Urinalysis: The Underappreciated Diagnostic Tool
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Outline
• Introduction: The value of the routine urinalysis
• Urine sample collection techniques
• Urine sample handling
• Urinalysis interpretation
  – Physical properties
  – Chemical properties
  – Sediment examination

Introduction
• Common reasons for performing a urinalysis:
  – Lower urinary tract signs
  – Change in urine character
  – Known or suspected renal disease or urolithiasis
  – Previous history of urinary tract infection
• Other reasons to consider performing a urinalysis:
  – Non-renal systemic disease
  – Suspected infectious disease
  – Fever
  – Preliminary assessment of renal function in dehydrated patient
  – Part of a “minimum database” in any patient with non-specific illness
  – Baseline reference point
  – Screening tool for geriatric patient
  – Pre-anesthetic screening tool
**Urine Sample Collection**

- The method of sample acquisition plays a major role in the results of the urinalysis and their interpretation.
- Timing of sample collection: It is usually acceptable to use a randomly timed sample, but if possible, collecting a sample prior to consumption of food or water in the morning is best.
- Try to collect samples PRIOR to initiating any sort of therapy (IV fluids, antibiotics).
- Voided urine samples:
  - Acceptable for initial evaluation—no need to evaluate further if the results of a voided urinalysis are normal.
  - Best technique for initial evaluation of hematuria (other techniques can cause iatrogenic bleeding).
  - Urine traverses several portions of the genitourinary tract, therefore results must be interpreted carefully.
  - Attempt to obtain a mid-stream voided sample.
  - Avoid bladder expression or catheterization of the bladder, and avoid catheter retention, vaginostomy, and amputation.
- Manual bladder expression is NOT recommended.
  - Can cause unnecessary bladder trauma.
  - Can cause reflux of infectious elements into ureters.

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**Catheterized Samples**
- More difficult in females than males.
- Contaminated by elements from the urethra.
- Requires chemical restraint in many patients.
- Risk of iatrogenic UTI—low in males, but up to 20% in females.
- Cystocentesis:
  - Not subject to contamination from distal urinary tract.
  - Up to 50 RBC/hpf can be seen due to trauma.
  - Best technique for collection of samples for urine culture.
  - Avoid bladder palpation for several hours to reduce risk of leakage.
  - Best technique for patients with complications or in patients with a devitalized bladder.
  - Can be performed blindly when the bladder can be easily palpated, or via ultrasound guidance.

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**Urine Sample Handling**
- Use a clean, airtight, ideally sterile container for sample transport.
- Ideally sample should be examined within 20 minutes; however, if this is not possible, sample should be refrigerated.
- Slowly warm samples to room temperature before testing, mix well prior to transfer to centrifugation tube.
- Chemical reagent strip analysis should be performed PRIOR to centrifugation, except if there is gross hematuria or marked urine turidity.
- Centrifuge at 1000 to 1500 RPM for 3-5 minutes, and bring centrifuge to slow, gradual stop.
- Examine stained and unstained sediment.
- Look for casts under low power near the margins of the cover glass.
- Examine under low power (for casts) AND high power (for bacteria, RBC, WBC, and epithelial cells).
Urinalysis Interpretation

Step 1: Physical properties

- Color
  - Reasons for abnormal colored urine:
    - Red/Reddish brown—hematuria, hemoglobinuria, myoglobinuria
    - Dark brown/black—methemoglobinuria
    - Yellow brown/green brown—concentrated sample, bilirubinuria, Pseudomonas infection
    - Dark greenish blue—canthaxanthinuria
    - Orange—uric aciduria

Illustration of the difference between hematuria (left side) and hemoglobinuria or myoglobinuria (right side).

Following centrifugation, red blood cells will come out of suspension in a pellet in a patient with hematuria.

