past or current smoking history**
- **Occupational exposure to chemicals or dyes (benzenes or aromatic amines),**
- **History of gross hematuria**
- **History of irritative voiding symptoms**
- **History of chronic urinary tract infection**
- **History of pelvic irradiation**
- **History of exposure to cyclophosphamide**
- **History of a chronic indwelling foreign body**
- **History of analgesic abuse**

- **Low-risk patients for urothelial cancer are**
  - **women <50 years**
  - **men <40 years of age who never smoked,**
  - **3 to 10 erythrocytes/hpf**
  - **No additional risk factors for urothelial cancer**

Additional Risk Factors for Urothelial Cancer
Irritative lower tract symptoms
Prior pelvic radiation therapy
Prior chemotherapy with cyclophosphamide or ifosphamide
Family history of urothelial cancer or Lynch syndrome
Occupational exposure to benzene, rubber, petrochemicals, and/or dyes
Chronic indwelling foreign body in the urothelial tract

Low-risk patients should have a repeat urinalysis within 6 months and,

- **if normal, require no additional evaluation.**
- **If repeat urinalysis continues to show hematuria, these patients are reclassified as intermediate risk (<25 erythrocytes/hpf) or high risk (>25 erythrocytes/hpf).**

- **High-risk patients include those with any of the following features:**

1. **>60 years of age,**
2. **>30 pack-year history of smoking,**
3. **>25 erythrocytes/hpf**
4. **gross hematuria.**

High-risk patients require cystoscopy and CT urography, if there are no contraindications, or MR urography.

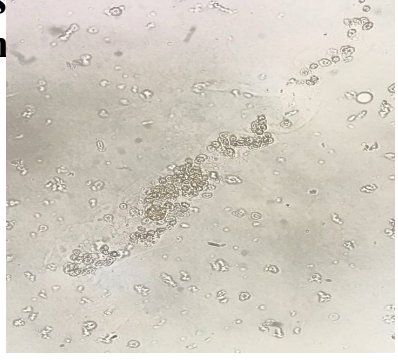
Intermediate-risk Patients Include All Others

Require Prompt Kidney Ultrasonography And Cystoscopy

A 45-year-old man is evaluated for one episode of macroscopic hematuria. He currently does not see blood in his urine. He reports no flank pain and no associated trauma or exertion. He is a nonsmoker and takes no medications.P/E and VS are normal.Lab. studies show a normal serum creatinine level; urinalysis shows 1+ blood, no protein, 10-15 isomorphic RBC/hpf, 0-2 WBC/hpf, no nitrites, and no leukocyte esterase.Contrast-enhanced CT urogram shows no kidney stones, masses, or cysts.Which of the following is the most appropriate diagnostic test to perform next?

1. **Cystoscopy**
2. **Kidney biopsy**
3. **Kidney and renal vein Doppler ultrasonography**
4. **Urine cytology**

A 27-year-old woman is evaluated for a 6-month history of fatigue, arthralgia, and myalgia. She has a history of urinary tract infections. Medications are an oral contraceptive pill and as-needed naproxen for pain. On physical examination, temperature is 38.2 °C (100.8 °F), blood pressure is 142/90 mm Hg, and pulse rate is 90/min. Cardiac, lung, and abdominal examinations are normal. Laboratory studies show a serum creatinine level of 1.4 mg/dL (123.8 µmol/L); urinalysis shows 2+ blood, 3+ protein, positive leukocyte esterase, no nitrites, 10-15 erythrocytes/hpf, 5-10 leukocytes/hpf, and no crystals. Urine microscopy is shown. Which of the following is the m diagnosis?



