

April 2015 - 7th Issue

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Preface

It gives me great pleasure to be addressing all of you through the medium of the 7th edition of Suyash Uro Times.

I would like to congratulate Dr Sharad Somani & his team for this unique initiative of bringing out this news letter. In spite of his busy schedule, to come out with this academic activity is indeed praiseworthy. Keep it up!

Suyash Uro Times not only deals with urological problems faced by so many urologists, but also serves the dual purpose of providing an academic platform to everyone.

This issue contains detailed information regarding most common and basic urological investigation of urine analysis written by a pathologist and a biochemist making it comprehensive but all inclusive.

My association with Dr Somani goes back to his student days and continues even today. I wish him all the best for the future.



DR. ANAND MALIK Prof & Head, Dept of Surgery IIMSR Medical College, Badnapur, Jalna

From Editors Desk

Dear colleagues,

Warm greetings from team "Suyash Uro Times" It is my immense pleasure to publish 7th issue of the newsletter.

We started this activity as a continuous medical education. I am happy to inform you that we are getting overwhelming response from the doctors all over. General practitioners, specialists & super specialists have communicated personally and appreciated the activity.

This issue highlights basic urological investigations and will definitely be of help for every practitioner. Please feel free to write to us on suyashnursinghome@gmail.com regarding suggestions, advice or criticism so as to make us improve on the newsletter.

Looking forward to communicate with you time to time through this newsletter.

Dr. Sharad Somani

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URINE ANALYSIS

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INTRODUCTION

Urine analysis is the most basic test that should be performed in all urologic patients.

A complete urinalysis includes

- 1. Physical examination
- 2. Chemical examination
- 3. Microscopic analysis.

Urine culture is indicated in specific cases.

COLLECTION OF URINARY SPECIMENS

1. Males :- A midstream urine sample is to be collected

2. Females:- Collect a midstream specimen. If infection is suspected, however, the midstream specimen may be unreliable and a catheterized urine sample may need to be collected.

3. Neonates and Infants :- Place a sterile plastic bag with an adhesive collar over the infant's genitalia.

TIMING OF EVALUATION

Urine sample should be examined within 1 hour of collection and plated for culture and sensitivity if indicated. If it is not possible to examine the urine promptly, it should be refrigerated at 5° C.

PHYSICAL EXAMINATION OF URINE

This includes an evaluation of

- a) Color
- b) Turbidity
- c) Specific gravity
- d) Osmolality
- e) pH.

a) <u>**Colour:**</u>- The normal colour pale yellow due to the presence of urochrome.

b) **Turbidity** :- Freshly voided urine is clear.

Cloudy due to phosphaturia, pyuria, chyluria.

1. Phosphaturia is a benign process in which excess phosphate crystals precipitate in an alkaline urine.

2. Pyuria : is usually associated with a UTI. The large numbers of white blood cells causes the urine to become turbid.

Pyuria can be distinguished from phosphaturia by smell (infected urine has pungent odor)

3. Chyluria : in which lymph fluid mixes with urine and can be confirmed by finding chylomicrons in urine.

c) Specific Gravity :- Reflects the state of hydration and renal concentrating ability. Determined from a urinary dipstick and usually varies from 1.001 to 1.035.

*A specific gravity less than 1.008 is regarded as dilute,

**and a specific gravity greater than 1.020 is considered concentrated.

***A fixed specific gravity of 1.010 is a sign of renal insufficiency, either acute or chronic.

Conditions that decrease specific gravity include

(1) Increased fluid intake

- (2) Diuretics
- (3) Decreased renal concentrating ability
- (4) Diabetes insipidus.

Conditions that increase specific gravity include

- (1) Decreased fluid intake
- (2) Dehydration owing to fever, sweating, vomiting, and diarrhea
- (3) Diabetes mellitus (glucosuria)
- (4) Inappropriate secretion of antidiuretic hormone.

Specific gravity will also be increased above 1.035 after intravenous injection of iodinated contrast and in patients taking dextran.

