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CHAPTER

Urine and Kidney function test

URINE

Formation of Urine

(Function of Nephron)

Function of nephron means function of glomerulus, *i.e.*, filtration and function of renal tubule i.e., modification of the filtrate to urine (Fig. 7.32).

Filtration

It is the process by which an **ultrafiltrate** of plasma, called **glomerular filtrate** is formed from blood in the glomerular capillaries (p. 272). This filtrate is the starting material for urine formation. Its composition and reaction are same as plasma except that the larger molecules like proteins, lipids etc., are absent. It is called ultrafiltrate, as it does not contain even very minute (ultramicroscopic) particles.

Tubular modification

As this filtrate collects in the Bowman's space positive pressure develops and it flows through the renal tubule as tubular fluid (TF) and undergoes severe transformation and volume contraction to form urine.

In the PCT there occurs reabsorption of about 2/3rd of the total volume (it is **load dependent**, *i.e.*, whatever amount is presented to PCT, 2/3rd will be reabsorbed). The tubular wall here is permeable to both water and solute, hence, as the solutes are reabsorbed actively, water follows and the tubular fluid in PCT remains iso-osmolar. Here 2/3rd of filtered Na^+ and water is reabsorbed along with anions (Cl^- and HCO_3^-). K^+ is reabsorbed in part I and II but secreted in part III. Urea is reabsorbed passively as its concentration rises with reabsorption of water. There is secretion of H^+ in exchange of Na^+ in PCT. All the filtered glucose and amino acids are reabsorbed in proximal tubule, uric acid is both reabsorbed and secreted. Reabsorption of Ca^{2+}, Mg^{2+}, lactate, citrate also occur in proximal tubule.

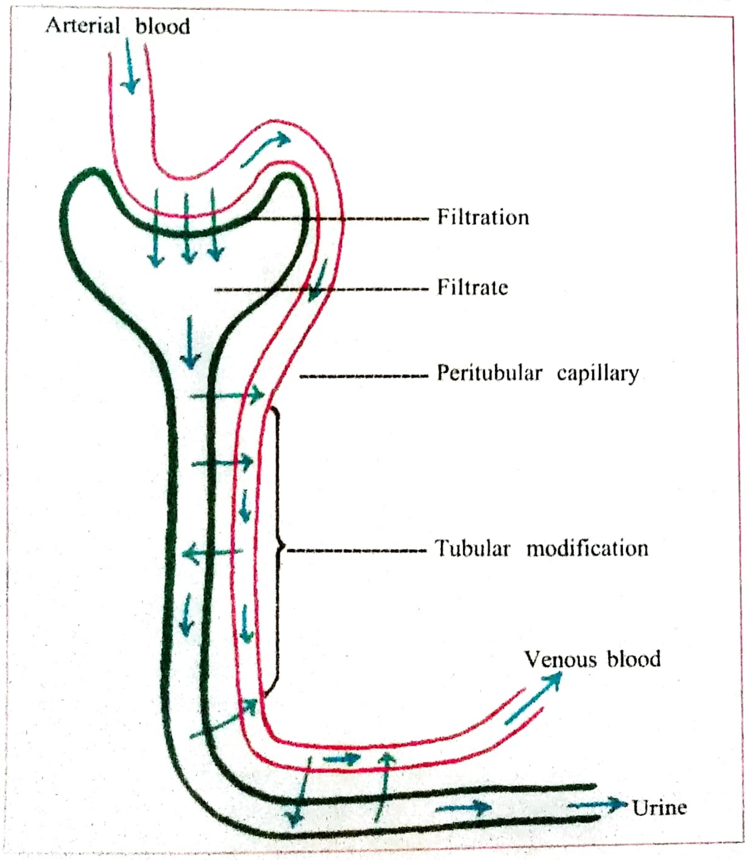

Fig. 7.32. *Formation of urine.*

The tubular fluid (now 1/3rd of its original volume and iso-osmolar), is delivered to the loop of Henle. Descending limb of the loop is highly permeable to water, but not to solutes; so, water leaves the tubular fluid as it passes down through more and more concentrated zone (Medullary concentration gradient). The fluid becomes concentrated and its volume is reduced due to absorption another 20% of water. Highest concentration of tubular fluid occurs at the hair pin bend (for juxtamedullary nephrons it may be up to 1200 mosm and for cortical nephrons 600 mosm). There is secretion of some negligible amount of solute in this segment.

