تفريغ كلينكال

المحاضرة: Renal failure

الصيدلاني/ة: ياسمين خليل

Soul Academy

لجان الدفعات

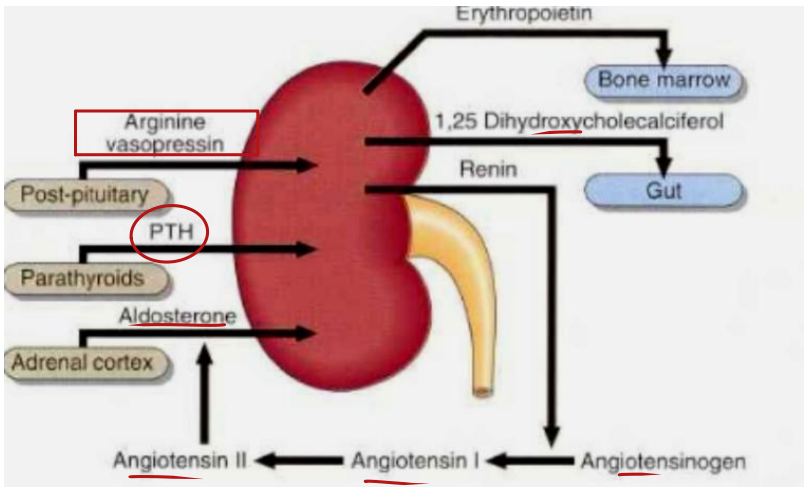
Renal failure

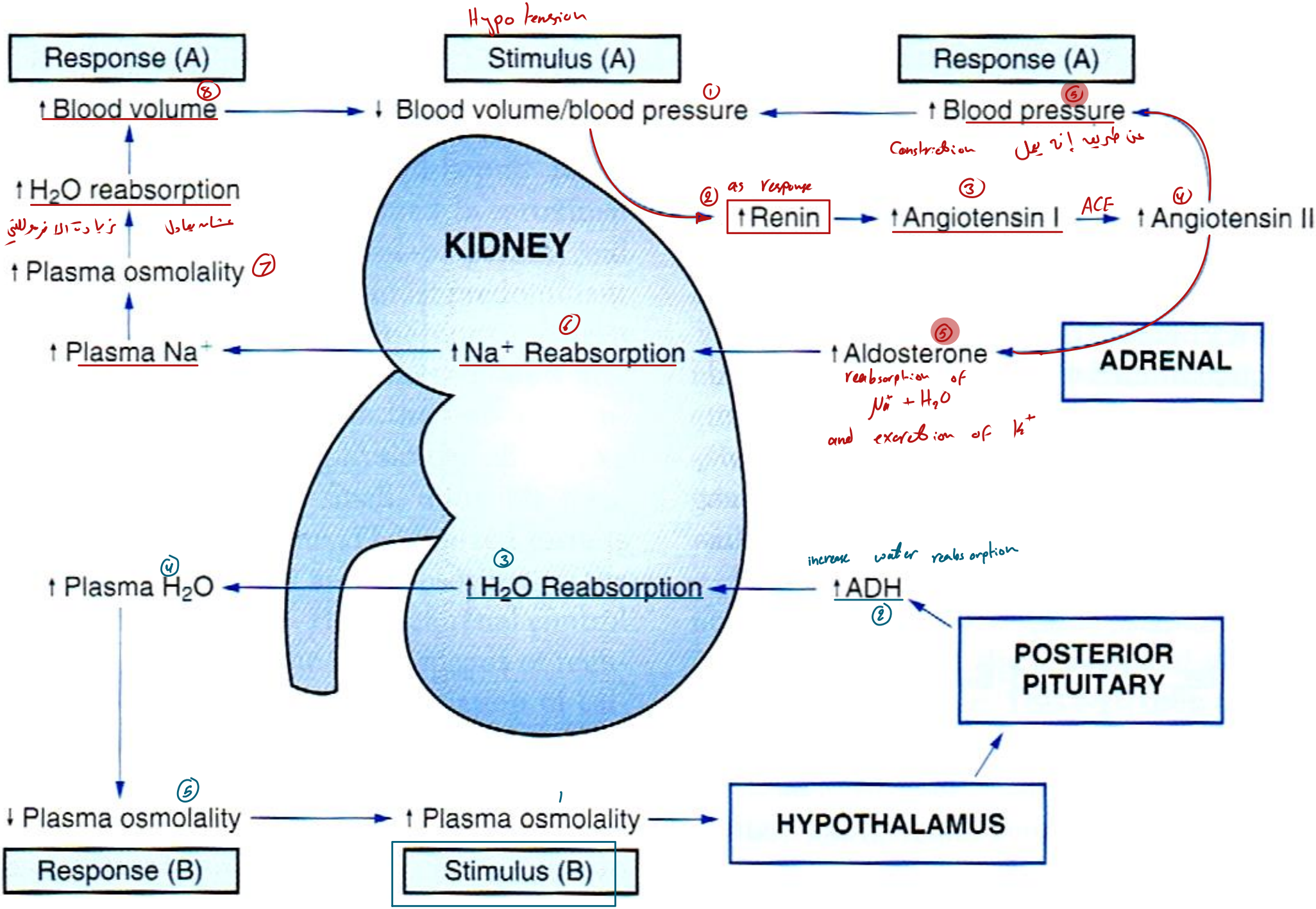
Dr. Iman Mansi

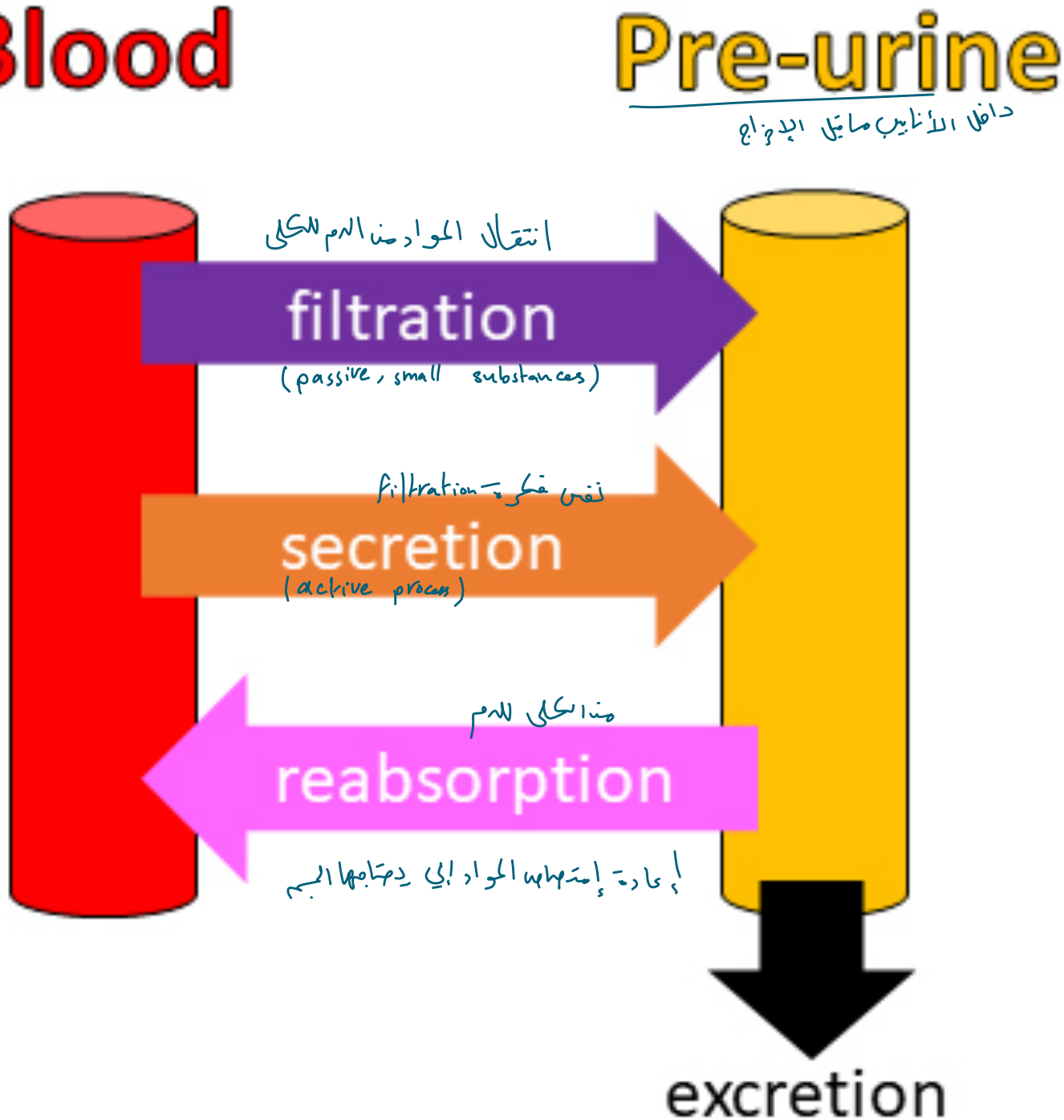
اللهم ارحم أبيهم واغفر له
وعافه و اعف عنه
واجمعه وأهله في الجنة والمسلمين آمين

Kidney Functions

- Urine formation (مخلفات البول كلها)
  Concentrated or diluted وظيفتها هي ، سواء كانت
- Fluid and electrolyte balance (by reabsorption or excretion to keep the range at normal)
- Regulation of acid-base balance
  renal is : long term buffering system (يحافظ على pH)
- Excretion of the waste products of protein metabolism
  هاي الـ waste إذا تراكمت لح تعمل toxic eff ف بتتخلص منهم أول بأول
