KIDNEY FUNCTION TEST

Dr. Zeiba khan

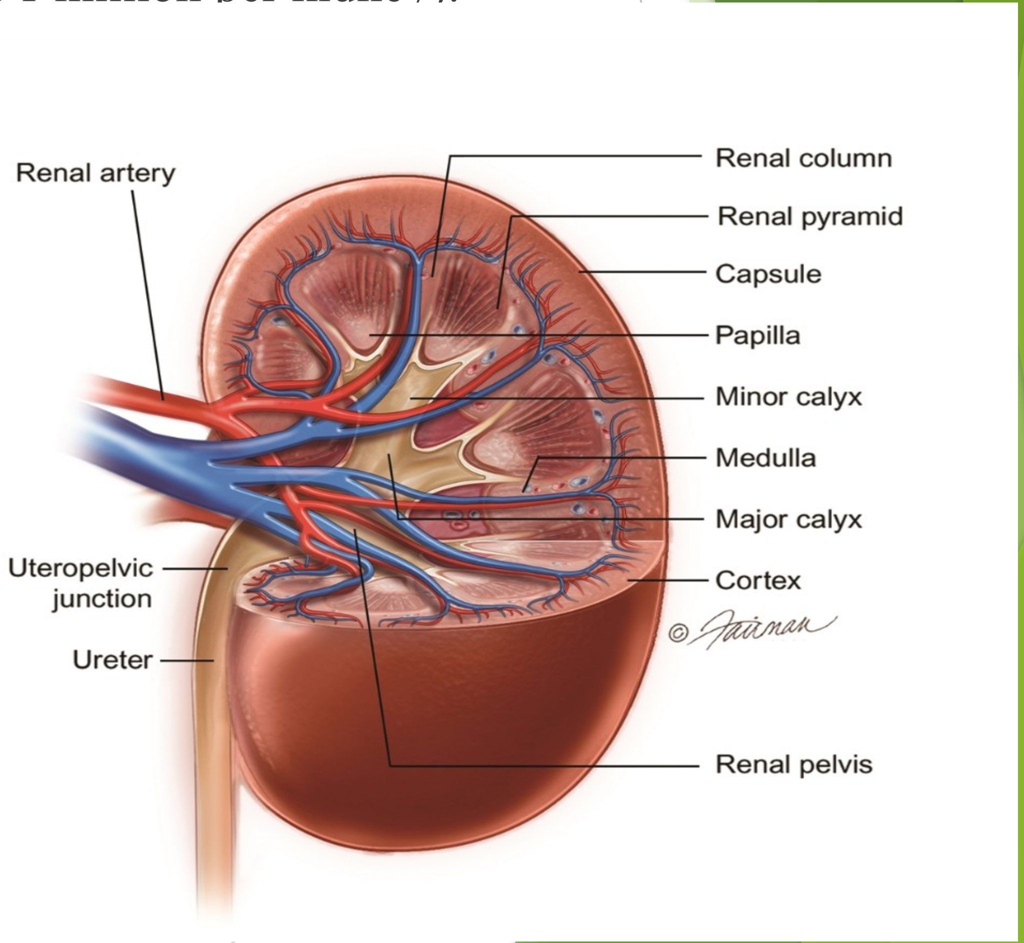
Anatomy and Physiology

- Nephron - Structural & Functional unit of kidney (about 1 million per kidney).
- Kidney is a retroperitoneal organ.
- Rt. Kidney lies slightly lower than the Lt. kidney.
- Bean shaped, Weight ~150 gm
- Dimensions-

  Length- 11-14cm, 6cm- wide, 4cm thick.
- At rest it receive about 25% of the total CO.
- Filters about 180 L per day.

(of w/c 178L of water and most of the organic & inorganic solutes are reabsorbed)

- About 2 L urine produce per day.



