KIDNEY FUNCTION TEST (KFT)

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What is Kidney function test (KFT)?

- Kidney function test is a group of blood tests that are done
- To determine how well the kidneys are working and
- To evaluate the health of the kidneys
- Kidneys are an important organ of our body
- That removes the waste products from our body
- Maintain water and electrolyte balance in our body
- And forms urine

Which tests are included in the Kidney function test (KFT)?

The tests included are:

- Creatinine
- Uric acid
- Blood Urea Nitrogen (BUN)
- BUN / Creatinine ratio

WHY IS KIDNEY FUNCTION TEST DONE?

- To diagnose any suspected kidney disease in patients with
- Increased or decreased frequency of urination
- Abnormal swelling around the eyes and body
- Or other symptoms
- To monitor the efficacy of a therapy given for treating a kidney disease
- As a part of preventive health checkups
- To screen people who are at risk of kidney disease

When should we assess renal function?

- Older age
- Family history of Chronic Kidney disease (CKD)
- Decreased renal mass
- Low birth weight
- Diabetes Mellitus (DM)
- Hypertension (HTN)
- Autoimmune disease
- Systemic infections
- Urinary tract infections (UTI)
- Nephrolithiasis
- Obstruction to the lower urinary tract
- Drug toxicity

WHAT TO EXAMINE???

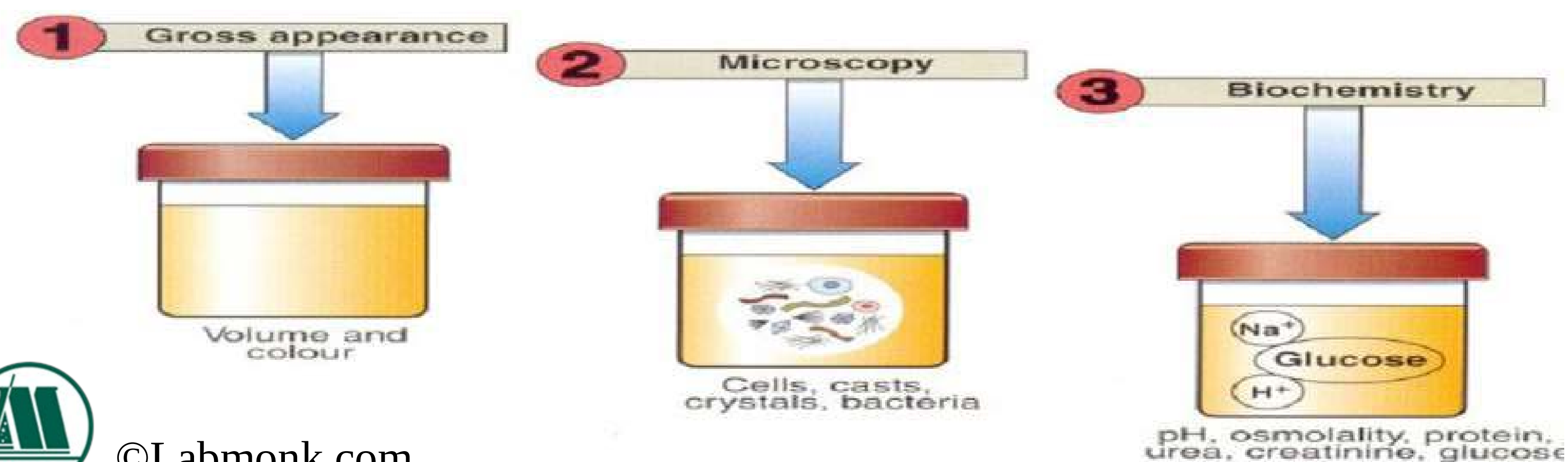
Renal function tests are divided into the following:

- Urine analysis
- Blood examination
- Glomerular Function Test
- Tubular Function Test

Urine Analysis

- Urine examination is an extremely valuable and most easily performed test for the evaluation of renal functions.

- It includes physical or macroscopic examination, chemical examination and microscopic examination of the sediment.



1. Macroscopic examination (Gross appearance)

Colour

- Normal- pale yellow in colour due to pigments urochrome,urobilin and uroerythrin.

- Cloudiness may be caused by excessive cellular material or protein, crystallization or precipitation of salts upon standing at room temperature or in the refrigerator.