- Excretion of drugs and toxins
- Secretion of hormones: سواء هرمونات من إنتاج الكلى أو هرمونات تشتغل على الكلى
  - Renin, Erythropoietin, 1,25-Dihydroxy vitamin D_3, Prostaglandins



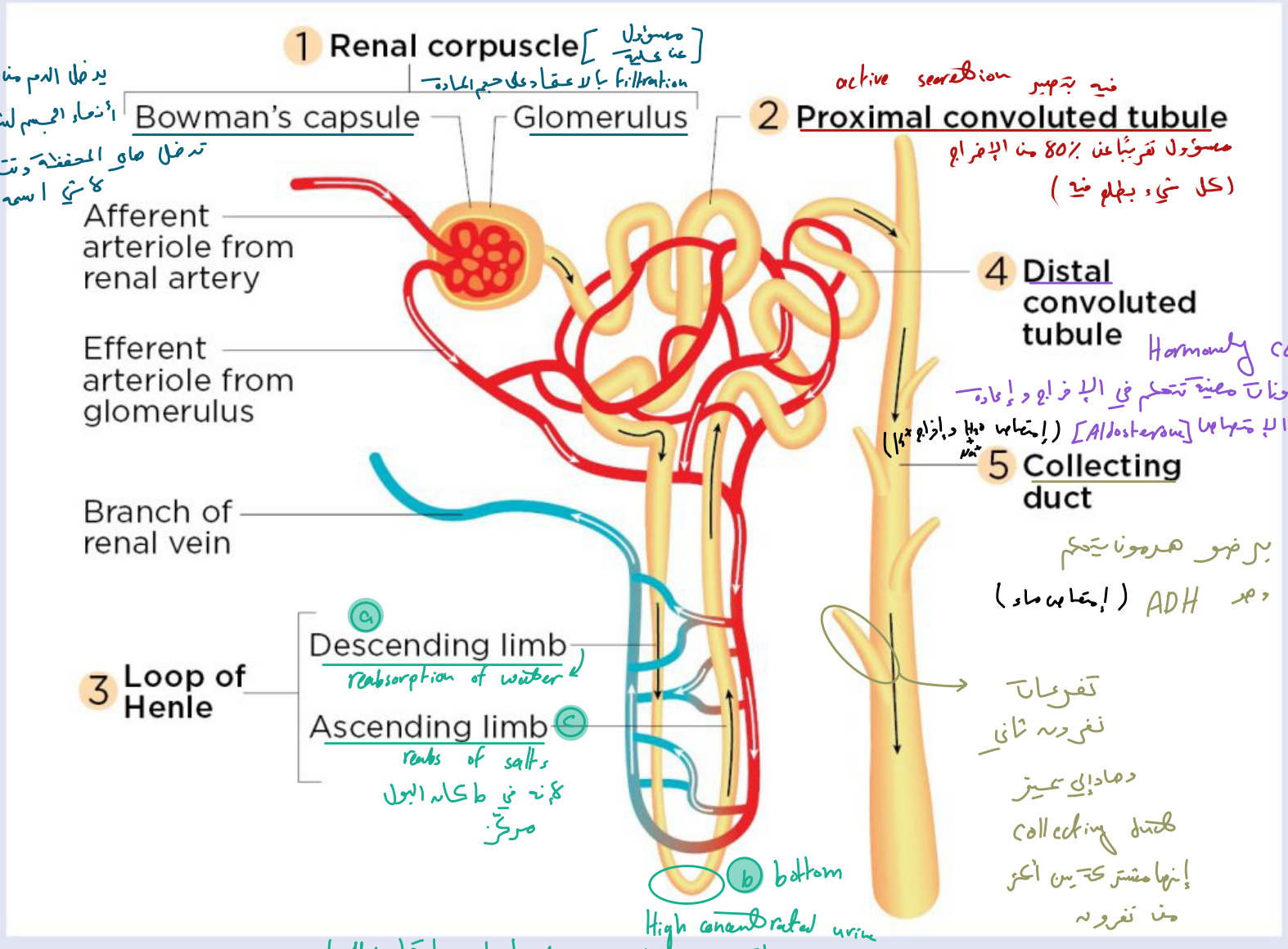

Response (A)
Stimulus (A)
Hypo tension
Response (A)
↑ Blood volume
↓ Blood volume/blood pressure
↑ Blood pressure
Constriction
من طريق إنه يعل
↑ H2O reabsorption
as response
↑ Renin
↑ Angiotensin I
ACE
↑ Angiotensin II
KIDNEY
↑ Plasma osmolality
↑ Plasma Na+
↑ Na+ Reabsorption
↑ Aldosterone
ADRENAL
reabsorption of Na+ + H2O and excretion of K+
↑ Plasma H2O
↑ H2O Reabsorption
increase water reabsorption
↑ ADH
POSTERIOR PITUITARY
↓ Plasma osmolality
↑ Plasma osmolality
HYPOTHALAMUS
Response (B)
Stimulus (B)