The thin ascending limb as well as the thick segment is not permeable to water. In the thin segment some passive transfer of solutes occurs (reabsorption of Na^+, Cl^- and secretion of urea) and active reabsorption occurs in the thick ascending limb. There occurs reabsorption of 25% of filtered Na^+, (load dependent). This Na^+ reabsorption is Cl^- linked. There is no reabsorption of water, hence the tubular fluid becomes hypo-osmolar when delivered to the DCT. This can be prevented by preventing Na^+ reabsorption by loop diuretics like furosemide, ethacrynic acid. Ca^{2+} is also reabsorbed in the thick ascending limb. The fluid in the distal convoluted tubule becomes further hypotonic due to active reabsorption of Na^+ (15% of filtered load is left to the distal nephron, of which 8 to 10% is reabsorbed normally). Many DCT then drain via the connecting tubules to a collecting system and the mixture becomes of about 150 mosm concentration.

In the collecting system most of the water received is reabsorbed under the influence of ADH (only about 1.5 L is left). Na^+ reabsorption throughout the distal nephron is under the influence of aldosterone. There occurs reabsorption of urea here. Ca^{2+}, Mg^{2+}, phosphate, creatinine, etc., are also reabsorbed in the distal nephron and there is secretion of K^+ and H^+.

Due to presence of tight junctions, the later part of the distal nephron is more impermeable and retention of anions render the lumen negative with respect to outside. H^+ ions are actively secreted here and free H^+ accumulate in the fluid, lumen negativity helps the process. (H^+ ions are secreted in all parts, but in PCT these are neutralised by HCO_3^- within the TF). The free H^+ are buffered to some extent by Na_2HPO_4 by forming NaH_2PO_4 and by combining with NH_3.

The final fluid is delivered to the urinary tract is called urine which is slightly acidic. The volume, reaction and osmolarity depend upon the body conditions, *e.g.*, dehydration, water intake, acidosis, alkalosis, etc.

Usually 1 to 1.5 litre of acidic urine is produced per day.

Composition of Urine

(Total volume = 1500 ml, Total solid = 60 gm)

Urine

- Water (96%)
- Solid (4%)
  - Organic (60%)
    - Nitrogenous
    - Non-nitrogenous
  - Inorganic (40%)
    - Cations
    - Anions

Nitrogenous	Non-nitrogenous	Cations	Anions
Urea	Hormones	Na^+	SO_4^{2-}
Uric acid	Hormone metabolites	K^+	PO_4^{3-}
Creatinine	Citrate	Ca^{2+}	Cl^-
Hippuric acid	Lactate	Mg^{2+}	HCO_3^-
Indican	Ketone bodies (small amt.)	NH_4^+	

Note : Some importants constituents of urine are urea, uric acid, creatinine, sodium chloride, hormones, hormone metabolites.

Characters of urine

(1) **Volume** : Normal volume of urine is 0.5 to 2.5 L/day.

Obligatory urine volume : Minimum volume of urine that must be produced to excrete the solute load. It is produced in conditions of dehydration and with full ADH action.

Oliguria is the condition where less amount of urine is produced which may be caused by dehydration and the volume of urine is less than 400 ml/day.

Anuria means no urine formation. Causes are urinary obstruction, severe dehydration, hypovolaemic shock, renal shutdown, etc. Clinically, anuria is said to occur when urine volume is less than 100 ml/day.

Polyuria means high volume of urine (more than 3 litre/day). It occurs in absence of ADH, *i.e.*, diabetes insipidus (*low sp. gr., high volume*). This also occurs after excessive water intake or drinking. In diabetes mellitus polyuria occurs due to osmotic effect of sugar present in the urine (*high sp. gr. with high volume.*).