- **Bladder cancer**
- **Glomerulonephritis**
- **Tubulointerstitial nephritis**

A 16 years old male patient with no previous medical history presented to the ER complain of change of urine color which turned red in the last 2 days, no h/o trauma , Family history insignificant

The patient claimed that 3 days ago he suffered an episode of URTI with sore throat and fever and resolved with paracetamol

The patient denied vomiting , diarrhea , or abdominal pain

Urine analysis: full of RBC , WBC : 40-60 , red cell cast positive and dysmorphic RBC positive

What is the most likely diagnosis :

A. **Ig A nephropathy**

B. **Postinfectious GN** ✗ presentation after 2-3 days

C. **Renal cell cancer** ✗ age . No weight loss , urinary retension, Smoking

D. **pyelonephritis** ✗ No fever, flank pain, vomiting

2-Patients Who Present With Proteinuria ⇒ Serious Condition

- **Proteinuria is an increased amount of protein in the urine and is typically a marker for renal or cardiovascular disease, a risk factor for kidney disease progression, and/or a manifestation of systemic disease in the kidney.**

Risk of Endstage renal failure (ESRF)
Risk for CV diseases → MI, strokes

Normally its accepted ⇒ 150 mg protein in urine daily (30mg albumin 120 Non-albumin)

Types Of Proteinuria: >150mg (clinical proteinuria)

- **Glomerular proteinuria** (albuminuria) results from increased glomerular permeability to large-molecular-weight proteins such as albumin. risk of glomerulonephritis, ESRF

  المرحلة الاولية هينزل albumen (albuminuria) لانه أقل MW بعدها هتنزل more higher MW proteins as HB, transferrin , myoglobin
- **Tubular proteinuria** results from incomplete tubular reabsorption of low-molecular-weight proteins that are normally filtered at the glomerulus. risk for ESRF

  This occur in monoclonal gammopathies (gamma globulin) as MM, light and heavy chain disease, amylodosis, M shape on plasma protein electrophoresis
- **Overflow proteinuria** results from increased plasma concentration of low-molecular-weight proteins such as immunoglobulin light chains, which overwhelms the proximal tubule's capacity for reabsorption.
- **Proteinuria resulting from abnormalities of the lower urinary tract.**

  Urinary bladder(blood with few amounts of protein)
- **Transient proteinuria** (which typically follows a benign, self-limited course and may be caused by congestive heart failure, dehydration, exercise, fever, and acute illnesses), and orthostatic proteinuria.

Benign Condition

Degrees Of Proteinuria:

- < 150 mg/24 hours is normal (normal limit increases to < 300 mg/24 hours during pregnancy)
- 150-500 mg/24 hours is moderate proteinuria
- 500-3,500 mg/24 hours is severe proteinuria
- > 3,500 mg/24 hours is nephrotic-range proteinuria

Total Urine Protein		
Urine Collection Method	Normal	Clinical Proteinuria
24-Hour Excretion	<150 mg/24 h	≥150 mg/24 h
Spot Urine Protein-Creatinine Ratio	≤150 mg/g ≈ ≤150 mg/24 h	>150 mg/g ≈ >150 mg/24 h

Albuminuria

- **Albuminuria as a marker of kidney damage (increased glomerular permeability) is defined as albumin excretion rate ≥ 30 mg/24 hours (approximately equivalent to urine albumin-to-creatinine ratio ≥ 30 mg/g [or 3 mg/mmol] in a spot urine sample).**

Degrees Of Albuminuria

Urine Albumin			
Urine Collection Method	**Normal**	**Moderately Increased Albuminuria (Microalbuminuria)** Now / at first	**Severely Increased Albuminuria (Macroalbuminuria)**
24-Hour Excretion	**<30 mg/24 h**	**30-300 mg/24 h**	**>300 mg/24 h**
Conventional Spot Urine Dipstick	**Negative**	**Negative**	**Positive**
Albumin-Specific Spot Urine Dipstick	**<3.0 mg/dL Negative**	**≥3.0 mg/dL Positive**	**Positive**
Spot Urine Albumin-Creatinine Ratio	**<30 mg/g ≈ <30 mg/24 h** < 3 mg/mmol	**30-300 mg/g ≈ 30-300 mg/24 h** 3 - 30 mg/mmol	**>300 mg/g ≈ >300 mg/24 h** > 30 mg/mmol