اللهم ارزقنا الصبر للنهاية

Kidney and nephrons

Fig 3. **Anatomy of a nephron**



Kidney

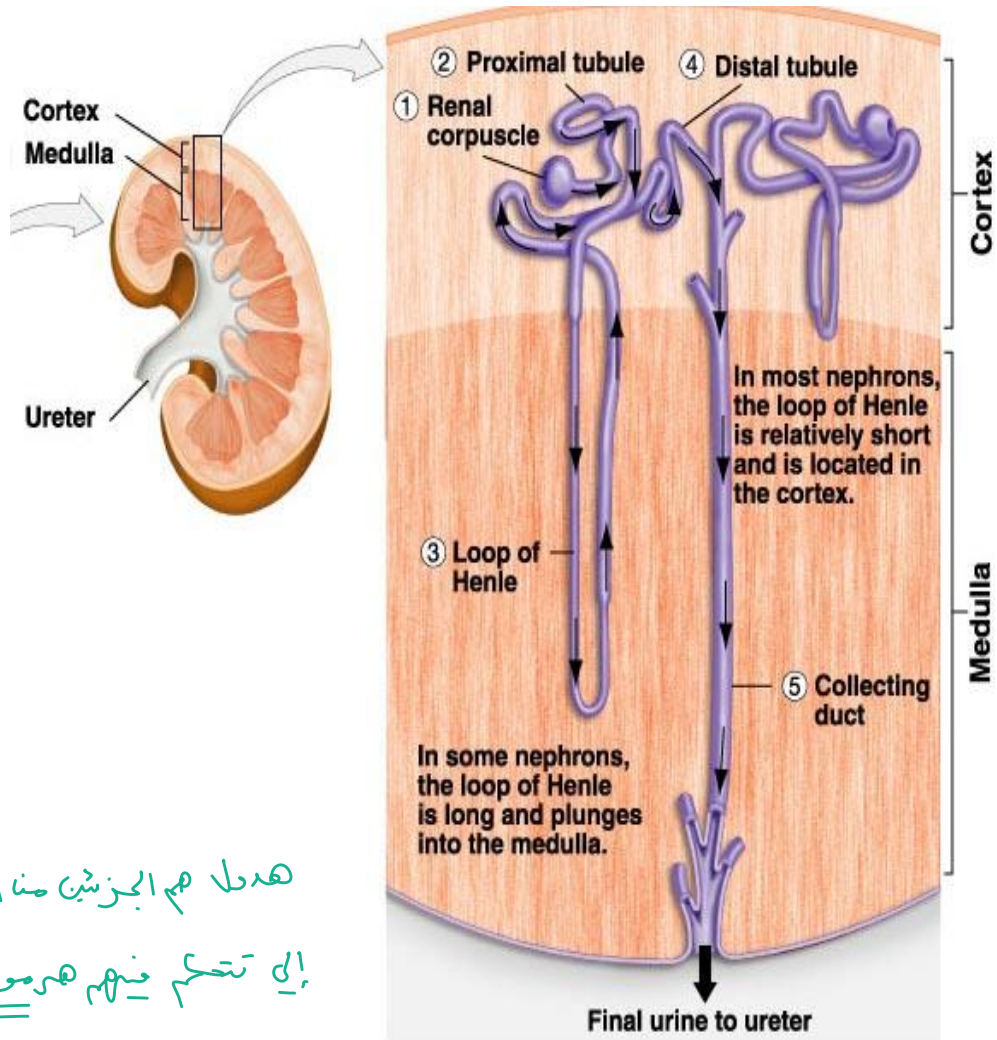
Nephron, functional unit of kidney, consists of glomerulus, Bowman's capsule, proximal tubule, loop of Henle, distal tubule, collecting duct (shared by many nephron).

- Glomerulus: ball of fenestrated capillaries.
- Bowman's capsule: Cup/Capsule that surrounds the glomerulus.
- Proximal tubule: convoluted tubule on the side of the Bowman's capsule. It is the major site for reabsorption (nutrient, salts and water) and secretion (except for K^+, the secretion of which is the job of distal convoluted tubule in response to aldosterone).
- Loop of Henle: U shaped loop that dips into the renal medulla. countercurrent multiplier mechanism occurs here
  - Descending limb:water reabsorption by osmosis (permeable to water, but not to solute).
  - Bottom of U: most concentrated.
  - Ascending limb: salt reabsorption (permeable to salt, but not water).

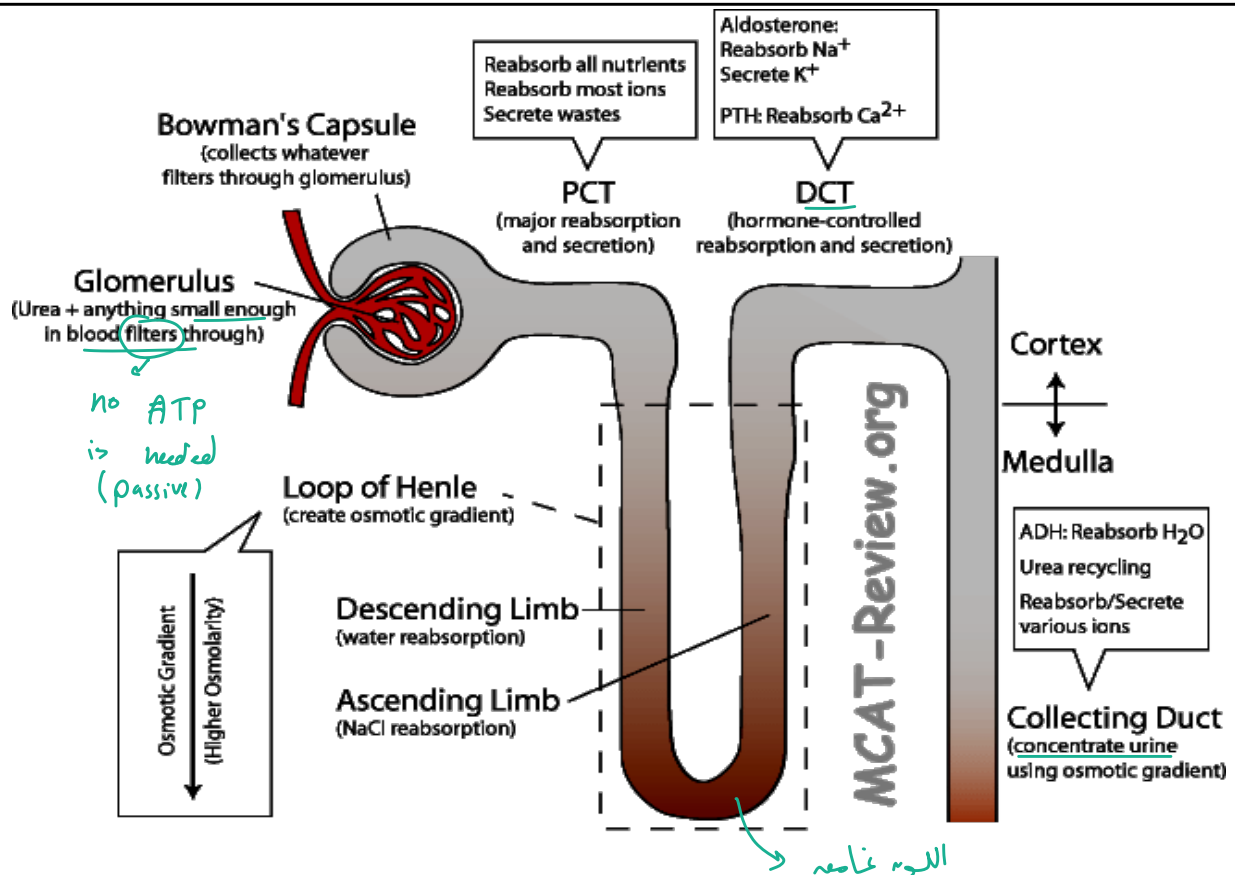
Kidney

- Distal tubule: convoluted tubule on the side of the collecting duct. hormone-controlled (fine tunes the work done by the proximal tubule) reabsorption of salts and water. Aldosterone-controlled secretion of K^+

