

Urinalysis Interpretation: A Practical Guide

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URINALYSIS INTERPRETATION: PRACTICAL GUIDE

PA/Medical Student Handout

LEARNING OBJECTIVES

By the end of this module, you will be able to:

1. **Understand dipstick chemistry** and limitations
 2. **Interpret proteinuria** (dipstick vs. quantitative measures)
 3. **Differentiate hematuria** from other causes of color
 4. **Recognize false positives/negatives** in proteinuria and hematuria
 5. **Interpret microscopy findings** (casts, crystals, cells)
 6. **Apply urinalysis to clinical scenarios** (UTI, GN, CKD, nephrotic syndrome)
 7. **Know when to send urine cultures** and specialized tests
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SECTION 1: DIPSTICK BASICS

How Dipstick Works

Reagent Pads on Standard Dipstick:

| Component | Chemical Reaction | What It Detects |
|---------------------------|---------------------------------|--|
| Protein | pH indicator (bromophenol blue) | Albumin primarily; insensitive to Bence Jones proteins |
| Glucose | Glucose oxidase | Free glucose (filtered at normal GFR) |
| Ketones | Nitroprusside reaction | Ketones (DKA, starvation) |
| Blood/RBC | Peroxidase-like activity | Heme, hemoglobin, myoglobin |
| Nitrites | Griess reaction | Gram-negative bacteria (<i>E. coli</i>) |
| Leukocyte esterase | Indoxyl carbinol | WBC (neutrophil granules); also some bacteria |
| pH | Methyl red/methylene blue | Urine pH |
| Specific gravity | Change in pKa | Urine concentration |

| Component | Chemical Reaction | What It Detects |
|---------------------|-------------------|----------------------|
| Bilirubin | Diazo reagent | Conjugated bilirubin |
| Urobilinogen | Ehrlich reaction | Urobilinogen |

Timing and Storage

- **Read at correct time:** Usually 60 seconds (varies by manufacturer)
- **Exposure to light:** Degrades reagents
- **Temperature:** Cold urine may give false negatives
- **Air exposure:** Nitrites and leukocyte esterase degrade
- **Refrigeration:** Prolongs accuracy; room temperature deteriorates within 2 hours

SECTION 2: PROTEIN IN URINE

Dipstick Proteinuria Interpretation

Dipstick Grading: - **Negative:** <10 mg/dL - **Trace:** 10-15 mg/dL - **1+:** 30 mg/dL - **2+:** 100 mg/dL - **3+:** 300 mg/dL - **4+:** ≥1000 mg/dL (nephrotic-range)

Critical Limitations of Dipstick

False Positives (positive dipstick with low actual protein): 1. **Concentrated urine** (high specific gravity, dehydration) 2. **Alkaline urine** (pH >7; dipstick more sensitive in alkaline conditions) 3. **Gross hematuria** (hemoglobin itself positive with dipstick) 4. **Contaminating blood** (even from traumatic catheterization) 5. **Quaternary ammonium compounds** (residual anti-septic on collection containers) 6. **Contrast agents** (from recent imaging)

False Negatives (negative dipstick with actual proteinuria): 1. **Bence Jones proteins** (immunoglobulin light chains; multiple myeloma) - Dipstick primarily detects albumin - Light chain proteins may not react - Require specialized tests (serum/urine protein electrophoresis, free light chains)

2. **Myoglobin** (rhabdomyolysis)
 - Small molecular weight
 - May be missed or underestimated by dipstick
3. **Dilute urine** (excessive hydration)
 - Protein concentration too low to trigger dipstick

Quantifying Proteinuria

When to use QUANTITATIVE measures: - Dipstick ≥1+ (significant) - Ongoing monitoring needed - Nephrotic syndrome workup - CKD monitoring

Available Tests:

| Test | Specimen | Advantages | Disadvantages |
|--|----------------------|---|---------------------------------------|
| Spot Urine ACR | Random (most common) | Easy, convenient, best for ongoing monitoring | Affected by timing, posture |
| Spot Urine PCR | Random | Includes all proteins | Albumin-specific assay needed for ACR |
| 24-Hour Urine | Timed collection | Gold standard; captures variation | Burdensome; collection errors common |
| Urinary Protein Electrophoresis | Random or 24h | Identifies protein type | Specialized; expensive |
| Serum/Urinary Free Light Chains | Serum + random urine | Detects light chain disease | Expensive; not routine |

