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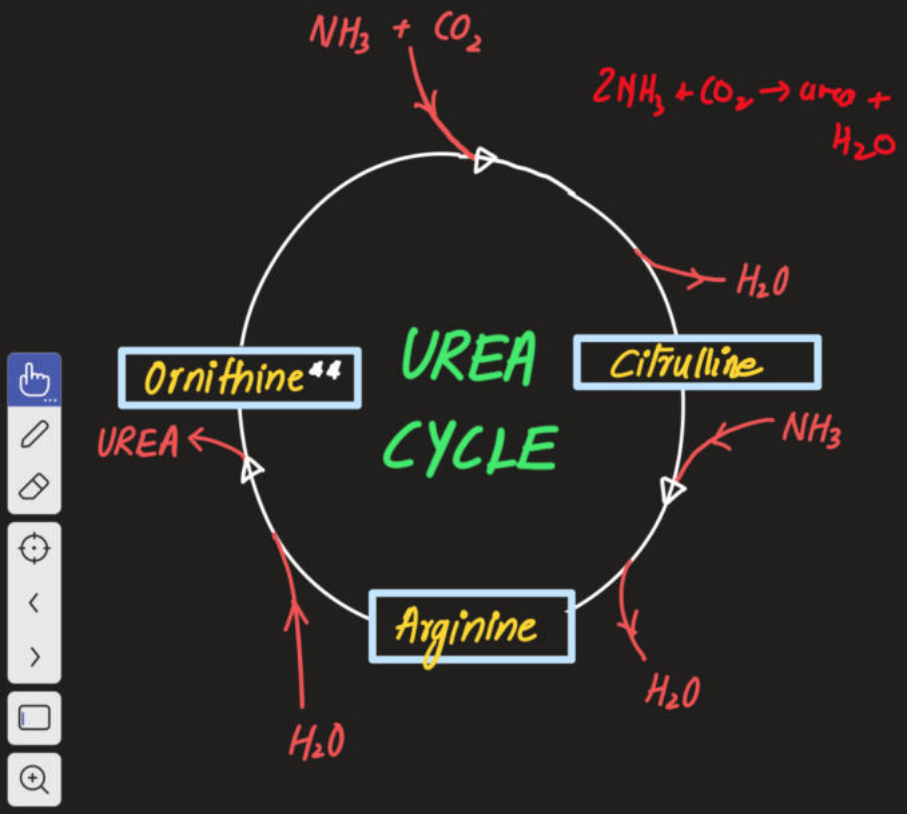
Homeostasis



* Urea is less Toxic and less soluble in water than ammonia
* Urea is primarily excreted via kidneys.

With

Mohammad Hussham Arshad, MD

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ADVANCED LEVEL BIOLOGY 9700

UNIT 14: Homeostasis

Learning Objectives:

- Excretion and Nitrogenous waste
- Structure of the kidney and associated blood vessels
- Nephron 1

Video Lecture 1 Slides

Mohammad Hussham Arshad, MD
Biology Department

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HOMEOSTASIS

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HOMEOSTATIS

* Homeostatis refers to the maintenance of a constant internal environment.
* Homeostatis can be subdivided into:

(A) Homeostatis in mammals

e.g; (1) Osmoregulation
(2) Thermoregulation
(3) Regulation of blood glucose

* All three achieved via NEGATIVE FEEDBACK.

(B) Homeostatis in plants

e.g; (1) Stomatal closure due To abscisic acid

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* This chapter is therefore subdivided into subsections:

(I) Excretion and nitrogenous waste products

(II) Kidneys and osmoregulation

(III) Skin and thermoregulation

(IV) Pancreas and control of blood glucose

(V) Guard cells and stomatal closure.

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I · Excretion and nitrogenous waste

Differentiating egestion and excretion....

* Egestion refers to the removal of undigested waste from the body.

* Excretion refers to the removal of metabolic waste from the body. Examples of excreta include:

① Nitrogenous waste (NH_3, urea, uric acid)
② Bile pigments
③ Respiratory waste (CO_2 and H_2O)

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Nitrogenous waste

* There are three common forms of nitrogenous waste products.

① NH_3
② Urea
③ Uric acid

* Mammals (including humans) primarily excrete urea as the nitrogenous waste.

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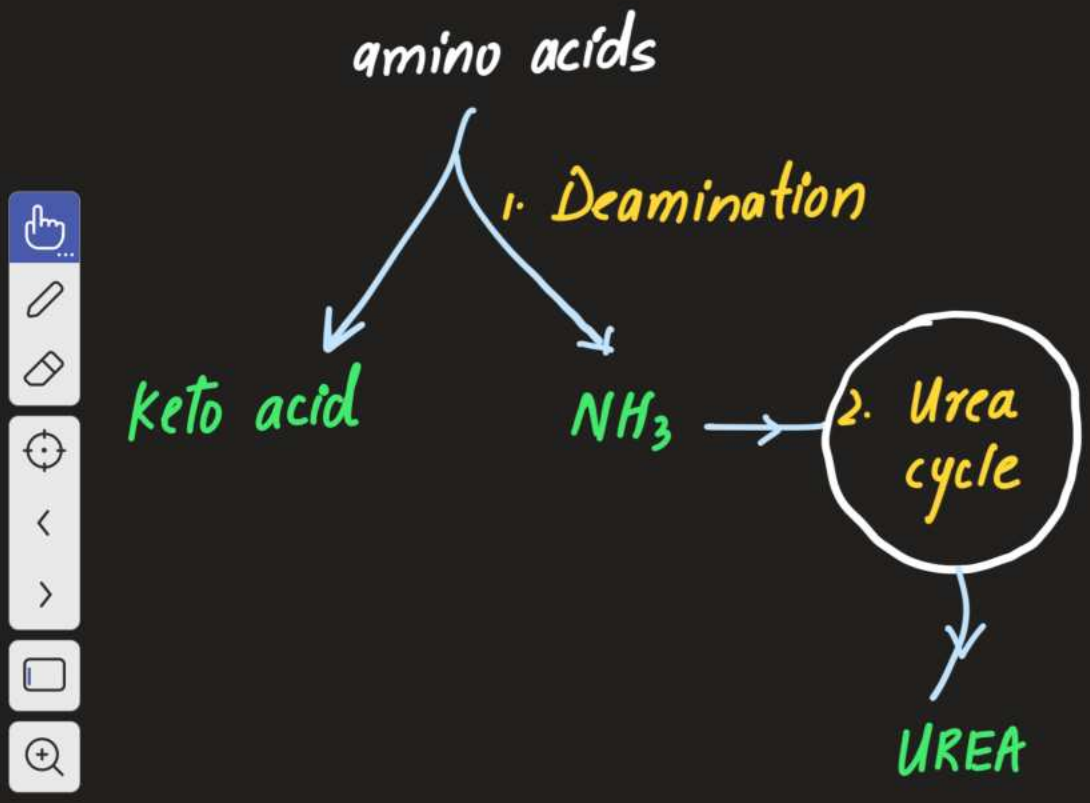
* Given below is a summary of how urea is produced:



① Amino acids undergo deamination to form NH_3

② NH_3 is used in the urea cycle to form urea.

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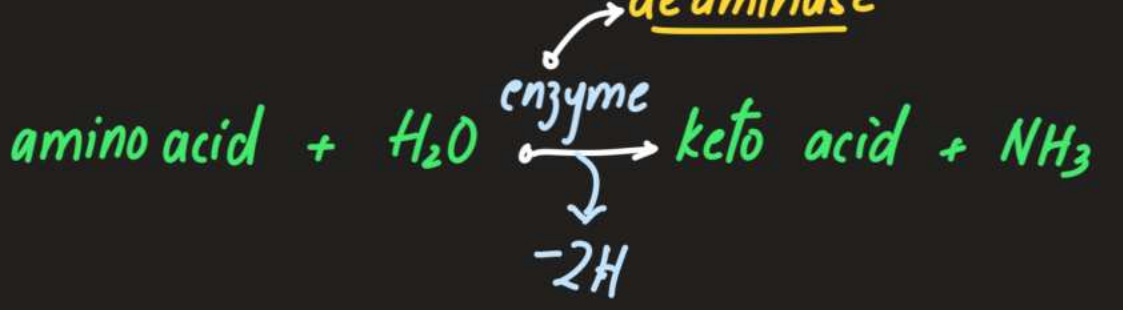
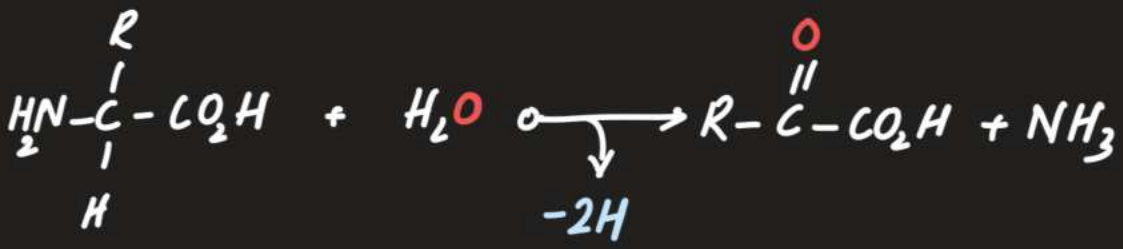
DEAMINATION

* occurs primarily in the liver.
* defined as the removal of the amine group from the amino acid in the form of ammonia.





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* The keto acid can be used in:
  1. Kreb's cycle to release energy via respiration
  2. formation of glucose (gluconeogenesis)

* The NH_3 produced is HIGHLY TOXIC and is rapidly converted into urea via the urea cycle.

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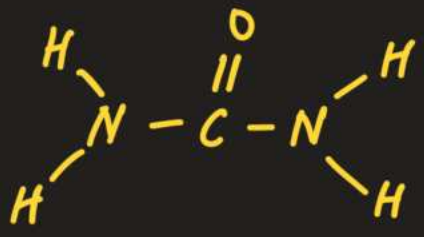
UREA CYCLE

* also termed as The ornithine cycle.
* occurs in the liver
* Summary of the reaction:

$$2NH_3 + CO_2 \longrightarrow \text{urea} + H_2O$$

* Displayed formula of urea:



$(NH_2)_2CO$

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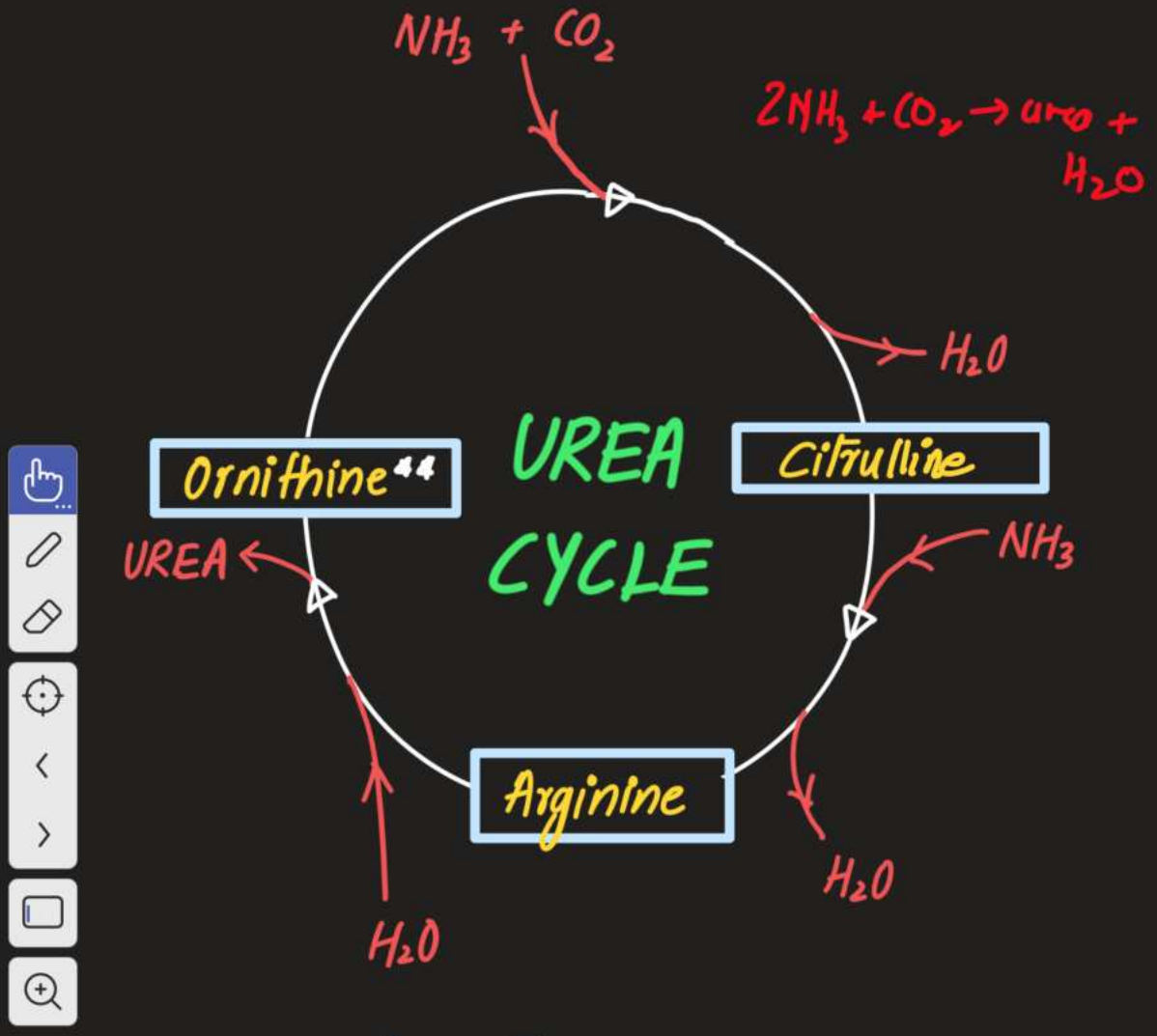

* Urea is less Toxic and less soluble in water than ammonia
* Urea is primarily excreted via kidneys.

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URIC ACID production in humans

* Humans form uric acid from breakdown of purine bases in the liver.

* The process occurs in the liver and is known as the inosinic pathway.

* Uric acid is excreted via kidneys.

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Main features of nitrogenous waste

	NH_3	Urea	Uric acid
No. of nitrogen atoms/molecule	1	2	4
Toxicity	high	1000	
Water solubility	high	1000	
Examples of main organisms	aquatic organisms (most fish species)	mammals primarily	birds, insects, reptiles

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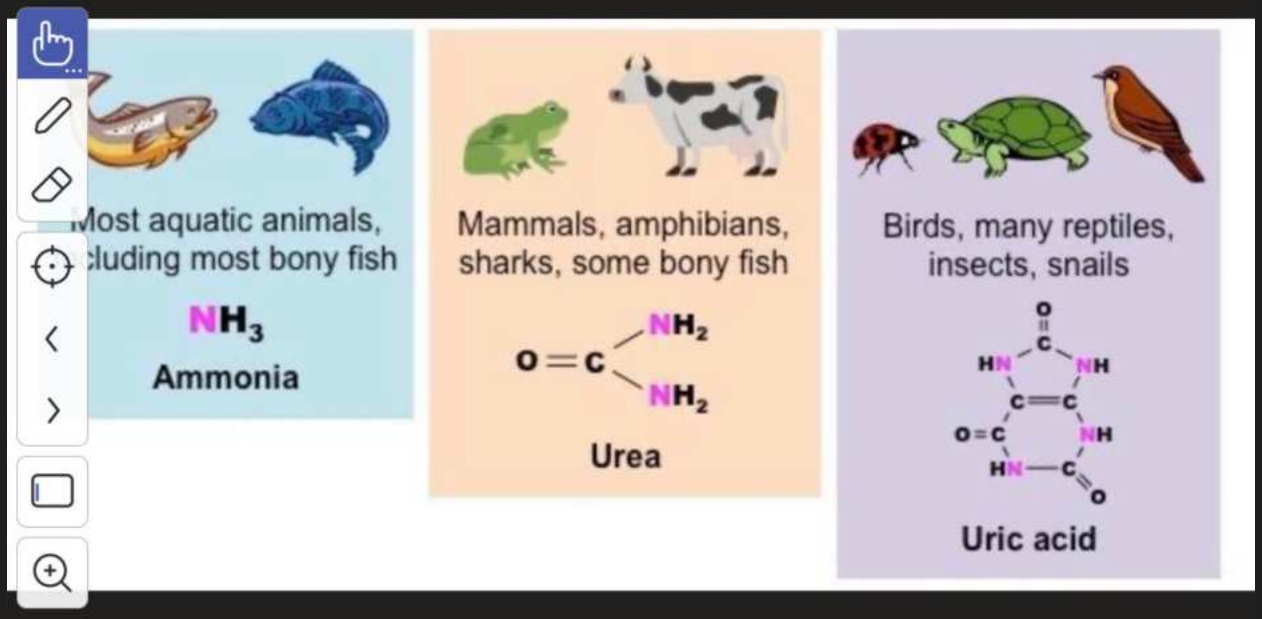
Most aquatic animals, cluding most bony fish
NH3
Ammonia
Mammals, amphibians, sharks, some bony fish
Urea
Birds, many reptiles, insects, snails
Uric acid

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Kidneys and Osmoregulation

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Gross anatomy of The Urinary System

* Mammalian urinary system is made up of:

① a pair of kidneys

② a pair of ureters

③ a bladder

④ a urethra

⑤ associated blood vessels.

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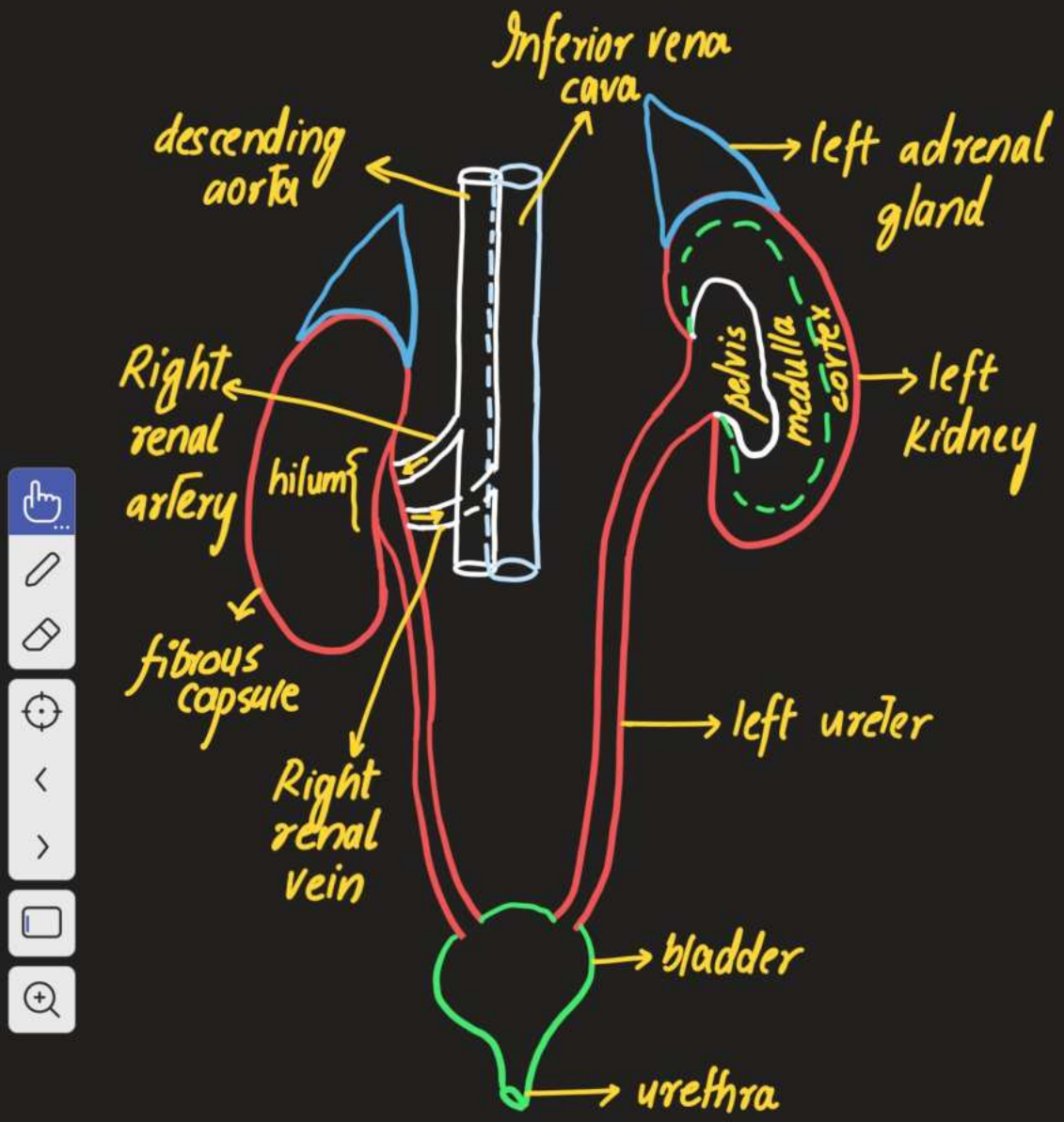

* The right kidney is lower than the left kidney due to the presence of the liver on the right side.