(2) **Colour** : Normal colour of urine is pale yellow due to presence of a pigment named urochrome. It changes in disease, *e.g.*, yellow in jaundice.

(3) **Reaction** : Slightly acidic, pH 6.5, range 5 to 7.5. Urine is alkaline in **post prandial alkaline tide,** in hyperventilation as in high altitude or voluntary. Limiting pH is 4.5. Urine on standing, outside the body, becomes alkaline due to formation of ammonia from the urea present in it by the organism '*Micrococcus ureae*'. In kidney disease urine cannot be acidified properly (renal acidosis).

(4) **Specific gravity** : Sp. gr. of urine is highly variable and may be between 1001 to 1050, usual value is 1010 to 1025. It increases in dehydration, after a high protein diet, in glycosuria, proteinuria, etc., and decreases in diabetes insipidus (lack of ADH action) after high water intake.

Fixed sp. gr. of urine is 1010. It is found in case of chronic kidney disease, when kidney function is abnormal and urine cannot be concentrated or diluted by kidney.

Microscopic examination of Urine

This is done by examining the centrifuged deposit of urine. Substances seen under the microscope are as follows :

(a) **Casts** : These are solidified protein (Tamm-horsfell) substances in the shape of the renal tubules, hence called tubular casts. These may be :

(i) hyaline casts (pure cast),
(ii) Granular cast with fragmented epithelial cells,
(iii) RBC cast with RBC, and
(iv) WBC cast with pus cells.

Normally a few casts may be present, but the number increases in some kidney diseases.

(b) **Pus cells** : Dead leucocytes are called so. Normally very few are present but increases in disease (infection). In urine of female patients, pus cell is normally more frequent. More than 10 pus cells per high power field is considered pathological.

(c) **Epithelial** cells are also found in urine.

(d) **RBCs** are present in case of haematuria.

(e) **Bacteria,** crystals of oxalate etc. are also found.

Abnormal constituents of Urine

These are the substances which are normally not present in urine. The substances, which are normally present in small amount, if increase, are also considered as abnormal constituents. These are as follows :

(1) **Glucose** : When present in urine in sufficient amount to be able to reduce alkaline copper sulphate solution, the condition is called **glycosuria.** Normally very small amount (150 mg/day) is present which cannot reduce alkaline $CuSO_4$. Glycosuria is found in diabetes mellitus (DM) due to high plasma level of sugar and also in renal disease (Renal glycosuria). There are also **alimentary glycosuria** (glycosuria after a large carbohydrate meal in early diabetics) and **nervous glycosuria** (due to high blood sugar from glycogenolysis by adrenalin). **Endocrine glycosuria** is caused due to increased GH, cortisol, thyroxine, etc., or due to decreased insulin.

(2) **Protein** : Normally trace amount (up to 150 mg) is present. When present in sufficient amount to be detected by tests (*e.g.*, heat coagulation), it is called **proteinuria.** It may be due to :

(a) Prerenal cause as in multiple myeloma when excess Bence-Jones Protein is found in plasma and it comes out through urine. In pregnancy also, proteinuria can occur without kidney defect.

(b) Renal : It is due to disease in kidney, *e.g.*, glumerulonephritis, where the negative charge of the capillary wall is probably lost, so albumin (anion) passes through easily.

(c) Post renal : Here protein is added by exudation from the inflamed urinary tract, as in urinary tract infection (UTI).

Proteinuria is classified in various ways, *e.g.*, glomerular, tubular, overflow, secretory and others.

(3) **Casts** : These are present in high amount in diseased condition (see microscopic examination of urine).

(4) **Ketone bodies** : Normally trace amount is present, but increases in diabetes mellitus and starvation. When ketosis develops. When sufficient ketone bodies are present in urine the condition is called **Ketoneuria.** Ketone bodies are **acetone, aceto-acetic acid** and **β-hydroxybutyric acid** (p. 312).