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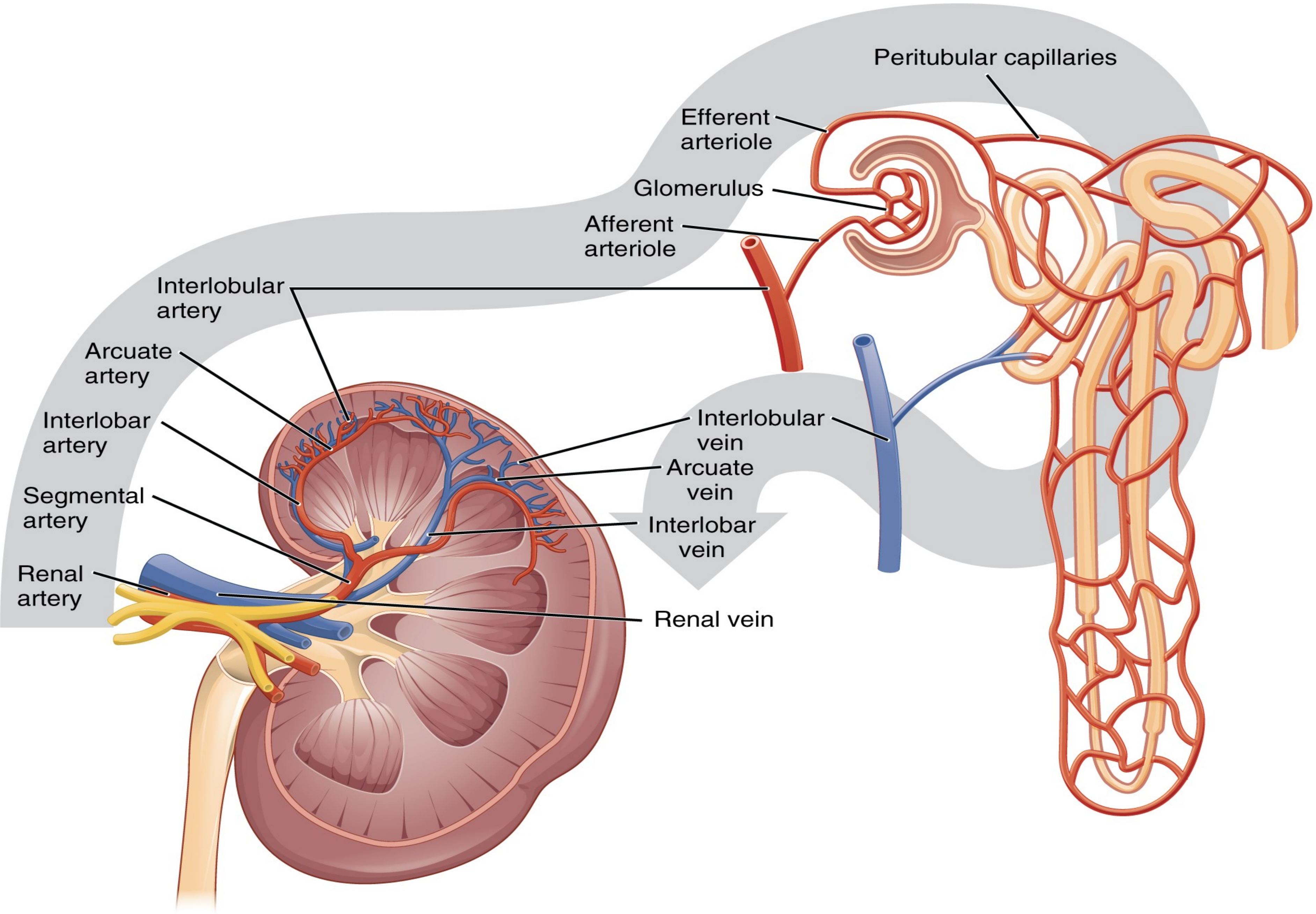

Peritubular capillaries
Efferent arteriole
Glomerulus
Afferent arteriole
Interlobular artery
Arcuate artery
Interlobar artery
Segmental artery
Renal artery
Interlobular vein
Arcuate vein
Interlobar vein
Renal vein

Renal Functions

- Urine Formation (4 stage: glomerular filtration, tubular reabsorption, tubular secretion, excretion)
- Excretion of waste/harmful/toxic substances (like urea, uric acid, creatinine)
- Homeostasis

  -Electrolyte Balances.

  -Acid-Base Balances.
- Metabolic & Hormonal function

  -Erythropoietin (stimulating production of RBCs)