- If the sample contains many red blood cells, it would be cloudy as well as red.

Blue Green	Pink-Orange-Red	Red-brown-black
Methylene Blue	Haemoglobin	Haemoglobin
Pseudomonas	Myoglobin	Myoglobin
Riboflavin	Phenolpthalein	Red blood cells
	Porphyrins	Homogentisic Acid
	Rifampicin	L -DOPA
		Melanin
		Methyldopa

- Colour of urine depending upon it's constituents

Volume

- Normal- 1-2.5 L/day

- Oliguria- Urine Output < 400ml/day

Seen in
– Acute glomerulonephritis
– Renal Failure

- Polyuria- Urine Output > 2.5 L/day

Seen in
– Increased water ingestion
– Diabetes mellitus and insipidus.

- Anuria- Urine output < 100ml/day

Seen in
– Renal shut down

Specific Gravity

- Measured by urinometer or refractometer.

- It is measurement of urine density which reflects the ability of the kidney to concentrate or dilute the urine relative to the plasma from which it is filtered.

- Normal :- 1.001- 1.040.

S.G	Osmolality (mosm/kg)
1.001	100
1.010	300
1.020	800
1.025	1000
1.030	1200
1.040	1400

Increase in Specific Gravity seen in

- Low water intake
- Diabetes mellitus
- Albuminuruia
- Acute nephritis.

Decrease in Specific Gravity is seen in

- Absence of ADH
- Renal Tubular damage.

Isosthenuria-Persistent production of fixed low Specific gravity urine isoosmolar with plasma despite variation in water intake.

pH

Urine pH ranges from 4.5 to 8

- Normally it is slightly acidic lying between 6 – 6.5.
- After meal it becomes alkaline.
- On exposure to atmosphere, urea in urine splits causing NH_4^+ release resulting in alkaline reaction.

2. Microscopic examination

- A sample of well-mixed urine (usually 10-15 ml) is centrifuged in a test tube at relatively low speed (about 2000-3,000 rpm) for 5-10 minutes which produces a concentration of sediment (cellular matter) at the bottom of the tube.
- A drop of sediment is poured onto a glass slide and a thin slice of glass (a coverslip) is place over it.
- The sediment is first examined under low power to identify crystals, casts, squamous cells, and other large objects. "Casts" are plugs of material which came from individual tubules.
- The numbers of casts seen are usually reported as number of each type found per low power field (LPF). For an example: "5-10 hyaline casts/L casts/LPF."

- Then, examination is carried out at high power to identify crystals, cells, and bacteria.

- The various types of cells are usually described as the number of each type found per average high power field (HPF). For example: "1-5 WBC/HPF.“

- Epithelial cells and 1-2 WBC or pus cell/HPF is normally seen

  - ✓ If more leukocytes per each high power field appear in non contaminated urine, the specimen is probably abnormal showing pyuria. Leukocytes have lobed nuclei and granular cytoplasm.

  - ✓ Usually, the WBC's are granulocytes. White cells from the vagina, in the presence of vaginal and cervical infections, or the external urethral meatus in men and women may contaminate the urine.

- Presence of Granular Casts, RBC, bacteria, Glucose, Albumin and Ketone bodies is abnormal.

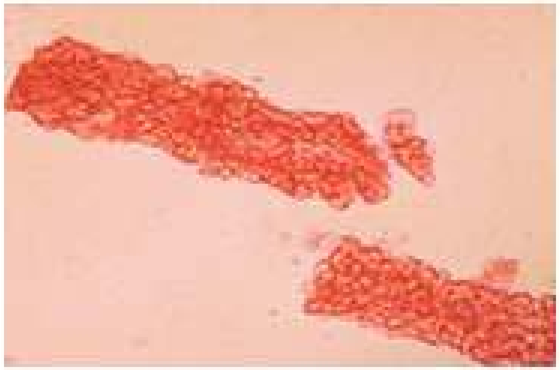
- Hematuria is the presence of abnormal numbers of red cells in urine due to any of several possible causes.

