The Minimum Diagnostic Database: Urinalysis

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The minimum database includes three types of diagnostics: chemistry, hematology, and the complete urinalysis. It is not just for occasions when urologic disease is suspected. The complete urinalysis is an important part of the minimum database and without it we are likely going to take much longer to get to the root of the problem. Potentially, we could even miss it altogether. The complete urinalysis is relevant across a wide variety of patient visit types and provides invaluable information for other organ systems including:

- Kidney health
- Lower urinary conditions
- Liver disease
- Diabetes mellitus and diabetic ketoacidosis
- Hydration status
- Other endocrine disease as Cushing’s disease (hyperadrenocorticism)
- Acid-base status
- Hemolytic diseases

The complete urinalysis comes in three parts:
- The physical examination
- The chemical examination
- Microscopic examination of the sediment

The physical examination

The physical examination consists of visualizing the collected urine and recording the color and clarity of the sample. Urine color is analyzed by visual inspection. Change in urinary color from its normal appearance – light yellow to amber – indicates the presence of pigments in the urine which can indicate lower urinary tract disease or systemic disease. Clarity is analyzed by visual inspection of the urine sample. Change in urine clarity is most often due to the presence of red blood cells, white blood cells, or crystals in the urine. Samples may be judged as clear, hazy, cloudy, opaque, turbid. The final element of the physical examination is the determination of the urine specific gravity (USG). The specific gravity is a measure of the urine’s concentration. Specific gravity varies in normal dogs and cats, but consistent readings above 1.030 for dogs and 1.035 for cats is considered normal. Urine specific gravity should be measured by a calibrated refractometer. Dry reagent strips are designed for human medicine, not veterinary medicine and are not useful in evaluating the USG of dogs and cats.

The chemical examination
The chemical examination of the urine uses dipsticks to provide semi-quantitative measurement of various urine chemicals that serve as important markers for major disorders or conditions. There are numerous suppliers of reagent strips —nearly all intended for use with human urine. IDEXX is veterinary specific. Since the reagents can expire, verify they are in date. To properly perform a urine chemistry evaluation, follow these steps:

- Use a fresh urine sample or, if refrigerated, use a sample returned to room temperature.
- Centrifuge bloody or turbid samples and test supernatant.
- Apply sample to the dipstick using pipette (do not dip).
- Remove excess by tipping the dipstick horizontally (see on screen image). Tipping vertically might mix pad chemicals.
- Following the careful timing and considerations in the dipstick’s instructions, compare color reactions with the standards on bottle.
- Record results.

The chemistry will be looking at these parameters:

**pH** — The pH of urine is an index of acid-base balance but is not a reliable indicator of blood pH. Normal urine pH in dogs and cats: 6.0-7.5, but can vary based on diet.

**PRO** — Protein in the urine can be an indicator of renal disease (interpret in conjunction with urine concentration) or lower urinary tract disease, when pre-renal causes of proteinuria have been ruled out.

**GLU** — Glucosuria is an indicator of increased blood glucose or an inability of the proximal renal tubule to reabsorb glucose.

**KET** — Ketonuria is primarily an indicator of diabetic ketoacidosis. Normally, ketones are completely resorbed by the proximal tubules.

**BLD/HGB** — Blood/hemoglobin on the reagent strip is most often an indicator of hematuria (RBC in the urine). Erythrocytes, free hemoglobin, methemoglobin, or myoglobin may be a source of heme. Red blood cells should be confirmed with sediment exam to help differentiate between hematuria and pigmenturia (erythrocytes may lyse in very alkaline or dilute urine).

**BIL** — Bilirubinuria is an indicator of conjugated bilirubin in the urine. Excessive bilirubinuria in a dog or any bilirubinuria in a cat is an indication to evaluate serum bilirubin concentrations.

**UBG** — Urobilinogen can be an indicator of increased serum bilirubin. However, there is a poor correlation between increased levels of urobilinogen and either hepatobiliary disease or hemolysis in dogs and cats.

**LEU** — Detects the enzyme leukocyte esterase, not white blood cells (WBCs). The accuracy is very questionable (especially in cat urine), therefore evaluation of WBCs must be done with sediment examination.
Other chemistry parameters have been proposed including nitrite, calcium, ascorbic acid, creatinine, and microalbumin. These parameters are not useful in assessing our veterinary patients for many different reasons, and have limited if any clinical usefulness.

Microscopic examination of the sediment

The final portion of the complete urinalysis is the sediment examination. This is the most technically demanding portion of this diagnostic test. Traditionally, urine sediments have been performed via microscope by a technician, veterinarian, or trained assistant. The microscope must be set up properly. To do this, the substage condenser needs to be lowered or the diaphragm on the substage condenser needs to be adjusted to allow for light scattering. In addition, the light source may need to be turned down to optimize refractility. Next, the urine must be centrifuged, and then set up on a slide for reading. The reading and recording is a time-consuming process as most resources recommend the scanning and recording of information of 10 LPFs (low-power fields = 10X) and 10 HPFs (high power fields = 40X). For the LPF examination, the parameters evaluated include casts and crystals. There are 2 main types of casts, hyaline and non-hyaline.

