Biochemistry (Renal module)

❑ Urine composition and renal stones

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Urine composition

Definition:

Urine is a fluid formed by the kidneys as a result of 3 processes:

1. **Filtration** of blood plasma by glomeruli
2. **Selective reabsorption** of certain substances by renal tubules: as salts, water, glucose and amino acids which are required by the body.
3. **Secretion** of certain substances by renal tubules: as potassium, uric acid, organic acid and hydrogen ions.

Non-protein nitrogenous compounds (NPN) in urine:

1. **Urea:** 25-30 g / day
2. **Uric acid:** 100 – 500 mg / day
3. **Creatinine:** 1.4 g / day
4. **Creatine:** 50 -150 mg /day
5. **Ammonia:** 0.7 g / day
6. **amino acids:** 100 – 200 mg / day

Urine composition

Urine NBN:

1. **Urea:** the main end product of protein catabolism
   - Its excretion is directly related to the protein intake
   - It comprises 80 – 90 % of the total urinary nitrogen
   - With low protein diet, its amount in urine decreases

- ↑ **Urea excretion in cases of increased protein catabolism:** e.g. fever, DM, hyperactivity of the adrenal cortex and thyroid gland.
- ↓ **Urea excretion** in cases of increased protein synthesis (pregnancy), renal failure (↓ excretion), severe liver disease (↓ production) and acidosis (↑ ammonia production)

Urine composition

Urine NBN:

2. Ammonia: formed from the renal tubular epithelium, 60% by glutaminase enzyme, the remainder by deamination of the other amino acids.

- It passes into the tubular lumen where it combine with H^+ forming $NH4^+$, thus lowering the H^+ concentration and allowing further passage of H^+ into the lumen in exchange with Na^+

Ammonia excretion is increased in:

1. Acidosis e.g. ketosis, ingestion of acids or acids forming substances
2. High protein diet (↑ production of acids)

Ammonia excretion is decrease in:

1. All cases of alkalosis
2. Acidosis of renal origin (failure of ammonia excretion)

Urine composition

Urine NBN:

3. Creatinine and creatine:

Creatine: It is not excreted in significant amount in urine, since it is completely reabsorbed by the renal tubules at the normal levels

Creatinine: formed from creatine in constant amounts daily corresponding to 2% of the body creatine, all of which is excreted in urine.

- The excretion is determined by the muscle mass.
- Creatinine is excreted by glomerular filtration and tubular excretion.
- The value for creatinine clearance is > 100 ml / minute (it is ↓ in conditions of impaired GFR)

Urine composition

Urine NBN:

4. Amino acids: are excreted in urine both free and combined e.g. hippuric acid (benzoic acid and glycine).

Causes for presence of amino acids in abnormal conditions (aminoaciduria):

- **Physiological:** early in life (newborn) & during pregnancy
- **Pathological:**

a. ↑ amino acids in plasma (overflow aminoaciduria):

- Severe liver diseases (↓ deamination)
- Inherited defect in amino acids metabolizing enzymes e.g. phenylalanine hydroxylase (phenyl ketonuria, histidase (histidinemia), branched chain ketoacid decarboxylase (maple syrup urine disease)

b. Renal aminoaciduria: as a result of renal tubular damage or due to genetic defect e.g. cystinuria & glycinuria

Urine composition

Urine NBN:

5. Uric acid: (the main end product of purine metabolism)

- At urine pH 6.0, uric acid is present as Na & K salts.
- The amount excreted depends on the amount of nucleoprotein ingested (exogenous) & that formed from tissue nucleic acids (endogenous).
- On a purine free diet, uric acid excretion is constant (0.1 – 0.5 gm daily)
- Its excretion is increased in metabolic gout

Urine composition

Abnormal constituents of urine:

1. Protein (proteinuria)
2. Sugars or glucosuria (see CHO metabolism)
3. Ketone bodies (see ketosis)
4. Bile pigment (see jaundice)

Urine composition

Abnormal constituents of urine:

1. **Proteinuria:** is the presence of protein mainly albumin in abnormal concentrations > 300 mg / day. **Types:**

a. Physiological Proteinuria:

- Following severe muscle exercise
- After high protein meal
- Orthostatic or postural (temporary impaired of renal circulation)

a. Pathological Proteinuria:

- **Pre-renal:** in heart failure & hypertension
- **Renal:** by ↑ permeability of renal glomeruli due to kidney diseases e.g. glomerulonephritis, nephrotic syndrome and heavy metal poisoning (mercury & arsenic)
- **Post-renal:** in inflammation of the urinary tract

c. Bence Jones proteinuria: special globulin of low molecular weight, found in serum & excreted in urine in myeloid leukemia & multiple myeloma, precipitate at 45 – 60°C but re-dissolve on boiling and re-precipitate on cooling.