– glomerular damage,
– tumors which erode the urinary tract anywhere along its length,
– kidney trauma,
– urinary tract stones,
– acute tubular necrosis,
– upper and lower urinary tract infections,
– nephrotoxins

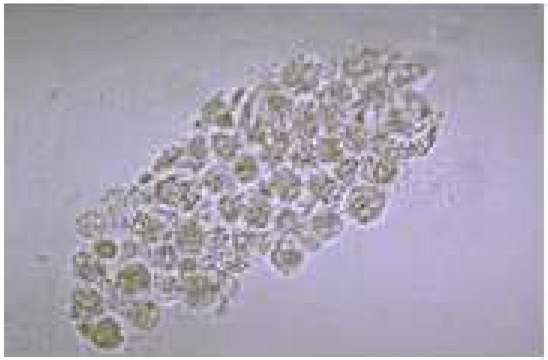
- Red blood cells may stick together and form red blood cell casts. Such casts are indicative of glomerulonephritis, with leakage of RBC's from glomeruli, or severe tubular damage.

- White blood cell casts are most typical for acute pyelonephritis, but they may also be present with glomerulonephritis. Their presence indicates inflammation of the kidney.

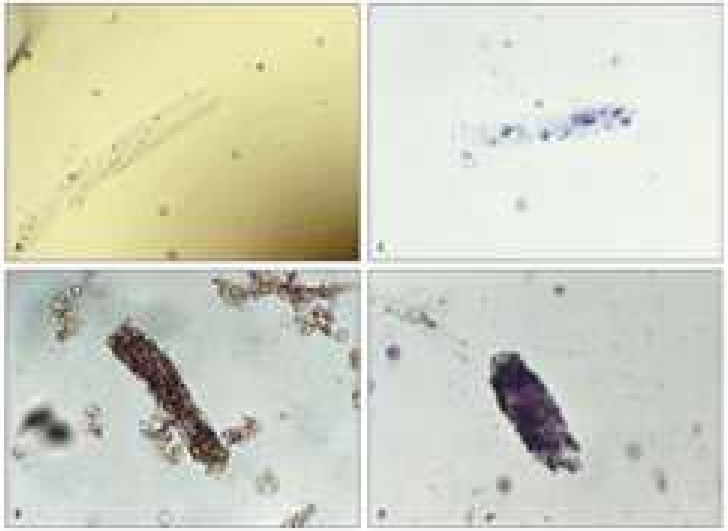
PHOTOGRAPH OF DIFFERENT CELL CAST IN URINE



Red blood cell cast in urine



White blood cell cast in urine

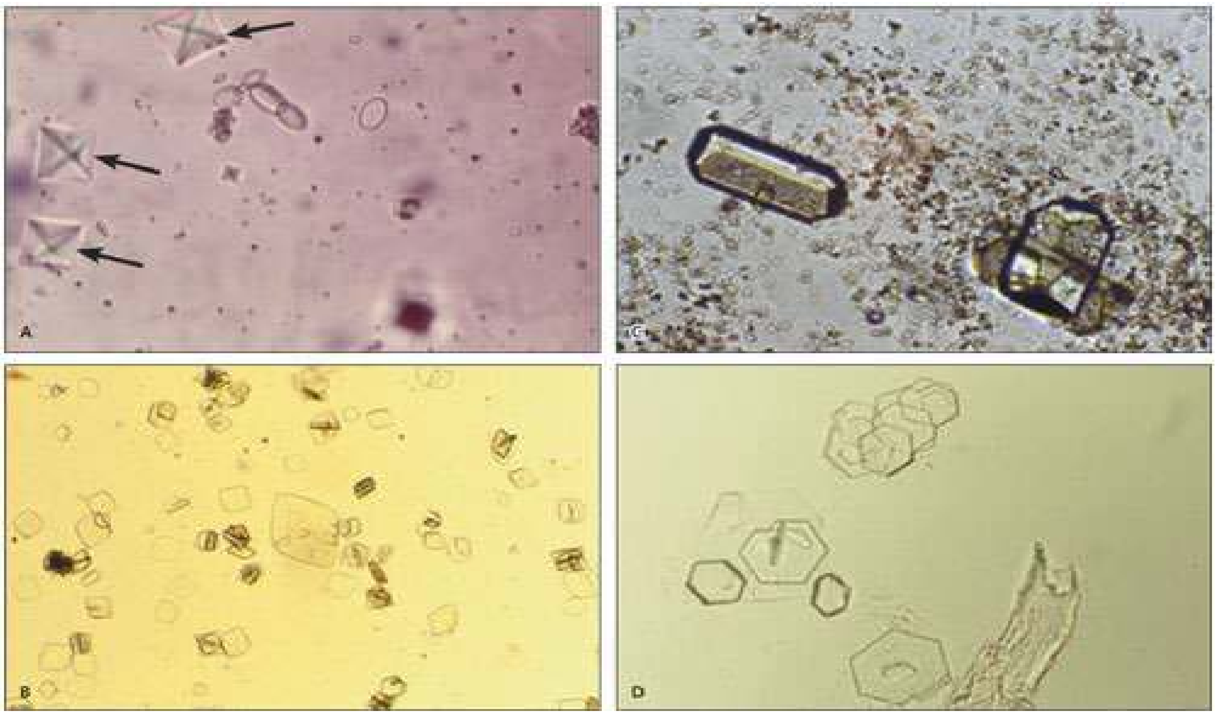


Urinary casts. (A) Hyaline cast (200 X); (B) erythrocyte cast (100 X); (C) leukocyte cast (100 X); (D) granular cast (100 X)

CRYSTALS

- Tyrosine crystals with congenital tyrosinosis

- Leucine crystals in patients with severe liver disease or with maple syrup urine disease.



Urinary crystals. (A) Calcium oxalate crystals; (B) uric acid crystals (C) triple phosphate crystals with amorphous phosphates ; (D) cystine crystals.

3. BIOCHEMICAL EXAMINATION

BLOOD EXAMINATION

- Done to measure substance in blood that are normally excreted by kidney.
- Their level in blood increases in kidney dysfunction.
- As markers of renal function creatinine, urea,uric acid and electrolytes are done for routine analysis

Serum creatinine

- Creatinine is a breakdown product of creatine phosphate in muscle, and is usually produced at a fairly constant rate by the body depending on muscle mass.
- Creatinine is filtered but not reabsorbed in kidney.
- Normal range is 0.8-1.3 mg/dl in men and 0.6-1 mg/dl in women.
- Not increased above normal until GFR<50 ml/min.
- The methods most widely used for serum creatinine are based on the Jaffe reaction. This reaction occurs between creatinine and the picrate ion formed in alkaline medium (sodium picrate); a red-orange solution develops which is read colorimetrically at 520 nm .

INCREASED SERUM CREATININE:

– Impaired renal function

– Very high protein diet

– Anabolic steroid users

– Vary large muscle mass: body builders, giants, acromegaly patients

– Rhabdomyolysis/crush injury

– Athletes taking oral creatine.

– Drugs:

- Probenecid
- Cimetidine
- Triamterene
- Trimethoprim
- Amiloride

Blood urea

