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DOCTORS CASE MEDICALS CME SERIES

July 2020

Intro.

- UA is an array of tests performed on urine to detect and measure various compounds that pass through the urine.
- Used as both a screening and diagnostic test.
- Obtained for numerous reasons;
 - √ Suspected infection
 - ✓ Evaluation of kidney and metabolic d/o

Ct'n

- Analyzed within 30-60 min. after the patient voids → for accurate results.
- Urinalysis can be divided into 3 parts.
 - ✓ Macroscopy
 - ✓ Dipstick (chemical) analysis
 - ✓ Microscopy
- Urine culture
 - Typically takes 1-3 days to result
 - ❖Is to identify specific organism causing infection (if any)

Proper Specimen Collection

Teach every patient how to collect proper specimen

- ➤ Clean-catch midstream (Patient should waste first 5 mL, then catch 5 10 mL mid-stream). Its used for urine culture and cytological analyses, and it is most important in females coz it reduces contamination from vaginal secretions.
- In patients with indwelling urinary catheters, a recently produced urine sample should be obtained (directly from the catheter tubing)
- ➤ Best examined when fresh. Chemical composition of urine changes with standing and formed elements degenerate with time
- > Refrigerated is best when infection is suspected
- First voided morning urine is ideal when evaluating suspected glomerulonephritis. It is also used to evaluate the ability of the kidneys to concentrate urine during the normal dehydration that occurs during sleep.

Macroscopy

Gross visual inspection/ observation of the urine for;

✓ Color

✓ Clarity/ turbidity

√ Odor

Turbidity.

- Normal urine is transparent.
- Turbid or cloudy urine may result from;
 - ✓ Infection
 - ✓ Presence of blood cells, bacteria or yeast (eg Candida).

A foamy urine may indicate either the presence of glucose or

protein.



Odor / Smell

- The normal smell of urine can be described as urinoid.
 Other smells of interest include:
 - √ Faecal smell: gastrointestinal-bladder fistula
 - ✓ Fruity or sweet smell: diabetic ketoacidosis
 - √Smell of ammonia: alkaline fermentation.
 - ✓ Smell of asparagus: eating a lot of asparagus.

Color

- Normal urine color is often described as straw, yellow or amber.
- This color may be altered by medications, food sources or



Color change	Medication	Other causative agent
Dark/brown	Cascara, Ferrous salts/iron dextran Methocarbamol, Metronidazole Nitrofurantoin, Senna (in laxatives) Chloroquine, Levodopa Methyldopa, Nitrates Quinine, Sulfonamide	Liver disorders, such as acute hepatitis, cirrhosis, and liver cancer, which cause bilirubin to be excreted in the urine (foamy if urine shaken)
Yellow- brown	Bismuth, Cascara Nitrofurantoin, Senna Chloroquine, Metronidazole Primaquine, Sulfonamides	Liver disorders that cause bilirubin to be excreted in the urine
Blue or blue green	Amitriptyline Triamterene Methylene blue Methocarbamol Indomethacin Cimetidine Phenergan	Artificial food coloring Asparagus Hypercalcemia

Color change	Medication	Other causative agent
Orange/yellow	Chlorzoxazone Heparin Rifampin Warfarin Dihydroergotamine Phenazopyridine (Pyridium®) Sulfasalazine Vitamin B complex Carotene	Liver disorders Carrot juice Dehydration
Red/pink	Daunorubicin or doxorubicin Ibuprofen, Phenothiazines Phenylbutazone, Propofol Salicylates, Heparin Methyldopa, Phenytoin Rifampin Senna	Blackberries Beets Blood (may relate to disease, exercise, or medications) Artificial food coloring Rhubarb Chronic lead or mercury poisoning

Dipstick Introduction

Plastic strip dipped in urine sample

- ✓ Test for various chemical components of urine
- √ Results in seconds to minutes
- Often performed in emergency departments or ambulatory clinics that do not have a micro lab available

Associated with false negatives

- √ Use caution if a negative dipstick test results in a patient with symptoms of a UTI
- ✓ Dipstick is specific, but not very sensitive
 - > Sensitivity related to bacterial load

Chemical analysis --- tests

- 1. Specific gravity
- 2. pH
- 3. Leukocyte esterase
- 4. Nitrites
- 5. Urobilinogen
- 6. Bilirubin
- 7. Glucose
- 8. Ketones
- 9. Protein
- 10. Blood



Dipstick Methodology

Paper tabs impregnated with chemical reagents

- Reagents are chromogenic
- Reagents are timed developed
- Some rxns are highly specific
- Other are sensitive to the presence of interfering substances or extremes of pH
- Rapid, semiquantitative assessment of urinary characteristics



Specific Gravity:

- The specific gravity (SG) of urine signifies the concentration of dissolved solutes and reflects the effectiveness of the renal tubules to concentrate it (when the body needs to conserve fluid). If there were no solutes present the urines SG would be 1.000, the same as pure water.
- The SG of urine is around 1.010 but can vary greatly.