- Collecting duct: the distal tubules of many nephrons drain here. ADH-controlled reabsorption of water, hormone-controlled reabsorption/secretion of salts.



Kidney and nephrons



Quick facts:

PCT	proximal convoluted tubule
DCT	distal convoluted tubule
pH homeostasis	tubules secrete H+ if blood too acidic don't reabsorb (same effect as secrete) HCO_3^- if too basic
urea recycling	urea diffuse out of collecting duct back into loop of Henle help maintain osmotic gradient
Wastes secreted by PCT	NH_4^+, Creatinine, Organic Acids
Loop of Henle	The longer the loop of Henle, the more concentrated the urine can be produced
Countercurrent Mechanism	Powered by NaCl pumps in upper ascending limb. Results in osmotic gradient down loop of Henle

Formation of urine

- **Glomerular filtration**
  - Filtration is a passive process which is powered by hydrostatic pressure.
  - All substances and ions are filtered out, as long as its small enough.
  - The amount of filtrate that flows out of all the renal corpuscles of both kidneys every minute is called the **glomerular filtration rate (GFR).** In the normal adult, this rate is **about 125 ml/min**
  - Proteins with molecular weights lower than that of albumin (68,000 daltons) are filterable
  - Negatively charged molecules are less easily filtered than those bearing a positive charge

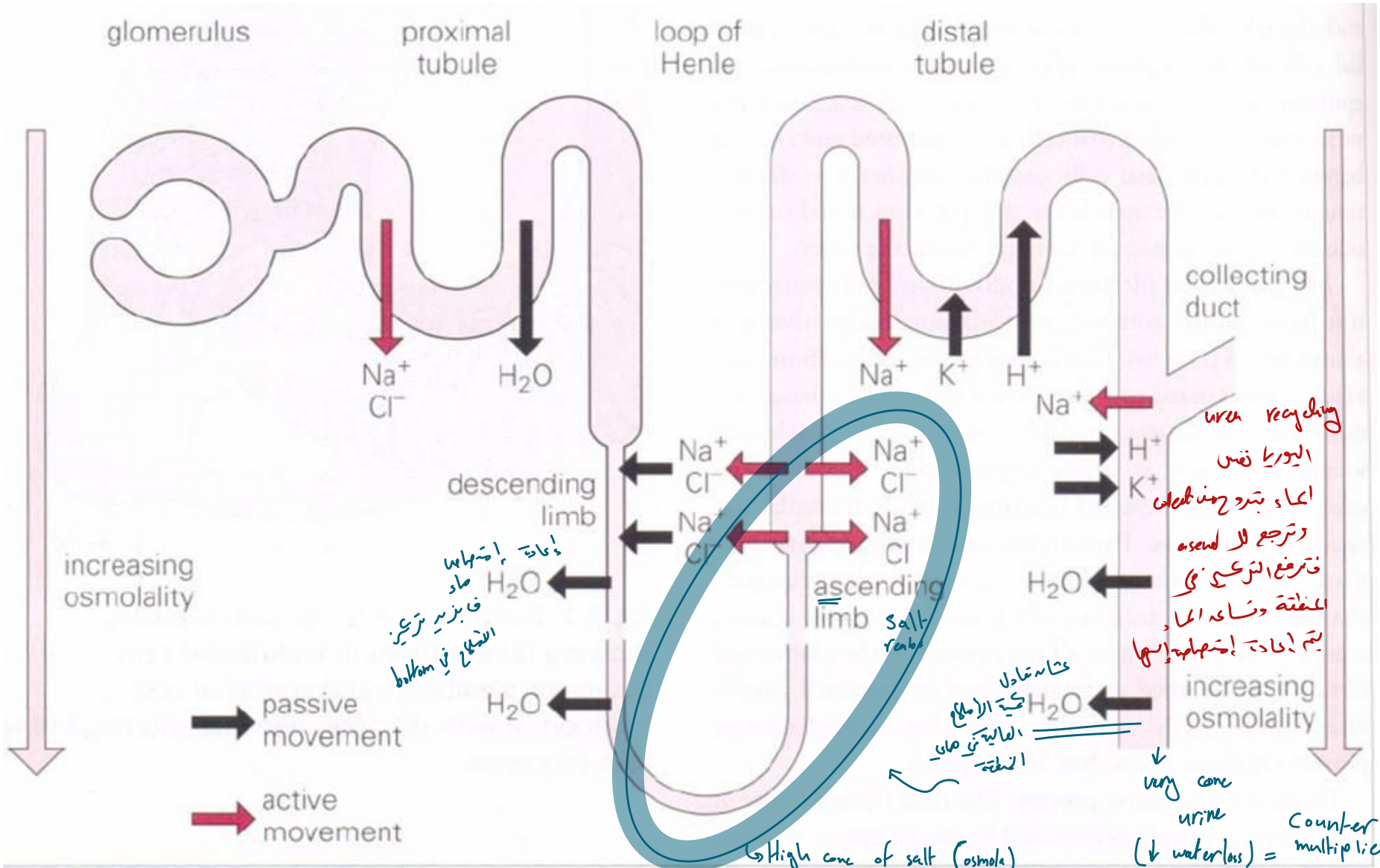
Formation of urine

- **Secretion and reabsorption of solutes**
  - Proximal convoluted tubules reabsorb all the nutrients and most of the ions.
  - Materials that are reabsorbed include water, glucose, amino acids, urea (partially), and ions such as Na^+, K^+, Ca^{2+} , Cl^-, HCO_3^-, and HPO_3^- .
  - Waste products are left in the filtrate (as urea), And also actively excreted (NH_4^+, creatinine, organic acids).
  - Glucose and amino acids are reabsorbed by an active process co-transpotred with (Na^+) ions.
  - Loop of Henle reabsorbs water and salt using the countercurrent mechanism.
  - Distal convoluted tubules selectively reabsorb or secrete substances based on hormonal control.
  - Collecting duct reabsorb water to concentrate urine if ADH present. (Also can secrete and reabsorb substances based on hormonal control)
  - Regulation of blood pH: secrete H^+ when blood too acidic, not to reabsorb HCO_3^- when blood too basic.