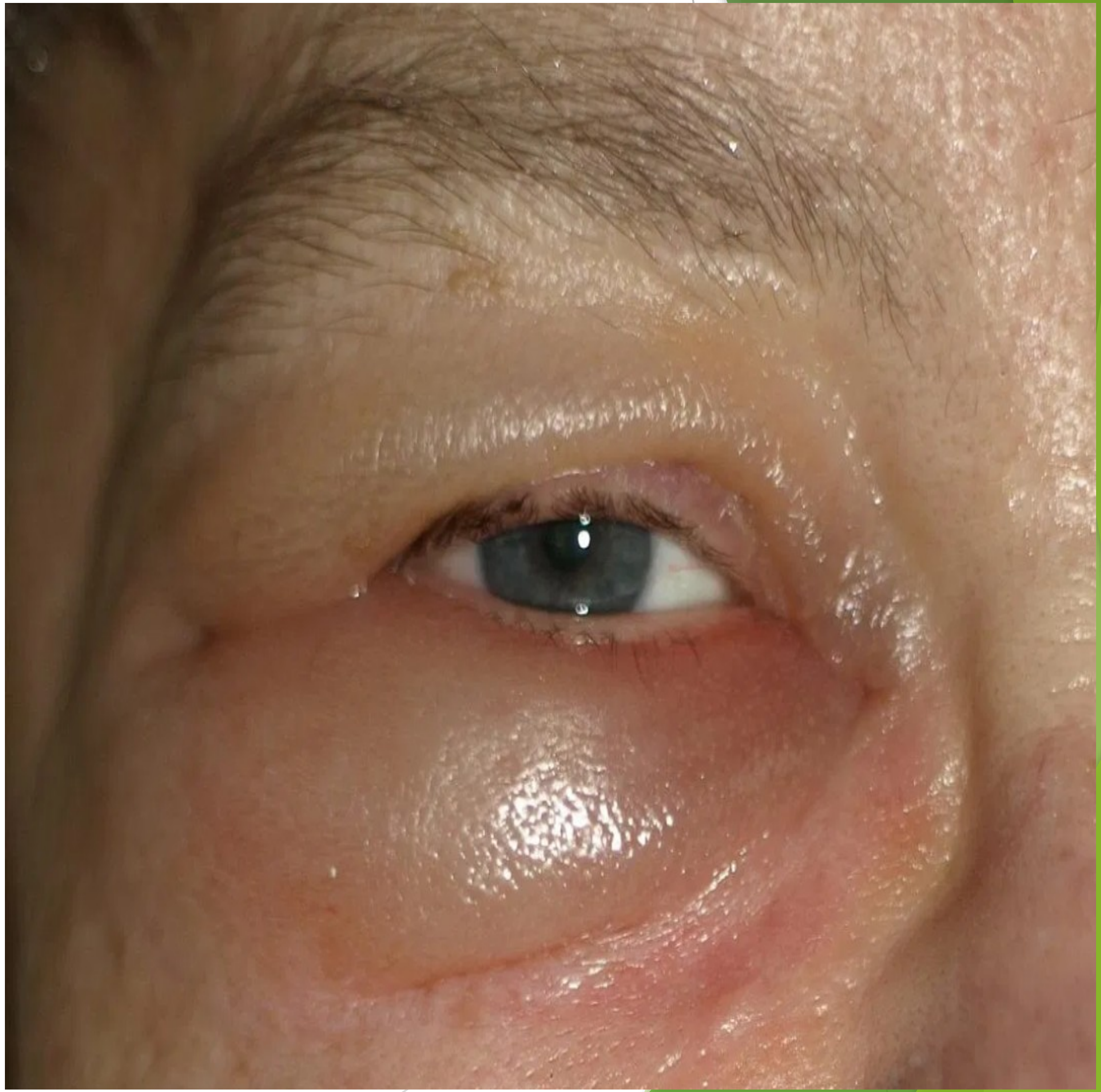
  -Prostaglandins Synthesis

  -Renin (Regulates blood pressure)

  -Synthesis of Vit. D.

Signs and Symptoms of Renal Disorders

- Polyuria, Oligouria, Anuria Seizures or coma in severe case
- Nausea, vomiting Confusion
- Weight loss Muscle cramps
- Fluid retention e.g. Periorbital edema Need to urinate at night
- General ill feeling Hematuria
- Fatigue Decreased alertness
- Headache
- Abdominal pain
- Generalized itching (pruritus)

Why do we test renal functions?

- To identify renal dysfunction.
- To diagnose renal disease.
- To monitor disease progression.
- To monitor response to treatment.
- To assess changes in function that may impact therapeutic efficacy (e.g. Digoxin, chemotherapy).

Classes of Renal Function Tests

- **Urine Analysis**

  -Physical, Chemical and Microscopic Examination of urine.
- **Biochemical Tests of Renal Function**