Specific gravity

Increased Urine Specific Gravity:

- Diarrhea that causes dehydration
- Heart failure
- Dehydration
- Diarrhea/emesis
- Renal artery stenosis
- Glycosuria
- Syndrome of inappropriate antidiuretic hormone secretion(SIADH).
- Hepatorenal syndrome

Decreased Urine Specific Gravity:

- ✓ Acute tubular necrosis
- ✓ Interstitial nephritis
- ✓ Diabetes insipidus
- ✓ Drinking too much fluid
- √ Kidney failure
- ✓ Pyelonephritis

Urine ph

- Measures the hydrogen ion concentration of the urine.
- It is important that a fresh sample be used as urine becomes more alkaline over time as bacteria convert urea to ammonia (which is very alkaline)
- Urine is normally acidic but its normal pH ranges from 4.5 to 8.
- Not sufficiently accurate to be used for diagnosis of renal tubular acidosis (check ABG and urine lytes)
- Changing urine pH to either acidic or alkaline may prevent development of certain types of kidney stones

pH cnt'n

Low pH (acidic):

- ✓ Foods such as acidic fruits (cranberries) can lower the pH.
- ✓ As urine generally reflects the blood pH, metabolic or respiratory acidosis can make it more acidic.
- ✓ Other causes of acidic urine include diabetes, diarrhoea and starvation.

High pH (alkaline):

- ✓ Low carb or vegetarian diet
- ✓ May be associated with renal calculi.
- √ Respiratory or metabolic alkalosis
- ✓ Urinary tract infection

NORMAL URINE



Squamous Epithelial Cells



RBCs



RBC Cast



WBCs



WBC Cast



Yeast



Granular Cast



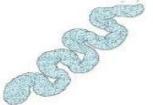
Spermatozoa



Hyaline Cast



Waxy Cast



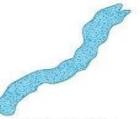
Convoluted Hyaline Cast



Mucus Threads

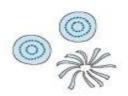


Renal Tubular Epithelial Cells

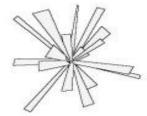


Cylindroids

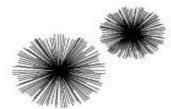
ACID URINE



Leucine Spheres



Sodium Urate Crystals



Tyrosine Needles



Cystine Crystals



Amorphous Urates



Calcium Oxalate Crystals



Uric Acid Crystals

ALKALINE URINE



Triple Phosphate Crystals 15 July 2020



Calcium Phosphate Crystals



Ammonium Urate Crystals CME SERIES: URINALYSIS BY JULIAN M.



Calcium Carbonate Crystals



Amorphous Phosphates

Leukocyte Esterase

- Detects esterase, an enzyme released by WBC
- Reflects presence of pyuria and may be used to detect > 10 leukocytes per HPF
- False negatives can occur in the presence of
 - ✓ Glycosuria
 - ✓ High specific gravity
 - ✓ Cephalexin or tetracycline Tx
 - ✓ Excessive oxalate excretion
- False positives can occur with contamination of vaginal debris and trichomonas infection

Nitrites

- Screening test for bacteriuria
- Reflects presence of >10(5)CFU of Enterobacteriaceae per ml of urine
- Relies on ability of gram-negative bacteria to convert nitrate nitrite
- False negative can occur
 - √ 1. Bacteria that cannot convert nitrate nitrite: EX: Enterococcos
 - ✓ 2. Presence of ascorbate
 - √3. Retention of urine in bladder <4 hours
 </p>
 - √4. Decrease in urine pH
- False positive can occur with substances that turn urine red such as use of bladder analgesic phenazopyridine or ingestion of beets

Urobilinogen and Bilirubin

- Urobilinogen produced in the gut from metabolism of bilirubin.
 Excreted in feces and urine.
- In obstructive jaundice, bilirubin does not reach bowel, so urinary excretion of urobilinogen is diminished
- In other forms of jaundice, urinary urobilinogen is increased
- Better tests are available to diagnose obstructive jaundice
- Presence of bilirubin in the urine may therefore indicate; liver disease, biliary tract infection, pancreatic causes of obstructive jaundice.

