Medicine

Nephrology

5th year – lecture 1

الدكتور

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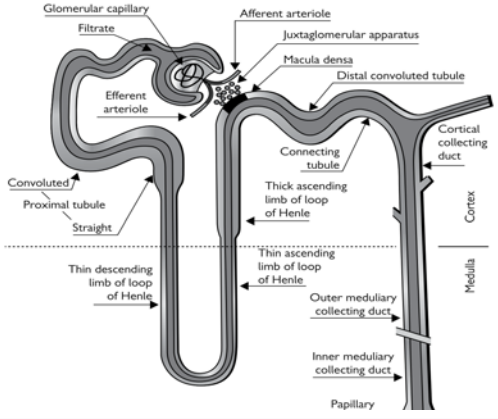
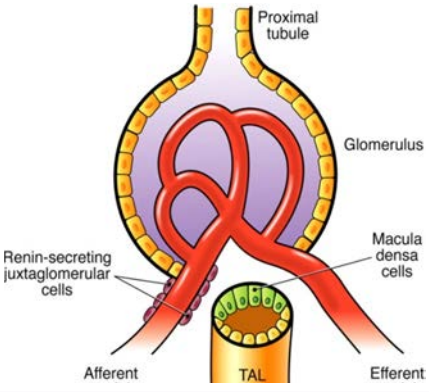
Functional anatomy and physiology

The kidneys are paired bean shaped organs situated in the retroperitoneum on either side of the vertebral column against the psoas major muscle. Each kidney weighs about 150 gram, and is about 12 cm in length, 6 cm in breadth and 3 cm in thickness. The specific components of the kidney are the nephrons, the collecting ducts, and a unique microvasculature. The kidney of humans contains about 1 million nephrons, although this number varies considerably. The number of nephrons is already established during prenatal development; after birth, new nephrons cannot be developed, and a lost nephron cannot be replaced.

The Nephron

- basic structural and functional unit of the kidney
- 2 main components: glomerulus and attached renal tubule
- filtration occurs across the glomerular filtration barrier (endothelium, glomerular basement membrane GBM, podocytes) into Bowman's space
- particles are selectively filtered by size (<60 kDa) and charge (negative charge repelled)
- The juxtaglomerular apparatus comprises 1)the macula densa : monitor the NaCl content of the filtrate entering the distal convoluted tubule (cortical thick ascending limb), 2) the extraglomerular mesangium, 3) the terminal portion of the afferent arteriole with its renin-producing granular cells (also often termed juxtaglomerular cells), and 4) the beginning portions of the efferent arteriole.





Major Functions of the Kidneys

1. Waste Excretion :

Excretion of nitrogenous products of protein metabolism (urea) , Excretion of organic acids and organic bases . Breakdown and excretion of drugs and peptide hormones .

2. Electrolyte Balance and Osmoregulation

Controls volume status and osmolar balance , Controls potassium concentration , Acid-base balance

3. Hormonal Synthesis

- **Erythropoietin** production (cortex) : Fibroblast like cells that lie in the interstitium of the renal cortex are responsible for production of erythropoietin, which in turn is required for production of red blood cells.
- Vitamin D activation: 25(OH)VitD converted to 1,25(OH)2VitD
- Renin production (juxtaglomerular apparatus)

4. Blood Pressure Regulation

Na^+ excretion ,Renin production , Alters ECF volume

5. Glucose Homeostasis :Gluconeogenesis (from lactate, pyruvate, and amino acids), Glucose supply maintained in prolonged starvation

Ways to Estimate glomerular filtration rate (eGFR) Using Serum Creatinine Concentration

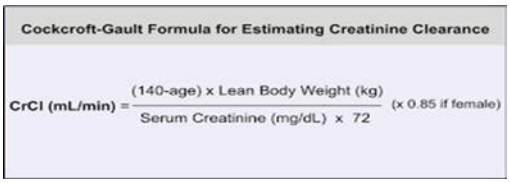
(GFR is reported as mL/min/1.73 m^2 body surface area)