Urine sediments (deposits)

Deposits are collected by centrifuging urine. The sediments are examined by microscope. They are organized & unorganized:

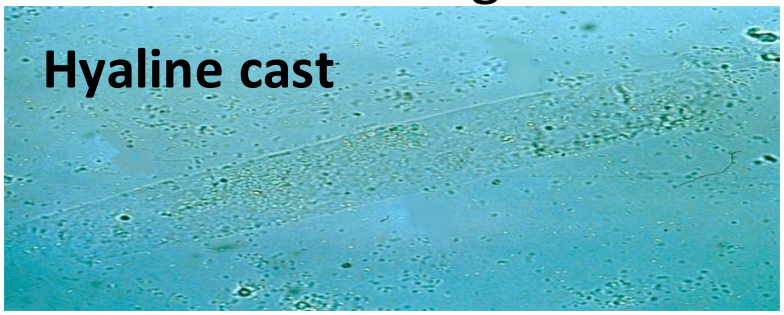
A. Organized urinary sediments:

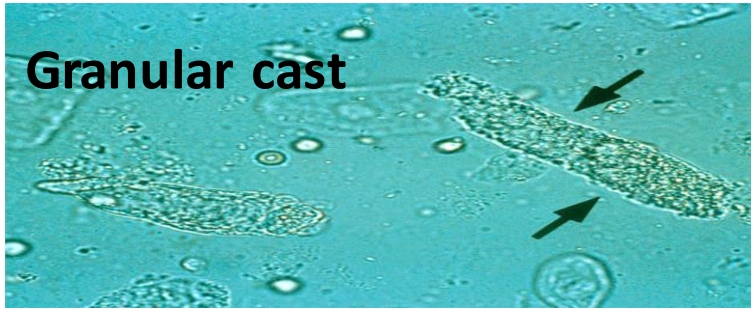
1. **Epithelial cells:** normally few, increased in inflammation of urinary tract.
2. **Red cells:** in case of hematuria
3. **Pus cells:** normally few, increase in infection
4. **Sperms:** in male urine after ejaculation
5. **Bacteria:** normally few, increase in infection
6. **Casts:** formed in the collecting tubules by coagulation of albuminous material.

Urine sediments (deposits)

Urine casts:

1. **Hyaline casts:** transparent, refractile tubular structures, normally few but increase after exercise.
2. **Granular casts:** similar to hyaline cast, but dotted with albuminous granules, occurs in late stages of acute nephritis.
3. **Epithelial, blood & leucocyte casts:** have a central core usually provided by a hyaline or granular cast around which the cells adhere. Their presence indicate acute phase of nephritis.
4. **Waxy casts:** in chronic renal failure and acute and chronic renal allograft rejection. Unusual broad waxy casts are renal failure casts. Theses dilated casts are created in dilated tubules of end stage renal disease.

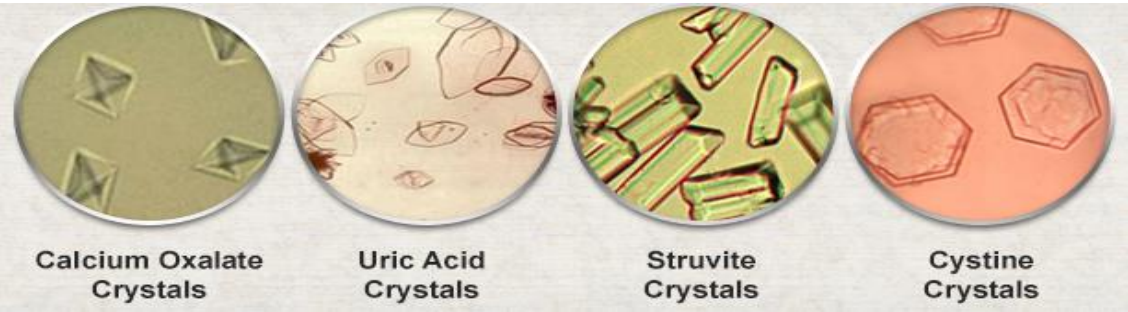




Urine sediments (deposits)