Formation of urine

- Concentration of urine
  - The distal convoluted tubule contains dilute solution of urea.
  - The collecting duct concentrates it by water reabsorption (facilitated diffusion) when ADH is present.
  - Water reabsorption in the collecting duct is possible because the loop of Henle has very high osmolarity (very concentrated) at the bottom.
- Countercurrent multiplier mechanism (basic function)
  - NaCl pump on ascending limb creates an osmotic gradient down the loop of Henle, which is used by the collecting duct to concentrate urine.
  - Descending limb: water flow out of filtrate, impermeable to salt. Ascending limb: salt flow out of filtrate, impermeable to water.
  - The gradient-producing power of each individual NaCl pump multiplies down the length of the loop of Henle. Longer the loop of Henle, greater the osmotic gradient, more concentrated urine can be produced.
  - What is urea recycling? Urea at the bottom of collecting duct leaks out into the interstitial fluid and back into the filtrate. Contributes to the high osmolarity at the bottom of the loop of Henle.

Urine formation



Endocrine function of kidney

الهرمونات المفرزة من الكلى وو ظائفها !

- Secretion of hormones:

  في حالة bp ↓

  - Renin: produced by juxtaglomerular cells of the renal medulla as a result of reduced kidney perfusion

    يُفرز لما تقل كمية الدم و ضخه إلي رايح للكلى

    بحول ang I إلى ang II و إلي يرفع ضغط الدم عن طريق ① vasoconstriction ② secr aldosterone

  - Erythropoietin: secreted by cells near to proximal tubule as a response to blood oxygen levels. It affects bone marrow to produce erythrocytes RBCs

    يُفرز لما يكون الدم الواصل للكلى فيه O_2 بنسبة ضعيفة، شغله في bone marrow على إفراز RBCs محملين (بـ هيموغلوبين)

    ← هاد السبب إنه دايما بكون دم المدخن 18 أو 19 لأنه الدم الواصل للكلى فيه نسبة O_2 قليلة

  - active form of vit D_3

    1,25-Dihydroxy vitamin D_3: act in the formation of the active form of vitamin D3

    في liver تتم إضافة OH على C رقم 25 و المرة الثانية على C-1 في kidney فبصير الشكل الفعّال

    في الناس إلي عندها renal failure الله يعافينا بنعطيهم activated vit D_3 جاهز لأنه مارح يقدر الكلى عنده تفعله من حالها.

  - لحماية الكلى

    Prostaglandins: increases renal blood flow, sodium and water excretion, and renin release

    الناس إلي تأخذ NSAIDs إلي تثبط COX-1 و COX-2

    رح يثبط من إنتاج prostaglandins فممكن يصير عنده م فشل كلوي لو كان يأخذ كمية كبيرة من NSAIDs

Elimination of Nonprotein Nitrogen Compounds

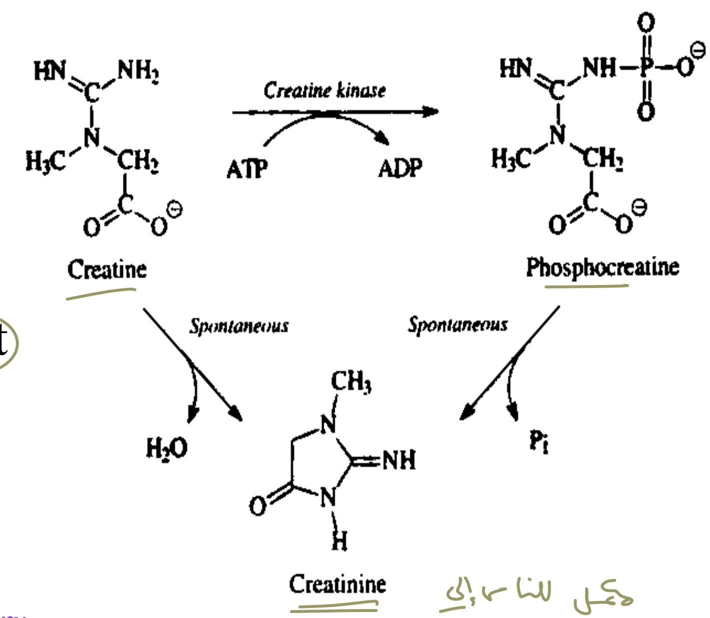
- Nonprotein nitrogen compounds (NPN) are waste products formed in the body as a result of the degradative metabolism of nucleic acids, amino acids, and proteins. The three principal compounds are urea, creatinine, and uric acid.

  - **Urea**
    - Urea makes up the majority (>75%) of the NPN waste. Urea synthesis occurs in the liver from ammonia
    - The kidney is the only significant route of excretion for urea.
    - It is readily filtered by the glomerulus. In the collecting ducts, 40-60% of urea is reabsorbed. The reabsorbed urea contributes to the high osmolality in the medulla, which is one of the processes of urinary concentration

Elimination of Nonprotein Nitrogen Compounds

Creatinine

- Muscle contains creatine phosphate, a high-energy compound for the rapid formation of ATP catalyzed by creatine kinase (CK).
- Every day up to 20% of total muscle creatine (and its phosphate) spontaneously dehydrates and cycles to form the waste product creatinine.
- Crearinine is readily filtered by the glomerulus but not reabsorbed by the tubules.



Uric acid

- uric acid is the primary waste product of purine metabolism (adenine and guanine)
- like creatinine, uric acid is readily filtered by the glomerulus, but undergoes a complex cycle of reabsorption and secretion as it crosses through the nephron

Renal assessment

- Renal function tests focus largely on glomerular clearances, as assessed by creatinine and urea measurements
- Tubular functions are assessed by protein measurements (eg, urine electrophoresis)
- The analysis of urine for analytes, such as pH, glucose, ketones, and bilirubin, continue to be important screening tests for many non- renal diseases, such as diabetes mellitus, ketoacidosis, hemolysis, and liver disease

Renal assessment

- Measurement of GFR
  - Clearance tests [filtration without reabsorption such as creatinine] ↑ better kidneys health
  - Plasma creatinine [↑ Plasma creatinine ↓ bad kidneys health] →
  - Urea, uric acid and β2-microglobulin →
- Renal tubular function tests (proximal + distal) secretion + reabsorption
  - Osmolality measurements proximal tubule (solutes reabsor)
  - Specific proteinurea →
  - Glycouria
  - Aminoaciduria
- Urinalysis →
  - Appearance
  - Specific gravity and osmolality
  - pH
  - Glucose
  - Protein
  - Urinary sediments turbid

Analytic procedures

- To assess the various aspects of nephron function, including glomerular filtration and proximal and distal tubular secretion and reabsorption, many tests are performed

أقيس أن مادة المفروض ما تكون في الدم ولكن بسبب خلل في الكلى تراكمت في الدم (waste products as urea + creatinine)

Clearance Measurements

- All laboratory methods rely on the measurement of waste products in blood, usually urea and creatinine. which accumulate when the kidneys begin to fail

و يبدأ التراكم بمعدل كانت فقط 20-30% من وظائف الكلى سليمة (نصف كلية)

- Renal failure must be advanced, with only about 20-30% of the nephrons still functioning, before the concentration of either substance begins to increase in the blood. The rate at which creatinine and urea are removed or cleared from the blood into the urine is termed clearance

هي السرعة إلي يتم فيها إزالة creatinine + urea من الدم للبول

- Clearance is defined as that volume of plasma from which a measured amount of substance can be completely eliminated into the urine per unit of time expressed in ml/minute

- Measurement of clearance is used to estimate the rate of glomerular filtration

Creatinine

- Creatinine is a nearly ideal substance for the measurement of clearance
- It is an endogenous metabolic product synthesized at a constant rate for a given individual and cleared essentially only by glomerular filtration (it is not reabsorbed and is only slightly secreted by the proximal tubule).
- Analysis of creatinine is simple and inexpensive using colorimetric assays.