1. **Measure Creatinine clearance CrCl** : calculation provides reasonable estimate of GFR . Creatinine clearance = **U ×V /P** = **(urine [Cr] x urine volume/d)/(plasma [Cr])**

 must use same units for urine [Cr] and plasma [Cr]

2. **Estimate CrCl using Cockcrof-Gault formula**

 serum Cr used along with age, gender, and weight (kg) to estimate GFR



3. **Estimate GFR using Modification of Diet in Renal Disease (MDRD) study formula**

 most common way in which GFR is estimated which is complex formula incorporating serum Cr, age, sex, and race (African descent) , ***does not include weight***

 4. **Estimate GFR using CKD Epidemiology Collaboration equation (CKD-EPI equation**) :the **best** current equation calculated using serum Cr, age, sex, and race , ***does not include weight.***

Examination of urine:

❖ Dipsticks (chemical testing):

1. Specific Gravity

• Urine specific gravity is a measure of the weight of dissolved particles in urine, whereas urine osmolality reflects the number of such particles.
• values <1.010 reflect dilute urine, values >1.020 refect concentrated urine
• value usually 1.010 in ESRD (isosthenuria: same specifc gravity as plasma)

2. pH

• urine pH is normally between 4.5-7.0; if persistently alkaline, consider
 renal tubular acidosis (RTA) type 1 or UTI with urease-producing bacteria (e.g. *Proteus*)

3. Glucose

• freely fltered at glomerulus and reabsorbed in proximal tubule
• causes of glucosuria include
1. hyperglycemia >9-11 mmol/L leads to fltration that exceeds tubular resorption capacity ,2. increased GFR (e.g. pregnancy) ,3. proximal tubule dysfunction (e.g. Fanconi's syndrome),4. sodium-glucose cotransporter 2 (SGLT2) inhibitors (also known as -flozin drugs)

4. Protein

• dipstick only detects albumin ,• Most reagent strips can detect protein if albuminuria exceeds 300 mg/day. They react primarily with albumin and are relatively insensitive to globulin and Bence Jones proteins.
• Gold standard: 24 h timed urine collection for total protein

5. Leukocyte Esterase

• enzyme found in WBC and detected by dipstick
• presence of WBCs indicates infection (e.g. UTI) or infammation (e.g. AIN)

6. Nitrites

• nitrates in urine are converted by some bacteria to nitrites
• high specifcity, low sensitivity for UTI

7. Ketones

• positive in alcoholic/diabetic ketoacidosis, prolonged starvation, fasting

8. Hemoglobin

• positive in hemoglobinuria (hemolysis), myoglobinuria (rhabdomyolysis), and **true hematuria (RBCs seen on microscopy)**

Urine Microscopy: Detect following

RBCs (erythrocytes): which are indicative of bleeding

1) Isomorphic RBCs from the urogenital tract (anywhere from kidney to tip of penis);
2) dysmorphic RBCs which suggest the presence of glomerulonephritis;

Red cell casts: indicative of glomerular disease;

WBCs (pus) : The presence of leucocytes and bacteria in urine is indicative of renal tract infection.

White cell casts: are strongly suggestive of pyelonephritis.

Crystals: which may be observed in patients with renal stone disease.

Renal biopsy :

Indications

1. Acute kidney injury that is not adequately explained
2. CKD with normal-sized kidneys
3. Nephrotic syndrome in adults
4. Nephrotic syndrome in children that has atypical features or is not responding to treatment
5. Isolated haematuria (dysmorphic RBCs) or proteinuria (more than 1g per day) with renal characteristics.

Contraindications

1. Disordered coagulation or thrombocytopenia. Aspirin and other antiplatelet agents increase bleeding risk.
2. Uncontrolled hypertension
3. Kidneys < 60% predicted size
4. Solitary kidney (except **kidney transplant**) , Relative contraindication.

Complications

1. Pain, usually mild
2. Bleeding into urine (hematuria) or ,Bleeding around the kidney (page kidney)
3. Arteriovenous fistula, rarely significant clinically.