Qualitative → Present or Not Quantitative → detect amount

Detection And Measurement Of Total Urinary Protein Excretion

كل ما زادت الكمية وقربت على ال 3g/24h , 300mg albumin /24 h كل ما
sever condition and related to glomerular cause كان الاشي

- **Semiquantitative measurement**

1. **Standard urine dipstick** → شريط يعطي لون معين ونحطه في الurine cup وحسب اللون نحدد عدد الشرطات +1,+2+3
   But it's not accurate as it depends on the conc of urine يعني لو مريض مش شارب مية
   منيح هتكون الارقام اعلى ولو شارب مي كثير هيكون الارقام اقل
   Also it doesn't detect all types of proteins especially tubular proteins (overflow)
   والمريض عنده negative يعني ممكن يعطي MM
2. **Sulfosalicylic acid test** Detect other types of proteins but not present here

- **Quantitative measurement** → الأدق , الأهم
- **24-hour versus spot urine collection**
- **Random (spot) urine protein-creatinine ratio (PCR)**
- **Albumin-creatinine ratio (ACR)**

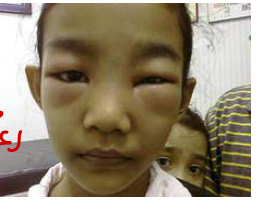
نحسب الأرقام

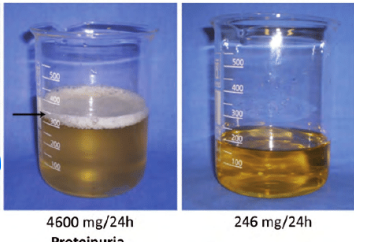
Evaluation Of Patient With Proteinuria

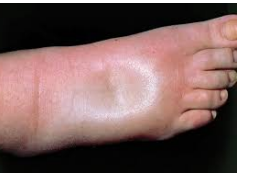
Clinical presentation

- Often **asymptomatic**
- Symptoms , if present, may include:
  - Early morning **periorbital puffiness** due to ↓ oncotic pressure (loss of protein)
  - **Lower extremity edema** in evening — pitting edema
  - Generalized **anasarca** in severe cases — ↳ generalized edema

• foaming urine
• changes in
↳ urine color
↳ volume
↳ odor







History

vasculitis . HF

- **Medical history may reveal a cause, such as diabetes mellitus, malignancy, systemic autoimmune disease, or a prior history of kidney disease.** SLE
- **Ask about recent exercise, fever, or acute illnesses, which may cause transient proteinuria (especially in adolescents and young adults)**
- **Ask about recent fever, heart failure, or seizures (≤ 1 g proteinuria commonly found with these conditions)**
- **Ask about medications or substances known to cause kidney disease**

↳ it's important in proteinuria more than hematuria

With different Mechanism → glomerulonephritis, tubulointerstitial nephritis, change in kidney vascularity (vasoconstriction, vasodilation)

Drugs That May Cause Proteinuria

1. **Nonsteroidal anti-inflammatory drugs** → cause interstitial nephritis
2. **Anabolic steroids interferon**
3. **Penicillamine** → interstitial nephritis
4. **Skin lightening creams (which may contain mercury)**
5. **Pamidronate**
6. **Cyclosporine**
7. **Tacrolimus**
8. **Mitomycin C**
9. **Oral contraceptives**
10. PPI → interstitial nephritis

with different Mechanism → glomerulonephritis, tubulointerstitial nephritis, change in kidney vascularity (vasoconstriction / vasodilation)

Drugs That May Cause Proteinuria

1. **Nonsteroidal anti-inflammatory drugs** → cause interstitial nepheritis
2. **PPIs (omeprazole , esomeprazole, pantoprazole,lansoprazole,etc..)** = & penicillin
3. **Anabolic steroids interferon**
4. **Penicillamine** → cause interstitial nepheritis
5. **Skin lightening creams (which may contain mercury)**
6. **Pamidronate** chemotherapy
7. **Cyclosporine**
8. **Tacrolimus**
9. **Mitomycin C**

- ACIs, ARBs ⇒ treat proteinuria & itself cause proteinuria → affect efferent: efferent arteriole pressure → ↑ permibility