Creatinine Clearance and GFR

- Calculation of creatinine clearance has become the standard laboratory method to determine glomerular filtration Rate (GFR).
- This value is derived by mathematically relating the serum creatinine concentration to the urine creatinine concentration excreted during a period of time, usually 24 hours
- Specimen collection must include both a 24-hour urine specimen and a serum creatinine value, ideally collected at the midpoint of the 24-hour urine collection.
- The urine container (clean, dry and free of contaminants or preservatives) must be kept refrigerated throughout the duration of both the collection procedure and the subsequent storage period until laboratory analysis can be performed
- The concentration of creatinine in both serum and urine is measured by the applicable methods

اللهم ارحم والديَّ كما ربياني صغيرًا

Creatinine Clearance and GFR

- The total volume of urine is carefully measured, and the creatinine clearance is calculated using the following formula (Cockcroft-Gault formula)

$$C_{Cr}\ (\text{mL/minute}) = \frac{U_{Cr}\ (\text{mg/dL}) \times V_{Ur}\ (\text{mL/24 hours})}{P_{Cr}\ (\text{mg/dL}) \times 1440\ \text{minutes/24 hours}} \times \frac{1.73}{A}$$

normal surface area for person has 70 kg

where Cr_{Cl} = creatinine clearance

U_{Cr} = urine creatinine concentration

V_{Cr} = urine volume excreted in 24 hours

P_{Cr}= serum creatinine concentration

- 1.73/A normalization factor for body surface area

Reference ranges for creatinine clearance

- Male: 97- 137 mL/minute per 1.73 m^2
- Female: 88-128 mL/minute per 1.73 m^2
- Creatinine clearance normally decreases with age, with a decrease of about 6.5 ml/minute per 1.73m^2 for each **decade** of life

Estimated Glomerular Filtration Rate

- The estimated GFR (eGFR) is calculated each time a serum creatinine is reported.
- The equation is used to predict GFR and is based on serum creatinine, age, body size, gender, and race, without the need of a urine creatinine
- Because the calculation does not require a timed urine collection, it should be used more often than the traditional creatinine clearance and result in earlier detection of chronic kidney disease

$$\text{GFR (mL/minute)} = \frac{(140 - \text{Age}) \times \text{Weight (kg)}}{72 \times S_{Cr}\,(\text{mg/dL})} \times 0.85$$

(0.85 if female)* **(Eq. 24–6)**

- If serum creatinine is measured in mg/dl, serum creatinine is multiplied by factor 72
- If serum creatinine is measured in µmol/L, the constant is 1.23 for men and 1.04 for women

If S_{cr} mg/dl

male

$$\frac{(140 - age) * w}{S_{cr}\,(mg/dl) * 72}$$

female

$$\frac{(140 - age) * w * 0.85}{S_{cr}\,(mg/dl) * 72}$$

If S_{cr} μmol/L

male

$$\frac{(140 - age) * w * 1.23}{S_{cr}\,(\mu mol/L)}$$

female

$$\frac{(140 - age) * w * 1.04}{S_{cr}\,(\mu mol/L)}$$

Renal failure stages (ml/min):

Stage 1: 90 or higher 2: 60-89 3: 30-59 4: 15-29 5: lower than 15

Urea

→ كنا نستخدمها قديمًا لـ GFR بس لما إنه بصير لجزء منها reabsorption في collecting duct أفضل creatinine

- Urea clearance was one of the first clearance tests performed.
- Urea is freely filtered at the glomerulus and approximately 40% reabsorbed by the tubules. For this reason, it does not provide a full clearance assessment and is no longer widely used

  عشان مايصير water loss urea recycle بتصير

  لأنه المادة إلي لازم نستخدمها لازم عليها يصير لها filtration بدون secretion و absorption

- Older clearance tests used administration of inulin, sodium [^{125}I] iothalamate, or p-aminohippurate to assess glomerular filtration or tubular secretion

  هدول المواد بعطيهم administration عشان أشوف كيف رح يطلعهم المريض (مش مواد بتتصنع داخل الجسم)

- These tests are time-consuming, expensive, and difficult to administer and, for the most part, have been discontinued.

  فبضل creatinine الخيار الأفضل

لا حول ولا قوة إلا بالله العلي العظيم

Urine Electrophoresis

- Owing to the efficiency of renal glomerular filtration and tubular reabsorption, normal urinary protein excretion is only about 50-150 mg/24 hours
- Proteinuria may develop when there are defects in renal reabsorption or glomerular capillary permeability or when there is a significant increase in serum immunoglobulins.
- As a result, urine electrophoresis is used primarily to distinguish between acute glomerular nephropathy and tubular proteinuria
- It is also used to screen for abnormal monoclonal or polyclonal globulins.
- Positive identification and subtyping of the urinary paraproteins can be performed by immunofixation electrophoresis

Urine Electrophoresis

- Newer protein assays, such as urine microalbumin, serum β2-M, cystatin C, and serum and urine myoglobin, can provide important prognostic information useful for patient management.

- **Microalbuminuria** is useful for early detection of **diabetic nephropathy**
- **β2-M** is useful for **early renal transplant rejection**
- **Myoglobin** clearance rates are helpful in predicting **rhabdomyolysis induced acute renal failure**.
- **Cystatin C** is used in detecting **early changes in kidney function**

Microalbumin

- Urine microalbumin measurement is important in the management of patients with diabetes mellitus, who are at serious risk of developing nephropathy over their lifetimes
- Type 1 has a 30-45% risk, and Type 2 has a 30% risk
- In the early stages of nephropathy there is renal hypertrophy hyperfunction, and increased thickness of the glomerular and tubular basement membranes

تضخم الكلى = كلما تصير تشتغل أكثر

too much urination

renal failure وضع الوقت بصير

لا إله إلا أنت سبحانك
إني كنت من الظالمين

β2-Microglobulin

- β2-Microglobulin (β2-M) is a small, nonglycosylated peptide (MW, 11.8 KDa) found on the surface of most nucleated cells
- The plasma membrane sheds β2-M as a relatively intact molecule into the surrounding extracellular fluid so stable levels in normal patients
- Its serum elevated levels indicate increased cellular turnover as seen in myeloproliferative and lymphoproliferative disorders, inflammation, and renal failure
- β2-M is easily filtered by the glomerulus. About 99.9% is then reabsorbed by the proximal tubules and catabolized
- Measurement of serum β2-M is used clinically to assess **renal tubular function in renal transplant patients** (high when organ rejection)
- β2-M is more efficient marker of renal transplant rejection than serum creatinine values (independent on lean muscle mass)

Myoglobin → in cardiac + skeletal muscles to store 4 molecules of O_2

- Myoglobin is associated with **acute skeletal and cardiac muscle injury**
- In rhabdomyolysis, myoglobin release from skeletal muscle is sufficient to overload the proximal tubules and cause acute renal failure
- Early diagnosis and aggressive treatment of elevated myoglobin may prevent or lessen the severity of renal failure. Recently, myoglobin clearance has been proposed as an effective early indicator of myoglobin-induced acute renal failure. A high clearance or a low clearance and low serum concentration indicates low risk and a low clearance and high serum concentration indicates high risk.
- Serum and urine myoglobin can be measured easily and rapidly by **immunoassays**. Urine myoglobin can also be measured by dipstick methods after removing hemoglobin, but this method has a lack of sensitivity and specificity.