- Urea is major nitrogenous end product of protein and amino acid catabolism, produced by liver and distributed throughout intracellular and extracellular fluid.
- Urea is filtered freely by the glomeruli.
- Many renal diseases with various glomerular, tubular, interstitial or vascular damage can cause an increase in plasma urea concentration.
- The reference interval for serum urea of healthy adults is 10-40 mg/dl.
- Plasma concentrations also tend to be slightly higher in males than females. High protein diet causes significant increases in plasma urea concentrations and urinary excretion.

- Measurement of plasma creatinine provides a more accurate assessment than urea because there are many non renal factors that affect urea level.

- Non-renal factors can affect the urea level (normal adults is level 10-40mg/dl) like:

- Mild dehydration,
- high protein diet,
- increased protein catabolism, muscle wasting as in starvation,
- reabsorption of blood proteins after a GIT haemorrhage,
- treatment with cortisol or its synthetic analogous

- States associated with elevated levels of urea in blood are referred to as uremia or azotemia.

- **Causes of urea plasma elevations:**

- Prerenal: renal hypoperfusion
- Renal: acute tubular necrosis
- Postrenal: obstruction of urinary flow

- Blood urea is normally doubled when the GFR is halved.
- Parallel determination of urea and creatinine is performed to differentiate between pre-renal and post-renal azotemia.
- Pre-renal azotemia leads to increased urea levels, while creatinine values remain within the reference range. In post-renal azotemias both urea and creatinine levels rise, but creatinine in a smaller extent.
- Enzymatic Berthelot Method is used for blood urea estimation:

Principal:

Urea + H_2O Urease > Ammonia + CO_2

Ammonia + Phenolic Chromogen + Hypochlorite > Green Colored Complex whoose absorbance is read at 570nm

Serum Uric Acid

- In human, uric acid is the major product of the catabolism of the purine nucleosides, adenosine and guanosine.
- Purines are derived from catabolism of dietary nucleic acid and from degradation of endogenous nucleic acids.
- Overproduction of uric acid may result from increased synthesis of purine precursors.
- In humans, approximately 75% of uric acid excreted is lost in the urine; most of the reminder is secreted into the GIT

- Renal handling of uric acid is complex and involves
- four sequential steps:

– Glomerular filtration of virtually all the uric acid in capillary plasma entering the glomerulus.