19 oral contraceptive

gold product → cause membranous glomerulonephritis (heavy metal)

- **Family history (FH)**
- **Ask about hereditary nephropathies such as Alport syndrome, familial focal segmental glomerulosclerosis, or immunoglobulin A disease**
- **Ask about family history of autosomal dominant polycystic kidney disease**
- **Social history (SH)**
- **Ask about heroin use (associated with increased risk of glomerular disease)**

↑B.P with DM, CKD, ESRD, atherosclerosis

- **Physical examination** Sec or malignant HT → cause hematuria proteinuria
- **General physical**
- **Check for**
  - **Elevated blood pressure (BP)**
    - **Nephritic syndrome (characterized by low urine output, hematuria with red blood cell casts, renal insufficiency, and edema) or chronic glomerulonephritis may cause elevated blood pressure**
    - **Chronic hypertension may cause renal injury and proteinuria**
  - **Generalized anasarca**

Xanthoma → yellowish plaques at tendon inseration

- **Skin**
- **check for**
  - **white nails and xanthelasmas (yellowish plaques, most commonly near inner canthus of eyelid), which are suggestive of nephrotic syndrome** due to hyperlipidemia
  - **Rash , which may suggest vasculitis**

SLE rash
Henoch-Schönelin purpura
Acute interstitial nepheritis (patient with fever, take NSAIDs, proteinuria, maculopapular rash)

Diagnostic Testing

- **For initial testing of proteinuria, an <u>early morning urine sample</u> is preferred and the following measurements are suggested (in descending order of preference) (<u>KDIGO Level 2, Grade B</u>)**

1. **Urine albumin-to-creatinine ratio (ACR)** → Most accurate as albumin is the first protein to appear
2. **Urine protein-to-creatinine ratio (PCR)**
3. **<u>reagent strip</u> urinalysis for total protein (detects predominantly albumin) with automated or manual reading.**

in Cases required early detection as DM we use ACR

1- urine ACR is preferred over PCR

- **Greater sensitivity than protein to creatinine ratio (PCR) for low levels of proteinuria** early dignosis
- **ACR ≥ 30 mg/g (3 mg/mmol) is considered clinically important proteinuria**
- **if initial ACR is between 3 and 70 mg/mmol (30-700 mg/g), confirm with a subsequent early morning urine sample;**
- **If initial ACR is > 70 mg/mmol (700 mg/g), repeat testing not required**

- **Measure proteinuria with ACR in adults with**

1. **Type 1 or type 2 diabetes**
2. **Estimated glomerular filtration ratio (GFR) < 60 mL/minute/1.73 m2**
3. **Estimated GFR ≥ 60 mL/minute/1.73 m2 if strong suspicion of CKD**

Urinary ACR may be influenced by a variety of factors:

Transient elevation in albuminuria may be caused by:

1. **Menstrual blood contamination of urine sample**
2. **Symptomatic urinary tract infection**
3. **Exercise**
4. **Upright posture (orthostatic proteinuria)**
5. **Heart failure**
6. **Seizures**
7. **Other conditions that increase vascular permeability (such as sepsis)**

So preferred for female out of menstruation

Urine protein-to-creatinine ratio (PCR)

- **PCR - if ACR > 70 mg/mmol, PCR may be an alternative method for measuring and monitoring proteinuria**
- **PCR should be used instead of ACR once albuminuria exceeds 500-1,000 mg/g (50-100 mg/mmol).**

according to differintial diagnosis

Another tests

IgA nephropathy → biopsy . IgA level

Hepatitis B. C → Hepatitis serology

Hepatitis B cause membranous glomerulonephritis
Hepatitis C cause membranoproliferative glomerulonephritis or meseangiocapillary glomerulonephritis
HIV cause focal segmental glomerulisclerosis

- **Microscopic urinalysis may help determine nature of renal pathology**
- **S.Electrolytes**
- **Creatinine and blood urea nitrogen**
- **Albumin**
- **Lipid panel**
- **Fasting blood glucose**
- **Uric acid**