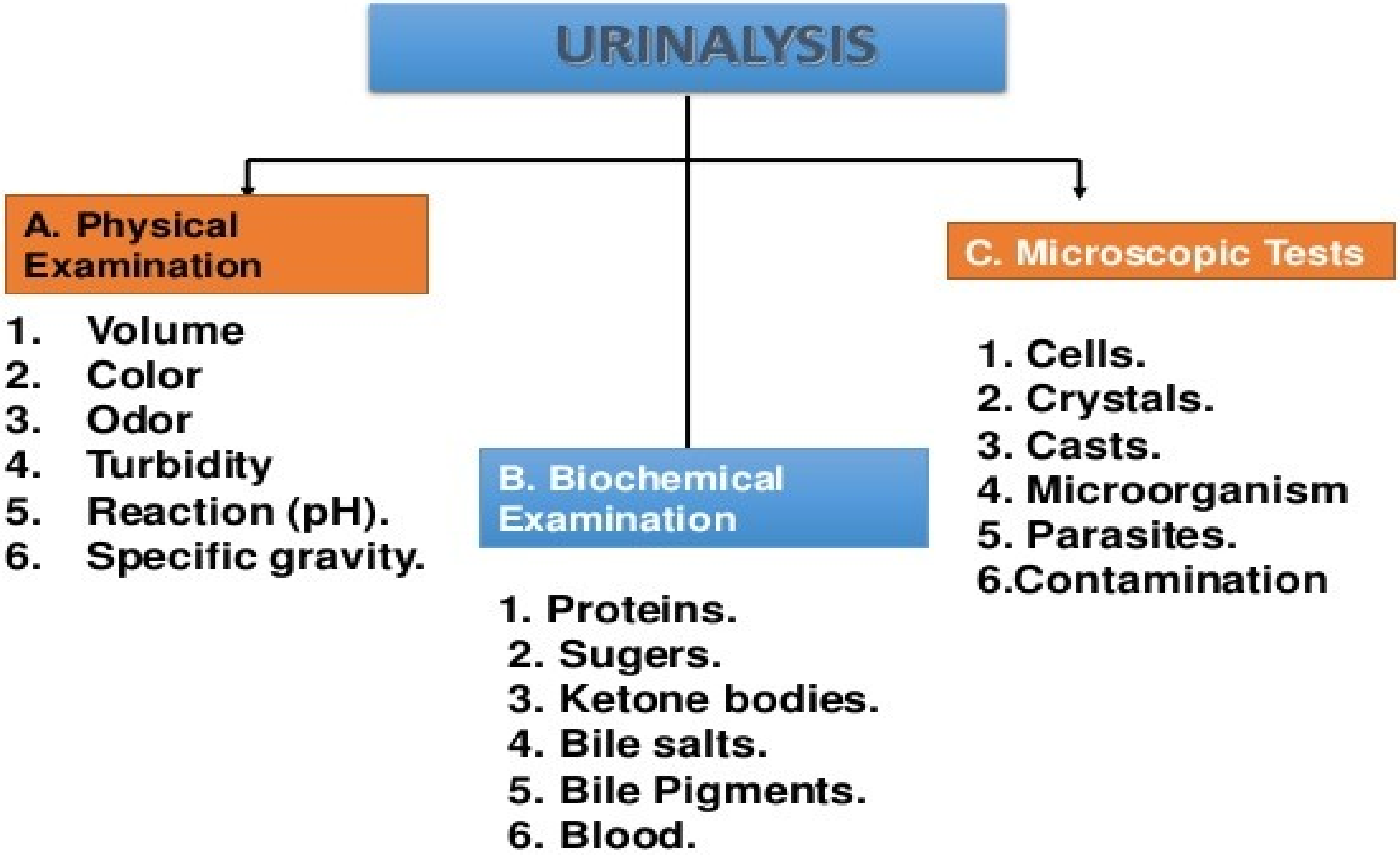
  -Urea, Uric acid, Creatinine
- **Glomerular Filtration or Renal Clearance**

  -Creatinine clearance test

  -inulin clearance test
- **Tubular Function**

  -Specific Gravity

  -serum and urine osmolarity



URINALYSIS
A. Physical Examination
1. Volume
2. Color
3. Odor
4. Turbidity
5. Reaction (pH).
6. Specific gravity.
B. Biochemical Examination
1. Proteins.
2. Sugers.
3. Ketone bodies.
4. Bile salts.
5. Bile Pigments.
6. Blood.
C. Microscopic Tests
1. Cells.
2. Crystals.
3. Casts.
4. Microorganism
5. Parasites.
6.Contamination

Biochemical Tests of Renal Function

Serum Creatinine

Normal values Men 0.7–1.3 mg/dL (Ramnik sood 6th ed.)

Women 0.6–1.1 mg/dL

- It is a by-product in the breakdown of muscle creatine phosphate (a compound found in skeletal muscle tissue) resulting from energy metabolism.
- It is produced at a constant rate depending on the muscle mass of the person and is removed from the body by the kidneys.
- A disorder of kidney function reduces excretion of creatinine, resulting in increased blood creatinine levels.

- This test diagnose impaired renal function. It is more specific and sensitive indicator of kidney disease than BUN.

Clinical Implications of Sr. Creatinine

Increased levels of creatinine levels occur in following conditions:

- Impaired renal function   Shock
- Obstruction of urinary tract   Dehydration
- Muscle disease   Rhabdomyolysis (breakdown of skeletal muscle)

    -Gigantism   A diet high in meat

    -Acromegaly

    -Myasthenia Gravis

    -Muscular Dystrophy

    -Poliomyelitis

- Congestive heart failure

Decreased levels of creatinine levels occur in following conditions:

1. Small stature
2. Decreased muscle mass
3. Advanced and severe liver disease
4. Inadequate dietary protein
5. Pregnancy (due to increase plasma volume)

Methods for detection Sr. Creatinine

Jaffe reaction-

- Commonly used
- creatinine react with an alkaline picrate reagent produce yellowish-red color.

Blood Urea

Normal range 15-45 mg/dl **(3rd ed. Praful B. Godkar)**

- Urea is a nonprotein nitrogen (NPN) compound produced in the liver from ammonia as an end product of protein metabolism.
- It accounts more than 75% of total NPN.
- More than 90% of urea is excreted through kidneys, rest 10% are excreted through GIT & Skin.
- The rate at which the urea level rises is influenced by-

  -Degree of tissue necrosis

  -Protein catabolism

  -High protein intake

  -Rate at which kidney excrete

Clinical Implications of Urea

Increase urea levels (uremia) occur in following conditions:

- Acute renal failure
- Congestive heart failure
- Decreased renal perfusion.
- DM with ketoacidosis.
- Hypovolemia.
- Chronic kidney disease like glomerulonephritis and pyelonephritis.
- Excessive protein intake
- GI bleeding (digested blood produces urea)