Cystatin C

- Cystatin C is a low-molecular-weight protein produced by nucleated cells. It is freely filtered by the glomerulus and reabsorbed and catabolized by the proximal tubule

- Produced at a constant rate, levels remain stable if kidney function is normal

- Measurement of cystatin C to be at least as useful as serum creatinine and creatinine clearance in detecting **early changes in kidney function**. Cystatin C can be measured by immunoassay methods

Urinalysis
Physical Characteristics

Color, odor, pH ...

- Initial morning specimens are preferred, particularly for protein analyses, because they are more concentrated from overnight retention in the bladder
- The urine should be freshly collected into a clean, dry container with a tight-fitting cover

في حرارة الغرفة نفحصها خلال ساعة فقط ، أو في حرارة °8-2 لـ 8 ساعات بس

- It must be analyzed within 1 hour of collection if held at room temperature or else refrigerated at 2°-8°C for not more than 8 hours before analysis

السبب

- Bacterial multiplication will cause false-positive nitrite tests, and urease-producing organisms will degrade urea to NH3 and alkalinize pH

ممكن العينة ما يكون فيها nitrate ولكن لما طولنا في الفحص

انتجت البكتيريا nitrate خلال فترة التخزين ، ورح يكون PH تبعت urine قاعدية بسبب urease production ← NH_3 ← basic

- Loss of CO_2 by diffusion into the air adds to this pH elevation, which causes cast degeneration and red-cell lysis

وجود CO_2 في العينة ← بخليها حمضية لأنه عنده خواص حمضية

فخروجه من العينة بخليها قاعدية وهاد بسبب تحلل خلايا الدم الحمراء RBCs

- The urine container must be sterile if the urine is to be cultured

لأنه لو ما كان الوعاء معقم ممكن نفحص بكتيريا الوعاء مش urine

Urinalysis
Physical Characteristics

- **Visual Appearance**. Color intensity of urine correlates with concentration: the darker the color, the more concentrated the specimen
  - Yellow and amber are generally due to urochromes (derivatives of urobilin), whereas a yellowish-brown to green color is a result of bile pigment oxidation.
  - Red and brown after standing are due to porphyrins, whereas reddish-brown in fresh specimens comes from hemoglobin or red cells.
  - Brownish- black after standing is seen in alkaptonuria (a result of excreted homogentisic acid) and in malignant melanoma (in which the precursor melanogen oxidizes in the air to melanin). Drugs and some foods, such as beets, also may alter urine color.

- **Odor**: The characteristic pungent odor of fresh urine is due to volatile aromatic acids
  - Urinary tract infections impart a noxious, fecal smell to urine, whereas the urine of diabetics often smells fruity as a result of ketones.

Urinalysis
Physical Characteristics

- **Turbidity** The cloudiness of a urine specimen depends on pH and dissolved solids composition.
  - Thread-like cloudiness is observed when the specimen is full of mucus. In alkaline urine, suspended precipitates of amorphous phosphates and carbonates may be responsible for turbidity whereas in acidic urine, amorphous urates may be the cause

- **Volume**. The volume of urine excreted indicates the balance between fluid ingestion and water lost from the lungs. sweat, and intestine
  - Polyuria is observed in diabetes mellitus and insipidus (in insipidus, as a result of lack of ADH). as well as in chronic renal disease. acromegaly (overproduction of the growth hormone)

Renal diseases

أي مشكلة في الكلى ٢٧ تؤثر على وظائفها
وترفع BUN و blood creatinine ← يؤدي إلى

- Common renal diseases include infectious and inflammatory processes to the glomerulus, tubules, and urinary tract, obstructions of normal kidney function, and acute and chronic renal failure.

NSAIDs → acute renal failure

- rapid deterioration of renal function → accumulation in blood of nitrogenous wastes that would normally be excreted in urine.

- Patient presents with rapidly ↑ blood urea nitrogen (BUN) & serum creatinine (SrCr).

أستغفرك ربي و أتوب إليك

Etiology

Acute Renal Failure

1. **Prerenal Causes**

- Patients who are dependent on prostaglandin-mediated vasodilation to maintain renal perfusion can develop RF simply from ingestion of NSAIDs.

  Protective mechanism of kidney by increase renal perfusion and excretion of Na^+ + H_2O so ↓ of kidney load.

  (as diclofenac)

- Patients with renal hypoperfusion (e.g., from renal artery stenosis, congestive heart failure, or intrarenal small vessel disease) who are dependent on angiotensin II-mediated vasoconstriction of efferent renal arterioles to maintain renal perfusion pressure may develop ARF on ingesting **ACE inhibitors**.

Etiology

② Intrarenal Causes

- can be divided into
  - specific **inflammatory diseases** (e.g., vasculitis, glomerulonephritis, drug-induced injury)
  - **acute tubular necrosis** resulting from many causes (including ischemia, poisons, & hemolysis).
- **Tubular damage can commonly be due to aminoglycoside antibiotics & rhabdomyolysis**, in which myoglobin, released into bloodstream after crush injury to muscle, precipitates in renal tubules.
- **Sepsis** is one of the most common causes of acute renal failure - combination of prerenal & intrarenal factors.

③ Postrenal Causes

- result in **urinary tract obstruction**, such as renal stones.

Pathogenesis

لو ما صار تدخل طبي بعد ما صار ARF ممكن يصير موت للنفرونات ATN

- All forms of ARF, if untreated, result in **acute tubular necrosis (ATN)**, with sloughing of cells that make up renal tubule.

- ARF **may be reversible** depending on timing of intervention between onset of initial injury & eventual ATN

سبحان الله وبحمده

سبحان الله العظيم

Clinical Manifestations

ARF

- Initial symptoms: fatigue & malaise, probably early consequences of loss of ability to excrete water, salt, & wastes via kidneys.
- Later, more profound S&S of loss of renal water & salt excretory capacity: dyspnea, orthopnea, rales, prominent S3, & peripheral edema.
- Altered mental status reflects toxic effect of uremia on brain, with ↑ blood levels of nitrogenous wastes & fixed acids.
- Clinical manifestations depend on cause & stage of disease at which patient comes to medical attention.
  - Patients with renal hypoperfusion first develop **prerenal azotemia** (↑BUN without tubular necrosis), a direct physiologic consequence of ↓ GFR.
  - Without treatment, prerenal azotemia may progress to **ATN** - often requiring supportive dialysis before adequate renal function is regained.

Clinical Manifestations

- The earliest manifestation of prerenal azotemia is ↑ ratio of BUN to SrCr. Normally 10–15:1, this ratio may ↑ to 20–30:1 in prerenal azotemia, with a normal or **near-normal serum creatinine**.
- Urinalysis:
  - Urine is maximally concentrated (up to 1500 mOsm/L) in prerenal azotemia.
    - However, with progression to acute tubular necrosis, the ability to generate a concentrated urine is largely lost (< than 350 mOsm/L)
    - granular casts, tubular epithelial cells, & epithelial cell casts are found in ATN.