↑ cholestrol → nephrotic syndrome

diapetic nephropathy

- **CBC**
- **ESR**
- **Serologic tests (antistreptolysin O, antinuclear antibody, antineutrophil cytoplasmic antibodies (ANCA), viral titers)**
- **Serum protein electrophoresis**
- **liver enzymes**
- **Complement levels**
- **Serum Free light chains**

→ P-ANCA . C-ANCA

→ for vasculitis

MM

SLE ⇒ double stranded DNA , RNA , anti histon antibody

HF ⇒ ECG

post streptococcal → antistreptolysin antibody , ↓ Complement levels

Microscopic Urinalysis

- **Presence of WBC typically suggests UTI, but may also be seen with**
  - **Glomerulonephritis**
  - **Allergic (usually drug-induced) acute interstitial nephritis**
- **RBCs**
- **Casts**

Granular muddy cast → Acute tubular interstitial nephritis

  - **Erythrocyte casts suggest glomerular disease or vasculitis**
  - **Granular casts (with tubular cells) may suggest acute tubular necrosis**
  - **White blood cell casts may be seen with acute pyelonephritis, tubulointerstitial disease such as acute interstitial nephritis, or glomerular disease**
  - **Fat and/or Maltese crosses (present under polarized light) associated with nephrotic-range proteinuria and nephrotic syndrome**
  - **Granular and waxy casts may be present with any proteinuric condition**
  - **hyaline casts are present in normal urine and are not associated with renal disease**
- **Hexagonal cystine crystals indicate hereditary cystinuria**

Other tests

- **Renal ultrasound for evidence of structural renal disease**
- **Renal biopsy may be indicated to confirm diagnosis of underlying disease in patients without reduced glomerular filtration rate but with:**

1. **Microscopic hematuria and any proteinuria after exclusion of infection and urologic causes (usually associated with hypertension and presence of serum biomarkers such as ANCA or double-stranded DNA)**
2. **Proteinuria > 1-2 g/day and bland urinary sediment**
3. **Signs or symptoms of systemic disease such as collagen vascular diseases or infectious diseases with or without positive serologies but with urinary abnormalities (hematuria, proteinuria)**
4. **Diabetes < 5-10 years without retinopathy or neuropathy**
5. **Transplant is being considered** transplanted kidney

Rule Out Transient Proteinuria

- Transient proteinuria is common, especially in young individuals.
- Transient proteinuria has been reported in 8 - 12 % of individuals younger than 18 years and in approximately 4 % of college-aged adults.
- Transient proteinuria is diagnosed if a repeat qualitative test is no longer positive for proteinuria.
- These patients need no further evaluation and should be reassured that they do not have kidney disease.

- **Transient proteinuria can occur with fever and exercise, perhaps mediated by angiotensin II or norepinephrine-induced alterations in glomerular permeability, as well as with symptomatic urinary tract infection.**
- **When quantified, proteinuria in such patients is generally less than 1 g/day.**
- **With marked exercise, protein excretion can exceed 1.5 mg/min in normal subjects (which is the equivalent of more than 2 g/day if sustained).**
- **Exercise is also associated with hematuria and occasionally red blood cell casts, suggesting that the proteinuria is likely glomerular in origin.**

Rule out orthostatic proteinuria

- **Orthostatic proteinuria is characterized by increased protein excretion in the upright position but normal protein excretion when the patient is supine.**
- **The mechanism by which orthostatic proteinuria occurs is unclear, but neurohumoral activation and altered glomerular hemodynamics may be important.**
- **Total protein excretion is generally less than 1 g/day in orthostatic proteinuria but may exceed 3.5 g/day in selected patients**
- **Orthostatic proteinuria is a relatively common finding in adolescents (occurring in 2 to 5 percent) but an uncommon disorder in adults over the age of 30 years.**
- **It is a benign condition that does not require extensive evaluation (such as a kidney biopsy) or specific therapy.**
- **However, kidney function and proteinuria should be followed yearly**

How to diagnose orthostatic proteinuria?