D) **Osmolality:** is a measure of the amount of material dissolved in the urine and usually varies between 50 and 1200 mOsm/L. Indicator of renal function

E) pH:- Urinary pH may vary from 4.5 to 8

A urinary pH between 4.5 and 5.5 is considered acidic, whereas a pH between 6.5 and 8 is considered alkaline.

In patients with a presumed UTI, an alkaline urine with a pH greater than 7.5 suggests infection with a urea-splitting organism, most commonly **Proteus.**

Urinary pH is usually **acidic** in patients with **uric acid** and **cystine lithiasis.**

Chemical Examination of Urine

Urine Dipsticks:-

Quick and inexpensive method for detecting abnormal substances within the urine.

The abnormal substances commonly tested for with a dipstick include

(1) Blood

- (2) Protein
- (3) Glucose
- (4) Ketones
- (5) Urobilinogen and bilirubin
- (6) White blood cells.

PROCEDURE:

- 1. Immerse reagent areas on dipstick completely in a fresh uncentrifuged urine specimen.
- 2. Withdraw immediately **dipstick** to prevent dissolution of the reagents into the urine.
- 3. Hold horizontally for the appropriate time and then compare with the color chart.

1) Hematuria

Principle : The chemical detection of blood in the urine is

Cont....

Dr. D. Bhale Biochemist

based on the peroxidase-like activity of hemoglobin.

The degree of color change is directly related to the amount of hemoglobin present in the urine specimen Hematuria can be distinguished from hemoglobinuria and myoglobinuria by

(a) Microscopic examination of the centrifuged urine :

The presence of a large number of erythrocytes establishes the diagnosis of hematuria.

If erythrocytes are absent, examination of the serum will distinguish hemoglobinuria and myoglobinuria.

A sample of blood is obtained and centrifuged.

Hemoglobinuria : Supernatant will be pink.

Hematuria of nephrologic origin is frequently associated with <u>casts</u> in the urine and almost always associated with significant proteinuria.

Even significant hematuria of urologic origin <u>will not elevate</u> the protein concentration in the urine into the 100 to 300 mg/dL or 2+ to 3+ range on dipstick that almost always indicates glomerular or tubulointerstitial renal disease.



2) Proteinuria :-

Normally healthy adults excrete 80 to 150 mg of protein in the urine daily.

Proteinuria is first indication of renovascular, glomerular, or tubulointerstitial renal disease, or it may represent the overflow of abnormal proteins into the urine in conditions such as multiple myeloma.

Proteinuria can also occur secondary to nonrenal disorders and in response to various physiologic conditions such as strenuous exercise.

Pathophysiology:-

Most causes of proteinuria can be categorized into one of three categories:

1.Glomerular

2.Tubular

3.Overflow.

Glomerular proteinuria:

Most common type of proteinuria

Results from increased glomerular capillary permeability albumin

Occurs IgA nephropathy or in glomerulopathy associated with systemic illness such as diabetes mellitus.

Glomerular disease should be suspected when the 24-hour urine protein excretion exceeds 1 g and is almost certain to exist when the total protein excretion exceeds 3 g.

Tubular proteinuria:

24-hour urine protein loss seldom exceeds 2 to 3 g and the excreted proteins are of low molecular weight rather than albumin.

Disorders are associated with other defects of proximal tubular function such as glucosuria, aminoaciduria, phosphaturia, and uricosuria (Fanconi syndrome).

Overflow proteinuria :

Due to an increased plasma concentration of abnormal

 $immunoglobulins \, and \, other \, low-molecular-weight \, proteins \, .$

Occurs in the absence of any underlying renal disease .

The most common cause of overflow proteinuria is multiple myeloma, in which large amounts of immunoglobulin light chains are produced and appear in the urine (Bence Jones protein).

Detection:- Qualitative detection of abnormal proteinuria is most

easily accomplished with a dipstick impregnated with tetra-

bromophenol blue dye.