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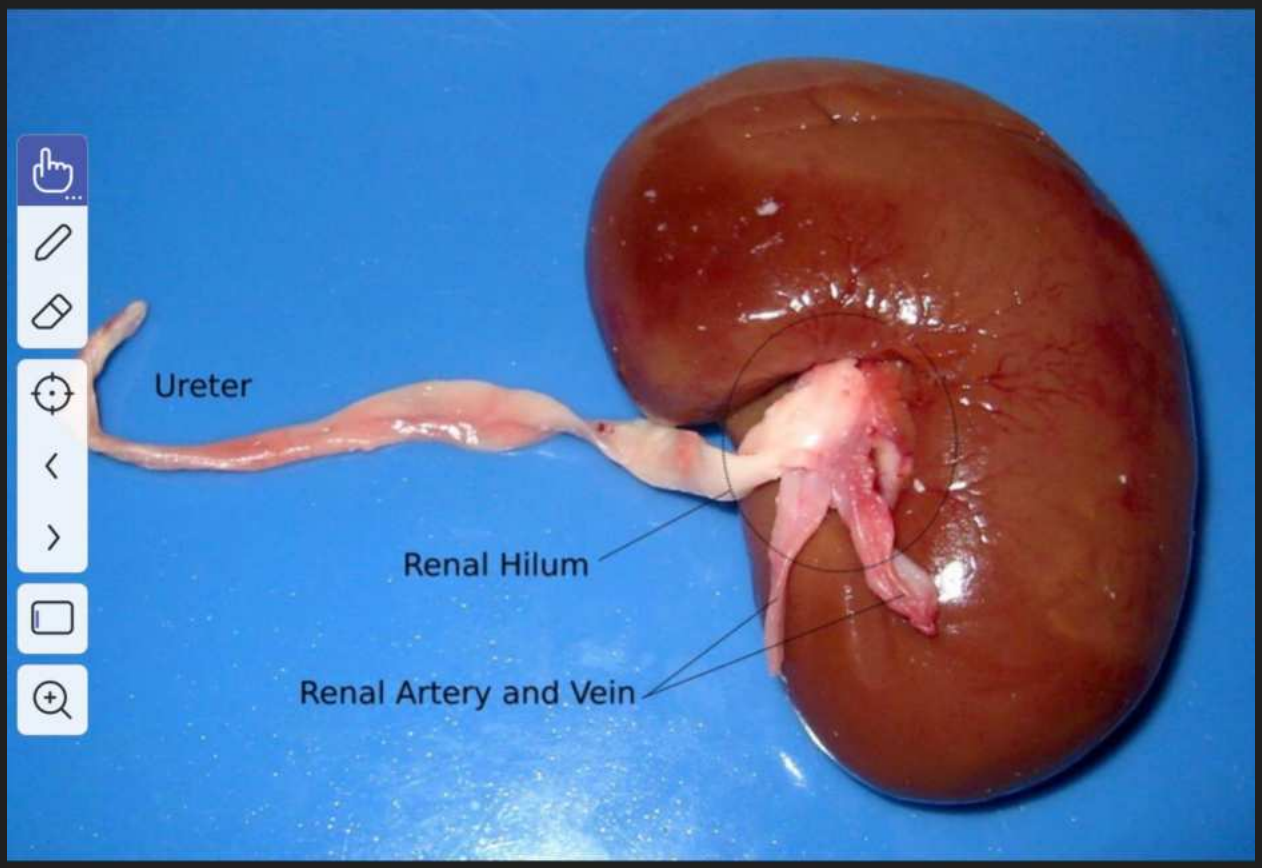

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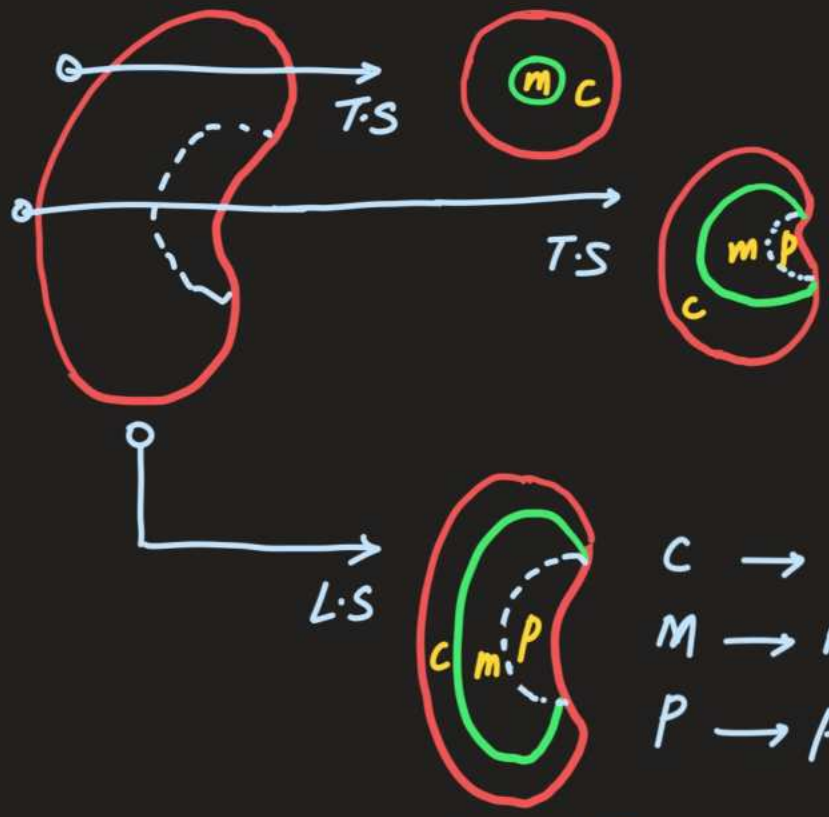
Internal details of a kidney



C → Cortex
M → Medulla
P → pelvis

T.S. Transverse section
L.S. Longitudinal section

* Each kidney contains a million nephrons.
* A nephron is said to be the functional unit of the kidney.

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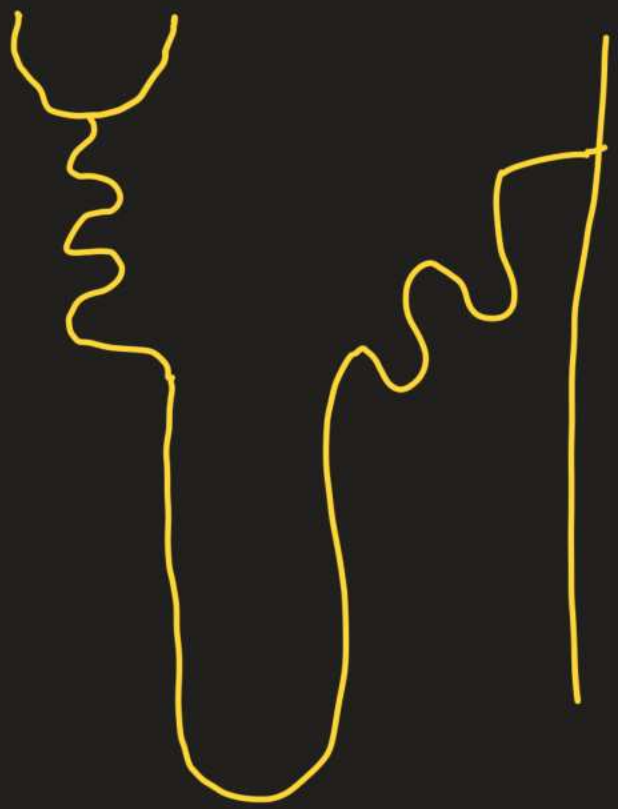
Nephron → Structural details

Tubular segments

Vascular Segments



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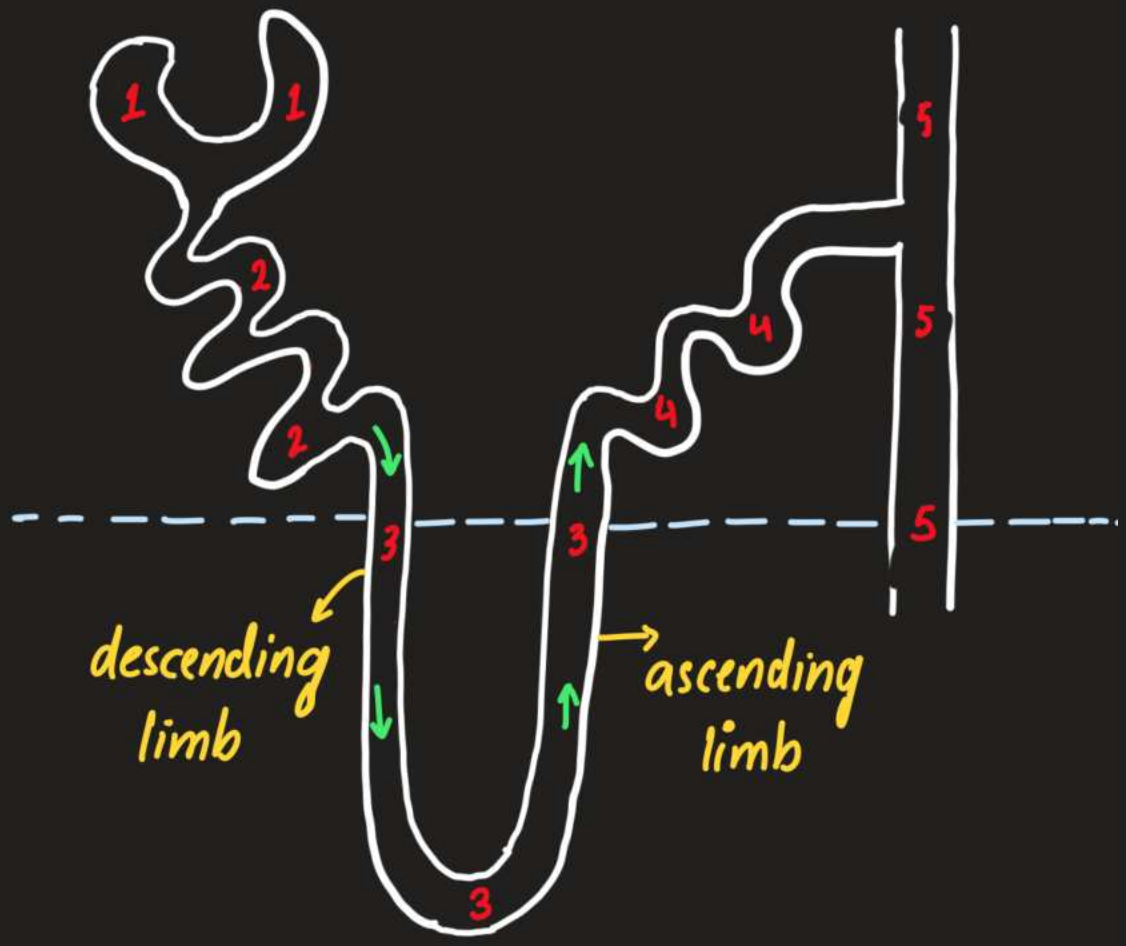
Nephron → Structural Details

* The structure of the nephron contains:
  - (a) tubular segments
  - (b) vascular segments

* The tubular segments of the nephron include:



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1 → Bowman's capsule (renal capsule)

2 → Proximal convoluted tubule

3 → Loop of Henle

4 → Distal convoluted tubule

5 → Collecting duct

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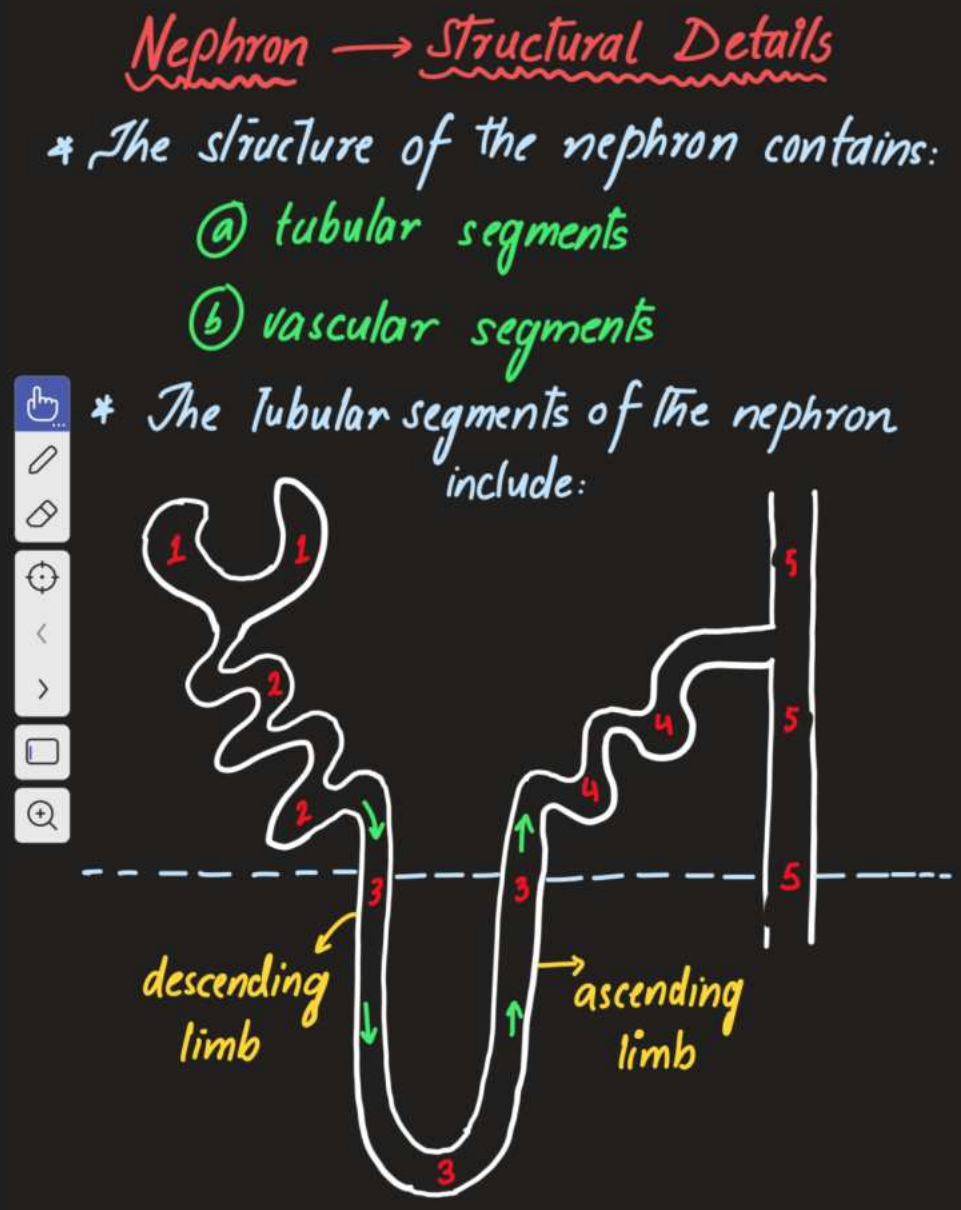
Homeostasis



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UNIT 14: Homeostasis

Learning Objectives:

- Nephron 2
- Urine formation 1

Video Lecture 2 Slides

Mohammad Hussham Arshad, MD
Biology Department

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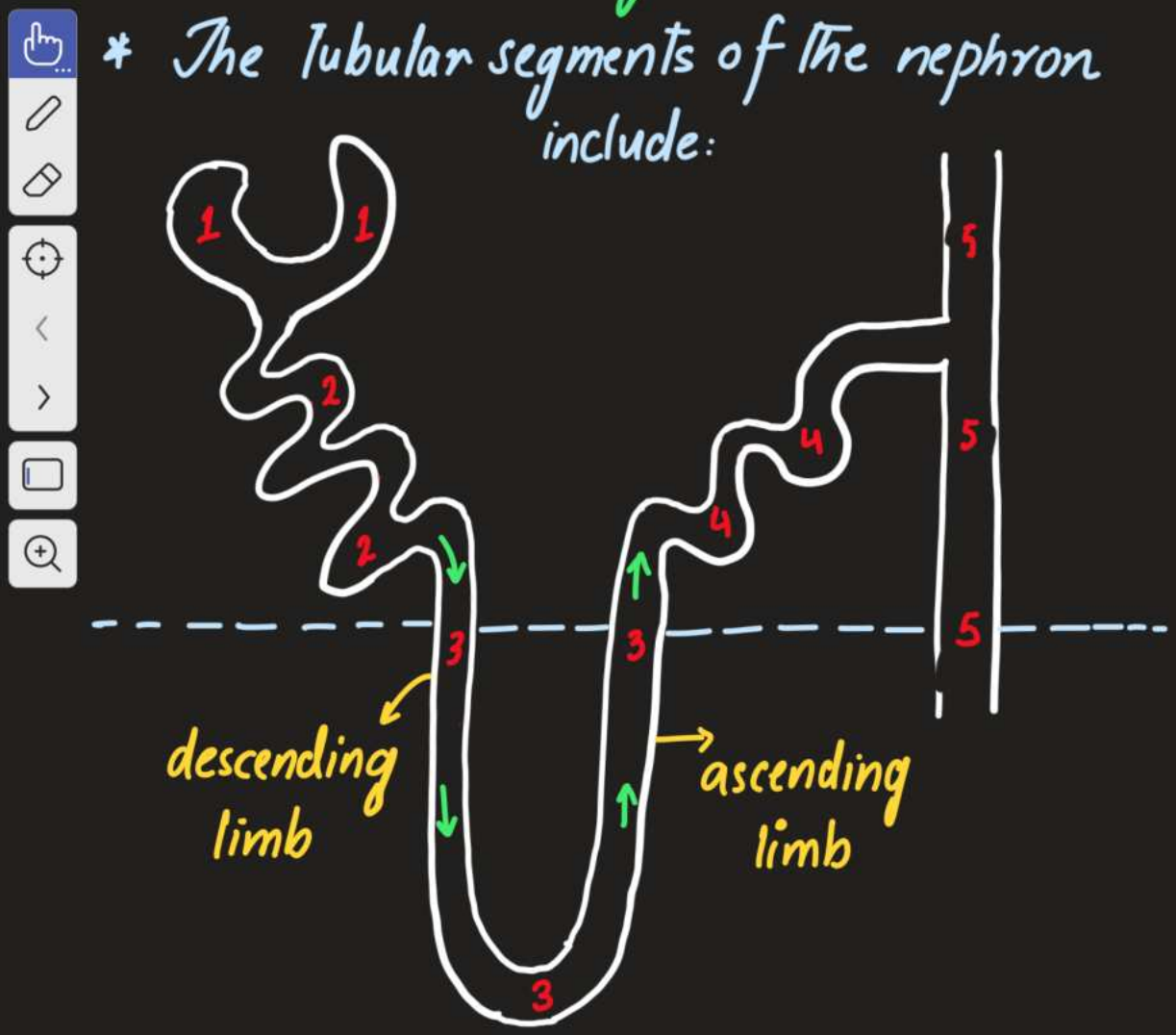
Nephron → Structural Details

* The structure of the nephron contains:
  - (a) tubular segments
  - (b) vascular segments

* The tubular segments of the nephron include:



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1 → Bowman's capsule (renal capsule)
2 → Proximal convoluted tubule (PCT)
3 → Loop of Henle (LoH)
4 → Distal convoluted tubule (DCT)
5 → Collecting duct (CD)

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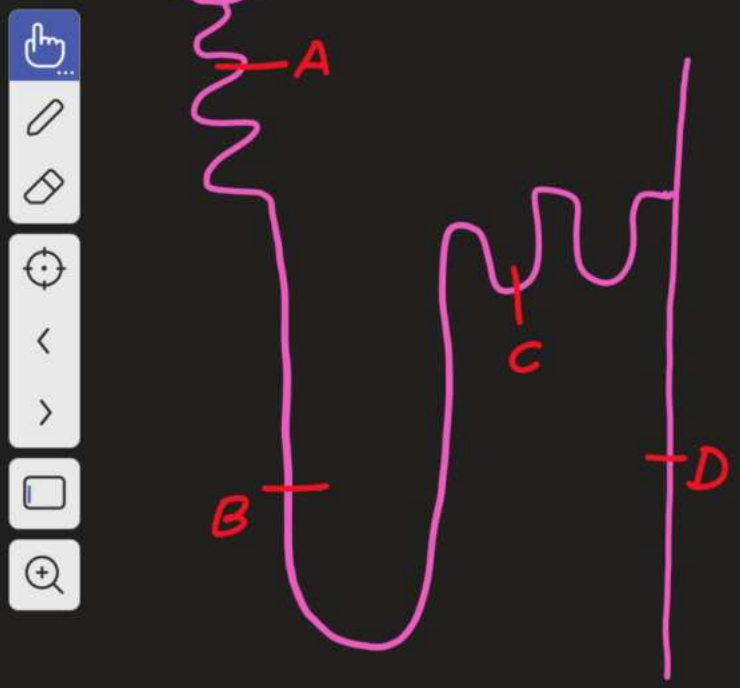
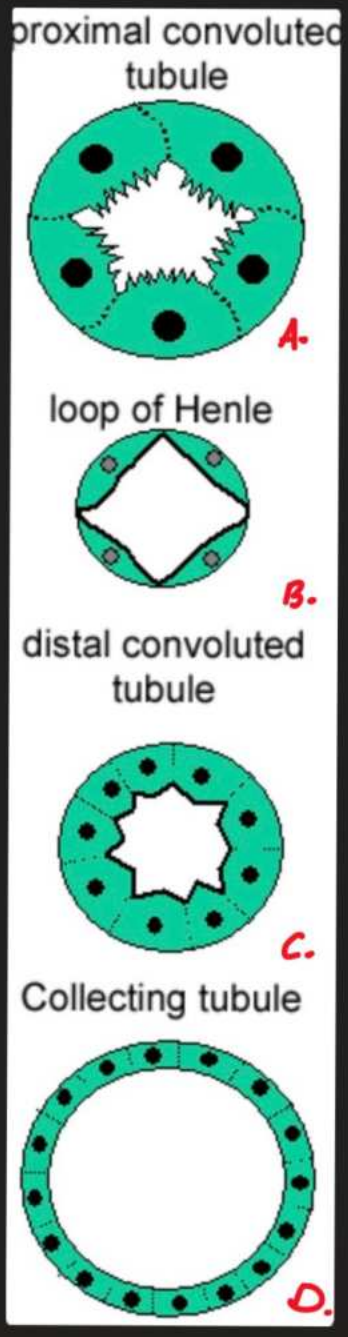

A
B
C
D


proximal convoluted tubule
A.
loop of Henle
B.
distal convoluted tubule
C.
Collecting tubule
D.