A. Unorganized urinary sediments:

1. **Phosphate:** in alkaline urine. The commonest form is the ammonium magnesium phosphate (triple phosphate)
2. **Calcium oxalate:** in acidic urine, envelope shaped.
3. **Cystine crystals:** hexagonal-shaped under the microscope. The other amino acids that are not absorbed do not create crystals in urine.
4. **Uric acid crystals:** of different shapes; barrel, plate-shaped, or diamond. They can be found in normal urine when caused by a protein-rich diet, which increases uric acid in urine. They are also caused by kidney stones, gout, chemotherapy or tumor lysis syndrome.



Kidney stones

Definition: Kidney stone diseases (urolithiasis) occurs when a solid material (stone) develops in the urinary tract.

Sites of formation: Develop any where along the urinary tract (kidney, ureter, urinary bladder & urethra)

Predisposing factors:

1. **Dehydration:** due to low fluid intake (a major factor)
2. **Obesity:** a leading risk factor
3. **High dietary intake:** animal ptn, sodium, grapefruit & apple juices
4. **Metabolic disorders:**

- Distal renal tubular acidosis
- Dent's disease (tubular proteinuria, excess Ca in urine, calcium kidney stones, nephrocalcinosis & chronic kidney failure)
- Hyperparathyoidism
- 1ry hyperoxaluria
- Crohn's disease: associated with hyperoxaluria & malabsorption of magnesium

Kidney stones

N.B. A person with recurrent kidney stones may be screened for such disorders. This done with a 24-hour urine collection. Urine is analysed for features that promote stone formation.

Types of stones:

1. Calcium stones: (calcium oxalate & Calcium phosphate)

- Ca stones are the most common of kidney stones
- Calcium oxalate stones > calcium phosphate stones
- Dietary calcium does not increase the chance of stone formation
- Excess calcium not used by bones or muscles goes to the kidney to be excreted. If this does not happen, calcium stays in the urinary tract & precipitates with other waste products to form stones.

Kidney stones

Types of stones:

2. Uric acid stones:

- It forms when there is too much uric acid in urine.
- Eating fish, shellfish and meat (especially organ meat) may increase urate stone.

3. Struvite stones: may form after urinary tract infection. They can develop suddenly and become large quickly

4. Cystine stones:

- They result from cystinuria (a disease passes down families)
- Cystinuria causes cysteine amino acid leak into urine

Kidney stones

Pathogenesis (mechanism of stone formation):

- Formation of crystals in supersaturated urine
- Crystals adhere to the urothelium creating a nidus for subsequent stone growth
- The biological process that anchor crystals to the urothelium is incompletely understood
- Many, but not all, calcium oxalate stones develop on Randall's plaques which are compose of calcium phosphate (= hydroxyapatite)
- They grow to erode the urothelium, forming a nucleus for calcium oxalate deposition

Kidney stones

Symptoms:

- Foul smelling urine
- Discolored urine: pink, red, brown or blood in urine
- Frequent urgent need to urinate
- Fever and chills
- Nausea and vomiting
- Shifting pain in the lower abdomen and groin
- Varying intensities of pain that comes and goes

Kidney stones

Diagnosis:

1. **Computerized tomography (CT) scan**
2. **X ray:** radiolucent stones as cystine & urate stones may not be identified with X-ray
3. **Ultrasonography**
4. **Intravenous urogram (IVU) or intravenous pyelogram (IVP):**

- In this procedure, a radio-opaque dye is injected through a vein in the arm. This dye highlights the presence of stones on X-ray. The dye passes out from the body in urine.
- A patient informs the doctor about all his current medications and allergies before this procedure
- The doctor makes sure that the patient is not allergic to the dye used.

Kidney stones

Complications:

- Recurrent kidney stones: the chance of recurrence is 80%
- Obstruction of the urinary tract
- Renal failure
- Injury to the ureter (during surgical removal of tone)
- Urinary tract infection
- Sepsis (after treatment of a large stone)
- Severe pain
- Heavy bleeding during surgery