Chronic Renal Failure (CRF)

Clinical Presentation

- in addition to those observed in ARF:
- Osteodystrophy,
- Neuropathy,
- Bilateral small kidneys by abdominal x-ray film or ultrasonography,
- Anemia

Etiology

- The most common cause of CRF is **diabetes mellitus**, followed closely by hypertension & glomerulonephritis.
- Polycystic kidney disease, obstruction, & infection are among the less common causes

Pathogenesis

Development of Chronic Renal Failure

- Irreversible loss of nephrons → > functional burden is borne by fewer nephrons → ↑ glomerular filtration pressure & hyperfiltration → ("hypertension" at level of nephron) → fibrosis & scarring **(glomerular sclerosis)** → the rate of nephron destruction & loss ↑→ **uremia**
- In CRF there is combination of toxic effects of:

  (1) retained products normally excreted by kidneys (e.g., nitrogen-containing products of protein metabolism) Same as ARF

  (2) normal products such as hormones now present in ↑ amounts

  (3) loss of normal products of kidney (e.g., erythropoietin)
- Excretory failure results also in fluid shifts, with ↑ intracellular Na+ & water & ↓ intracellular K+.
- **Effects on metabolism:**

  (1) ↓ in basal body temperature (perhaps because of ↓ Na+-K+ ATPase activity)

  (2) ↓ lipoprotein lipase activity with accelerated atherosclerosis.

Clinical Manifestations

ما في كدرة – للكلى تقل إفراز

Na+ Balance & Volume Status

- Some degree of Na+ & water excess, reflecting loss of renal route of salt & water excretion.
- Continued excessive Na+ ingestion contributes to CHF, HTN, ascites, peripheral edema, & weight gain.
- Excessive water ingestion contributes to hyponatremia.

كتجمع سوائل في منطقة البطن

كاستهلاك ماء وملح بس ماء أكثر

اللهم اغفر لي ولوالدي وللمسلمين

والمسلمات والمؤمنين والمؤمنات

الأحياء والأموات

Clinical Manifestations

K+ Balance

- Hyperkalemia is a serious problem especially when GFR ↓ below 5 mL/min → aldosterone-mediated K+ transport in distal tubule ↑ in compensatory fashion.
  - Treatment with K+-sparing diuretics, ACE inhibitors, or β -blockers—drugs that may impair aldosterone-mediated K+ transport—can, therefore, precipitate dangerous **hyperkalemia** in a patient with CRF.
- CRF patients are at > risk of hyperkalemia in the face of sudden loads of K+ from either endogenous sources (e.g., hemolysis, infection, trauma) or exogenous sources (e.g., stored blood, K+-rich foods, or K+-containing medications).

Metabolic Acidosis

- ↓ capacity to excrete acid & generate buffers
- Can usually be corrected with 20–30 mmol (2–3 g) of sodium bicarbonate by mouth daily.

Clinical Manifestations

Mineral & Bone

- Several disorders of phosphate, Ca2+, & bone metabolism
- Key factors:

(1) ↓ absorption of Ca2+ from gut,

(2) overproduction of PTH,

(3) disordered vitamin D metabolism,

(4) chronic metabolic acidosis → **enhanced bone resorption**.

- Hyperphosphatemia contributes to development of hypocalcemia → serves as additional trigger for secondary hyperparathyroidism →↑ blood PTH levels.
- →further depletion of bone Ca2+ → **osteomalacia** & **osteoporosis** of CRF

Clinical Manifestations

renal failure يؤدي إلى احتباس

السوائل والأملاح في يؤثر على حجم الدم في يزداد الثقل على القلب فا يؤدي إلى مشاكل في القلب ← Hypertension ...

Cardiovascular & Pulmonary Abnormalities

- ① CHF & ② pulmonary edema are most commonly due to volume & salt overload.
- ③ HTN is a common finding, usually on the basis of fluid & Na^+ overload.
  - ④ **Hyperreninemia** (↓ renal perfusion triggers failing kidney to overproduce renin →↑ elevate systemic BP.

    ارتفع CRF لأن كمية الدم الواصلة للكلى أقل من الطبيعي في دائماً محفز عنده إنتاج renin

    direct vaso constriction due to angio II
- ↑ cardiovascular risk remains the leading cause of mortality in this population (⑤ MI, ⑥ stroke, & ⑦ peripheral vascular disease).

  الكلى صامة إنه كمية الدم قليلة في تبهل في تشتغل إنها ترفع ضغط الدم م إنه عند القلب و الأوعية الدموية الدم مرتفع تشكل اوفر
- Cardiovascular risk factors: HTN, hyperlipidemia, glucose intolerance, chronic ↑ cardiac output, & valvular & myocardial calcification due to ↑ Ca^{2+} x PO_4^{3-} product

  صار الـ complex

  يترسب على القلب و صمامات القلب

  فا بصير تكلس في عضلة القلب

  جزء أتعب صادا بي يضلي أمراض عضلة القلب

  هو أكثر سبب للموت لمرضى فشل الكلى.

اللهم إنا نسألك الجنة ونعوذ بك من النار

Clinical Manifestations

Hematologic Abnormalities

Kidneys produce Erythropoietin when the oxygen of blood, it will not be produced when someone has renal failure → anemia

- Normochromic, normocytic anemia, with hematocrits typically in the range of 20–25%, is a consistent feature. Because of
  - Lack of production of erythropoietin (mainly)
  - Bone marrow suppressive effects of uremic poisons
  - Bone marrow fibrosis due to ↑ blood PTH → تليين تحاتم العظم
- Abnormal hemostasis (↑ bruising, ↑ blood loss at surgery, ↑ incidence of spontaneous GI & cerebrovascular hemorrhage.
- ↑ susceptibility to infections, due to leukocyte suppression by uremic toxins.
- Acidosis, hyperglycemia, malnutrition, & hyperosmolality also contribute to immunosuppression.
- Invasiveness of dialysis & use of immunosuppressive drugs in renal transplant patients also contribute.

Clinical Manifestations

Endocrine and Metabolic Abnormalities

- Women have low estrogen levels → amenorrhea & inability to carry pregnancy to term.
- Low testosterone levels, impotence, oligospermia are common findings in men
- ↑ half-life of insulin → stabilizing effect on diabetic patients whose blood glucose was previously difficult to control.

Dermatologic Abnormalities

- Pallor because of anemia,
- Hematomas as a result of clotting abnormalities,
- Pruritus & excoriations as a result of Ca^{2+} deposits from secondary hyperparathyroidism.

Treatment of chronic renal failure

- In situations of chronic renal failure, aggressive therapeutic approaches based on **dialysis** and **transplantation** have enabled prolonged survival of what was once a terminal condition

بس بده يضل ياخذ أدوية تثبيط مناعة عشان الخلية ما تهاجم العضو

- Variations in dialysis techniques have made this process more available and convenient and, with the implementation of powerful immunosuppressive drugs, widespread renal transplantation is now limited only by the availability of appropriate donor organs.

① ②

جدًا صعب يكون في شخص متطابق مع المريض مناعيًا 100٪

الحمد لله رب العالمين