Interpreting Spot ACR/PCR:

| Protein Level | ACR (mg/g) | PCR (mg/g) | Clinical Significance |
|-------------------------|------------|------------|--|
| Microalbuminuria | 30-300 | 50-500 | Diabetes, early CKD; requires intervention |
| Nephrotic range | >300 | >500 | Nephrotic syndrome; requires kidney biopsy |

SECTION 3: HEMATURIA

Dipstick Blood/RBC Interpretation

Dipstick Blood Positive Indicates: - RBCs - Hemoglobin (from lysed RBCs) - Myoglobin (muscle breakdown) - **Cannot distinguish between them**

Microscopy Differentiation

With RBCs on microscopy (dysmorphic): - True hematuria (from kidney or urinary tract) - If RBC casts present **glomerulonephritis** (RPGN, IgAN, etc.)

Without RBCs on microscopy (dipstick positive): - Hemoglobinuria (intravascular hemolysis) - Myoglobinuria (rhabdomyolysis) - **False positive** (from other causes below)

False Positives for Hematuria

Cause 1: Contaminating Blood - Traumatic catheterization - Menses in women - Hematospermia in men - Management: Repeat clean-catch specimen; wait 48 hours if traumatic catheterization

Cause 2: Pigmenturia (Hemoglobin-Like) - Hemoglobinuria (intravascular hemolysis) - Severe hemolysis □ hemoglobin exceeds renal reabsorption capacity - Dipstick positive; no RBCs on microscopy - Management: Check free plasma hemoglobin, LDH, bilirubin, reticulocyte count

- **Myoglobinuria** (rhabdomyolysis)
 - Muscle breakdown releases myoglobin
 - Dipstick positive; no RBCs on microscopy
 - Associated with CK elevation, brown urine color
 - Management: Check CK, urine myoglobin, creatinine (AKI risk)

Cause 3: Oxidizing Agents - Hydrogen peroxide contamination - Bleach exposure - Rare but documented

Clinical Approach to Hematuria

Step 1: Microscopy - RBCs present? (True hematuria) - RBC casts? (Glomerulonephritis) - No RBCs? (Hemoglobinuria or myoglobinuria)

Step 2: Additional Tests if Needed - Free plasma hemoglobin (hemolysis) - Creatine kinase (rhabdomyolysis) - LDH, bilirubin, reticulocyte count (hemolysis workup) - Urine myoglobin (rhabdomyolysis)

Step 3: Clinical Context - Dysmorphic RBCs + RBC casts = **Glomerulonephritis** (biopsy candidate) - Isomorphic RBCs without casts = **Lower urinary tract source** (cystitis, stone, malignancy) - No RBCs + positive dipstick = **Hemoglobinuria or myoglobinuria** (investigate cause)

SECTION 4: MICROSCOPY FINDINGS

Cells in Urine

| Finding | Normal | Abnormal Significance |
|-------------------------|---------|---|
| RBCs | 0-3/lpf | >5 = hematuria; dysmorphic = GN |
| WBCs | 0-5/lpf | >5 = pyuria (UTI, pyelonephritis, interstitial nephritis) |
| Bacteria | None | Present in UTI; should correlate with LE+ and nitrites |
| Epithelial cells | Few | Numerous = contaminated specimen (improper collection) |
| Squamous cells | Few | Numerous = contaminated (urethral epithelium) |

Casts

What are Casts? - Cylindrical protein precipitates formed in collecting duct - Composed of Tamm-Horsfall protein (uromodulin) + cellular inclusions - Always abnormal (except rare hyaline in concentrated urine)

| Cast Type | Meaning | Associated Condition |
|----------------------------------|----------------------------|---|
| RBC casts | RBCs in cast matrix | ALWAYS means glomerulonephritis (urgent biopsy) |
| WBC casts | WBCs in cast matrix | Pyelonephritis, interstitial nephritis, SLE |
| Granular casts | Granular debris | Non-specific; CKD, acute illness |
| Muddy brown casts | Cellular debris, myoglobin | Acute tubular necrosis (AKI) |
| Waxy casts | Degenerated cellular cast | Chronic kidney disease (ominous) |
| Hyaline casts | Tamm-Horsfall protein only | May be normal in concentrated urine; otherwise abnormal |
| Fatty casts | Fat droplets in matrix | Nephrotic syndrome |
| Broad/renal failure casts | Large diameter casts | Severe CKD, renal failure |