– Reabsorption in the proximal convoluted tubule of about 98 to 100% of filtered uric acid.

– Subsequent secretion of uric acid into the lumen of the distal portion of the proximal tubule.

– Further reabsorption in the distal tubule.

- Hyperuricemia is defined by serum or plasma uric acid concentrations higher than 7.0 mg/dl (0.42mmol/L) in men or greater than 6.0 mg/dl (0.36mmol/L) in women

Glomerular function tests

- The GFR is the best measure of glomerular function.
- Normal GFR is approximately 125 mL/min
- When GFR decreases to 30% of normal → moderate renal insufficiency. Patients remain asymptomatic with only biochemical evidence of a decline in GFR
- As the GFR decreases further → severe renal insufficiency characterized by profound clinical manifestations of uremia and biochemical abnormalities, such as acidemia; volume overload; and neurologic, cardiac, and respiratory manifestations
- When GFR is 5% to 10% of normal → ESRD

- Inulin clearance and creatinine clearance are used to measure the GFR.

Creatinine Clearance:

- A simple, inexpensive bedside estimate of GFR.
- GFR= Ccr = {Ucr * Urinary flow rate(ml/min)} / Pcr

Normal	100-120ml/min
Dec.Renal reserve	60-100ml/min
Mild Renal imp	40-60ml/min
Moderate insuff.	25-40ml/min
Renal failure	<25ml/min
ESRD	<10ml/min

Cockroft Gault Formula

Creatinine Clearance =(140-age)* weight in kg / S.creat.*72

(multiplied by 0.85 for females)

MDRD Nomogram

- GFR(ml/min)=170*S.creat.-0.999 *age-0.176 * BUN-0.170 *albumin0.318

(multiplied by 0.742 if female)

Tubular function tests

Urine Concentration Test

- The ability of the kidney to concentrate urine is a test of tubular function that can be carried out readily with only minor inconvenience to the patient.
- This test requires a water deprivation for 14 hrs in healthy individuals.
- A specific gravity of > 1.02 indicates normal concentrating power.
- Specific gravity of 1.008 to 1.010 is isotonic with plasma and indicates no work done by kidneys.
- The test should not be performed on a dehydrated patient.

Vasopressin Test

- More patient friendly than water deprivation test.
- The subject has nothing to drink after 6 p.m. At 8 p.m. five units of vasopressin tannate is injected subcutaneously. All urine samples are collected separately until 9 a.m. the next morning.
- Satisfactory concentration is shown by at least one sample having a specific gravity above 1.020, or an osmolality above 800 m osm/kg.
- The urine/plasma osmolality ratio should reach 3 and values less than 2 are abnormal.

Urine Dilution (Water Load) Test

- After an overnight fast the subject empties his bladder completely and is given 1000 ml of water to drink.
- Urine specimens are collected for the next 4 hours, the patient emptying bladder completely on each occasion.
- Normally the patient will excrete at least 700 ml of urine in the 4 hours, and at least one specimen will have a specific gravity less than 1.004.
- Kidneys which are severely damaged cannot excrete a urine of lower specific gravity than 1.010 or a volume above 400 ml in this time.
- The test should not be done if there is oedema or renal failure; water intoxication may result.

- **Para Aminohippuric Acid Clearance**
- Maximum secretory capacity of tubules for PAH is nearly constantat about 80mg/min.
- A decrease in the TmPAH indicates tubular damage.

- **Micropuncturing**
- Micropuncturing various part of tubule and analysis of fluid for volume and composition.

- **Microcryoscopic study**
- Studying slices of renal tissue at different depths.

- **Microelectrode study**
- Measuring membrane potential of the tubular cells


Thank you!