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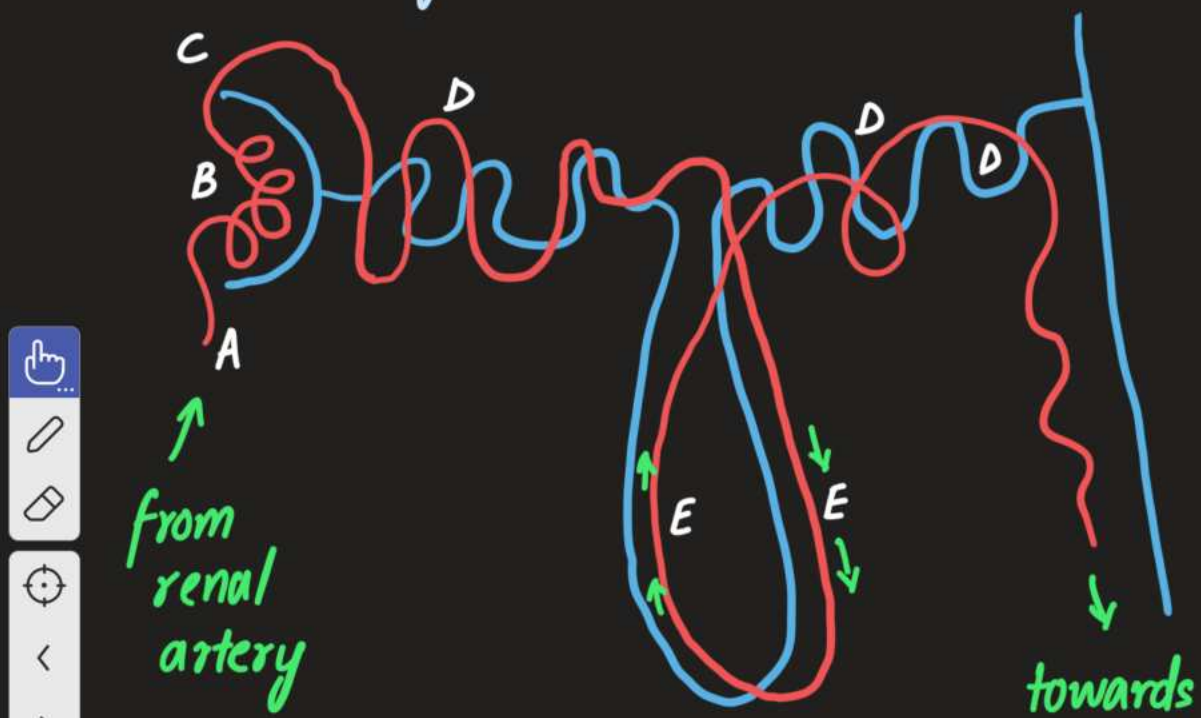
* Vascular segments of a nephron include:



(A) Afferent arteriole
(B) Glomerulus
(C) Efferent arteriole
(D) Peritubular capillary network
(E) Vasa recta

NOTE: glomerulus + Bowman's capsule ⇒ Malpighian body

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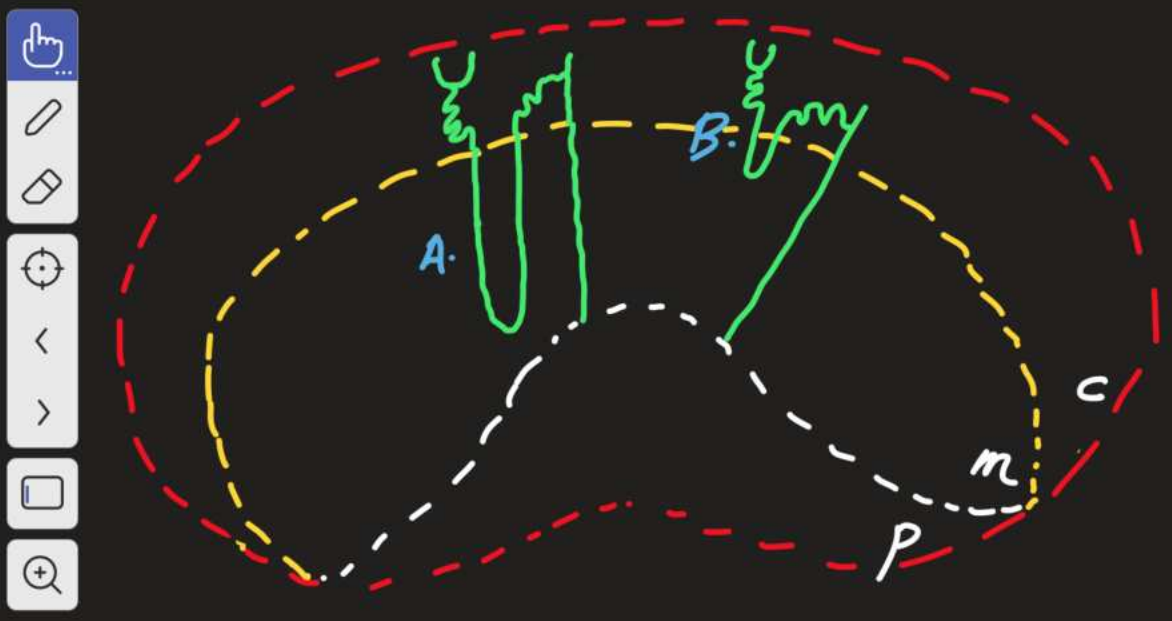
Organisation of a nephron within the kidney



A. Juxtamedullary nephron
B. Cortical nephron

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Q: Describe the structure of the kidney including the associated blood vessels ? [8 marks]

Ans: The kidney is externally covered with a tough fibrous capsule.Each kidney is supplied by a renal artery which is a direct branch of the aorta. Each kidney is drained by a renal vein which enters into the inferior vena cava. A longitudinal section of a kidney reveals an outer cortex, a central medulla and the innermost pelvis. The pelvis narrows to give rise to a ureter. Each kidney is made up of numerous nephrons. A nephron is a functional unit of the kidney. The parts of the nephron within the cortex include the Bowman's capsule, the PCT , the DCT and part of the collecting duct. The parts of the nephron in the medulla include the Loop of Henle and the remaining part of the collecting duct. Each nephron is supplied by an afferent arteriole which gives rise to a capillary network termed as the glomerulus. Blood leaves the glomerulus via the efferent arteriole which gives rise to another capillary network known as the peritubular capillary network.

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Functions of a kidney

- The roles of a kidney can be summarised into the following:

1. Urine formation
2. Osmoregulation
3. Maintenance of blood pH
4. Regulation of blood pressure
5. Regulation of bodily salts.

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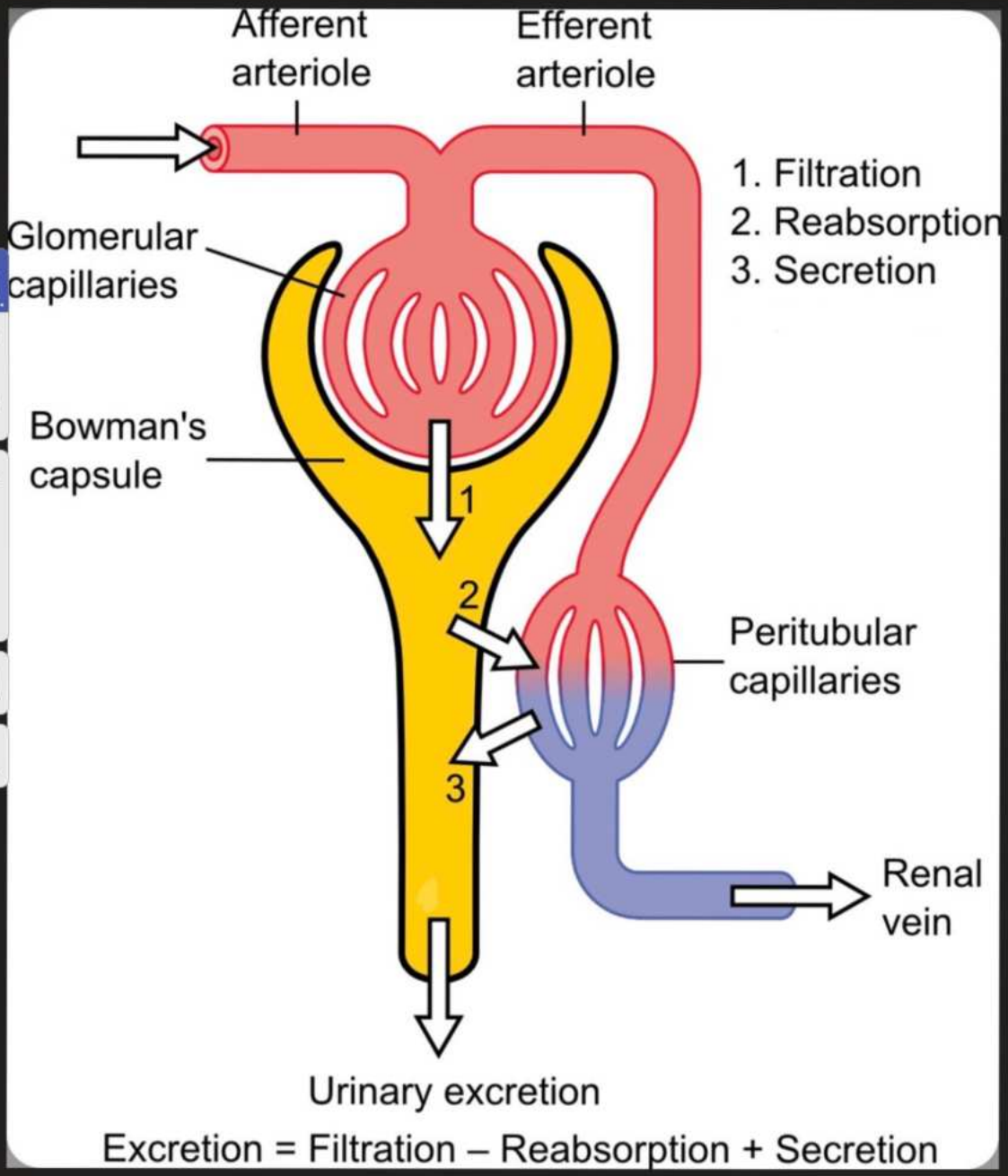
Urine Formation



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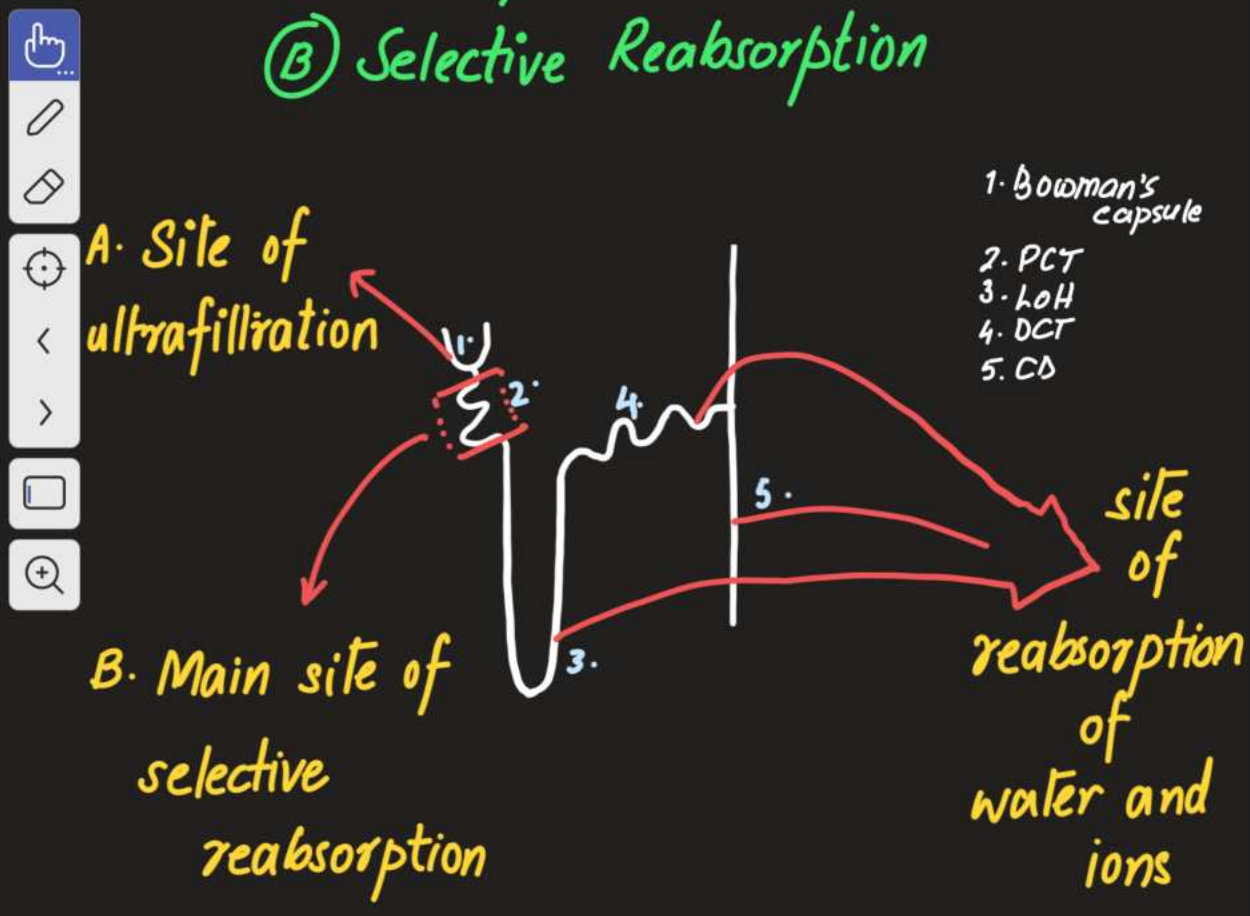
URINE FORMATION

* Urine formation involves two main stages:

(A) Ultra filtration

(B) Selective Reabsorption



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* Ultrafiltration is a passive process.
* Selective reabsorption is an active process.
* Before we move on to the details of ultrafiltration, let's understand the structure of the filtration barrier.

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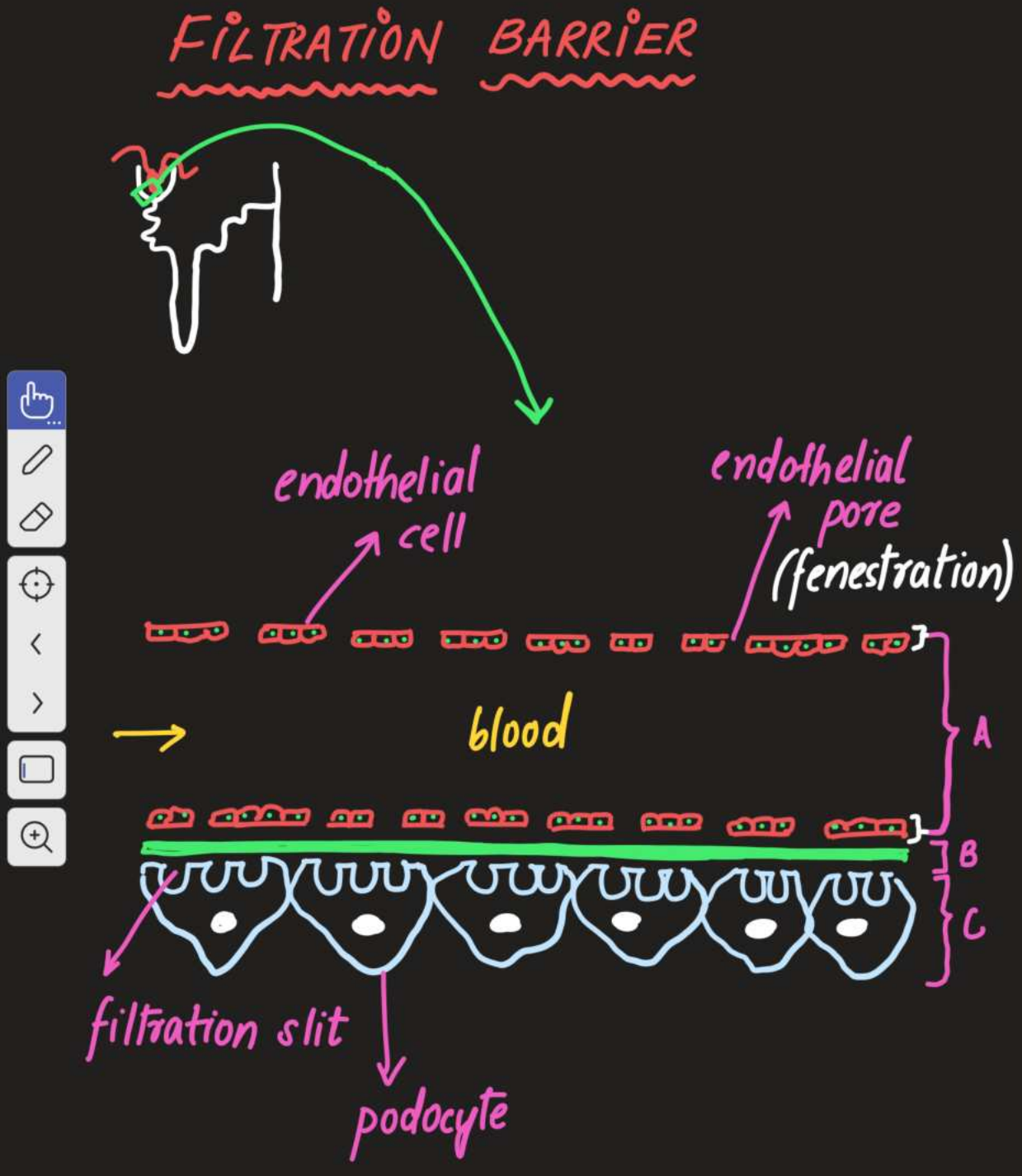
FILTRATION BARRIER
endothelial cell
endothelial pore (fenestration)
blood
A
B
C
filtration slit
podocyte

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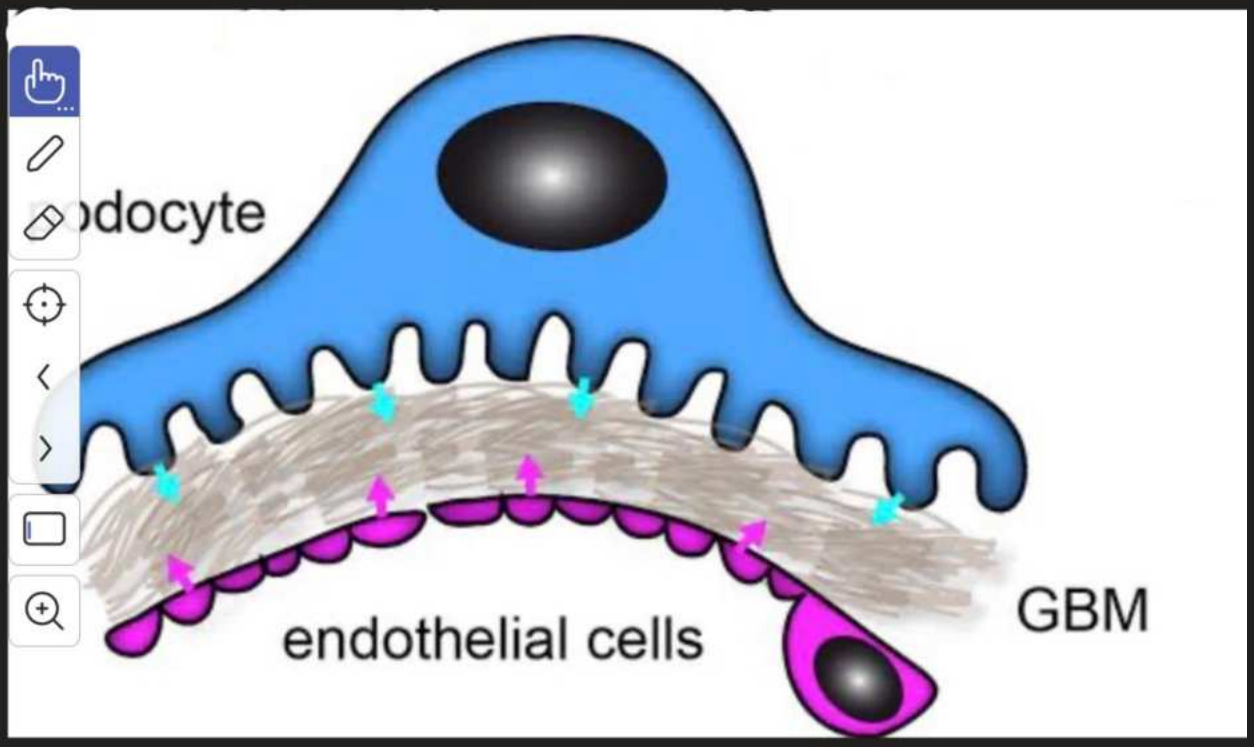

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* Filtration barrier = A + B + C
  - A = endothelium of the glomerulus
  - B = basement membrane
  - C = epithelium of the Bowman's capsule (made up of specialised epithelial cells known as podocytes)

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* Blood has to pass through all three of these layers before it gets filtered into the Bowman's capsule of the nephron.