Crystals

| Crystal | pH | Clinical Significance |
|--|----------|---|
| Calcium oxalate | Acidic | Normal finding; >100/lpf suggests stone disease |
| Uric acid | Acidic | Normal; excessive in gout, tumor lysis syndrome |
| Calcium phosphate | Alkaline | Normal |
| Triple phosphate (struvite) | Alkaline | Urease-producing bacteria (Proteus); stone disease |
| Bence Jones (immunoglobulin light chains) | Variable | Multiple myeloma (requires serum/urine protein electrophoresis for confirmation) |
| Cystine | Acidic | Cystinosis (genetic disorder) |

Microorganisms

Bacteria: - **None:** Normal - **Few:** Likely contamination - **Numerous (>5/lpf):** Suggests UTI; quantify with culture

Yeast (Candida): - Vaginal contamination (women) - True candiduria (catheters, immunocompromised) - Usually not clinically significant unless symptoms present

SECTION 5: SPECIAL SITUATIONS

Orthostatic Proteinuria

Definition: Protein present in daytime urine but absent in overnight urine

Characteristics: - More common in young, tall, thin males (5-15%) - Completely **benign**; excellent long-term prognosis - Due to postural changes and increased capillary pressure upright

Diagnosis: - Split collection: daytime vs. overnight urine - Daytime shows protein; overnight shows none - Can follow up with repeat spot urine in morning

Clinical Pearl: If orthostatic proteinuria diagnosed, reassure patient and no further workup needed

Transient Proteinuria

Causes: - Fever - Stress - Seizures - Extreme exercise (marathon running can reach nephrotic levels) - Vigorous physical activity

Management: - Repeat testing when patient returns to baseline - Usually resolves within 24-48 hours

Contamination Issues

Signs of Contamination: - **Numerous squamous epithelial cells** (>5/lpf) = improperly collected specimen - **Numerous bacteria without pyuria** = likely contamination - **RBCs + bacteria in female** = consider menses as source

Proper Collection: - Women: Cleanse urethral meatus; midstream catch - Men: Retract foreskin; midstream catch - Avoid external contamination

SECTION 6: URINE CULTURE

When to Culture

Send Culture When: - Pyuria (WBC >5/lpf) + symptoms of UTI - Hematuria + pyuria (rule out infection) - Fever + lower abdominal pain - Pyelonephritis symptoms (fever, flank pain, CVA tenderness) - Catheterized patients with symptoms - Asymptomatic bacteriuria (only in pregnancy, pre-urologic procedures)

Do NOT Culture: - Asymptomatic bacteriuria (except pregnancy) - Pyuria without symptoms (low positive predictive value) - Prophylactic culture in non-pregnant, non-procedure patients

Interpreting Culture Results

| Colony Count | Clinical Significance |
|--|---|
| <10,000 CFU/mL | Likely contamination |
| 10,000-100,000 CFU/mL | Borderline; repeat if symptomatic |
| >100,000 CFU/mL single organism | UTI (if symptoms present) |
| Multiple organisms | Likely contamination; repeat collection |

SECTION 7: CLINICAL PEARLS

- Dipstick is SCREENING tool**, not diagnostic
 - Protein dipstick limited**: Albumin-specific; misses light chains, myoglobin
 - Always correlate dipstick with microscopy** (never interpret in isolation)
 - RBC casts = GLOMERULONEPHRITIS until proven otherwise** (urgent evaluation needed)
 - Hematuria without RBCs on microscopy** = hemoglobinuria or myoglobinuria (investigate further)
 - Contaminating epithelial cells** indicate improper collection; repeat if present
 - Orthostatic proteinuria benign** and requires no further workup once recognized
 - 24-hour urine gold standard** but collection errors common; spot ACR acceptable alternative
 - Asymptomatic bacteriuria treatment NOT recommended** except in pregnancy
 - Urine culture only helpful if symptoms present** (high contamination rates in screening)
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PRACTICE QUESTIONS

Question 1: A 28-year-old woman presents with dysuria. Urinalysis shows: dipstick trace protein, 2+ blood, LE+, nitrites+. Microscopy: 15 RBCs/lpf, 25 WBCs/lpf, 1 RBC cast, gram-negative rods. What is your NEXT step?