The minimal detectable protein concentration by this method is 20 to 30 mg/dL

False-negative results can occur in alkaline urine, dilute urine, or when the primary protein present is not albumin.

Protein electrophoresis:

1.Is particularly helpful in distinguishing glomerular from tubular proteinuria.

2. In glomerular proteinuria, albumin makes up about 70% of the total protein excreted, whereas in tubular proteinuria, the major proteins excreted are immunoglobulins with albumin making up only 10% to 20%.

3.Immunoassay is the method of choice for detecting specific proteins such as Bence Jones protein in multiple myeloma.

Evaluation:- Proteinuria should first be classified by its timing into transient, intermittent, or persistent.

1.Transient proteinuria :

a) Occurs commonly, especially in the pediatric population, and usually resolves spontaneously within a few **days**.

b)It may result from fever, exercise, or emotional stress.

c)In older patients, transient proteinuria may be due to congestive heart failure.

d)If a nonrenal cause is identified and a subsequent urinalysis is negative, no further evaluation is necessary.

Obviously if proteinuria persists it should be evaluated further.

2.Proteinuria may also occur **intermittently**, **and** this is frequently related to postural change.

3. Persistent proteinuria requires further evaluation, and most cases have a glomerular etiology.

3) Glucose and Ketones :-

Urine testing for glucose and ketones is useful in screening patients for diabetes mellitus.

Renal threshold corresponds to serum glucose of about 180 mg/dL; above this level, glucose will be detected in the urine.

Glucose detection with the urinary dipstick is based on a double sequential enzymatic reaction yielding a colorimetric change. In the first reaction, glucose in the urine reacts with glucose oxidase on the dipstick to form gluconic acid and hydrogen peroxide.

In the second reaction hydrogen peroxide reacts with peroxidase causing oxidation of the chromogen on the dipstick producing a color change.

This double-oxidative reaction is specific for glucose and there is no cross-reactivity with other sugars. The dipstick test becomes less sensitive as the urine increases in specific gravity and temperature

<u>Ketones</u> : Present in urine in diseases diabetic ketoacidosis pregnancy and after periods of starvation or rapid weight reduction.

Ketones excreted include acetoacetic acid, acetone, and β -hydroxybutyric acid. With abnormal fat breakdown, ketones will appear in the urine before the serum.

Sodium nitroprusside on the dipstick reacts with acetoacetic acid to produce a purple color.

Dipstick testing will identify acetoacetic acid at concentrations of 5 to 10 mg/dL but will not detect acetone or β -hydroxybutyric acid.

4) Bilirubin and Urobilinogen :-

Normal urine contains no bilirubin and only small amounts of urobilinogen. Conjugated bilirubin has a low molecular weight, is water soluble, and normally passes from the liver into the small intestine through the bile ducts, where it is converted to urobilinogen. Therefore conjugated bilirubin does not appear in the urine except in pathologic conditions in which there is intrinsic hepatic disease or obstruction of the bile ducts.

Indirect bilirubin is of high molecular weight and bound in the serum to albumin. It is water insoluble and therefore does not appear in the urine even in pathologic conditions.

Urobilinogen is the end product of conjugated bilirubin metabolism. Hemolysis and hepatocellular diseases that lead to increased bile pigments can result in increased urinary bile pigments can result in increased urinary urobilinogen., obstruction of the bile duct or antibiotic usage that alters intestinal flora thereby interfering with the conversion of conjugated bilirubin to urobilinogen will decrease urobilinogen levels in the urine. In these conditions obviously serum levels of conjugated bilirubin rise.

False-negative results can occur in the presence of ascorbic acid which decreases the sensitivity for detection of bilirubin. False-positive results can occur in the presence of phenazopyridine because it colors the urine orange and similar to the colorimetric reaction for bilirubin turns red in an acid medium.

Urinary Sediment

Obtaining and Preparing the Specimen

1. If possible the first morning urine specimen is the specimen of choice and should be examined within 1 hour.

2.Ten to 15 milliliters of urine should be centrifuged for 5 minutes at 3000 rpm.