* The endothelium of the glomerulus (capillary) has endothelial pores about 10 nm wide.

* The epithelium of the Bowman's capsule is made up of cells with "foot-like" processes => thus termed as podocytes.

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* The filtration slits within the epithelium are 25nm wide.

* Basement membrane is the MOST IMPORTANT layer in the filtration barrier. It is made up of connective tissue containing collagen besides other components.

* Basement membrane is important for two reasons:

① Extremely small pore size
② it's negatively charged

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* During ultrafiltration through a NORMAL filtration barrier, the following never pass through the filtration barrier:

① Red Blood Cells

② Large plasma proteins (having a MW > 68000 Da)

* MW = Molecular weight
* Da = daltons.

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ULTRAFILTRATION

* Ultrafiltration is a passive pressure dependent process involving filtration of small molecules (both useful and waste) through the filtration barrier.

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* Examples of useful substances filtered include:
1- glucose
2- amino acids
3- water
4- mineral ions
5- small proteins (< 68kDa)

* Examples of waste substances include:
1- Urea
2- Creatinine
3- Excess water
4- Excess ions

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Factors determining ultrafiltration pressure

- ✓ Hydrostatic pressure (HP)
  - → HP_G
  - → HP_{BC}
- ✓ Diameter of the afferent & the efferent arteriole
- ✓ Renal blood flow
- ✓ Colloidal osmotic pressure

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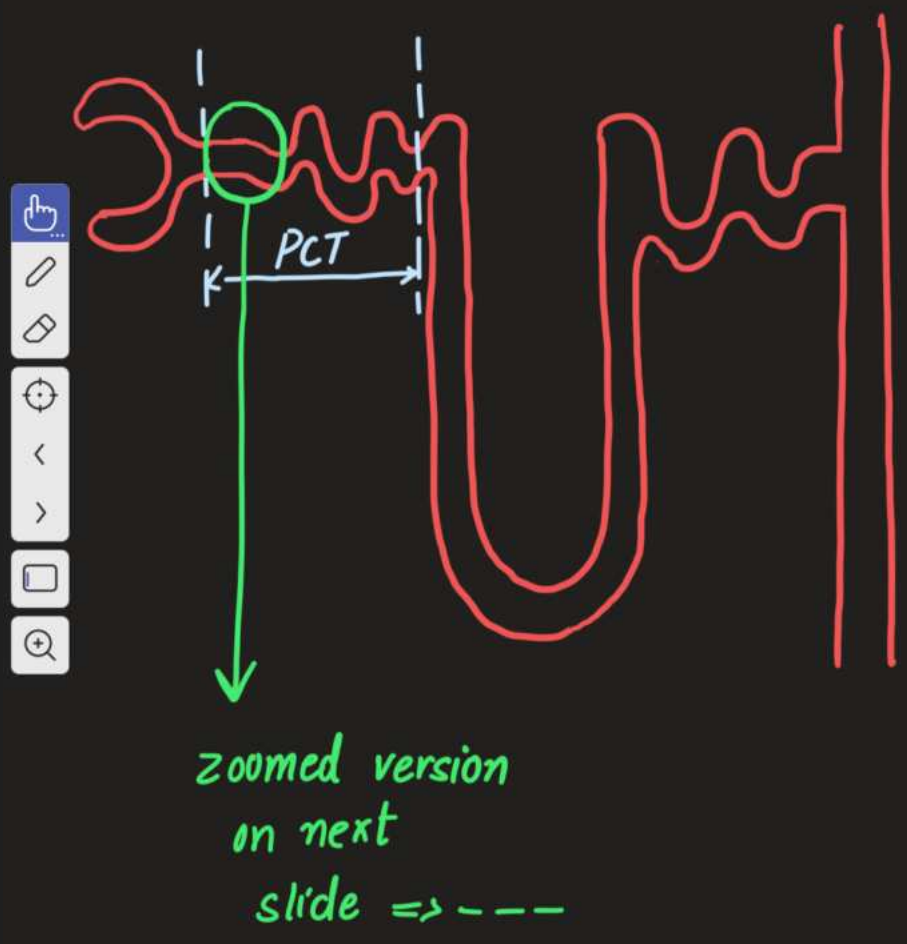
Homeostasis



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UNIT 14: Homeostasis

Learning Objectives:

- Urine formation-2
- Proximal Convoluted Tubule- structural & functional adaptations

Video Lecture 3 Slides

Mohammad Hussham Arshad, MD
Biology Department

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Previously,

* Excretion and egestion
* Excretory waste products
* Nitrogenous waste
* Deamination and urea cycle
* Urinary system + structure of the kidneys
* Nephron → structure
* Urine formation → ultrafiltration
  → selective reabsorption

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Factors determining ultrafiltration pressure

1. Hydrostatic pressure → glomerulus
   → BC
2. Diameter of the afferent & the efferent arteriole

3. Renal blood flow
4. Colloidal osmotic pressure

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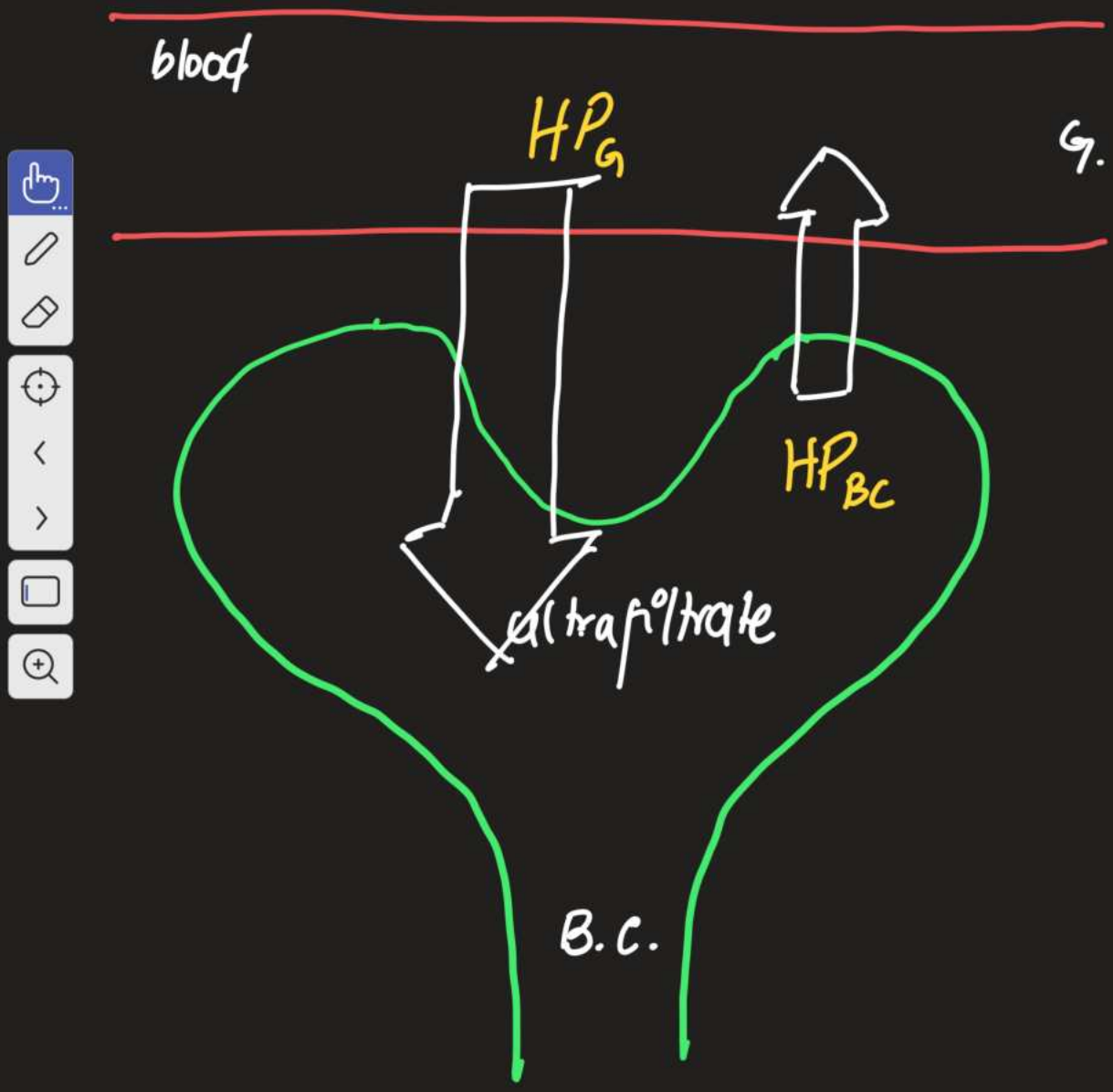
Yncterstanding hydrostatic pressure.....



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* The following factors influence the net ultrafiltration pressure:

A. Hydrostatic pressure (HP):

* HP of the glomerulus (HP_G) favours ultrafiltration.
* HP of the Bowman's capsule (HP_{BC}) opposes ultrafiltration.
* HP is the pressure due to water within the glomerulus / Bowman's capsule

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B. Diameter of the arterioles

* The diameter of the afferent arteriole is wider than the efferent arteriole.

* The narrower diameter of the efferent arteriole helps build up hydrostatic pressure within the glomerulus.

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C · Renal blood flow

* The greater the renal blood flow, the greater is the blood flow in the glomerulus.

=> and the greater is the hydrostatic pressure within the glomerulus.

* Greater renal blood flow thereafter increases the net ultrafiltration pressure.

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Winters and renal blood flow....

* In winters, vasoconstriction of arterioles supplying blood to skin capillaries SHUNTS the blood towards major organs such as kidney, thereafter increasing renal blood flow. This increases the rate of formation of urine in cold → a phenomenon termed **cold diuresis**

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D. Colloidal osmotic pressure (oncotic pressure - OP):

* Oncotic pressure is "the osmotic pull of water due to large plasma proteins.
* Oncotic pressure of the glomerulus (OP_G) opposes ultrafiltration.
* Oncotic pressure of the Bowman's capsule (OP_{BC}) favours ultrafiltration.
* OP_{BC} in a normal kidney is usually zero. WHY?

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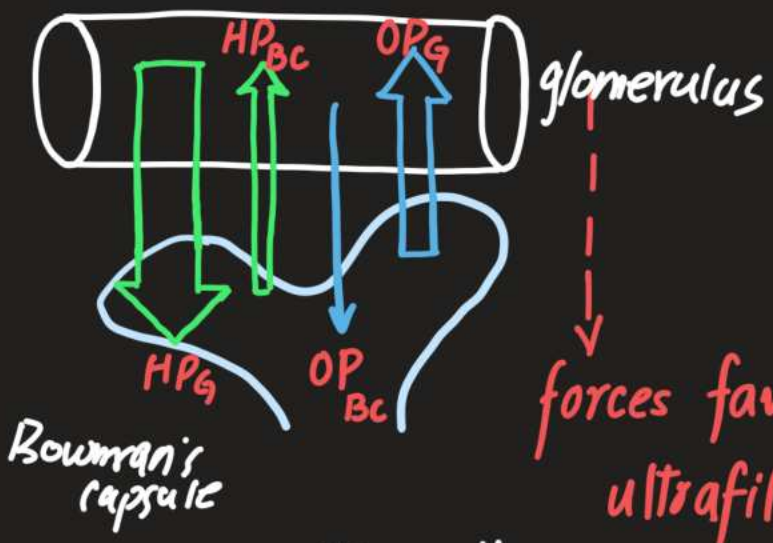
Sample scenario for calculation of net ultrafiltration pressure.



$HP_G = 70 mm Hg$

$HP_{BC} = 20 mm Hg$ (-)

$OP_G = 30 mm Hg$ (-)

$OP_{BC} = 0 mm Hg$

$$NUP = (HP_G + OP_{BC}) - (HP_{BC} + OP_G)$$

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Net ultrafiltration pressure =

$$(HP_G + OP_{BC}) - (HP_{BC} + OP_G)$$

$$(70 + 0) - (20 + 30)$$

$$\Rightarrow 20 \text{ mm Hg}$$

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Selective Reabsorption

* Selective reabsorption is an active process involving reabsorption of useful substances (e.g. glucose) filtered from the glomerulus into the Bowman's capsule.

* Examples of useful substances that are selectively reabsorbed include:

a) glucose
b) amino acids
c) small proteins (< 68 kDa)
d) water (variable)
e) Na^+ and other useful ions (variable)

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*The main site of selective reabsorption is the proximal convoluted tubule (PCT).

* PCT reabsorbs:

1. 100% glucose
2. 100% amino acids
3. 100% small proteins
4. 60-70% Na^+ and water

} The fluid leaving the PCT therefore has NO glucose, amino acids or small proteins.

Before we understand how these substances are reabsorbed, let's understand the structural features of the PCT, which make it suitable for selective reabsorption.

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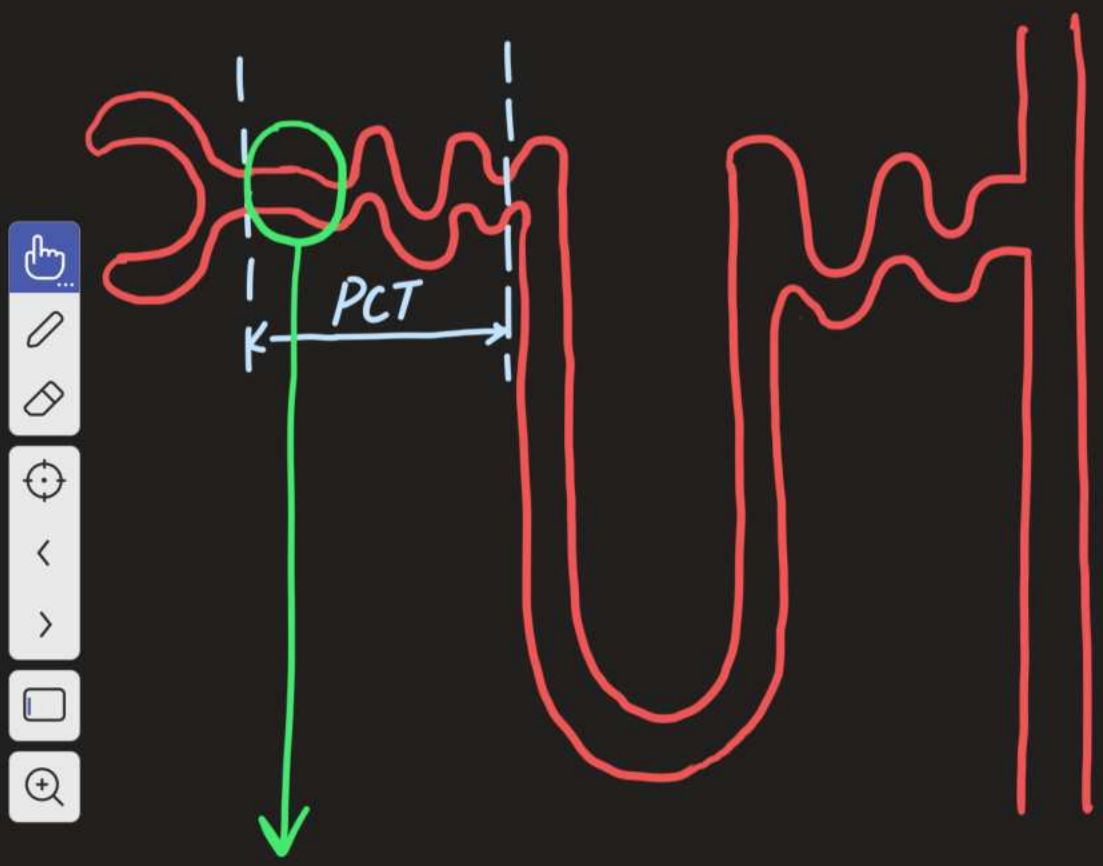

zoomed version
on next
slide =>

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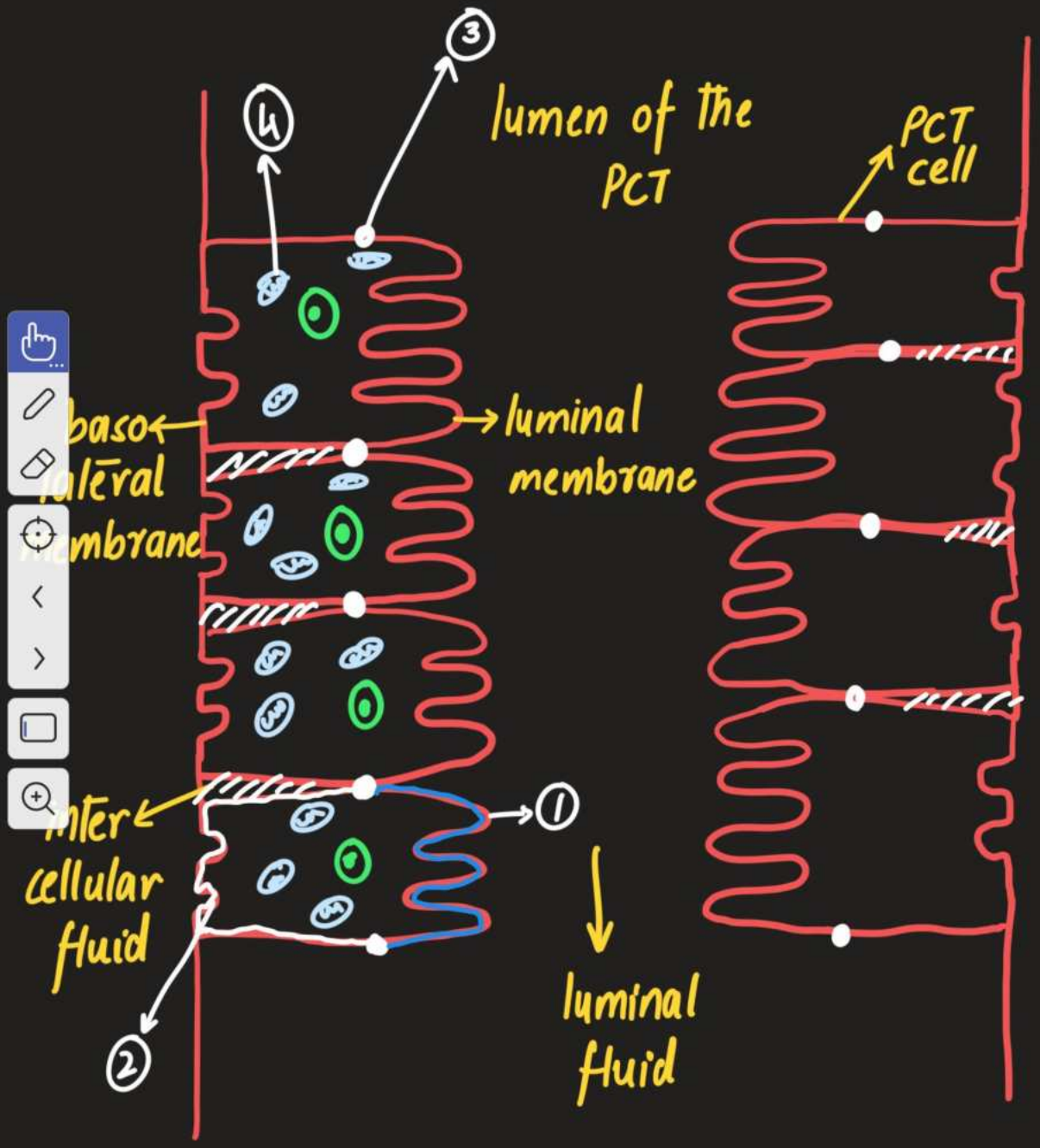
3
4
lumen of the PCT
PCT cell
baso lateral membrane
luminal membrane
inter cellular fluid
1
2
luminal fluid

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+ Main features of PCT cells;

① Microvilli on the luminal membrane (which form a brush border when observed under microscopy)

② Infoldings / invaginations on the baso-lateral membrane.

③ Tight junctions between adjacent cells.

④ Numerous mitochondria within PCT cells.

⑤ The luminal and basal membrane has numerous transport proteins.

⑥ PCT is surrounded by peritubular capillary network.

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Q: How do these structural features assist in selective reabsorption?

① Microvilli increase the surface area available for transport proteins required for selective reabsorption.

② Invaginations increase the surface area available for transport proteins required for selective reabsorption.

③ Tight junctions serve two functions:

a) prevent the luminal fluid from mixing with intercellular fluid.

b) prevent the migration of luminal or basolateral Transport proteins.

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④ Mitochondria provide ATP via aerobic respiration. Selective reabsorption is an active process.

⑤ Transport proteins (e.g → Na^+–K^+ pump, channel proteins, etc) enable reabsorption of different solutes such as glucose, amino acids, etc.

⑥ Capillary network carries away the substances reabsorbed to the main circulation.

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Past paper questions

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Question 1:

(a) The mammalian kidney is an organ involved in homeostasis.

Explain what is meant by the term *homeostasis*.

maintenance of a constant internal environment

..... [1]

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Question 2 :

(b) Fig. 1.1 shows a section through a kidney.

