Urine the Know: Interpreting the Urinalysis in Children
1 – 1:45 p.m.

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I have no relevant financial relationships to disclose.
Objectives

1. Utilize the urinalysis effectively in different pediatric case scenarios

2. Avoid the pitfalls of false positive results that can occur in the urinalysis in children
History of Urine Analysis
Urinalysis

• 400 B.C. Hippocrates wrote on the observations of urine as an indicator of health

• 1922 Stanley Benedict, a 17 year old medical student, published on detection of glycosuria; Benedict’s solution in JAMA

• 1956 arrival of the dipstick “Clinistix”

• 30 years later, the Multistix 10 S.G.
Urinalysis

• One of the most commonly ordered tests in pediatrics

• Utility is 2-fold:
  – Detect metabolic or endocrine derangements
  – Detect diseases of the kidney

• How to interpret and avoid the pitfalls of over interpretation
- Fresh specimen <1 hr old or refrigerated
- Bagged specimen or "clean catch", mid-stream void
Case 1

- The mother of a 6 year old boy calls you for concerns over “cloudy urine”. He has no urinary symptoms or fever
- In the office you collect a urinalysis and it shows a sp. gravity of 1.020, pH 5.5, negative leukocyte esterase and nitrites, negative heme, protein, glucose. A urine culture is negative
- This continues for a long time and mother remains concerned
Appearance: When “cloudy” is normal

Normal Crystals in Acid Urine

- Uric acid
- Amorphous Urates
- Calcium Oxalates
pH and specific gravity

- Urine pH ranges between 5-8.0 in normal health
- Western diets result in urinary pH ~6.0
- Urine pH is increased (alkaline) in vegetarian diets and high milk, dairy intake
- Urine pH is helpful in situations of metabolic acidosis or in kidney stone formation
Case 2

- A 1 year old is otherwise well but has fallen off his growth curve for both height and weight to <3 %ile
- Labs: Na 135, K+ 3.0, Cl 112; HCO3 15
- Anion gap is 11 (normal)
- UA shows sp. gr. 1.015, pH 7.5, negative heme, protein, glucose, ketones, nitrites, L.E.
- Kidney ultrasound shows nephrocalcinosis
Metabolic Acidosis

• Urine pH will reflect acidosis or alkalosis
• If the urine pH is “inappropriate”, then consider underlying renal disease
• Renal Tubular Acidosis: Inability to acidify the urine in the context of a metabolic acidosis
  – FTT (height and weight); hypokalemia, hypercalciuria, nephrocalcinosis
Specific Gravity

- Specific gravity = \( \frac{\text{Weight of urine}}{\text{Weight of water}} \)
- Normal 1.000-1.035
- **Fixed sp.grav \( \leq 1.010 \)** indicates a disturbance in urinary concentrating ability
Case 3

• A 2 year old boy is in the ED with 1 day of vomiting and found to be moderately dehydrated. His mother gives the history that he was toilet trained 6 months ago but is now wetting the bed every night.

• A UA showed a sp.grav. 1.010, pH 6 negative heme, protein, glucose, ketones, nit, L.E.
Urinary concentrating defect

• Na 146, K 4.5, Cl 105, BUN 28, creatinine 0.4
• Serum osm 308 (nl=298) and Urine osm is 300
• You later find out he has been observed drinking from the dog’s water dish over the past month.
The parents of a 2 year old boy are concerned that he seems to be always “drinking a lot”. He takes milk, juice, water from his cup all day long. They estimate he drinks 80 ounces per day and he cries if he does not get his bottle at bedtime. His diapers are soaked and changed 5-6x/day.
Is it a urinary concentrating defect?