The supernatant is then poured off and the sediment is resuspended in the centrifuge tube by gently tapping the bottom of the tube.

MICROSCOPY EXAMINATION :

Microscopic analysis of the urinary sediment should be performed

with both low-power (×100 magnification) and high-power (×400 magnification) lenses.

Under low power : Low-power magnification Identifies erythrocytes, leukocytes, casts, cystine crystals, oval fat macrophages and parasites such as Trichomonas vaginalis and Schistosoma hematobium.

High-power magnification is necessary to distinguish circular from dysmorphic erythrocytes to identify other types of crystals and particularly to identify bacteria and yeast.

In summary the urinary sediment should be examined microscopically for

(1) cells (2) casts (3) crystals (4) bacteria (5) yeast and (6) parasites.

CELLS

Erythrocyte morphology may be determined under high-power magnification. Although phase contrast microscopy has been used for this purpose, circular (nonglomerular) erythrocytes can generally be distinguished from dysmorphic (glomerular) erythrocytes under routine brightfield high-power magnification.

ERYTHROCYTES

May be confused with yeast or fat droplets Erythrocytes can be distinguished however because yeast will show budding and oil droplets are highly refractile.

LEUKOCYTES

can generally be identified under low power and definitively diagnosed under high-power magnification.

It is normal to find 1 or 2 leukocytes/ HPF in men and up to 5/HPF in women in whom the urine sample may be contaminated with vaginal secretions.

A greater number of leukocytes generally indicates infection or inflammation in the urinary tract. which are generally indicative of urinary tract pathology.

Fresh leukocytes are generally larger and rounder, and, when the specific gravity is less than 1.019 the granules in the cytoplasm demonstrate glitter-like movement so-called glitter cells.

EPITHELIAL CELLS

are commonly observed in the urinary sediment. Squamous cells are frequently detected in female urine specimens and are derived from the lower portion of the urethra the trigone of postpubertal females, and the vagina.

Squamous epithelial cells are large have a central small nucleus about the size of an erythrocyte and have an irregular cytoplasm with fine granularity.

Transitional epithelial cells may arise from the remainder of the urinary tractTransitional epithelial cells may arise from the remainder of the urinary tract (Transitional cells are smaller than squamous cells, have a larger nucleus and demonstrate prominent cytoplasmic granules near the nucleus.

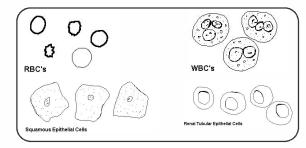
Malignant transitional cells have altered nuclear size and morphology and can be identified with either routine Papanicolaou staining or automated flow cytometry.

RENAL TUBULAR CELLS :

are the least commonly observed epithelial cells in the urine but are most significant because their presence in the urine is always indicative of renal pathology. Renal tubular cells may be difficult to distinguish from leukocytes, but they are slightly larger. **CASTS**

A cast is a protein coagulum that is formed in the renal tubule and traps any tubular luminal contents within the matrix.

Tamm-Horsfall mucoprotein is the basic matrix of all renal casts it originates from tubular epithelial cells and is always present in the urine.



HYALINE CASTS

Hyaline casts: When the casts contain only mucoproteins they are called hyaline casts and may not have any pathologic significance. Hyaline casts may be seen in the urine after exercise or heat exposure but may also be observed in pyelonephritis or chronic renal disease.

Red blood cell casts contain entrapped erythrocytes and are diagnostic of glomerular bleeding most likely secondary to glomerulonephritis.

White blood cell casts are observed in acute glomerulonephritis, acute pyelonephritis, and acute tubulointerstitial nephritis.

Casts with other cellular elements usually sloughed renal tubular epithelial cells are indicative of nonspecific renal damage.

Granular and waxy casts result from further degeneration of cellular elements.

Fatty casts are seen in nephrotic syndrome, lipiduria, and hypothyroidism.

CRYSTALS

Cystine crystals in urine establishes the diagnosis of cystinuria.