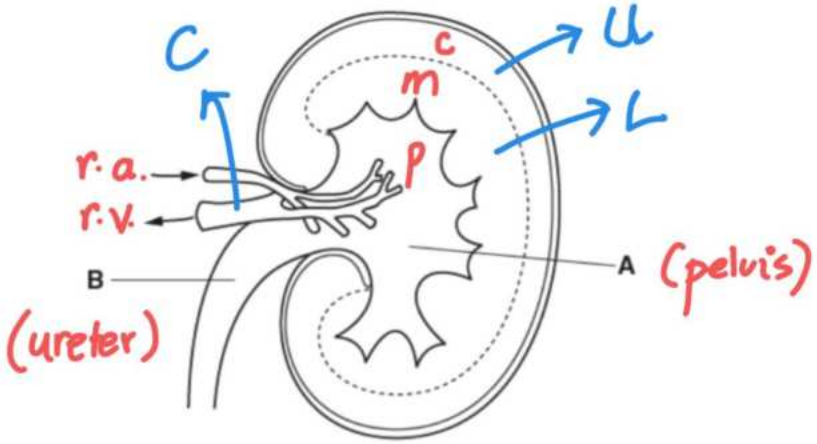

Fig. 1.1

(i) With reference to Fig. 1.1, name structures **A** and **B**.

A ..... pelvis .....

B ..... ureter ..... [2]

(ii) On Fig. 1.1, use label lines and letters to label where:

U – ultrafiltration occurs ✓

L – the loop of Henle is found ✓

C – blood urea concentration is low. ✓

[3]

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Question 3:

(a) Fig. 5.1 is a photomicrograph of part of the cortex of a kidney.

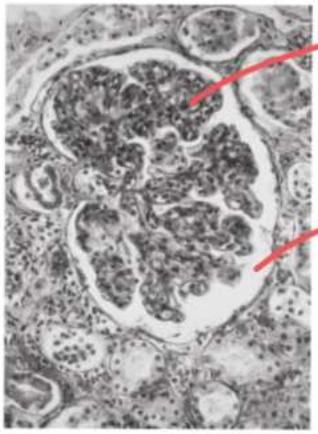

Fig. 5.1

(i) On Fig. 5.1, use label lines and letters to label:

G – the glomerulus

L – the lumen of the Bowman's (renal) capsule.

[2]

(ii) During ultrafiltration, components of blood in the glomerulus with a relative molecular mass greater than 68 000 are prevented from passing into the Bowman's capsule.

Name the structure that acts as this filtration barrier.

basement membrane ..... [1]

(b) The glomerular filtration rate (GFR) is the rate of flow of filtered fluid through the kidneys per unit time.

The afferent arterioles supply blood to the glomerulus of each nephron within the kidney and the efferent arterioles take blood away from each glomerulus. The lumen diameters of the afferent and efferent arterioles have a large effect on the GFR. Normally the lumen diameters of the afferent and efferent arterioles are different, but they can change to increase or decrease the normal GFR in response to changing conditions.

Complete Table 5.1 to indicate whether the GFR is normal, increased, or decreased for each combination of arteriole diameters shown.

The first row has been completed for you.

Table 5.1

afferent arteriole lumen diameter	efferent arteriole lumen diameter	GFR
normal	normal	normal
decreased	normal	decreased
normal	increased	decreased

[2]

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Question 4:

(a) In mammals, excess amino acids cannot be stored in the body.

Outline the formation of urea from excess amino acids by liver cells.

* deamination of excess amino acids produces NH_3
* NH_3 combines with CO_2 in the urea cycle
* to form urea

— reactions —

[3]

(b) The mammalian kidney is composed of many nephrons.

Describe the process of ultrafiltration in the nephron.

[4]

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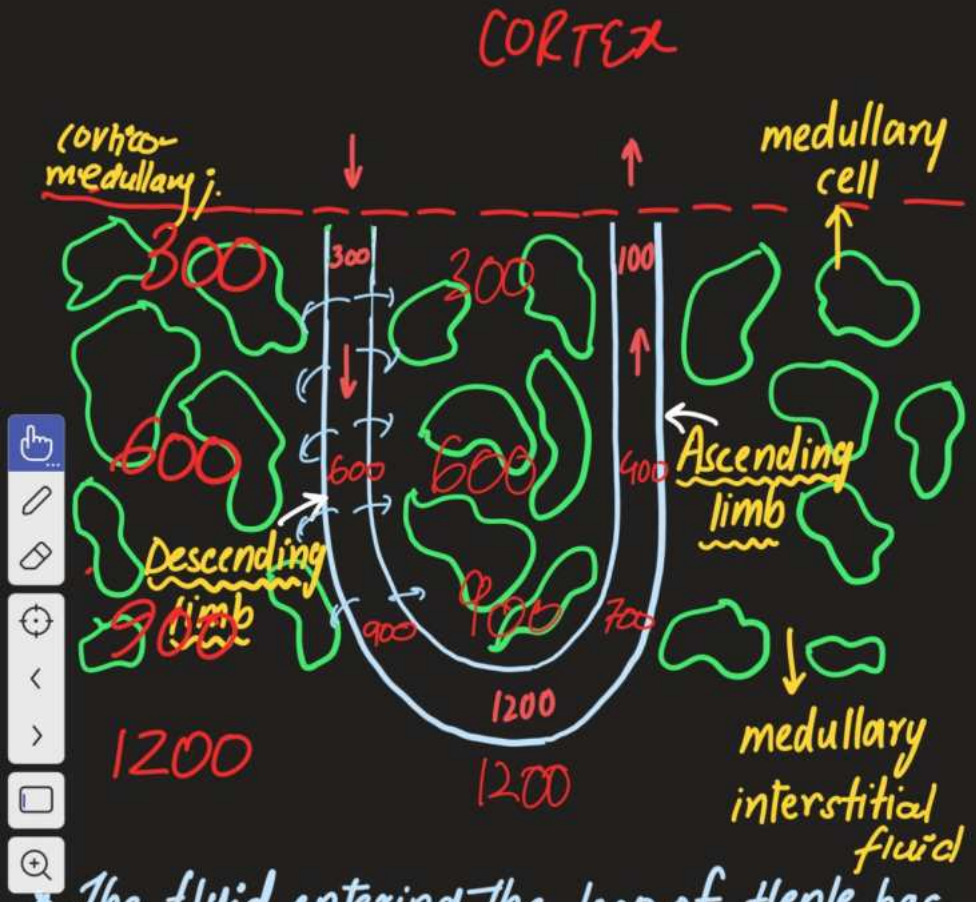
Homeostasis



* The fluid entering the loop of Henle has an osmolarity of 300 mOsm/L. The fluid leaving the loop of Henle has an osmolarity of 100 mOsm/L.

With
Mohammad Hussham Arshad, MD

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ADVANCED LEVEL BIOLOGY 9700
UNIT 14: Homeostasis

Learning Objectives:

- Selective Reabsorption 2
- Loop of Henle 1

Video Lecture 4 Slides

Mohammad Hussham Arshad, MD
Biology Department

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Previously,

* Excretion and egestion
* Excretory waste products
* Nitrogenous waste
* Deamination and urea cycle
* Urinary system + structure of the kidneys
* Nephron → structure
* Urine formation → ultrafiltration
  → selective reabsorption

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Question 5:

(b) Table 1.1 shows the quantities, per day, of some of the substances that are:

- removed from the blood by ultrafiltration
- reabsorbed into the blood by the pct
- excreted in the urine.

Table 1.1

substance	quantity removed by ultrafiltration and units		percentage reabsorbed into blood from pct	quantity excreted in urine and units	
urea	56.0	g	46.4	30.0	g
water	180.0	dm^3	99.2	1.4	dm^3
sodium ions	25200.0	arbitrary units	99.4	151·2	arbitrary units
glucose	800.0	nmol	100.0	0.0	nmol

Complete Table 1.1 by calculating the quantity of sodium ions excreted in the urine.

Write your answer in the table to one decimal place.

Show your working in the space below.

$$\frac{25200 \times 99.4}{100} = 25048.8$$

[2]

$$25200 - 25048.8 = 151.2$$

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Question 6 :

(b) (i) The urine of people on different types of diet was analysed.

- people on a low protein diet had a mean urea concentration of 2.40 g dm^{-3}
- people on a high protein diet had a mean urea concentration of 14.76 g dm^{-3}.

Calculate the percentage increase in the concentration of urea between the low and high protein diets.

Show your working.

$$\frac{14.76 - 2.40}{2.40} \times 100\% = 515\ \%$$

answer 515 % [2]

(ii) Explain why an increase in the quantity of protein in the diet leads to an increase in the concentration of urea in the urine.

* excess amino acids produced after hydrolysis of the protein
* excess amino acids cannot be stored
* deamination of excess amino acid to form NH_3 → converted to urea for excretion in urine [2]

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Question 7:

1 **(a)** Fig. 1.1 represents part of the wall of a proximal convoluted tubule (pct) in a kidney nephron.

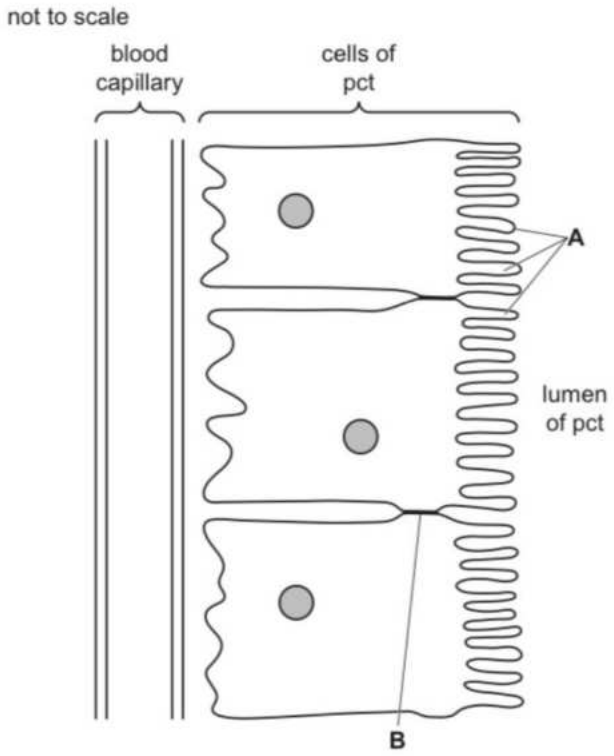

Fig. 1.1

(i) Name the features of the wall of a pct that are labelled **A** and **B** in Fig. 1.1.

A microvilli

B tight junction

[2]

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Selective reabsorption of....

1) Glucose
2) Amino acids
3) small proteins
4) water and ions

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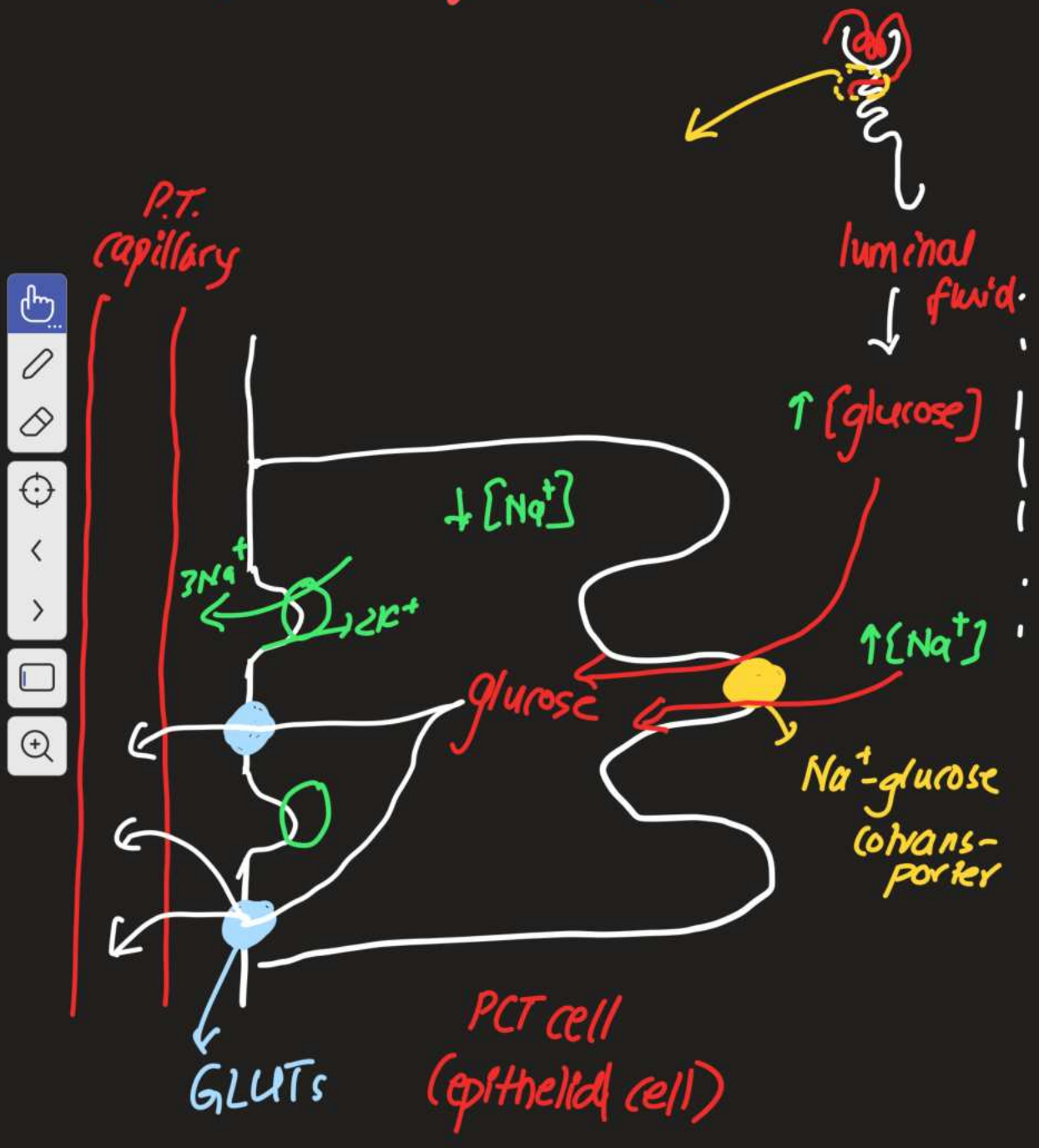
Reabsorption of glucose by the PCT cells



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Reabsorption of glucose by the PCT cells

* All the glucose is selectively reabsorbed by the PCT cells.
* The following is an outline of how glucose is reabsorbed;

① Na^+–K^+ pumps on the basolateral membrane actively transports 3Na^+ out and 2K^+ into the PCT cells lowering intracellular [Na^+].

② This creates a concentration gradient to allow Na^+ to move from the luminal fluid to the PCT cells.

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③ Na^+ are cotransported into PCT cells along with glucose via Na^+- glucose cotransporters.

④ This mechanism of glucose reabsorption into the PCT cells is known as secondary active transport.

⑤ Glucose thereafter ~~diffusion~~ moves via facilitated diffusion from the PCT cells into the neighbouring peri-tubular capillaries via GLUTs (glucose transporters).

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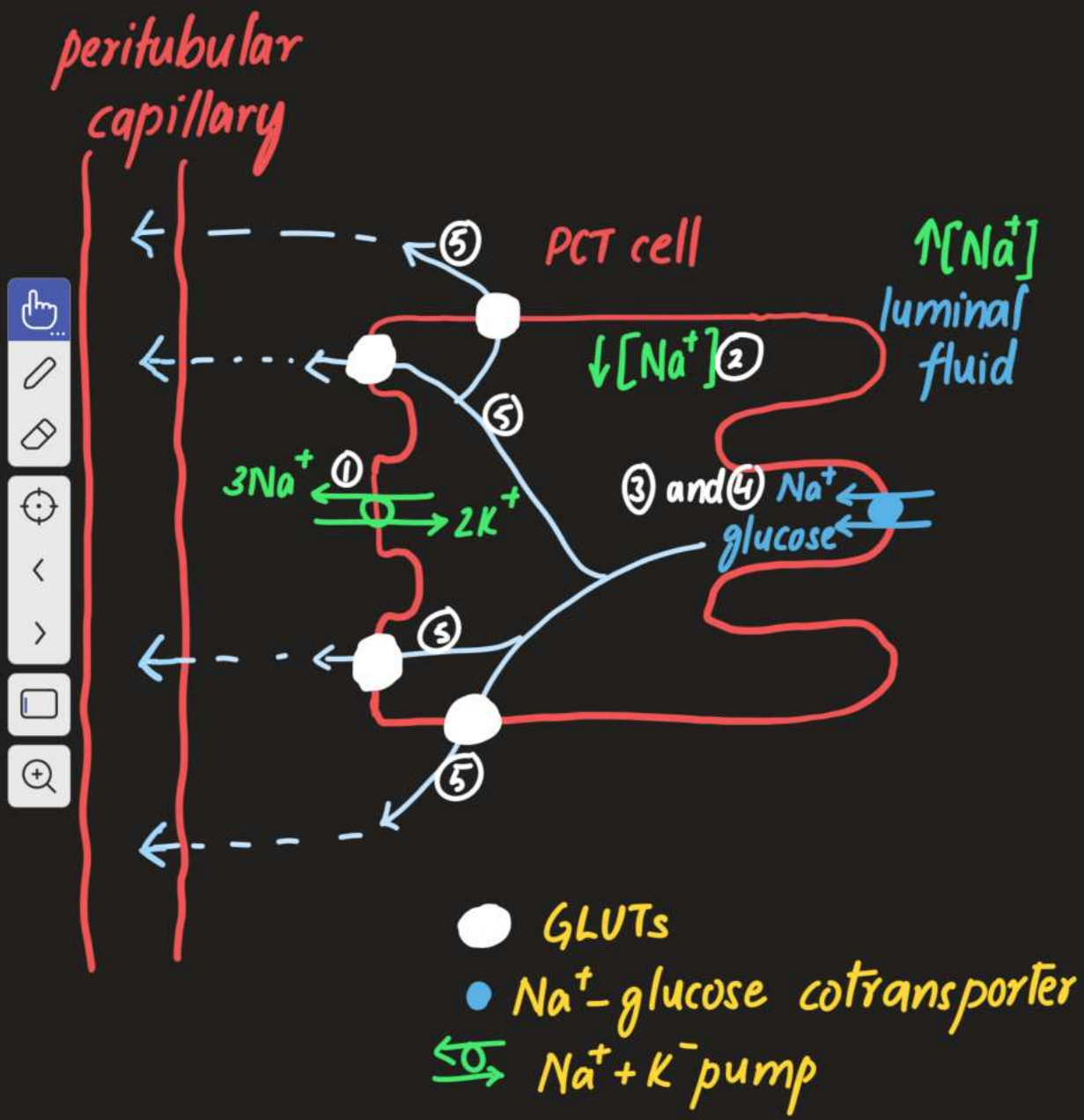
peritubular capillary
PCT cell
↑[Na+] luminal fluid
↓[Na+] ②
3Na+ ①
2K+
③ and ④ Na+ glucose
⑤
GLUTs
Na+-glucose cotransporter
Na+ + K- pump

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Reabsorption of amino acids

* Amino acids are reabsorbed into PCT via secondary active transport like glucose.
* Amino acids thereafter move via facilitated diffusion from PCT into the neighbouring peritubular capillaries through carrier proteins.

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Reabsorption of water

* Entry of Na^+ into PCT cells lowers the water potential.
* Water thereafter moves from a region of higher water potential in the luminal fluid to the region of lower water potential within the PCT cell via osmosis.

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Reabsorption of small proteins

* Small proteins (<68KDa) may get filtered through the filtration barrier.
* These proteins are reabsorbed into PCT cells via pinocytosis.
* They may be hydrolysed into amino acids which can move via facilitated diffusion through carrier proteins into neighbouring peritubular capillaries.

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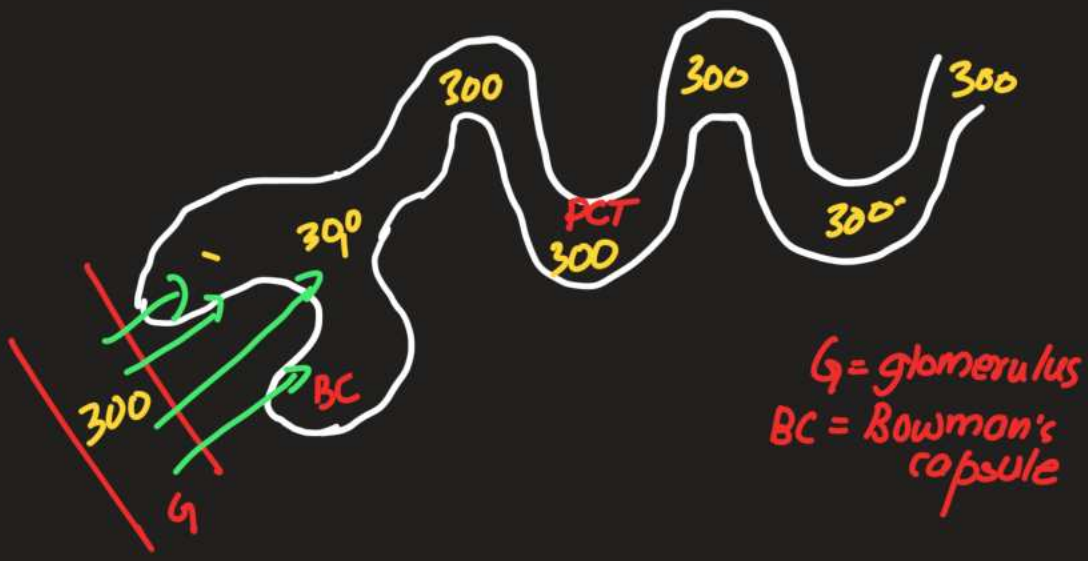
Osmolarity of the blood plasma and the tubular fluid

* The term osmolarity means concentration.
* Osmolarity of bodily fluids is primarily determined by Na^+
* Osmolarity is measured in mOsm/L.
* Osmolarity of blood plasma is equal to 300 mOsm/L
* Figure below shows the variation in osmolarity of the tubular (luminal) fluid as it moves through the Bowman's capsule and the PCT:



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Loop of Henle and it's function

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LOOP OF HENLE – STRUCTURE

* Loop of Henle is a tubular structure present within the medulla.