• Labs: Na 138, K 4.0, Cl 100, HCO3 24, BUN 10 creatinine 0.38
• UA: sp.gr. 1.010, pH 5.5, negative heme, protein, ketones, glucose, LE and nitrites
• Ht/Wt are both 50%ile; His P.E. is normal.
• Parents state that most nights he can sleep through the night
Mini-water deprivation testing at home

• You ask that he be NPO overnight for 8-10 hours

• Collect a first morning voided urine:
  – UA: sp.gr.1.020; negative glucose
  – Urine osm 710
  – Serum osm 298, Na 136

• Reassurance is given
Heme

- Dipstick is VERY sensitive and detects both RBCs and also free hemoglobin
- Transient hematuria is common in healthy children
  - 4% school age children tested positive for heme in at least 1 out 4 serial specimens
    - Of these pts, 6% had tested positive in 4/4
    - Testing at least 3 specimens on separate occasions is current recommended practice
• The dipstick detects free hemoglobin and myoglobin
  – May indicate hemolysis or rhabdomyolysis
  – Hematuria: If specimen stands long enough, the RBCs may lyse and still test positive
  – Normal UA should test negative, but “trace” heme readings are usually not clinically significant
Hematuria

• Extensive differential diagnosis: Helpful Tips
  – Gross hematuria vs. microhematuria
    • Blood clots indicate lower urinary tract bleeding
  – Associated with pain vs. being painless
    • Glomerular diseases have painless hematuria (except for rare c/o of vague flank pain)
  – Proteinuria vs. no proteinuria
    • >2+ is a “red flag” for glomerular disease
• A 7 year old presents with abdominal pain and a UA shows 2+ heme, negative protein, 10-20 RBC/hpf. The pain resolves, but repeat UA’s over the next 2 months continue to show microhematuria.
Asymptomatic microscopic hematuria

- Glomerulonephritis
- TBM disease
- UTI
- Urolithiasis
- Sickle cell
- Hypercalciuria
- Cystic kidney

UTI
Viral cystitis
Urethritis
Trauma
Tumor

- Tumor
- Vascular anomalies
- Thrombosis
- Urolithiasis
- Hydronephrosis

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Asymptomatic Microscopic Hematuria
Limited Evaluation

• History and physical
  – Family history: kidney disease (dialysis, kidney transplant), hearing loss, kidney stones
  – Review of systems: Pain, trauma, joints, skin, weight loss, fever, hearing loss, edema, urinary symptoms, medications

• Renal ultrasound: noninvasive, low cost

• Urine calcium to creatinine ratio

• Monitor with routine physical exams
Case 5: follow-up

- Renal US normal
- Urine calcium to creatinine ratio is 0.10 (nl <0.22)
- His mother later informs you his 40 year old maternal uncle has kidney disease and is awaiting a kidney transplant and wears a hearing aid
- Mother recalls she has hematuria noted during one of her pregnancies.
Asymptomatic microscopic hematuria

• Persistent with absence of proteinuria
  – Hypercalciuria
    • In absence of kidney stone disease, observe
  – Familial causes: Thin Basement membrane disease and Alport’s syndrome
    • Alport’s: X-linked disease most common, but autosomal dominant and recessive are known
    • “Benign familial hematuria” is considered a form of Thin Basement Membrane disease, an autosomal recessive form of Alport’s syndrome
    • Long-term outcomes may not be benign
Protein

- Normal excretion of small amount of albumin and low molecular weight proteins
  - Adults: 150 mg/day
  - Children: 4 mg/m²/hr
- Dipstick only detects albumin and misses LMW proteins
• Test Range
  Trace
  1+  30 mg/dl
  2+  100 mg/dl
  3+  300 mg/dl
  4+  >2000 mg/dl

• Urine concentration affects protein testing
  – Urine protein:creatinine ratio is better, semi-quantitative

• Alkaline urine pH >7.5 may cause false positivity
Proteinuria

• Intermittent
  – Exercise, stress, pregnancy, orthostatic

• Continuous
  – Glomerular disease
  – Chronic kidney disease (scarring)
  – Inflammation (infection, vasculitis, autoimmune)
  – Congestive heart failure, multiple myeloma, vascular thrombosis)
Case 6

• A 14 year old healthy girl is seen for 4 days of mild abdominal pain in Urgent Care
• UA showed 3+ protein, pH 6.0, neg heme, neg L.E. and nitrites
• Blood pressure is 124/80
• Physical exam is normal
• R.O.S. is negative except for NSAID use 3 days/month
• Repeat UA shows 4+ protein
Proteinuria