**Hyaline casts**— Hyaline casts in the urine are an indicator of renal injury/disease. Hyaline casts are cylindrical concretions made of Tamm-Horsfall mucoproteins produced by the epithelial cells lining the loops of Henle, distal tubules, and collecting ducts. Some hyaline casts may be seen in healthy animals from normal turnover of tubular epithelial cells or following physical activity or fever. These are less than approximately 1-2 per low power field in moderately concentrated urine of otherwise normal patients. Some casts are shed intermittently (or in showers), so the absence of casts does not preclude active renal tubular disease. Casts can also deteriorate rapidly, especially in dilute, alkaline, or aged samples. It is important to remember that the number of casts is not a reliable index of the severity, duration, or reversibility of the underlying disease.

**Non-hyaline casts**— These casts are also indicators of renal injury/disease and are composed of Tamm-Horsfall mucoproteins. However, these incorporate cellular material that can sometimes help provide clinical insights into the type and location of the disorder. The casts that are subdivided into this category include cellular, granular, and waxy casts. When cellular casts remain in the nephron for some time before they are flushed into the bladder urine, the cells may degenerate to become a coarsely granular cast, later a finely granular cast, and ultimately, a waxy cast. Granular and waxy casts are thought to be later stages of renal tubular cell casts.

Additionally, crystals are evaluated on the low-power field of view as well. 95% of all crystals in dogs and cats are either struvite or calcium oxalate dihydrate crystals. Other less common types of crystals include calcium oxalate monohydrate, cysteine, ammonium biurate, and bilirubin crystals. Crystals may or may not have significance in a urine sample, so it is important to evaluate the urine within 30 to 60 minutes of collection. This will minimize the effects of cooling that can lead to precipitation of crystals.

For HPF examination, the evaluator will be looking for cells and bacteria. The cells that will be scrutinized include:

**RBCs**— Red blood cells in the urine sediment are most often an indicator of inflammation, infection, or neoplasia in the urinary tract. However, rare erythrocytes detected on sediment examination of the urine may be found in healthy animals.
**WBCs**— White blood cells in the urine are an indicator of inflammation, infection, or neoplasia in the urinary tract. It is important to remember that pyuria, or the presence of white blood cells in the urine, does not always indicate a urinary tract infection.

The type of epithelial cells seen will depend on the method of collection. With voided or catheterized samples, squamous cells are common, but transitional epithelial cells may also be observed. One should not expect to see many squamous cells in a cystocentesis sample.

**Squamous Epithelial Cells**— Squamous epithelial cells line the distal urethra and external genitalia.

**Non-squamous Epithelial Cells**— Non-squamous epithelial cells line the renal tubules through the proximal urethra. There are 2 types of cells that are microscopically indistinguishable, renal tubular epithelial cells, and transitional epithelial cells.

- Renal epithelial cells line the renal tubules.
- Transitional epithelial cells line the mucosa from the renal pelvis through the proximal urethra.

**Bacteria** is the next element that is examined under the 40X scan and can appear in the urine sample for many reasons including a urinary tract infection (UTI), sample contamination from collection, or sample contamination post collection. To help discern if a patient has a UTI, a urine culture can be performed as this is the definitive test for a urinary tract infection. However, a negative test does not necessarily mean that a UTI is absent.

In evaluating the slide it may be difficult to discern bacteria (especially cocci) from small debris, lipids, etc. To help with this, look for uniformly sized rods or cocci, in short chains or doublets. Additionally, it may be helpful to make an air-dried sediment slide and stain using a cytological stain (e.g., Diff-quick) similar to validating hematology results with a blood film. The benefit to doing an air-dried cytological preparation is that it can be evaluated with oil-immersion (100X). This can increase confidence in whether or not bacteria is or is not present. The most common etiologic agent in a UTI in both cats and dogs is *E. coli* which is a rod-shaped bacteria.

In 2016 IDEXX introduced the SediVue DX, the first and only in-clinic urine sediment analyzer. With only 165 microliters of neat urine and a gentle, urine specific on-board centrifuge, the SediVue DX uses automated, precision cartridge microscopy to capture 70 high-resolution, high-contrast images of the urine sediment. A convolutional neural network then identifies, classifies and counts the formed elements in the sediment, using a process analogous to facial recognition technology, providing semi-quantitative results (e.g. struvite crystals: 6 to 20 per HPF). Both the semi-quantitative results and the high-resolution images are available in about three minutes, dramatically improving the urinalysis workflow. The numerical results and images are then integrated with the physical and chemical examination to provide the complete urinalysis report and seamlessly and immediately uploaded to practice management systems and the VetConnect PLUS account.

**References**