* It extends from the end of PCT till the start of DCT.

* Nephrons are divided into Two categories based on the length of the Loop of Henle:

1) Cortical nephrons → with a shorter loop of Henle

2) Juxtamedullary nephrons → with a relatively longer loop of Henle running deep into the medulla.

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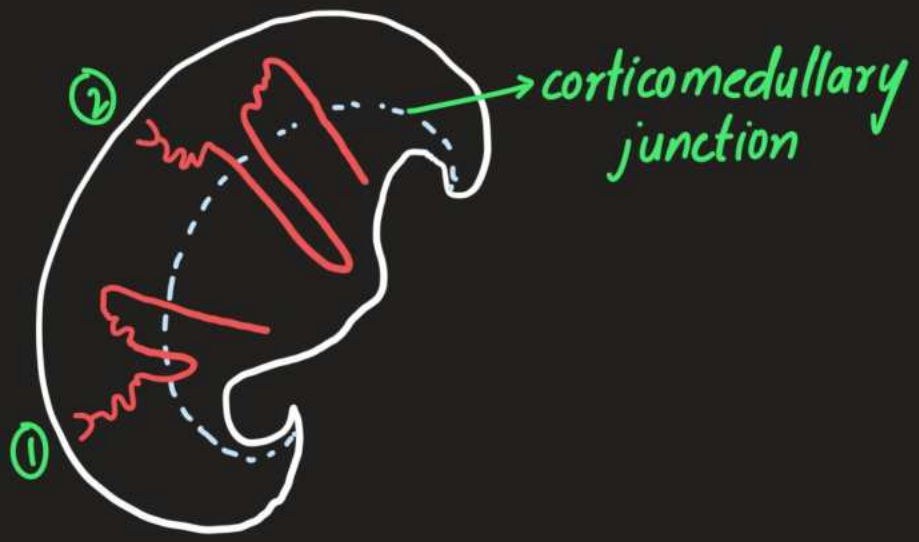

* The loop of Henle is made up of an ascending limb and a descending limb.

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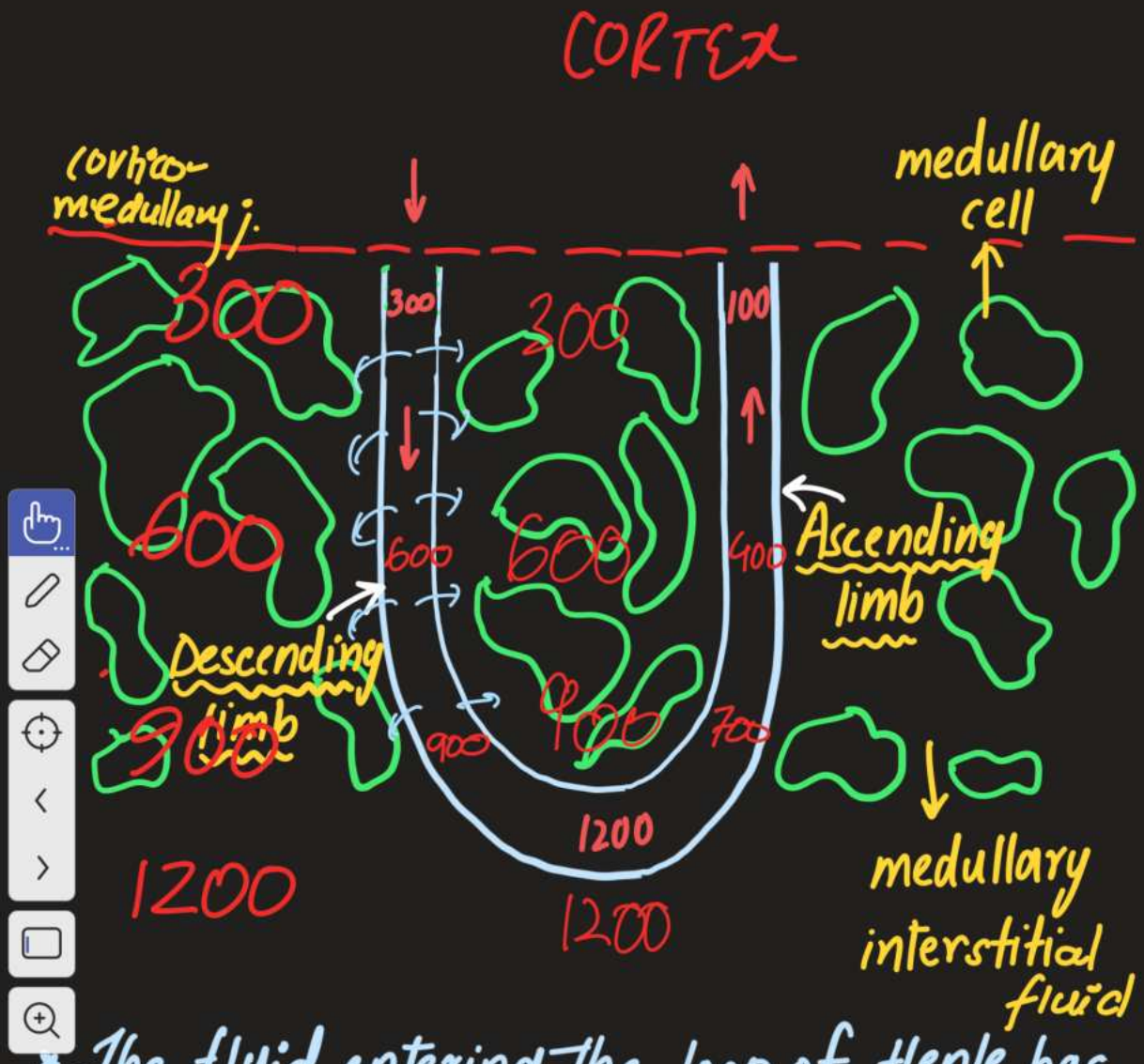

* The fluid entering the loop of Henle has an osmolarity of 300 mOsm/L. The fluid leaving the loop of Henle has an osmolarity of 100 mOsm/L.

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* The main features of the descending limb are:

① Permeable to water and impermeable to ions. The high permeability to water is due to the presence of aquaporins within the membranes of the cells lining the descending limb.

② Concentrates the luminal fluid as water is reabsorbed via facilitated diffusion.

③ No energy is required for reabsorption of water.

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* The main features of the ascending limb are:

① Impermeable to water but permeable to ions due to the presence of NKCC* pumps within the membranes of the cells lining the ascending limb.

* NKCC ⟶ Sodium-potassium-chloride pump

② Dilutes the luminal fluid due to reabsorption of sodium, potassium and chloride ions.

③ Energy is required for reabsorption of ions in the form of ATP.

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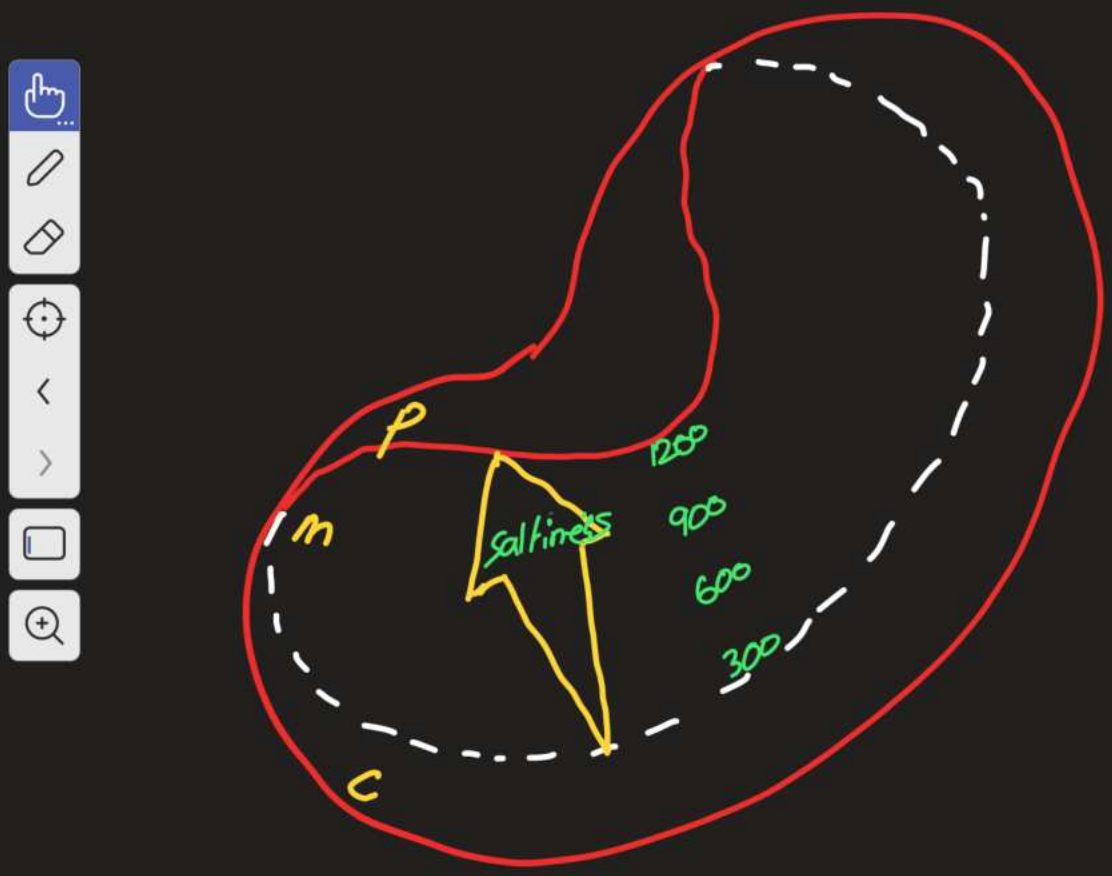
Medullary Concentration gradient

Q. What is medullary concentration gradient ?



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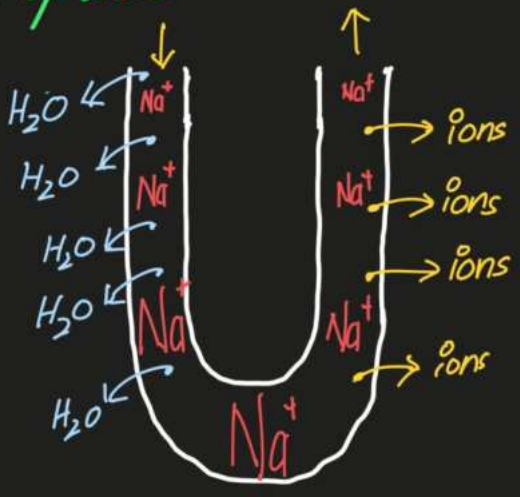
Homeostasis

Revisiting the features of the descending limb and the ascending limb

Descending	Ascending
* permeable to water	* impermeable to water
* impermeable to ions	* permeable to ions
* concentrates the luminal fluid	* dilutes the luminal fluid
* involves passive movement of water	* Involves active movement of ions



With
Mohammad Hussham Arshad, MD

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ADVANCED LEVEL BIOLOGY 9700

UNIT 14: Homeostasis

Learning Objectives:

- Loop of Henle 2
- Negative feedback and introduction to osmoregulation

Video Lecture 5 Slides

Mohammad Hussham Arshad, MD
Biology Department

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Previously,

* Excretion and egestion
* Excretory waste products
* Nitrogenous waste
* Deamination and urea cycle
* Urinary system + structure of the kidneys
* Nephron → structure
* Urine formation → ultrafiltration
  → selective reabsorption
* Loop of Henle → Structural and functional feature
* Medullary concentration gradient

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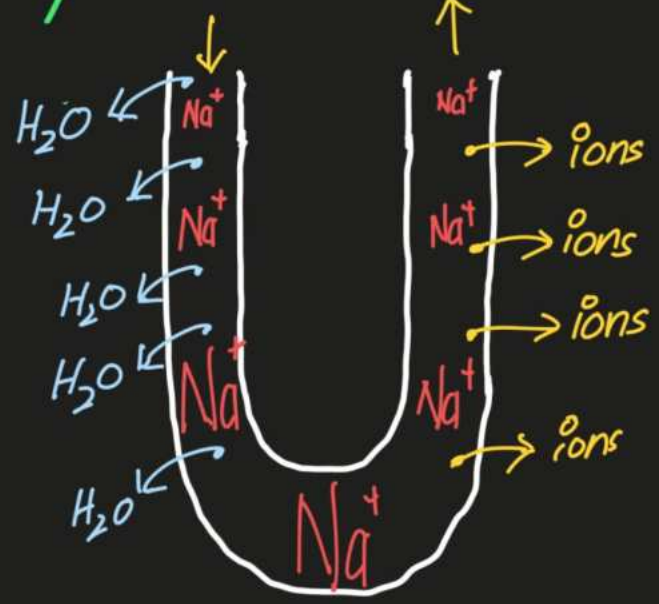
Revisiting the features of the descending limb and the ascending limb

Descending

* permeable to water
* impermeable to ions
* concentrates the luminal fluid
* involves passive movement of water

Ascending

* impermeable to water
* permeable to ions
* dilutes the luminal fluid
* involves active movement of ions



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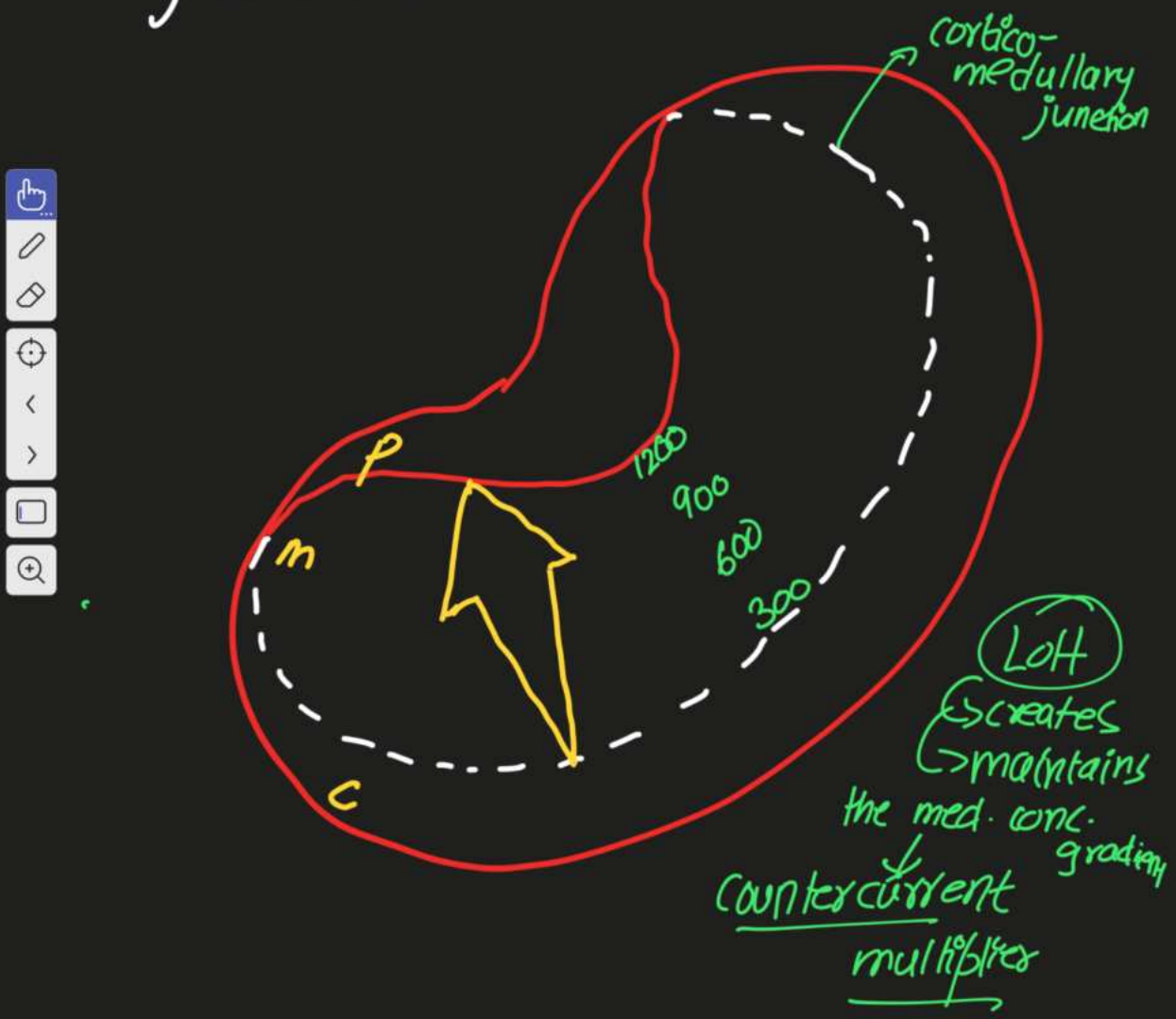
Medullary Concentration gradient

Q. What is medullary concentration gradient ?



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Medullary Concentration gradient

* The medullary interstitial fluid gets salty (concentrated) as we go from the cortico-medullary junction towards the pelvis.

* Medullary interstitial fluid is the tissue fluid surrounding the cells within the medulla.

* This medullary concentration gradient is created and maintained by the loop of Henle through the counter current multiplier mechanism.

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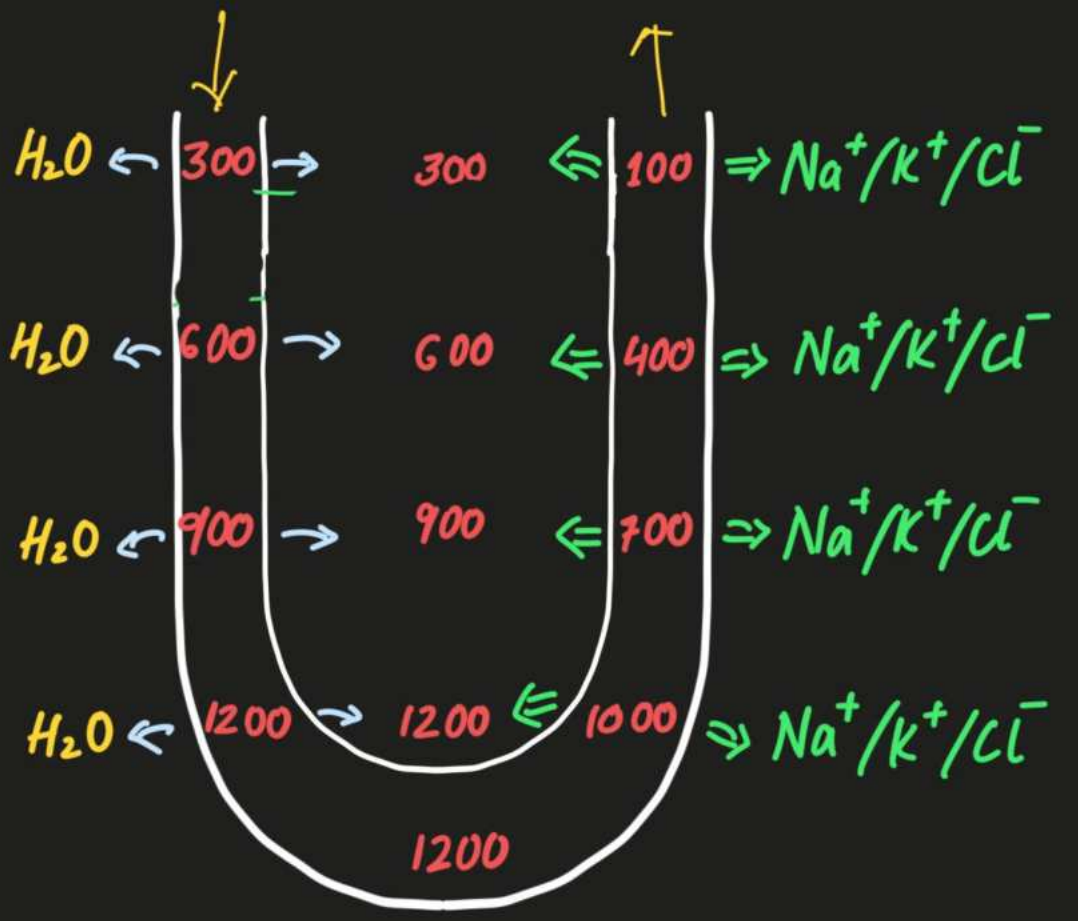
Counter-current multiplier



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Counter current multiplier

① The cells lining the descending limb of the loop of Henle have numerous aquaporins which enable water to move via facilitated diffusion into the interstitium.

② Water moves out of the luminal fluid such that the concentration of the luminal fluid is the same as the adjacent interstitial fluid.