Glucose (glycosuria)

Dipstick is specific for glucose.

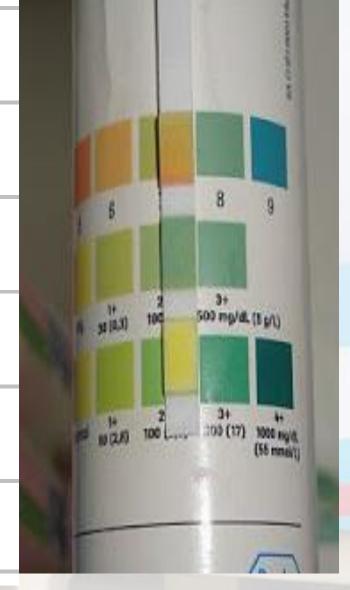
- Rely on glucose oxidase to catalyze the formation of hydrogen peroxide
- High concentrations of ascorbic acid can result in false-negative test
- Due to inability of kidney to reabsorb glucose in PT despite normal serum glucose or urinary spillage with high serum glucose
- Normal renal function: glycosuria does not generally occur until serum glucose exceeds 180mg/dl
- Diabetes, Liver disease, Medications such as tetracycline, lithium, penicillin, cephalosporins and in Pregnancy.

Ketones

- ✓ Created when body breaks down fat or fatty acids for energy instead of carbohydrates or sugar.
- ✓ Measures the presence of urine ketones
- ✓ False positive may occur with usage of levodopa, captopril (drugs containing free sulfhydryl group)
- ✓ Ordered when patient has Type 1 DM and diabetic ketoacidosis is suspected particularly when patient is sick.
- ✓ Monitored in a person...
 - On a low-carbohydrate and/or high-fat diet
 - Not able to eat (anorexia/fasting), is vomiting or diarrhea
 - Pregnant woman who has DM or gestational DM
 - Diabetes, Alcoholism, eclampsia



negative	0 mg/dL
trace	15-30 mg/dL
1+	30-100 mg/dL
2+	100-300 mg/dL
3+	300-1000 mg/dL
4+	>1000 mg/dL



Proteinuria

- Highly sensitive to albumin AND insensitive to other urinary proteins such as globumins, hemoglobin, or light chains
- Scored from trace to 4+ based on concentration
- Quantification is influenced by urine concentration:
 - dilute urine may give falsely low results
 - ✓ Ranges from 200-3000mg/24hrour are readily detected
 - ✓ Not sensitive enough to detect for MICROALBUMINURIA
 - ✓ Highly alkaline urine may produce false-positive rxns
 - ✓IF proteinuria other than albumin is suspected, more sensitive assays should be used (SPEP, UPEP IFE, serum free light chains)

Quantification of Proteinuria

- If presence of proteinuria is detected on dipstick, confirmation is required through quantification of proteinuria.
- Measurement of urinary protein
 - ≥24 hour total urinary protein
 - > Random protein/creatinine or albumin/creatinine.
- Adjustment for urinary concentration is made by relating the urine protein concentration to the urine creatinine concentration.

conditions which may lead to protein in the urine include:

- √ Kidney disease
- ✓ Injury to the urinary tract, bladder or urethra
- ✓ Inflammation.
- √ malignancies.
- ✓ Multiple myeloma.

VIERNITY & WOMEN'S CENTR

Hematuria.