- **The first-morning void is discarded.**
- **An upright collection is obtained during the waking hours while the patient is performing normal activities. The patient should finish this collection by voiding just prior to going to sleep.**
- **The patient should then assume the recumbent position and collect nighttime urine (including a void immediately after waking in the morning) into a separate container.**
- **The protein excretion is quantified on the upright collection (which should be abnormal) and the recumbent collection (which should be normal if the patient has orthostatic**

- A 65-year-old man is evaluated for a 2-month history of low back pain. The pain is worse with movement, but it does not radiate. He reports associated fatigue and a 4.5-kg (10-lb) weight loss. He has osteoarthritis and GERD. He has been taking ibuprofen without any pain relief. His only other medication is omeprazole.The P/E, including VS and neurologic examination, is normal. Laboratory studies:
- HGB 9.2 g/dL (92 g/L) , Creatinine 3.0 mg/dL (265.2 µmol/L), S.calcium 12.4 mg/dl
- Urinalysis: Trace protein; no erythrocytes, leukocytes, leukocyte esterase, or nitrites
- Urine protein-creatinine ratio 2500 mg/g
- US reveals normal-sized kidneys with slightly increased echogenicity; no hydronephrosis or abnormalities of the collecting system are seen. In addition to discontinuing ibuprofen, which of the following is the most appropriate next step in management?

1. Discontinue omeprazole
2. Obtain a 24-hour urine protein collection
3. Obtain a noncontrast helical abdominal CT
4. Obtain a urine protein electrophoresis

Approach to AKI

- **Acute kidney injury (AKI) is a rapid reduction in kidney function (within 48 hours) as measured by an increase in serum creatinine, decrease in urine output, and/or need for renal replacement therapy.**
- **It is characterized by either direct injury to the kidney or acute impairment of function or both.**

- **<u>Diagnose AKI</u> in patients with any of the following:**

1. **Increase in serum creatinine by ≥ 0.3 mg/dL (≥ 26.5 mcmol/L) within 48 hours**
2. **Increase in serum creatinine to ≥ 1.5 times baseline, which is known or presumed to have occurred within prior 7 days**
3. **Urine volume < 0.5 mL/kg/hour for 6 hours**

Causes of AKI

- **Prerenal azotemia** (often associated with elevated blood urea urea/ cr ratio > 20:1 and low fractional excretion of sodium)
- **Postrenal obstruction** (due to either extrarenal obstruction of urinary flow, or intrarenal obstruction due to crystals, clots, stones, or tumors)
- **Renal** causes:

1. Tubular disorders including **acute tubular necrosis** (which can be toxic or ischemic) or acute interstitial nephritis
2. Glomerulonephritis (such as systemic lupus erythematosus [sle], iga nephropathy, membranous glomerulonephritis, focal segmental glomerulosclerosis [fsgs], antineutrophil cytoplasmic antibodies [anca] associated vasculitis, antiglomerular basement membrane [anti-gbm] disease, and thrombotic microangiopathy)
3. Vascular diseases including renal atheroembolic disease and malignant hypertension

Clinical presentation

- Acute kidney injury (AKI) is generally asymptomatic until onset of kidney failure
- Patients may present with abnormal urinary output, which may include
  - Anuria
  - Oliguria
  - Polyuria
- Presentation may vary depending on cause of AKI
  - Symptoms and conditions that may suggest prerenal AKI
    - Thirst And Reduced Fluid Intake
    - Vomiting
    - Diarrhea
    - Bleeding

- **Symptoms and signs that may suggest intrinsic AKI (in addition to those seen with prerenal)**
  - **Weight Loss**
  - **Fever**
  - **Myalgias, Arthralgias, Or Arthritis**
  - **Rash**
  - **Cough including Hemoptysis**
- **Symptoms and signs that may suggest postrenal AKI (usually asymptomatic)**
  - **Urinary urgency or hesitancy**
  - **Blood in urine**
  - **Complete anuria**
  - **Renal angle pain**

Symptoms in severe cases may include

- **Confusion**
- **Lethargy**
- **Nausea and vomiting**
- **Weight gain due to fluid retention**