③ Since the descending limb is impermeable to ions, the luminal fluid gets concentrated as it's moves down the descending limb.

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④ The luminal fluid reaches a concentration of 1200 mOsm/L at the tip of Loop of Henle.

⑤ The luminal fluid gets diluted as it moves up the ascending limb.

⑥ This is due to the active pumping of $Na^+/K^+/Cl^-$ from the luminal fluid into the interstitium through NKCC pumps.

⑦ These pumps have a capacity of maintaining a gradient of 200mOsm/L at each horizontal level.

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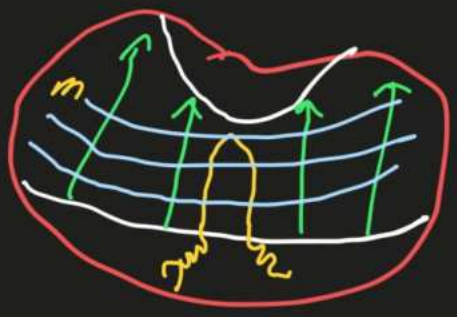
⑧ However, the counter-current flow of the fluid in the descending and the ascending limb multiplies the gradient vertically across the medulla.

⑨ This is termed as the counter-current multiplier mechanism.



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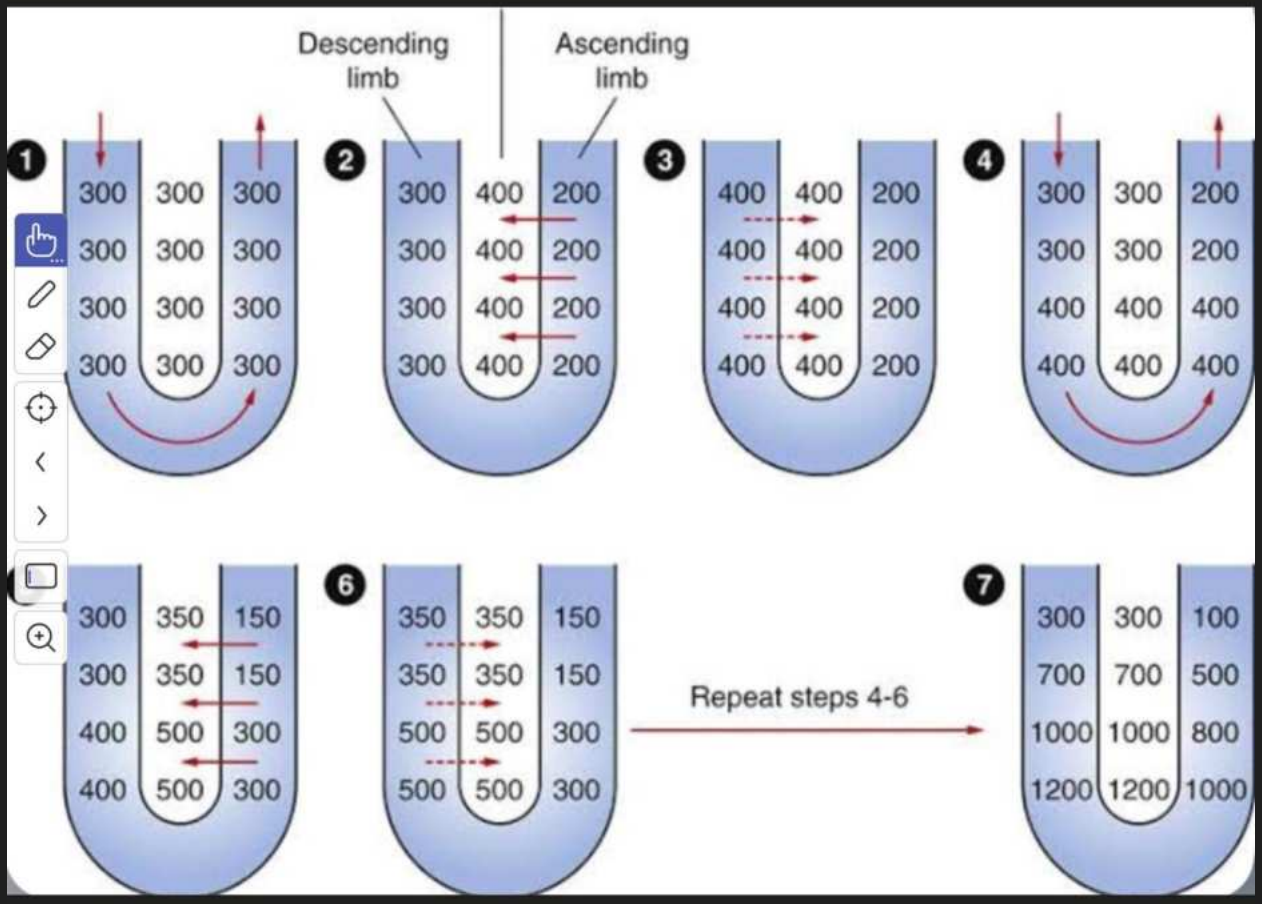
Creation of the medullary gradient



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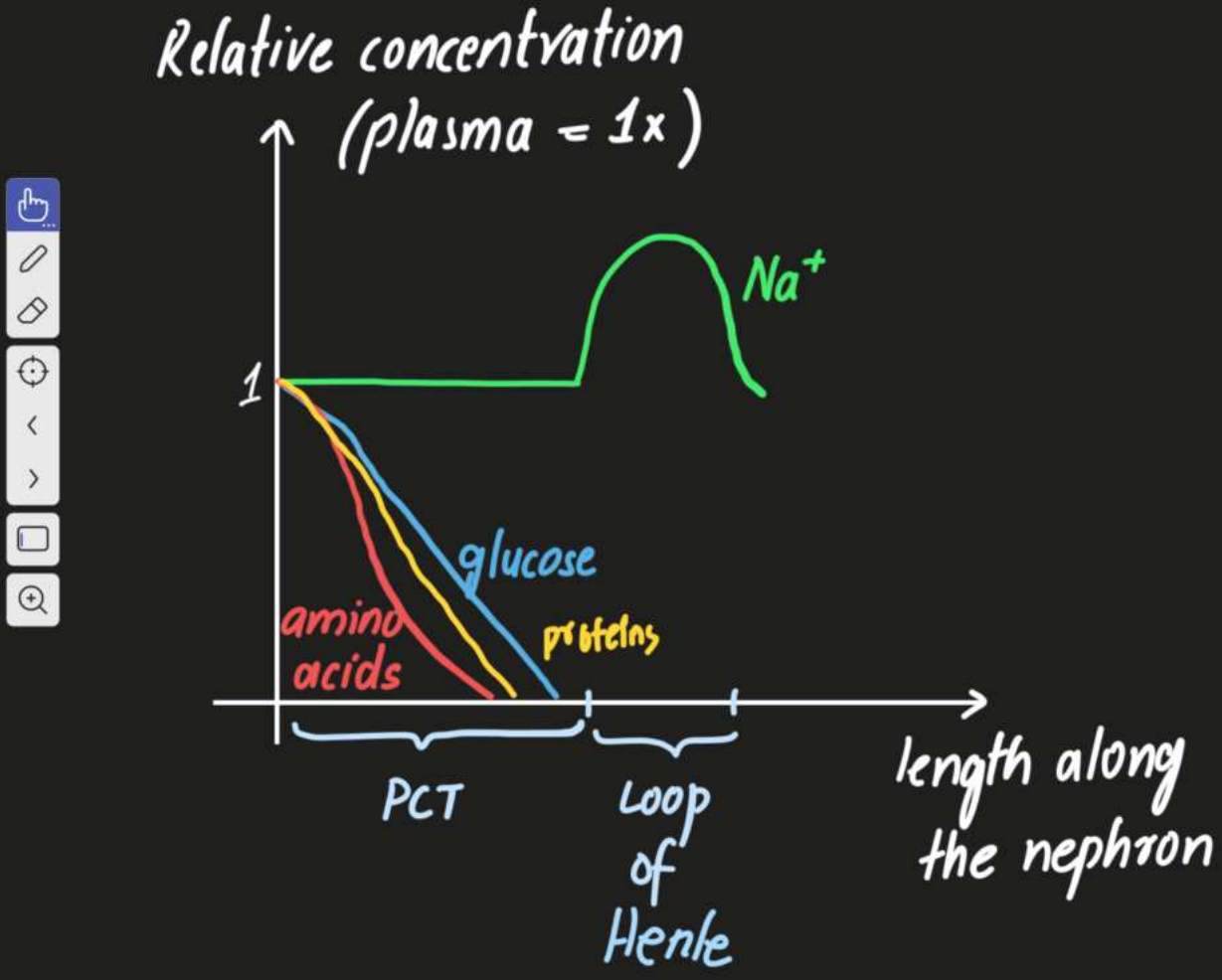
Variation in the relative concentration of different solutes along the nephron



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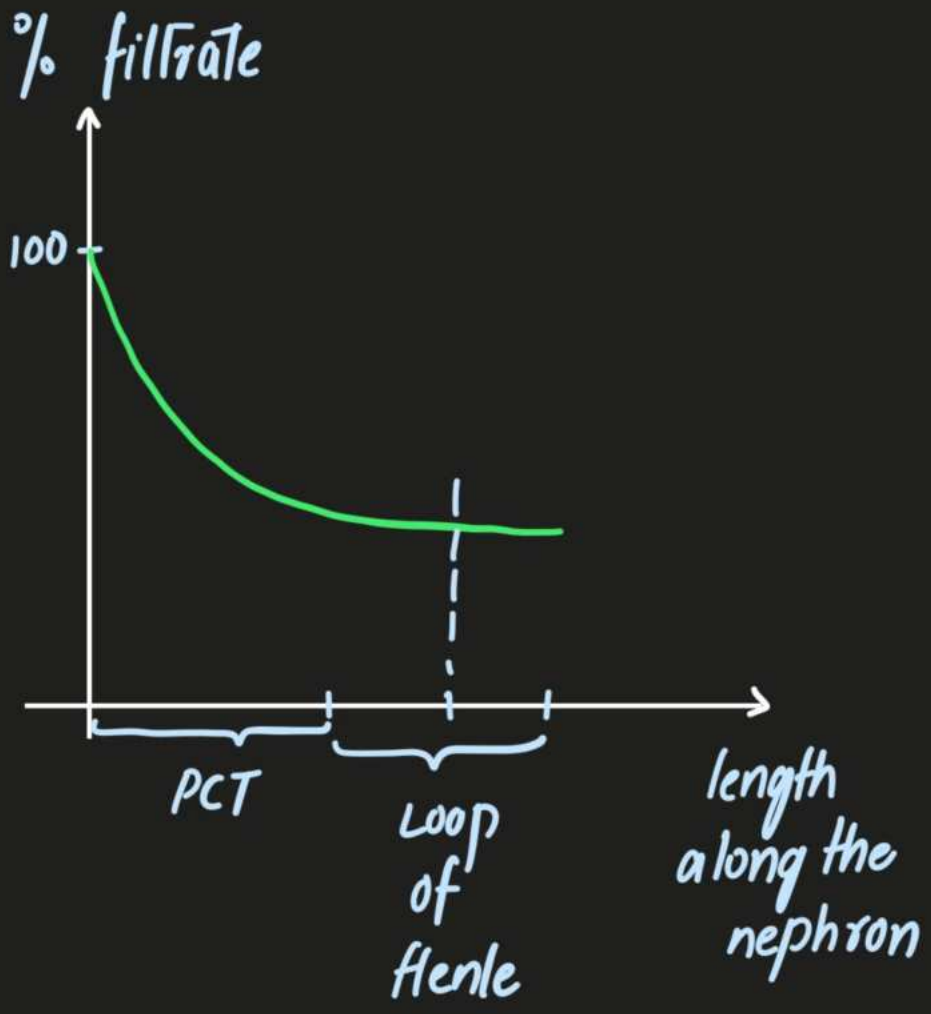
Volume of the filtrate along the nephron



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Negative feedback, ADH and osmoregulation

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Osmoregulation + Negative feedback

* Osmoregulation refers to the maintenance of a constant water potential in body fluids.
* Osmoregulation is achieved via negative feedback.
* Negative feedback involves a stimulus (deviation from norm/set point) detected by receptors which transmit the information to the control centre.

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* The control centre relays information to the effectors which perform corrective actions (response) to restore the norm or the set point.

* Negative feedback in osmoregulation involve the following:

1. Stimulus → Hyper osmolarity or hypo-osmolarity
2. Receptors → Osmoreceptors in hypothalamus
3. Control centre → Hypothalamus
4. Effector → Pituitary (posterior) gland/ collecting duct

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⑤ Response → Reabsorption of more/less water to restore plasma osmolarity

+ The main hormone responsible for achieving osmoregulation is ADH.

ADH → antidiuretic hormone

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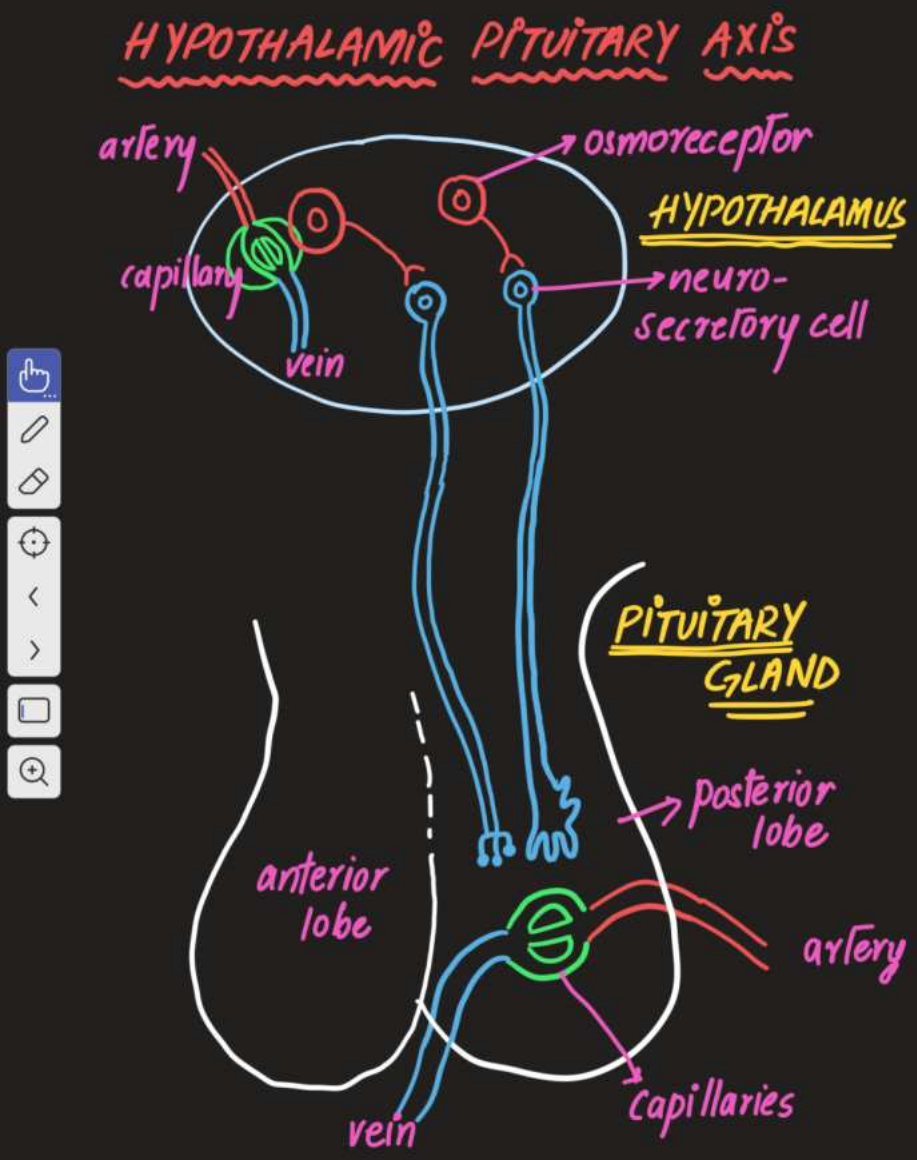
Homeostasis



With
Mohammad Hussham Arshad, MD

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ADVANCED LEVEL BIOLOGY 9700
UNIT 14: Homeostasis

Learning Objectives:

- ADH & osmoregulation
- Diabetes Insipidus

Video Lecture 6 Slides

Mohammad Hussham Arshad, MD
Biology Department

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Previously,

* Excretion and egestion
* Excretory waste products
* Nitrogenous waste
* Deamination and urea cycle
* Urinary system + structure of the kidneys
* Nephron → structure
* Urine formation → ultrafiltration
  → selective reabsorption
* Loop of Henle → Structural and functional feature
* Medullary concentration gradient
* Introduction to negative feedback and osmoregulation

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ADH and Osmoregulation

* ADH stands for anti-diuretic hormone (vasopressin).
* "anti-diuresis" literally means "reduction in the volume of urine excreted"
* ADH is a protein hormone made up of nine amino acids => and thus a nonapeptide.
* ADH is produced by the neurosecretory cells within the hypothalamus.
* It is stored and released by the posterior pituitary gland.

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* Both hypothalamus and pituitary gland (master gland) are present at the base of the brain.

* ADH acts only on the collecting duct cells/distal convoluted tubule cells. This is because the receptors of ADH are located on the cell surface membrane of these cells (target cells).

* Osmoreceptors (in the hypothalamus) are the receptors which detect changes in blood plasma osmolarity.

* NOTE: Both osmoreceptors and neurosecretory cells are specialised neurones.

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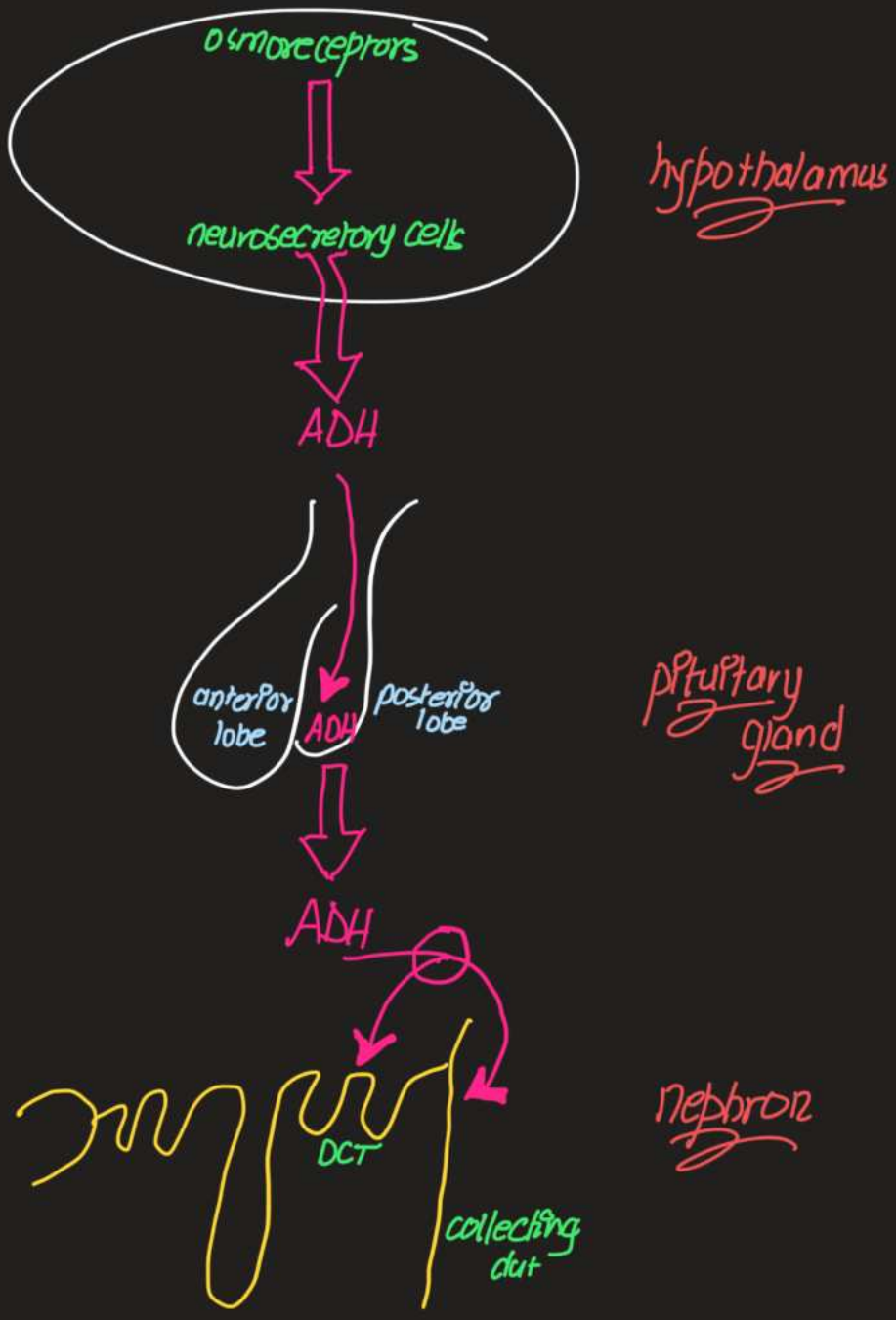
HYPOTHALAMIC PITUITARY AXIS