Hypovolemia

Neoplasms

Shock

Nephrotoxic agents

Starvation/muscle wasting

- Catabolic states: (Protein catabolism e.g. fever, severe infections, etc.)
- Drugs: Steroids (by causing increased Protein catabolism), Diuretics, etc.
- Due to obstruction of outflow of urine (e.g. enlarged prostate gland, stone in urinary tract or tumors of bladder)

NOTE

1. Conditions that result in decreased perfusion, such as hypovolemic shock or heart failure, cause BUN levels to increase.
2. Additionally, severe dehydration also increases BUN because the low fluid volume impairs the ability of the kidneys to excrete urea and other waste products.
3. BUN = mg% urea * 0.467 or mg% urea = BUN * 2.14

A decreased urea may be seen in:

1. Protein malnutrition
2. Overhydration
3. Severe liver disease such as resulting from like hepatitis, drugs, or poisoning
4. Malabsorption syndromes (celiac disease)
5. Pregnancy (bcoz increase plasma level)
6. Nephrotic syndrome
7. Syndrome of inappropriate anti-diuretic secretion (SIADH)
8. BUN is normally lower in children and women because they have less muscle mass than adult.

Methods for detection Urea

1. **Di-acetlymonoxime (DAM) method**

Urea reacts with DAM in hot acidic medium & in presence of thio-semicarbazide & ferric ions to forms a pink colored compound which can be measured on a green filter (520nm).

2. **Berthelot reaction method-** 546nm

3. **Rate of reaction method (uv- kinetic)-** 340nm

URIC ACID

- Normal values- Men 3.4–7.0 mg/dL (Ramnik sood 6th ed.)

  Women 2.4–6.0 mg/dL
- Uric acid is formed from the breakdown of nucleonic acids and is an end product of purine (chemicals that are the building blocks for DNA and RNA) metabolism.
- Two thirds of the uric acid produced daily is excreted by the kidneys, whereas the remaining one third exits by stool.
- The overproduction of uric acids occurs when there is excessive cell breakdown and catabolism of nucleonic acids (as in gout), excessive production and destruction of cells (as in leukemia), or an inability to excrete the substance produced (as in renal failure).

Clinical Implications of Uric acid

Elevated uric acid levels (hyperuricemia) occur in following conditions:

- Conditions of rapid turnover of cells due to cell damage (Leukemias, myeloma, lymphoma)
- Gout
- Renal diseases
- Lead poisoning
- Starvation, weight loss diets
- Hypothyroidism and hyperthyroidism
- Hemolytic anemia, sickle cell anemia

Alcohol (source of purine)

Metabolic acidosis

Conti.

- Hyperlipidemia, obesity (when people are obese, their bodies produce more insulin. Higher level of insulin inhabit uric acid elimination by the kidney)
- Psoriasis (due to rapid skin cell turn over)
- Liver diseases (as production of uric acid is mainly from the liver)
- Following excessive cell destruction, as in chemotherapy & radiation tx
- Purine rice diet e.g. liver, kidney, sweetbreads

Hyperuricemia and gout in thyroid endocrine disorders.

Giordano N, et al. Clin Exp Rheumatol. 2001 Nov-Dec.

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Citation
Clin Exp Rheumatol. 2001 Nov-Dec;19(6):661-5.

Abstract
OBJECTIVE: A significant correlation between thyroid function and purine nucleotide metabolism has been established in hypothyroidism. On the contrary, the relationship between hyperthyroidism and purine metabolism is more controversial. The present study evaluates the prevalence of hyperuricemia and gout in patients affected by primary hypothyroidism and hyperthyroidism.

METHODS: We studied 28 patients with primary hypothyroidism and 18 patients with

RESULTS: In comparison to the prevalence reported in the general population, a significant increase of both hyperuricemia and gout was found in the hypothyroid patients, and of hyperuricemia in the hyperthyroid patients. In hyperthyroidism the hyperuricemia is due to the increased urate production, while in hypothyroidism the hyperuricemia is secondary to a decreased renal plasma flow and impaired glomerular filtration.

Decreased levels of uric acid occur in following conditions:

1. Xanthinuria (deficiency of xanthine oxidase)
2. SIADH (Syndrome of inappropriate anti-diuretic secretion)
3. Wilson’s disease
4. Fanconi’ syndrome (disorder of kidney tubule function)
5. Heavy metal poisoning
6. Renal tubular defects
7. Drugs like aspirin (high dose), corticosteroids, allopurinol.

Glomerular Filtration or Renal Clearance

Clearance Test

Purpose:

- Used to calculate glomerular filtration rate **(GFR)**
- Evaluates progression of renal disease.

GFR is the volume (mL) of fluid filtered from the glomeruli into Bowman's capsule per unit time (min).

Avg Normal Value: "125 ml/min"

GFR is directly proportional to number of intact nephrons.