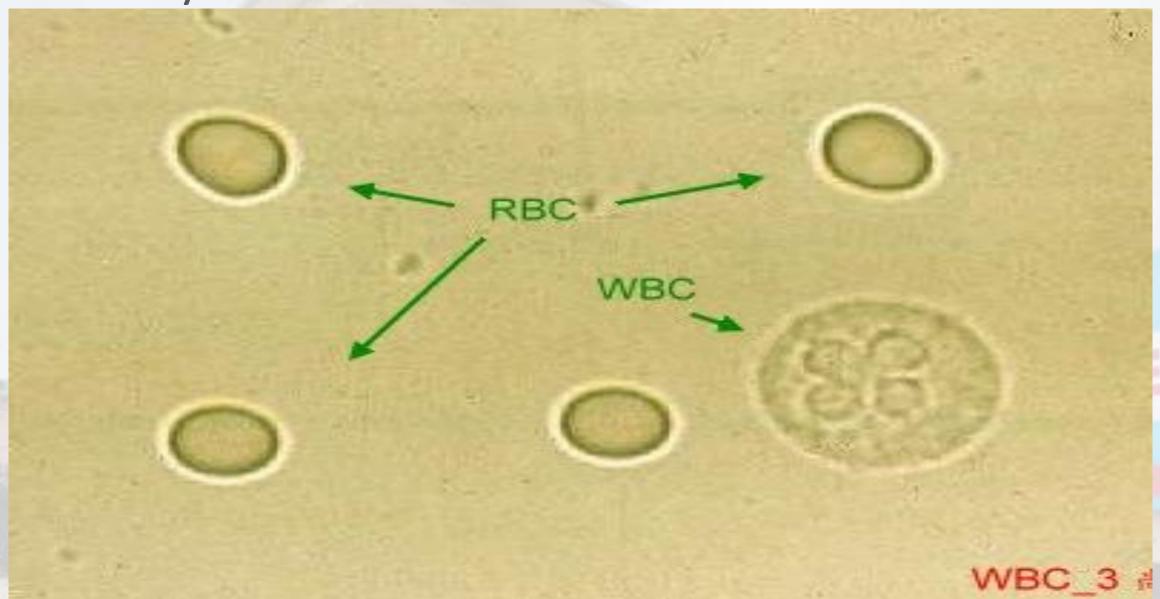




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Urinary RBC vs WBC



Hematuria

- ✓ Dipstick relies on the peroxidase activity of hemoglobin to catalyze an organic peroxide with subsequent oxidation of an indicator dye.
- ✓ Myoglobin is also detected because it has intrinsic peroxidase activity.
- ✓ Suspect myoglobinuria or hemoglobinuria with positive by dipstick but negative for urinary RBC by microscopic examination.
- ✓ Confirm all positive dipsticks with microscopic examination of spun urinary sediment vs supernatant.

False Positive Hematuria

- ✓ Presence of semen in urine may cause positive heme reaction
- ✓ Alkaline urine with pH>9 or contamination with oxidizing agents used to clean perineum
- ✓ Presence of myglobinuria

TERNITY & WOMEN'S CENT

Mimics of Hematuria

- ✓ Menstrual cycle: remember age and sex of patient
- ✓ Ingestion of beets, rhubarb, certain food dyes or senna: what is your

patient eating?

✓ Drugs: pyridium, phenytoin, rifampin, nitrofurantoin

Hematuria

- Is common, particularly young adult patients, hematuria is transient and of no consequence.
- Can be transient or persistent (history is very important)
- Grossly visible (macroscopic) or detectable only on urine examination (microscopic)
- Pathology represents the presence of 3 or more RBC per high power field (HPF) in a spun urine sediment.
- Dipstick for heme detect 1 to 2 RBC per HPF
- Dipsticks are at least as sensitive as urine sediment examination, but result in more false positive tests.
- Positive dipstick test needs to be confirmed with microscopic evaluation

Causes of Hematuria

- 1. Renal: renal mass, glomerular pathologies,
 - structural disease, pyelonephritis,
 - malignant HTN, renal vein thrombosis, AV
 - malformation, papillary necrosis(sickle cell)