(5) **Blood** : When present in small amount can be detected only by the presence of RBC in microscopic examination and it is called **microscopic haematuria.** It occurs in acute glomerulonephritis. Glomerular/renal haematuria is detected by dysmorphic RBC or RBC casts in urine. Excess blood may be present in urine making its colour red, then it is called **frank haematuria** (found in renal stone, malignancy, and in injury of the urinary tract).

(6) **Bile** : Normally urobilinogen is present in urine but in obstructive jaundice both bile salts and bile pigments (conjugated bilirubin) are found in urine.

(7) **Etherial sulphates (Indicans)** : These are the etherial sulphates of indoxyl and skatoxyl, and normally present in urine. In case of constipation these are present in high amount rendering the urine dark coloured and foul smelling. **Indole** and **skatole** are produced by bacterial degradation of proteins in stool, these compounds (indole and skatole are responsible for the foul smell of stool) are then absorbed and in the liver these are converted into indoxyl or skatoxyl which are then excreted as etherial sulphates.

(8) **Hormone metabolites** : Metabolites of most of the hormones are found in urine normally. These metabolites increase when there is more secretion of the hormones.

One important hormone metabolite is **17 ketosteroid.** It comes from the androgens and cortisol. In female, its source is adrenal cortex, but in male 2/3rd of it comes from the adrenal cortex and 1/3rd from the testes.

(9) **Creatine** : Creatinuria means presence of creatine in urine. Normally creatine is absent in urine except in children and in pregnancy. It is found in urine in conditions of muscle wasting (breakdown) as in starvation, thyrotoxicosis and myopathies, and in some other conditions.

KIDNEY FUNCTION TESTS

These are the different tests which are performed to assess the functions of the kidneys. Some of these tests are as follows :

Blood analysis

Blood or serum is analysed for urea (Normal value 10 to 40 mg/dl), creatinine (Normal value : 0.5 to 1.5 mg/dl). These substances accumulate in the body in kidney disease and concentration of these in blood increases; so, estimation gives an idea of kidney function.

Examination of urine

Urine has a normal character (see above), when the kidney is defective, urine changes in relation to volume, sp. gr., reaction, abnormal constituents, etc.

Analysis of blood and urine both

By this method GFR, renal plasma flow and clearance values are measured. Clearance test is highly sensitive. Clearance value is expressed as percentage of normal, *e.g.*, if a person has urea clearance 40 ml/min, then the value is 57% (Normal C_{urea} = 70 ml/min.). In clinical practice creatinine clearance is used and its normal value is 80 to 100 ml/minute.

Excretion test or Functional radiography (including IVP or isotope renal scan)

In this test various radio-opaque dyes (*e.g.*, conray 420) or radio-isotope dyes are injected intravenously and when the dye is excreted by kidney through urine, it is studied by radiography. Normal kidneys concentrate the dye sufficiently to make the kidneys and the urinary tract visible in X-ray plates. (As such soft tissues like kidneys cannot be seen properly in X-ray plates).

Water elimination test

A person is asked to drink water (2% of his body wt.). Normally 90% of the water is eliminated in 5 hours time. It can be detected by urinary dilution test through measurement of urine osmolarity.

Water deprivation test

If a person is deprived of water for some time, concentration of urine increases and if the specific gravity in a sample is found to be 1020 or more, kidneys are taken as normal. It is detected best by simultaneous measurement of urinary and plasma osmolarity by osmometer. It is actually a very good screening test for diabetes insipidus.

Other tests

Radiological tests like X-ray of Kidney-ureter-bladder (KUB), Computerised Tomography (CT), Magnetic resonance imaging (MRI) and Ultrasonographic (USG) tests also give plenty of information regarding structural abnormalities of kidney and urinary tract.

On the other hand functional magnetic resonance imaging and contrast CT give information about function of the kidneys.

Above tests are performed in groups to assess kidney function, depending upon the disease a person is suffering from.