GFR can be estimated by Clearance Tests

- Clearance test measure the actual excretory capacity of the kidney since they measure the amount of a substance excreted in the urine as compared to the concentration of the same substance in the plasma.
- Clearance tests are considerably more sensitive and clinically more useful than the tests measuring retention of substance such as urea; since these substances may not elevate in blood until there is a significant decrease in kidney function. (below 50% of normal substance)

GFR = Clearance of a Substance = (U / P) x V

- U = Conc. of the marker substance in Urine mg/dl
- P = Conc. of the marker substance in Plasma mg/dl
- V = Urine flow rate [Urine Vol. (ml)/24 h] i.e volume of the urine in ml / 1440
- *Marker substance used to measure GFR may be Exogenous (e.g. Inulin) or Endogenous (e.g. Creatinine)

Ideal Marker for GFR Measurement

- Constant rate of production (endogenous) or of delivery (i.v.) (exogenous).
- Freely filtered in the glomerulus i.e. no protein binding.
- Metabolically inactive
- No tubular reabsorption
- No tubular secretion
- Can be estimated in the Lab

Creatinine Clearance

Reference value (mL/min): Adult male: 85-125

Adult female: 75-115

Children: 70-140

Note: after 40yr age, values decrease 7 ml/min per decade.

- Creatinine is made at a steady rate, but with kidney disease that interferes with excretion, blood levels rise and urine levels fall.
- This test measures how effectively the kidneys remove creatinine from the blood.
- This test is done in conjunction with a creatinine blood test and amount of creatinine excreted during a specified time period (usually 24 hours).

Formulas:

- GFR (Cr. Cl)/ml/min = Urine Creatinine X Urine Volume (ml)

Serum Creatinine

1440

- GFR(ml/min/1.73m2)= Urine Creatinine X Urine Volume (ml) X 1.73

Serum Creatinine 1440

A (surface area of pt.)

Inulin Clearance

- Inulin is a fructose polysaccharide that gives very accurate estimations of GFR since it meets all the criteria of ideal marker.
- A loading dose of inulin can be administered iv, followed by a sustaining infusion (usually for 3 hr.)
- Inulin concentration in urine and plasma is determined and hence GFR can be calculated.
- Inulin clearance is infrequently used in clinical lab. (expensive)

Estimated Glomerular Filtration Rate (eGFR)

1. A simpler technique of estimating creatinine clearance and there by GFR is by using serum creatinine level. This eliminate the need for timed urine collections. A commonly used formula is **cockroft Gault** equation.

(140 - age) X weight (kg) X 0.85 (if females- assuming that they have 15% less muscle mass)

72 X serum creatinine

2. A more recent equation used in the **MDRD (Modification of Diet in Renal Disease)** study is more accurate. This equation directly estimates GFR.

eGFR (mL/min/1.73m2) = 186 × (Creatinine/88.4) -1.154 × (Age) – 0.203 × 0.742 (if female)

Sensitivity and Clinical utility

	accuracy	Clinical utility	Cost
Inulin clearance	++++	+	$$$$
Radiolabeled markers	+++	+	$$$
Nonisotopic contrast agents	+++	++	$$$
Creatinine clearance	++	+++	$$
Serum creatinine	+	++++	$

Staging of CKD

KDIGO 2017 Clinical Practice Guideline

(Kidney disease improving global outcomes)

GFR Category	GFR (mL/min/1.73 m2)	Terms
G1	≥90	Normal or high
G2	60-89	Mildly decreased
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	<15	Kidney failure

Cystatin C

- It is a small protein, produced throughout body by all cells that contains a nucleus.
- It is filter from the blood by the kidney, and broken down at a constant rate.
- If kidney function and GFR decline, the blood level of cystatin c rise.
- Serum levels of cystatin c are more precise test of kidney function (GFR) than serum creatinine levels because its levels are less dependent on age, diet, race, gender and muscle mass compared to creatinine.
- **Range** Men- 0.56 to 0.98 mg/l

  Women- 0.52 to 0.98 mg/l

Limitations

Not standardized

Not widely used

Expensive – compared to creatinine

Tubular Function

Specific Gravity

- Reference value 1.001 – 1.040 (Usually 1.015 with normal fluid intake)
- It measures the kidney's ability to concentrate or dilute urine in relation to plasma by comparing the weight of urine (particles) to the weight of distilled water (1.000).
- Because urine contains various substances, such as minerals and salts, the specific gravity is normally higher than that of water.
- SG may increase with an increase of other substance, such as protein, glucose, in the urine or if the fluid content falls, such as with dehydration.
- If abnormal substances (proteins, glucose, dyes) are not present in the urine and the kidney produces concentrated urine with an increased specific gravity, the primary causes include:

  - Dehydration (Most common).

  - Increased secretion of ADH- it increases tubular water reabsorption.

  (Various factors, such as trauma, stress, surgery, and medications, can result in an increased ADH secretion.)

A decreased SG occurs when the urine becomes more dilute:

- **Diabetes insipidus** occurs with absent or decreased anti-diuretic hormone (ADH) because of impairment of the pituitary gland.
- **Kidney disease**, such as glomerulonephritis or pyelonephritis, may interfere with the ability of the kidneys to filter and to reabsorb fluid, so the urine may have low specific gravity as well as overall decreased volume of urine
- **Renal failure** usually results in a fixed specific gravity between 1.007 and 1.010 as the functional nephrons hypertrophy in an effort to compensate.