2. Ureter:

- malignancy, stone, stricture,
- fibroepithelial polyp

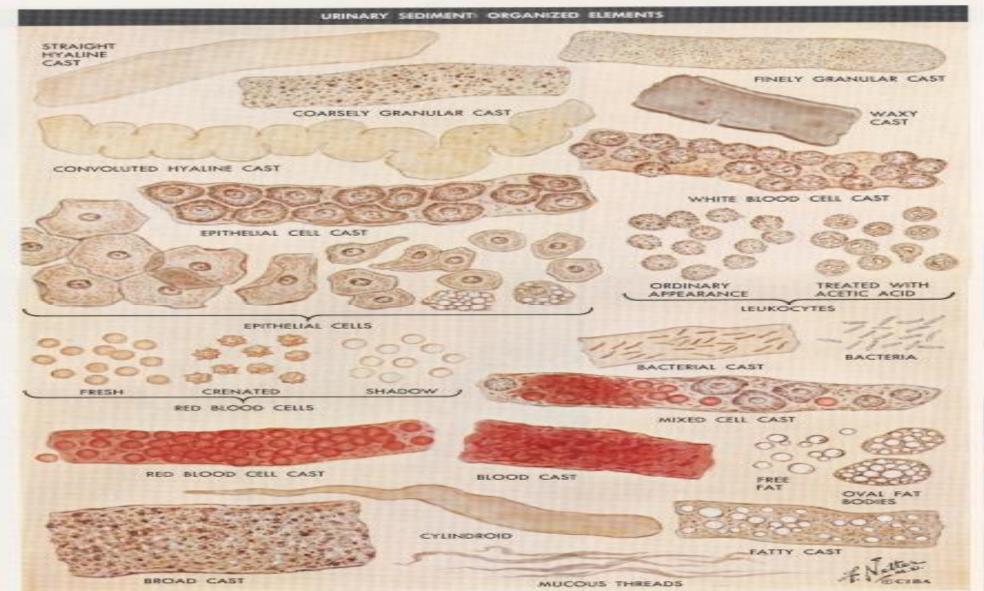
3. Bladder:

- Malignancy
- Radiation
- Cystitis

4. Prostate/urethra: BPH, malignancy,

- prostatic procedures, traumatic
- catheterizations, urethritis, urethral
- diverticulum

Urine Microscopy



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Microscopic Examination

- 1. Cellular elements
 - a. RBC
 - b. WBC
 - c. Renal tubular epithelial cells
 - d. Squamous cells of urethral, vaginal or cutaneous origin
 - e. Transitional epithelial cells line the renal pelvis, ureter, bladder and proximal urethra

2. Casts

Microscopic Urinalysis (cont.)

WBC

- Normal: 0 5 per hpf
- Men usually have < 2/hpf; women usually have < 5/hpf
- Presence of elevated WBCs indicates the body may be fighting infection in the urinary tract

RBC

- Normal: 0 1 per hpf
- Presence indicates damage to urinary tract(eg. infection, physical trauma, etc.)

Bacteria

- Normal: negative
- Presence of bacteria is not always predictive of a UTI (ex. asymptomatic bacteriuria, catheter colonization)
- Must use in conjunction with other factors

Microscopic Urinalysis (cont.)

Epithelial cells

- Squamous epithelial cells
 - Normal: 0 2 per hpf
 - Large numbers may indicate a poor sample (contamination)
- Renal epithelial cells
 - Normal: 0 1 per hpf
 - Large numbers may indicate renal tubular injury

Crystals and casts

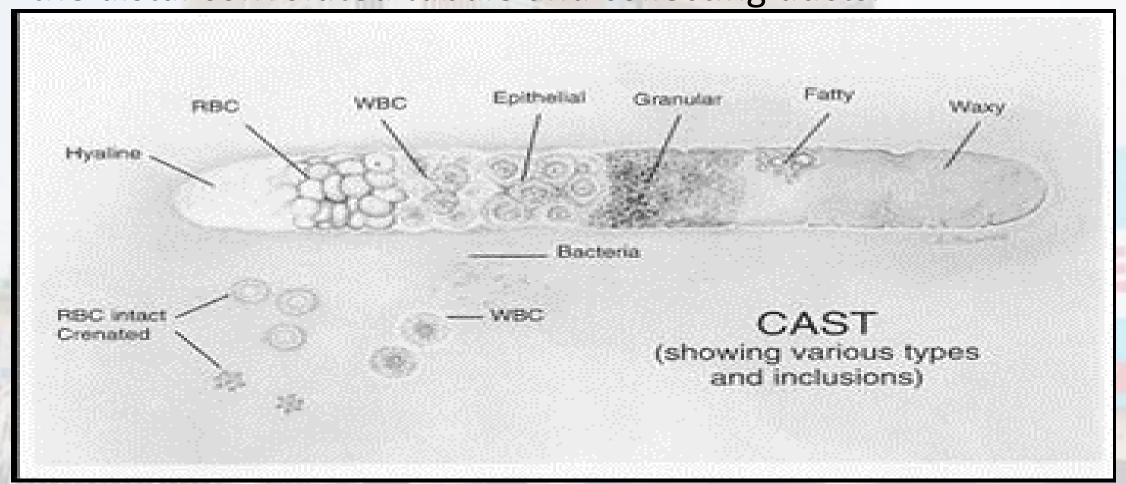
Typically indicative of inflammation, infection, or injury in the urinary tract

URINARY CASTS

- ✓ Named based upon shape and origin.
- ✓ Consist of a matrix of Tamm-Horsfall urinary glycoprotein in the shape of the distal tubular or collecting segment where they were formed.
- ✓ Matrix has a straight margin compared to clumps of cells or debris has seen in cellular elements
- ✓ Formation iS pronounced during low flow, concentrated salts and low Ph.