Pictures from: Chew DJ and Di Bartola SP. Interpretation of Canine and Feline Urinalysis

Step 1: Physical properties

- Transparency
- Odor
- Specific gravity
  - The ratio of the weight of urine compared to the weight of an equal volume of pure water at the same temperature
  - An estimate of solute concentration
  - Should be tested prior to initiating treatment
  - Repeatedly low urine specific gravity from inappropriate antidiuretic hormone concentration
  - Normal USG for a dog: 1.018 to 1.064
  - Normal USG for a cat varies based on diet
    - Dry food: >1.030
    - Canned food: >1.025

A refractometer, used to assess urine specific gravity

Urinalysis Interpretation

Step 1: Physical properties

- Urine specific gravity (continued)
  - Hyponatremia (USG 1.001-1.007)—osmolality is less than that of plasma
    - Indicates a relative water diuresis
    - Can be normal in an overhydrated patient
    - Diseases to consider; diabetes insipidus, hypothyroidism, hypothyroidism, hyperaldosteronism, hepatic insufficiency, pharmacologic polyuria
  - Isoosmotic (USG 1.007-1.017)—osmolality is the same as that of plasma
    - Indicates a normal renal disease
    - ALWAYS consider a patient’s hydration status when assessing the urine specific gravity. In a dehydrated patient, the urine specific gravity should be >1.040. Therefore, a USG of 1.030 in a dehydrated patient is lower than normal.
Urinalysis Interpretation

- Chemical properties
  - pH
    - Varies with diet and with patient’s acid/base status
    - Meat based, high protein diet → acidic urine pH
    - Vegetable based diet → alkaline urine pH
    - Postprandial → alkaline urine pH
    - Urinary tract infection → alkaline urine pH if urease producing bacteria present
  - Protein
    - Semi-quantitative assessment on a dip strip can be misleading (highly affected by urine specific gravity)
    - Proteinuria may be pre-renal, renal, or post-renal in origin
    - Consider whether the urine sediment is active—proteinuria cannot be adequately localized
    - Positive results should be further assessed with a urine protein to creatinine ratio
    - False positive dip strip results can occur if the urine pH is very alkaline

- Chemical properties
  - Occult blood
    - Reagent strip reacts with heme pigments
    - Slightly less sensitive to erythrocytes than hemoglobin or myoglobin.
    - Interpret results in light of urine sediment results
  - Glucose
    - May read falsely negative in patients receiving methenamine or in patients receiving large doses of vitamin C
    - False positive: contamination with hydrogen peroxide, chlorine, or hypochlorite
    - Causes of glucosuria: hyperglycemia exceeding renal threshold, altered proximal renal tubular function (e.g., Fanconi syndrome, proximal tubular toxicity due to toxins)

- Chemical properties
  - Ketones
    - Beta-hydroxybutyrate, acetoacetate, and acetone
    - Formed due to exaggerated, incomplete oxidation of fatty acids
    - Ketonuria often precedes ketonemia
    - False positive: highly pigmented urine
    - False positive: high protein intake
  - Bilirubin
    - Only conjugated bilirubin is present in urine
    - The canine kidney is capable of degrading unconjugated bilirubin
    - Bilirubin should never be present in feline urine
    - False negatives: large amounts of vitamin C or aspirin
    - False positives: recent administration of large doses of chlorpromazine
Urinalysis Interpretation

- Chemical properties
  - Leukocyte esterase reaction
    - In dogs, the test is specific for pyuria, but is not sensitive (i.e., a positive result does indicate pyuria but a negative result does not rule out pyuria).
    - In cats, there are many false positive results
  - Nitrites
    - Limited value in veterinary medicine
    - False negative results are common in dogs and cats, as not all bacteria are able to convert nitrates to nitrites, and urine must be held in the bladder for at least 4 hours for the conversion to occur.

Urinalysis Interpretation

- Sediment examination
  - Mix sample well prior to centrifugation
  - Red blood cells
    - May arise from kidney, ureter, bladder, urethra, and genital tract
    - Do not confuse lipid droplets for red blood cells!
  - White blood cells
    - Normal ratio of RBC:WBC is 1:0
    - Neutrophils are the most common WBC seen in the urine sediment
    - WBC may arise from any portion of the urogenital tract and are not always indicative of a urinary tract infection (e.g., urolithiasis, neoplasia)

Refractile lipid droplets in a urine sample

Urinalysis Interpretation

- Sediment examination
  - Epithelial cells
    - Very small numbers seen in a normal urine sediment
    - Smallest epithelial cells usually arise from the kidney
    - Largest epithelial cells arise from distal urogenital tract
    - Squamous cells are much larger than transitional cells
    - It is difficult to distinguish reactive transitional cells (due to inflammation), from neoplastic transitional cells (due to transitional cell carcinoma), and biopsy is typically required.