History of present illness (HPI)

- **Ask about symptoms that may suggest cause of AKI:**
  - **vomiting, diarrhea, significant blood loss, or shock may indicate systemic volume depletion**
  - **Trauma or prolonged immobilization may indicate rhabdomyolysis**
  - **fever, maculopapular erythematous rash, and arthralgias may suggest acute interstitial nephritis**
  - **Presence of flank pain or history of urolithiasis, GUT neoplasia, or retroperitoneal disease may suggest obstruction.**
  - **Dysuria , suprapubic pain, slow urine stream, and increased frequency of urination may indicate lower urinary tract disease**

- **Ask about previous urea, serum creatinine, and lytes results.**
- **Previous health checks.**
- **Ask about medications:**

- Angiotensin converting-enzyme inhibitors
- Angiotensin receptor blockers
- Direct renin inhibitors
- Calcineurin inhibitors
- NSAIDs
- Amphotericin
- Beta -lactam antibiotics
- Sulfonamides
- Vancomycin
- Acyclovir

- Cisplatin or carboplatin
- Ifosfamide
- PPI
- Herbal and dietary supplements
- vascular endothelial growth factor inhibitors (for example, pazopanib or sunitinib)
- Aminoglycosides
- Iodinated radiocontrast media
- Diuretics (overuse)
- Tenofovir
- Methotrexate

- **Past medical history (PMH)**
- **Ask about history of chronic illnesses, including**
  - **Chronic Kidney Disease**
  - **Diabetes Mellitus**
  - **Hypertension**
  - **Heart Failure**
  - **Peripheral Artery Disease (PAD)**
  - **Liver Failure**
  - **Infections such as HIV, hepatitis, or other infections**
  - **Autoimmune disease, such as SLE, rheumatoid arthritis , or systemic sclerosis**

- **If warranted, obtain information about exposure to waterways, sewage systems, and rodents to identify possible causes such as malaria, leptospirosis, or hantavirus.**
- **Ask about recent travel or exposure to infectious diseases**

Physical examination

- **Check blood pressure(BP)**
- **Evaluate fluid status by assessing**
- **Look for signs of acute and chronic heart failure, infection, and sepsis**
- **Fever may occur with infection or acute interstitial nephritis**
- **Skin exam may identify features of underlying causes or associated conditions skin lesions for example:**

1. **Palpable purpura may suggest vasculitis.**
2. **Fine maculopapular rash may suggest drug-induced interstitial nephritis.**
3. **Livedo reticularis, purple toes, and other signs may suggest atheroembolic disease**
4. **Skin thickening may suggest systemic sclerosis**

- **Neck exam for jugular venous pressure and carotid pulses and sounds may help detect HF**
- **Lungs : Pulmonary edema**
- **Heart : IE. Gallop rythm**

- **Abdominal findings suggestive of acute kidney injury (AKI) may include**
  - **Evidence of vascular disease including bruits or palpable abdominal aortic aneurysm**
  - **Masses that could be malignant**
  - **Enlarged or tender kidneys**
  - **Distended bladder**
  - **Possible sources of bacterial infection**
  - **Evidence of liver disease**
  - **Intra -abdominal pressure (may be assessed by measuring bladder pressure) > 20 mm Hg (may occur after trauma, abdominal surgery, or secondary to massive fluid resuscitation)**

Diagnostic Testing

- Measure serum creatinine and urine output to detect AKI
- Determine cause of AKI whenever possible
- Evaluate patients with AKI promptly to determine cause with special attention to reversible causes
- Determine staging of AKI by monitoring serum creatinine and urine output in patients with AKI