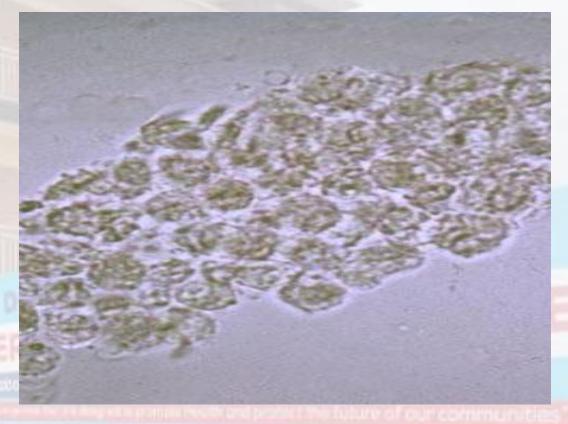
Urinary casts

• Formed via precipitation of Tamm-Horsfall mucoprotein in the distal convoluted tubule and collecting ducts.



Casts ct'n





RBC Cast

WBC Cast

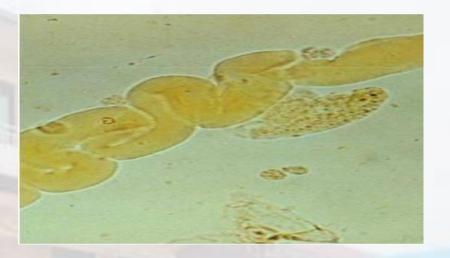
Casts ct'n



Hyaline Casts

- ✓ Consists of protein alone.
- ✓ Difficult to see b/c of refractive index close to that of urine.
- ✓ Nonspecific, solidified Tamm-Horsfall mucoprotein. Most common cast.

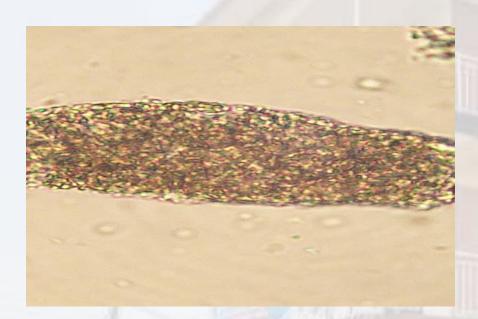
Ex: normal individuals in dehydration or vigorous exercise.



Waxy/Broad Casts

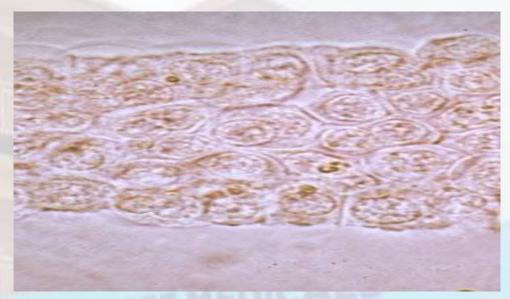
- ✓ Consists of hyaline material with a much greater refractive index.
- ✓ Form in tubules that have become dilated and atrophic due to chronic parenchymal disease.

Casts ct'n



Granular Cast.

- ✓ Consists of finely (altered serum protein) or coarsely (degeneration of embedded cells) granular material.
- ✓ Usually pathologic. Most often indicative of CKD.



Tubular Cell Cast

- ✓ Consists of sloughed epithelial tubular cells.
- ✓ Characteristically seen with acute tubular necrosis (ATN) and toxic ingestion such as mercury, diethylene glycol or salicylate. But can occur in concentrated urine

Urinary Crystals

- Formation is dependent on degree of
 - concentration of constituent molecules,
 - urine pH, and the presence of inhibitors of crystallization
- May be present spontaneously or may precipitate with refrigeration of urine



THE END.

- •Thank you for your time
- •Questions?