Crystals precipitated in acidic urine include calcium oxalate, uric acid, and cystine. Crystals precipitated in an alkaline urine include calcium phosphate and triple-phosphate (struvite) crystals.

Cholesterol crystals are rarely seen in the urine and are not related to urinary pH. They occur in lipiduria and remain in droplet form.



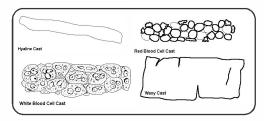
BACTERIA

*Normal urine should not contain bacteria and in a fresh uncontaminated specimen the finding of bacteria is indicative of a UTI. Because each HPF views between 1/20,000 and 1/50,000 mL,

* Each bacterium seen per HPF signifies a bacterial count of more than 30,000/mL. Therefore 5 bacteria/HPF reflects colony counts of about 100,000/mL.

This is the standard concentration used to establish the diagnosis of a UTI in a clean-catch specimen. This level should apply

only to women however in whom a clean-catch specimen is frequently contaminated.



The finding of any bacteria in a properly collected midstream specimen from a male should be further evaluated with a urine culture.

Under high power it is possible to distinguish various bacteria. Gram-negative rods have a characteristic bacillary shape, whereas streptococci can be identified by their characteristic beaded chains and staphylococci can be identified when the organisms are found in clumps.

YEAST

The most common yeast cells found in urine are Candida albicans.

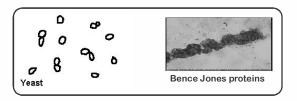
The biconcave oval shape of yeast can be confused with erythrocytes and calcium oxalate crystals

But yeasts can be distinguished by their characteristic budding and hyphae. Yeasts are most commonly seen in the urine of patients with diabetes mellitus or as contaminants in women with vaginal candidiasis.

TRICHOMONAS VAGINALIS :

It is a frequent cause of vaginitis in women and occasionally of urethritis in men. Trichomonads can be readily identified in a cleancatch specimen under low power.

Trichomonads are large cells with rapidly moving flagella that quickly propel the organism across the microscopic field.



BENCE JONES PROTEINS

- Bence Jones proteins are small proteins found in the urine. Testing for these proteins is done to diagnose and monitor multiple myeloma and other similar diseases.
- Bence Jones proteins are considered the first tumor marker.
- A tumor marker is a substance made by the body that is linked to a certain cancer or malignancy. Bence Jones proteins are made by plasma cells a type of white blood cell. The presence of these proteins in a person's urine is associated with a malignancy of plasma cells.

INTERESTING CASES – PEDIATRIC PCNL





3 years female 10 kg weight



X KUB showing large left renal calculus



Immediate post operative fluoroscopy image with patient in prone position showing total clearence

Case 2:



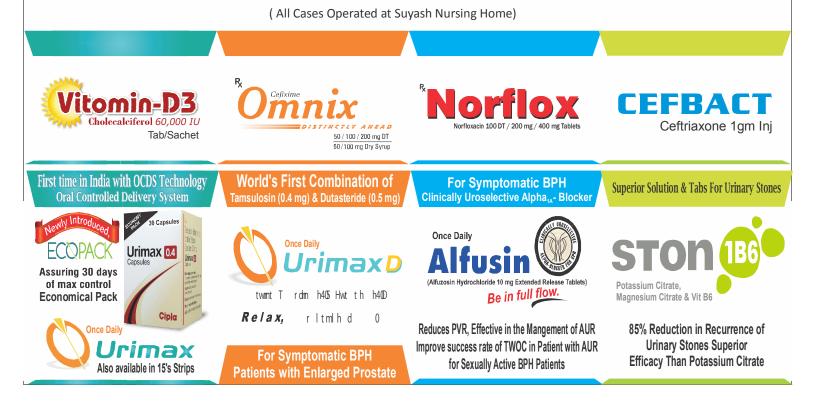
4 years old male 13 kg



X KUB showing Staghorn with multiple right renal calculi



Post PCNL KUB showing total clearance with nephrostomy tube in situ



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