- Labs: BUN 14, creatinine 0.7, albumin 4.0, total protein 7.0, LFTs normal
- Random urine protein:creatinine ratio is 1.5 (normal <0.20)
- Renal ultrasound: normal
Postural (Orthostatic) proteinuria

• 3-5% healthy adults
  – Adolescents, usually tall and thin
• Proteinuria in renal disease also shows an orthostatic pattern
• Benign orthostatic proteinuria
  – “Diagnosis of exclusion”
  – Collect first AM specimen and a PM specimen for urine protein to creatinine ratio
  – The morning specimen should be completely normal and the PM specimen is abnormal
  – Or a “split timed” 24 hr urine
  – Follow-up
Case 6 follow-up

• Labs:
  – First morning urine protein/creatinine ratio: 0.8 (nl <0.2)
  – Afternoon specimen urine protein/creatinine ratio = 1.5

• Her proteinuria was quantitated with a 24 hour urine that showed 2 gms protein/day

• A renal biopsy showed focal segmental glomerulosclerosis
Leukocyte esterase and nitrites

- Leukocyte esterase (L.E.) predicts UTI nearly as well as a Gram stain
- Nitrites: Produced by Enterobacteriaceae
- L.E.: Sensitivity is 88% for UTI
- Nitrites: Sensitivity is also 88% for UTI
- When both are present the false positive rate is only 4% for UTI
Case 7

- A 6 year old boy is seen in local ED for “dark urine” and fatigue. He denies pain, fever, but has a mild cough
- On exam he appears mildly ill. BP is 110/68, RR 24, T 99.0
- A UA shows 3+ heme, 2+ protein, large L.E., 10-20 RBCs/hpf, 10-20 WBCs/hpf
- A urine culture is sent and antibiotics are prescribed
Case 7 returns

- 3 days later, he develops facial swelling, increased abdominal girth and returns to your office
- BP 120/80
- Urine culture is negative
- UA shows 3+ heme, 3+ protein, 5-10 WBC’s hpf, >100 RBCs/hpf.
- Lab: Creatinine 0.8, BUN 20, albumin 3.0, C3=20 (low); C4=16 (nl), ASO >200
Pyuria in acute glomerulonephritis
Acute GN: Under the microscope

- **Imune deposits**
- **RBC cast**
- **WBC cast**
Case 8

• A 5 year old girl who otherwise healthy, is seeing you for dysuria and new onset enuresis

• UA: pH 6.0, sp.gr. 1.015, 3+ heme, neg. protein, large L.E., positive nitrites, 10-20 WBCs/hpf, 10-20 RBCs/hpf

• Clean catch urine culture is sent

• Started on Amoxicillin for UTI
Case 8 follow-up

- She feels better after 2 days of antibiotics
- Urine culture shows 50,000 col/ml E.coli and <10,000 Staph coagulase negative species
- Should her antibiotics be continued?
“Diagnosis of UTI: Liquid gold and the Problem of Gold Standards”

• J.Pediatrics: Commentary June 2015
• Urine culture and UA interpretation defined in UTI in 1956
  – $>10^5$ CFU/ml assigned as diagnostic criterion for defining true infection vs contamination
• 1970’s: Asymptomatic bacteriuria in young girls defined
  – Absence of pyuria is key lab finding
Pyuria

• American Academy of Pediatrics 2011 UTI guideline
  – Requires presence of pyuria as well as positive urine culture result
• Infants <3 months; pyuria was 96% sensitive for predicting true UTI
• Urine culture gold standard of $\geq 10^5$ CFU/ml can be lowered in individual cases
Summary

- Screening urinalyses are not recommended in preventative care.
- Use of pH and specific gravity can help understand metabolic acidosis and urinary concentrating defects.
- Positive results (especially for heme and protein) may often reflect transient abnormalities.
- Asymptomatic microhematuria requires a good H&P and a limited evaluation most times.
- Persistent proteinuria is often significant.
- Pyuria can be seen in glomerulonephritis too.
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