Serum And Urine Osmolality

Lab test	Purpose	Reference value
1. Serum osmolality	**Evaluates hyponatremia**	Adult: 275-295 m/Osmol/kg Newborn: ≥266 m/Osmol/kg
2. Urine osmolality	**Evaluates hydration, concentration and antidiuretic hormone**	adults: 250-900 mOsm/kg Newborn:75-300 mOsm/kg
3. Ratio of urine to serum osmolality	**Same**	3.0 or more

- Osmolarity = molarity X number of particles (ion or unionized molecules) resulting from ionization
- Osmolality refer to the osmotic concentration of fluids in the body, such as serum and urine.
- The predominate factors affecting serum osmolality are sodium, blood urea nitrogen and blood glucose.
- Serum osmolality evaluates hyponatremia while urine osmolality evaluates hydration.
- With dehydration, urine osmolality increases; and with overhydration, decreases.

- Healthy kidneys are usually able to maintain the appropriate fluid balance in relation to the fluids consumes, but renal impairment may interfere with the ability to concentrate urine, so the urine osmolaity may be similar to that of plasma (about 290 mOsm/kg).

- Like specific gravity, urine osmolality measures urine concentration; however, urine osmolality reflects the total number of osmotically active particles in a sample of urine (without relation to size or weight), so it's more accurate than specific gravity, which can increase with substances such as glucose, proteins, or dyes.

Urine Protein

Purpose - Urine protein testing is done to evaluate kidney function

Range - Negative or trace

- Normally, urine is free of protein, but proteinuria occurs with renal disease.
- Both albumin and globulin may be excreted in the urine, but albumin filters more readily than globulin, so protein in the urine is primarily albumin. Because of that, the term albuminuria is often used.
- Since proteins are necessary for the formation of casts, this sediment is often seen on microscopic examination of urine when proteinuria is present.
- Bence-Jones protein test is used to detect urine protein.

Interpretation of proteinuria

- **Minimal proteinuria** (<0.5 gm/day)

  -Fever, exercise, lower urinary tract infection, drug induced

- **Moderate proteinuria** (0.5-3 gm/day)

  -Diabetic nephropathy, chronic glomerulonephritis (moderate), pyelonephritis, pre-eclampsia. (it temporary damage filter)

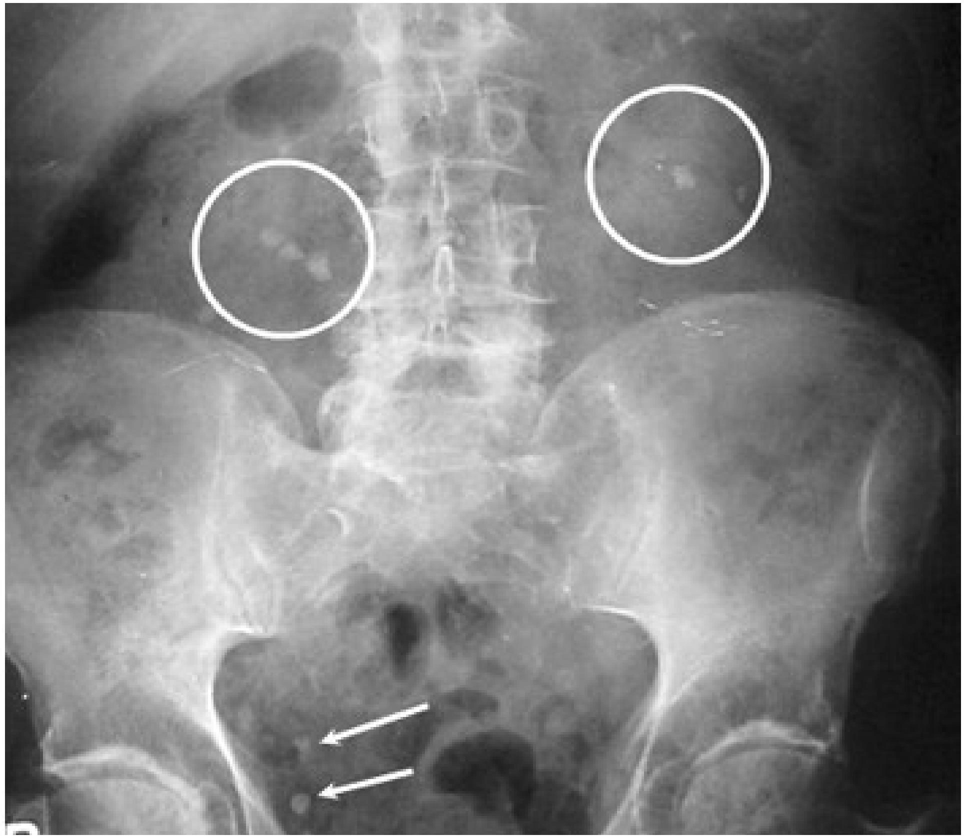
- **Marked proteinuria** (>3gm/day)