- A) Prescribe empiric nitrofurantoin for UTI
- B) Order blood cultures
- C) Refer for urgent kidney biopsy
- D) Send urine culture; repeat UA in 1 week

Answer: C - RBC CASTS = GLOMERULONEPHRITIS. This is NOT simple cystitis. The presence of RBC casts indicates glomerular disease (possibly IgAN, post-infectious GN, lupus, vasculitis). While LE+ and nitrites suggest bacterial infection, the RBC casts override this interpretation. She needs: - Urgent nephrology referral - Kidney biopsy for definitive diagnosis - Serologies (ANA, ANCA, anti-GBM, complement) - Blood cultures only if septic appearance

Question 2: A 35-year-old man with fever (102°F), flank pain, and dysuria presents with UA showing: dipstick 3+ blood, LE+, WBCs 50/lpf, bacteria abundant. Microscopy shows isomorphic RBCs, WBCs, no casts. Which diagnosis is MOST likely?

- A) Acute glomerulonephritis
- B) Acute pyelonephritis
- C) Rhabdomyolysis
- D) Hemolytic anemia

Answer: B - Pyelonephritis. The key findings: - Isomorphic RBCs (NOT dysmorphic/RBC casts) = lower urinary tract source - NO RBC casts = NOT glomerulonephritis - Abundant bacteria

+ LE+ + WBC + fever + flank pain = **PYELONEPHRITIS** - Management: Blood cultures, urine culture, empiric antibiotics (fluoroquinolone or cephalosporin)

Question 3: A 65-year-old woman with CKD Stage 4 has routine UA showing: 2+ protein, trace blood. Microscopy: 2 RBCs/lpf, no casts. What action is MOST appropriate?

- A) Start ACE-inhibitor and recheck UA in 3 months
- B) Urgent kidney biopsy
- C) Refer for dialysis
- D) Quantify with spot ACR/PCR; monitor CKD with regular labs

Answer: D - Proteinuria in CKD requires QUANTIFICATION, not just dipstick grading. The trace blood with normal RBC count (no casts) is NOT concerning for glomerulonephritis. Management: - Spot ACR or 24-hour urine PCR to assess protein burden - Blood pressure control, ACE-I/ARB if proteinuric - Monitor eGFR slope - Biopsy only if atypical features (sudden worsening, active urinary sediment with casts)

KEY TAKEAWAYS

- Dipstick is screening tool** with significant limitations; correlate with microscopy
 - RBC casts ALWAYS abnormal** = glomerulonephritis (urgent evaluation)
 - Hematuria without RBCs** = hemoglobinuria or myoglobinuria (investigate further)
 - Proteinuria requires quantification** with ACR/PCR (dipstick insufficient)
 - Bence Jones proteins missed by dipstick** = risk in myeloma patients
 - Orthostatic proteinuria benign** once recognized; no further workup
 - Contamination common** with improper collection; repeat if epithelial cells abundant
 - Culture only helpful if symptoms present** (high false-positive rate in asymptomatic patients)
 - Pyuria without bacteriuria** suggests non-infectious causes (interstitial nephritis, GN)
 - Always interpret UA in clinical context** (symptoms, vitals, other lab findings)
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RELATED CLINICAL NOTES

- Urinary Tract Infection - UTI diagnosis and treatment
 - Glomerulonephritis - GN classification and workup
 - Hematuria Evaluation - Detailed hematuria workup
 - Proteinuria Management - Proteinuria monitoring
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This handout is designed for PA/medical student education. Always consult institutional protocols and clinical context for patient management.