Normal transitional epithelial cells

Malignant transitional epithelial cells

Pictures from: Chew DJ and DiBartola SP. Interpretation of Canine and Feline Urinalysis
Urinalysis Interpretation

- Sediment examination
  - Casts
    - Cylindrical molds formed within renal tubular lamina
    - Tamm-Horsfall mucoprotein is the matrix for most casts, and is secreted in the loop of Henle, distal tubule, and collecting duct.
    - Anything that favors secretion or precipitation of Tamm-Horsfall mucoprotein promotes cast formation:
      - Acidic urine
      - Highly concentrated urine
      - Low tubular flow rate
      - Presence of serum proteins, hemoglobin, or myoglobin in tubular fluid
    - Up to 2 hyaline casts per low power field and 1 granular cast per low power field is normal
      - Cellular casts are NEVER normal

Urinalysis Interpretation

- Sediment examination
  - Casts
    - Addis theory of cast formation: Cellular casts undergo progressive degeneration to granular (coarse to fine), then to waxy casts. Hyaline casts are pure precipitates of matrix protein.

A hyaline cast (with a few fine granules) in a non-inflamed urine:

A hyaline cast (with a few fine granules) in a non-inflamed urine:

Hyaline casts—Precipitates of THM and small amounts of albumin
- Commonly found in patients with renal proteinuria or pre-renal proteinuria.
Urinalysis Interpretation

- Sediment examination
  - Cellular casts
    - Most commonly comprised of epithelial cells, but white blood cell casts and red blood cell casts can also be found
    - Epithelial casts are indicative of active sloughing of renal epithelium due to a disease process
    - White cell casts are associated with acute bacterial pyelonephritis
    - Red cell casts are associated with intrarenal bleeding

-from top: An epithelial cast, a white cell cast, and a red cell cast (degenerated red cell cast)
Pictures from Chew DJ and DiBartola SP. Interpretation of Canine and Feline Urinalysis

Urinalysis Interpretation

- Sediment examination
  - Organisms
    - Normal urine from the urinary bladder is sterile
    - The distal urethra and genital tract are colonized by bacteria, therefore voided urine specimens may be contaminated
    - Bacteruria without pyuria is suggestive of a contaminated specimen, but may still represent true infection in patients with diseases such as Cushings disease or diabetes mellitus
    - Yeast and fungal hyphae are typically contaminants, but fungal infections can occur in patients with urinary tract obstruction or after prolonged use of antimicrobial drugs or immunosuppressants.

Urine sediments containing (from top): Blastomyces organisms, rod shaped bacteria, and fungal hyphae.

Urinalysis Interpretation

- Sediment examination
  - Crystals
    - The presence of crystals in a urine sample is dependent upon: urine saturation with crystal precursors, urine pH, USG, crystal promoters/inhibitors in the urine, time between collection and sediment evaluation, and refrigeration
    - Alkaline urine: struvite, calcium phosphate, ammonium urate
    - Acidic urine: uric acid, calcium oxalate, cystine
    - Certain medications can cause crystalluria (eg. sulfonamides)
    - Crystalluria alone (ie. in the absence of calculus formation) is often clinically insignificant, and in most cases should not be treated

Urine sediments containing (from top): Calcium oxalate dihydrate crystals, struvite crystals, and sulfonamide crystals.
Urinalysis Interpretation

- Sediment examination
  - Artifacts
    - Foreign material
    - Plant matter
    - Spores
    - Fibers
    - Hair
    - Surgery glove powder
    - Sterile lubricant
    - Stain precipitate

Urinalysis- A few tips

- If possible, to obtain a cystocentesis, rather than a voided sample
- If the sample is a voided sample and there is evidence of a possible infection, obtain a new sample via cystocentesis for urinalysis and urine culture PRIOR to starting antibiotic therapy
- Always interpret the results of a urinalysis in light of the urine specific gravity
- If there are a large number of crystals in a urine sediment, check for calculi. If none are present, then treatment for crystalluria alone should be questioned.
- If there is proteinuria noted on a dip strip, use a urine protein to creatinine ratio (not microalbuminuria testing) to further evaluate the degree of proteinuria, and the need for treatment

Questions???