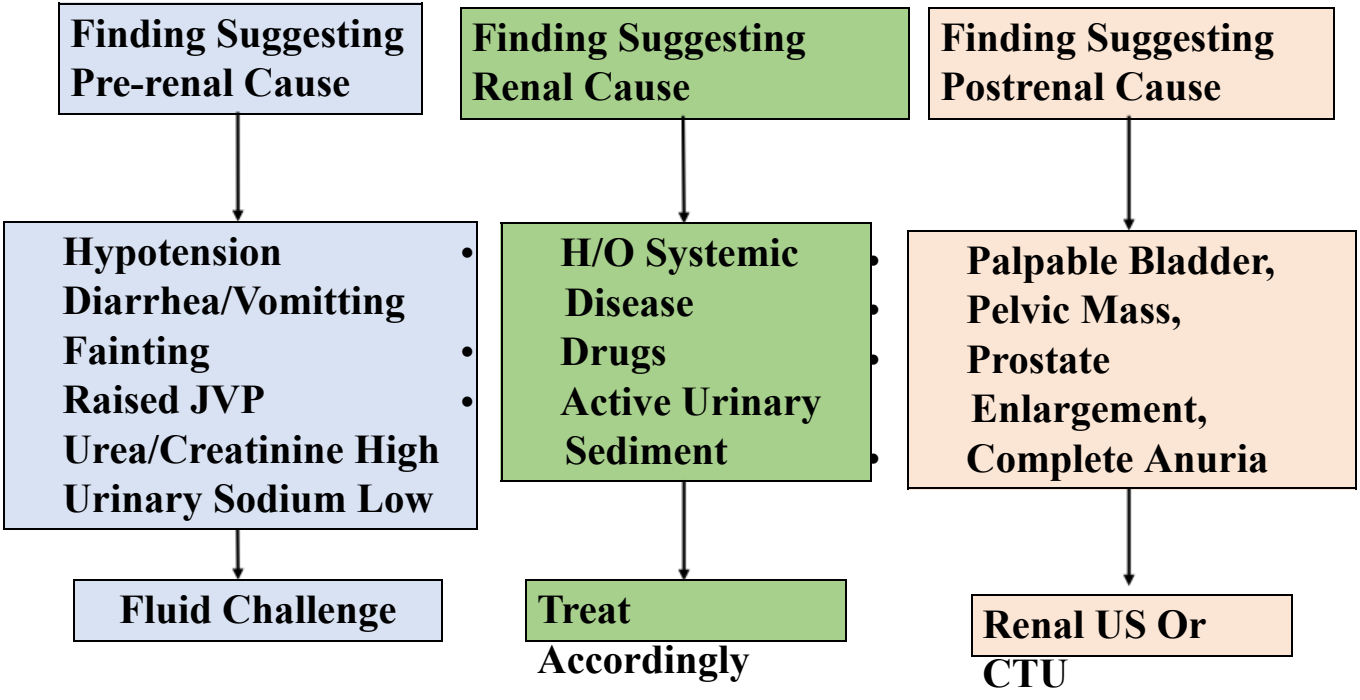
- **Initial testing for acute kidney injury (AKI) should include**
  - **Blood Urea Nitrogen (BUN)**
  - **Serum Creatinine**
  - **Electrolytes**
  - **Fractional Excretion Of Sodium (Fena)**
  - **Complete Blood Count**
  - **Urinalysis**
  - **Renal ultrasound as first-line imaging test to rule out obstruction**
- **Biopsy may be indicated where conditions such as glomerulonephritis or vasculitis are suspected**

Algorithm

- **Rule out presence of chronic kidney disease (CKD)evaluate**

1. **Renal size and cortical thickness using renal ultrasound (reduction in size may indicate CKD).**
2. **Previous serum creatinine measurement**

- **In absence of previous serum creatinine measurement, assess for anemia, hyperphosphatemia, hypocalcemia, nocturia, acute illness, and duration of symptoms**


Finding Suggesting Pre-renal Cause
Finding Suggesting Renal Cause
Finding Suggesting Postrenal Cause
Hypotension
Diarrhea/Vomitting
Fainting
Raised JVP
Urea/Creatinine High
Urinary Sodium Low
H/O Systemic Disease
Drugs
Active Urinary Sediment
Palpable Bladder, Pelvic Mass, Prostate Enlargement, Complete Anuria
Fluid Challenge
Treat Accordingly
Renal US Or CTU

Thank You