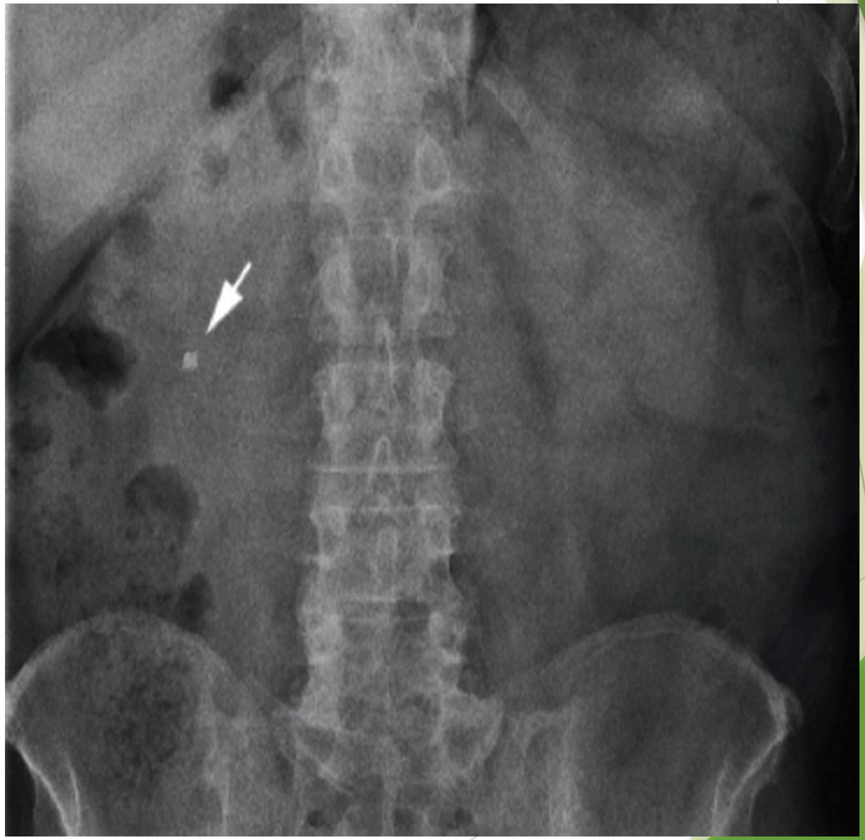
  -Acute glomerulonephritis, chronic glomerulonephritis (severe), nephrotic syndrome, severe diabetic

Reference- (Ramnik Sood 6th ed.)

Radiology and Renal Imaging

- **Plain radiograph** of abdomen is done to detect radiopaque stones or areas of calcification with in the urinary tract.





Ultrasonography

- To assess renal size , shape, position and thickness of renal.
- To detect solid tumours and their extension, cysts, polycystic disease and calculi.
- To evaluate residual urine volume, to detect bladder neck obstruction or enlargement of prostate.
- Prostate mass, size volume can also calculated.
- To carried certain procedures like cyst puncture and renal biopsy.
- Doppler ultrasonography for diagnosis of renal artery stenosis and renal vein thrombosis.


2D
42%
C 50
P Low
Gen
CF
75%
2.0MHz
WF Med
Med
Small stone with twinkling
G
R
-18.
cm/

- **Intervenous pyelography**
- **Renal angiogram**

-Gold standard for diagnosis of renal artery stenosis, arteriovenous malformations and persistent bleeding after truma.

- now a days CT angiography and MRI angiography are increasingly being used.

- **CT Scan**
- **MRI**
- **Renal biopsy**

-Useful in diagnosis of pt. with proteinuria of unknown origin, unexplained renal failure with normal sized kidneys.

Normal values of KFT

Test name	Definition	Normal value
Sr. Creatinine	• By-product in the breakdown of muscle creatine phosphate	0.7 -1.3 mg/dl in male 0.6-1.1 mg/dl
Blood urea	• End product of protein • 1gm of protein can produce about 0.3g of urea	15-45 mg/dl
Sr. Uric Acid	• End product of purine	3.4 -7.0 mg/dl 2.4- 6.0 mg/dl
Total protein	Albumin and globulin	6-8.3 g/dl Albumin 3.5-5 mg/dl Rest is Globulin
Sr. Sodium	It is key to controlling the amount of fluid in body	135-145 mmol/L
Sr Potassium	Essential for proper muscle and nerve function	3.5-5.1 mmol/L (adult) 3.4-4.7 mmol/L (children)
Chloride	Helps to keep fluid and acid-base balance in body	98-106 mmol/L

Case study

A 2 year young man sustained multiple injuries in a motorcycle accident. He was clinically dehydrated and his BP was 85/50 mmHg. His laboratory test as follows:

		Reference range
Sr BUN	**48mg/dl**	7-21 mg/dl
Sr. creatinine	**2.3 mg/dl**	0.6-1.2 mg/dl

REASON- ???

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Thank you