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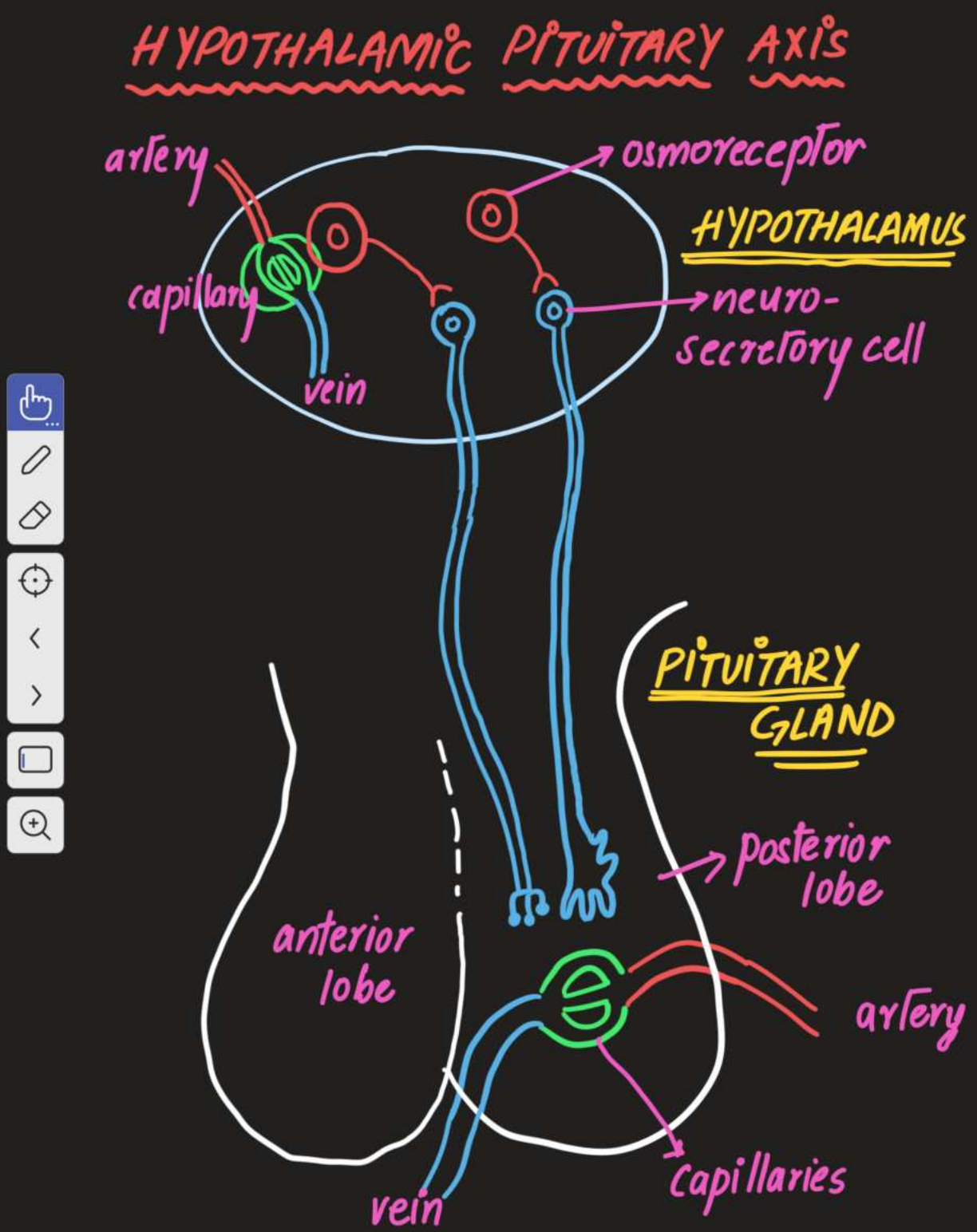
HYPOTHALAMIC PITUITARY AXIS
artery
osmoreceptor
HYPOTHALAMUS
capillary
neuro-
secretory cell
vein
PITUITARY
GLAND
posterior
lobe
anterior
lobe
artery
capillaries
vein

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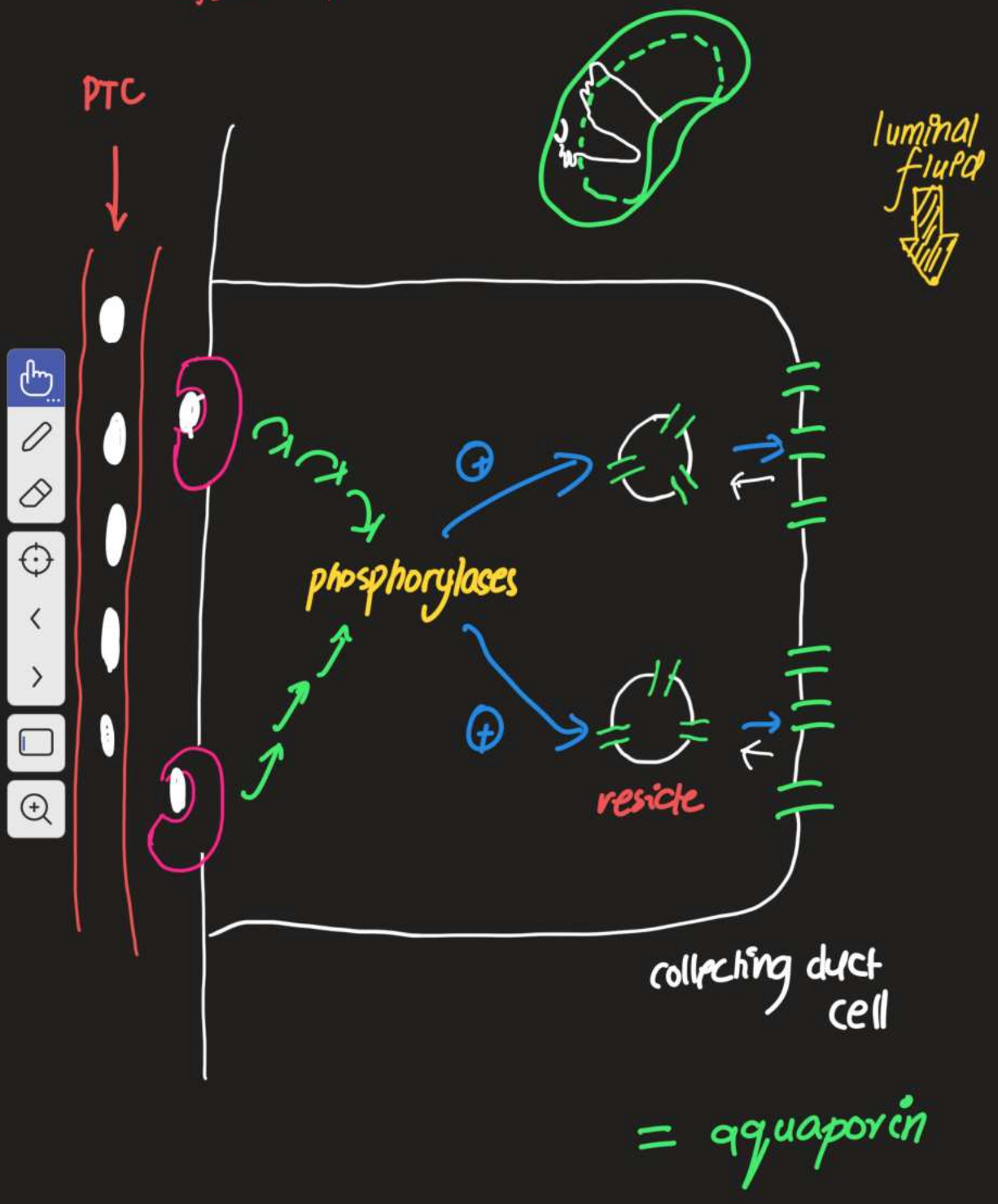
Effect of ADH on the nephron



= aquaporin

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* Consider the blood being hyperosmolar :

lower water potential (hyperosmolarity)

↓

osmoreceptors in hypothalamus stimulated

↓

hypothalamus produces ADH and transports it to posterior pituitary gland

↓

posterior pituitary releases ADH

↓

ADH travels in blood to its target cells → collecting duct cells

↓

ADH binds to its receptors on the cell surface membrane.

↓

Continued...

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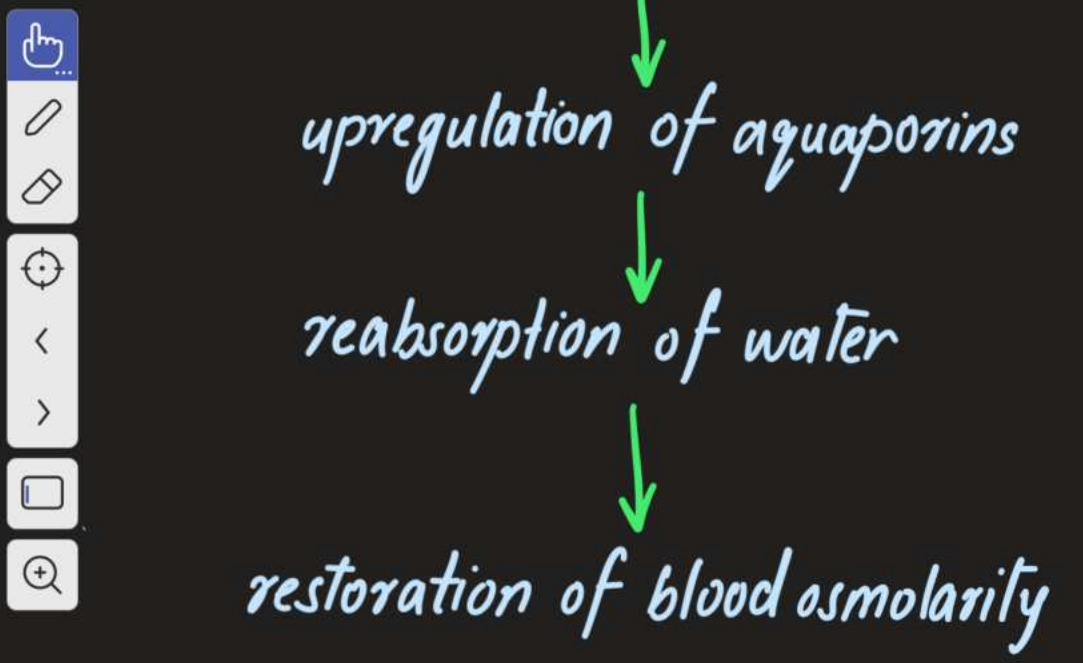
activates phosphorylases
vesicles fuse with membrane
upregulation of aquaporins
reabsorption of water
restoration of blood osmolarity

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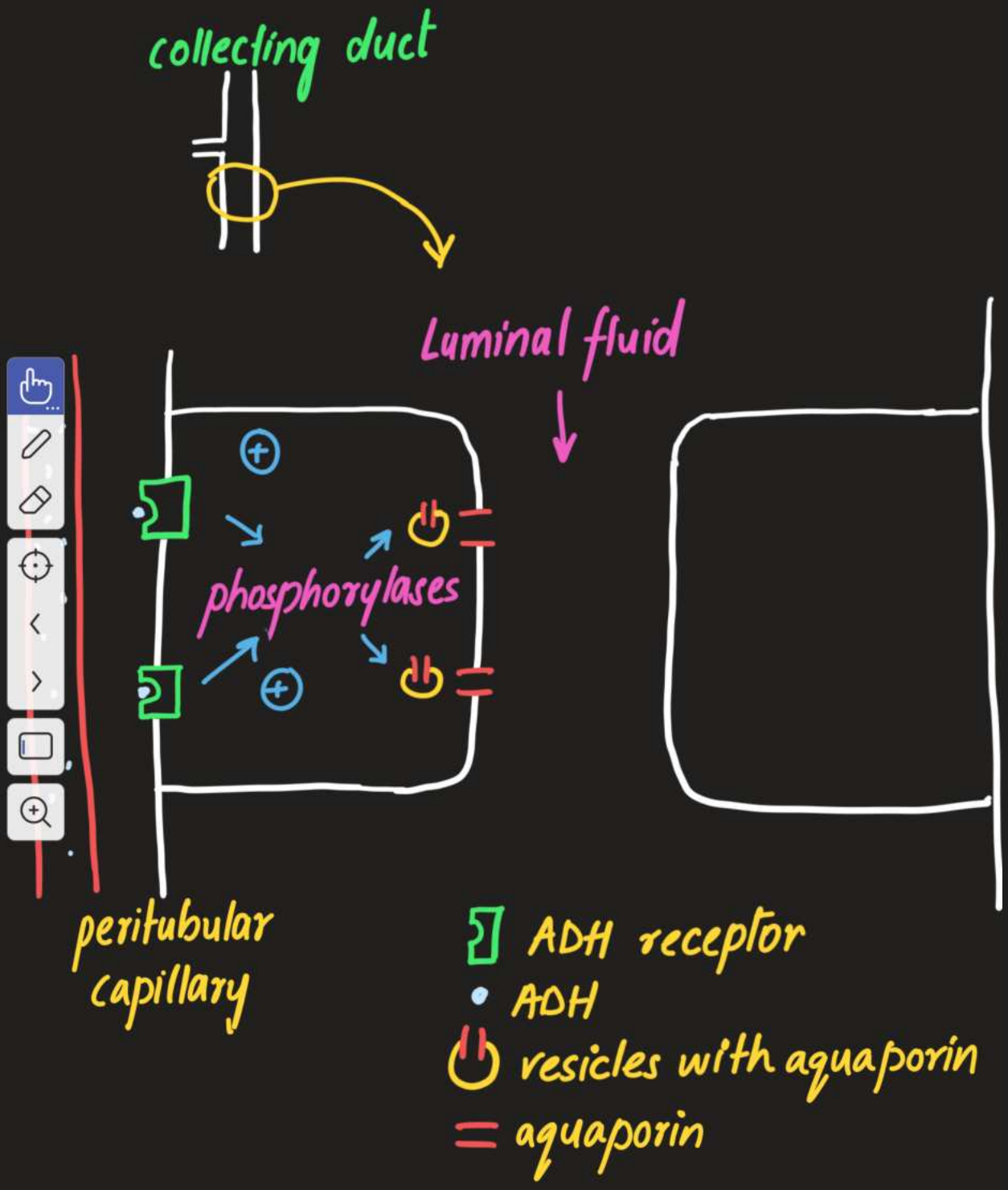
collecting duct
Luminal fluid
phosphorylases
peritubular capillary
ADH receptor
ADH
vesicles with aquaporin
aquaporin

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Diabetes Insipidus

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Diabetes Insipidus

→ It is a disease characterised by production of large amounts of dilute urine and excessive thirst (polydipsia).

→ Diabetes insipidus can occur due to:

① Lack of ADH production due to damage to the pituitary or the hypothalamus.

This type of Diabetes Insipidus is known as Central Diabetes Insipidus.

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② Reduced ADH sensitivity which results due to non-functional ADH receptors within the kidneys. This form of Diabetes Insipidus is known as Nephrogenic Diabetes Insipidus.

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→ Individuals with Diabetes Insipidus have the following signs and symptoms:

i) Production of 15-20L of urine per day
ii) Excessive thirst
iii) Dry skin
iv) Dizziness and confusion
v) Severe dehydration which can lead to seizures, permanent brain damage and even death.

→ There is no treatment available for Diabetes Insipidus.

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Essay Q and A

Q1: Describe the process of ultrafiltration in a nephron ? [6 marks]

Ans: Ultrafiltration is a passive process which involves filtration of useful and waste substances from the blood plasma into the Bowman's capsule. Useful substances which are filtered include glucose, amino acids, small proteins , salts and water. RBC's and large plasma proteins (>68kDa) are never filtered through a normal filtration barrier. There are three layers which collectively make up the filtration barrier. The include :
a) **the endothelium of the glomerulus** which contains **fenestrations** , b) **the basement membrane**, which is the most important layer. Basement membrane is negatively charged with very small pores. c)**the epithelium of the Bowman's capsule**, these epithelial cells have foot-like processes and are therefore termed as podocytes.

The hydrostatic pressure within the glomerulus is the most important factor enabling ultrafiltration. The narrower diameter of the efferent arteriole compared with the afferent arteriole helps build this hydrostatic pressure. The waste substances that are filtered include urea, excess water, and unwanted salts.

Q2: Explain how glucose is reabsorbed into the blood from a kidney nephron ?

Ans: All the glucose is selectively reabsorbed in the proximal convoluted tubule. The process requires energy in the form of ATP. Sodium ions are pumped out of the epithelial cells of the PCT using the Na^+/ K^+ pumps on the basolateral membrane. This lowers the intracellular sodium ion concentration . Sodium ions therefore move down the concentration gradient from the luminal fluid into the epithelial cells via sodium ion glucose co-transporter. Glucose therefore gains entry into the epithelial cells. These glucose molecules move via facilitated diffusion through GLUT proteins into the neighbouring peritubular capillaries. The microvilli present on the luminal membrane and the invaginations on the basolateral membrane maximise the surface area for selective reabsorption of glucose.

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Q3: Outline the role of Loop of Henle in reabsorption of water and ions?

Ans: Loop of Henle has an ascending limb and a descending limb. The descending limb is permeable to water due to the presence of numerous aquaporins. This allows passive reabsorption of water. The descending limb is impermeable to ions which causes the luminal fluid to become more concentrated as it travels down the descending limb. The ascending limb is permeable to ions but impermeable to water due to the absence of aquaporins. It reabsorbs sodium, potassium, and chloride ions actively using NKCC pumps. The Loop of Henle maintains the medullary concentration gradient in addition to reabsorption of water and ions via the counter current multiplier effect. The term counter current refers to the opposite flow of fluid in the two limbs of loop of Henle.

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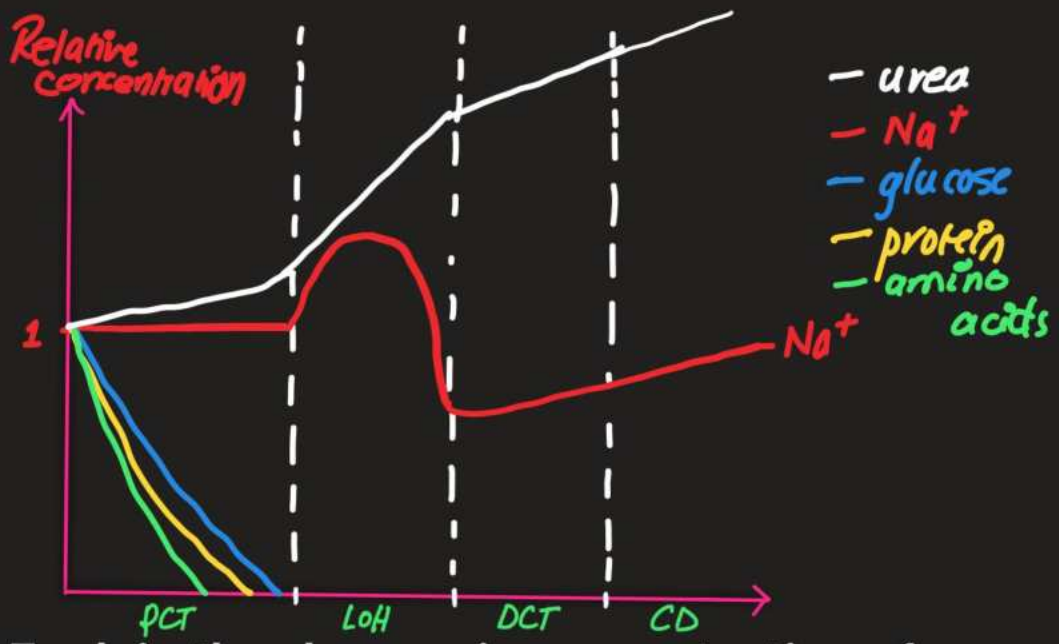

Q4: Explain the changes in concentration of glucose in the PCT?

Ans: The glucose concentration within the luminal fluid decreases to zero within the proximal convoluted tubule because all the glucose is selectively reabsorbed within the PCT.

Q5: Account for the constant [Na^+] in PCT?

Ans: Sodium ions move into the epithelial cells of the PCT via cotransporters and channel proteins. This lowers the water potential within the PCT cells enabling the water to move into the cells via osmosis. Therefore the concentration of sodium ions within the luminal fluid stays constant .

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Q6: Describe and explain the changes in the concentration of Na^+ in the Loop of Henle?

Ans: The concentration of Na ions within the Loop of Henle increases and then decreases.The descending limb of the Loop of Henle reabsorbs water which causes the sodium ion concentration to increase until it reaches its maximum . The descending limb is impermeable to sodium ions. The ascending limb reabsorbs Na^+ ions actively using sodium carrier pumps which explains the decrease in sodium ion concentration as the fluid travels up the ascending limb . The ascending limb is impermeable to water.

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Q7: Describe and explain the changes in [urea] along the nephron.

Ans :

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Question 1:

mammalian kidneys, the loop of Henle is closely associated with the process of smoregulation.

) Explain what is meant by osmoregulation.

maintain water potential of internal environment

..... [2]

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Question 2:

(a) In mammals, the water potential of the blood is constantly monitored by osmoreceptor cells in the hypothalamus of the brain. When the water potential of the blood decreases, ADH (antidiuretic hormone) is produced by cells in the hypothalamus and released into the blood via an endocrine gland.

(i) Explain what is meant by the term *water potential*.

tendency of water molecules to leave a system

.....[1]

(ii) Describe the effect on water potential of adding solute to a solution.

becomes lower (gets more negative)

.....[1]

(iii) State precisely where ADH is released into the blood.

posterior pituitary gland [1]

(iv) The decrease in the water potential of the blood is sometimes due to the loss of water from the body of a mammal.

List **two** ways by which water may be lost from the body.

sweat, urine

.....[1]

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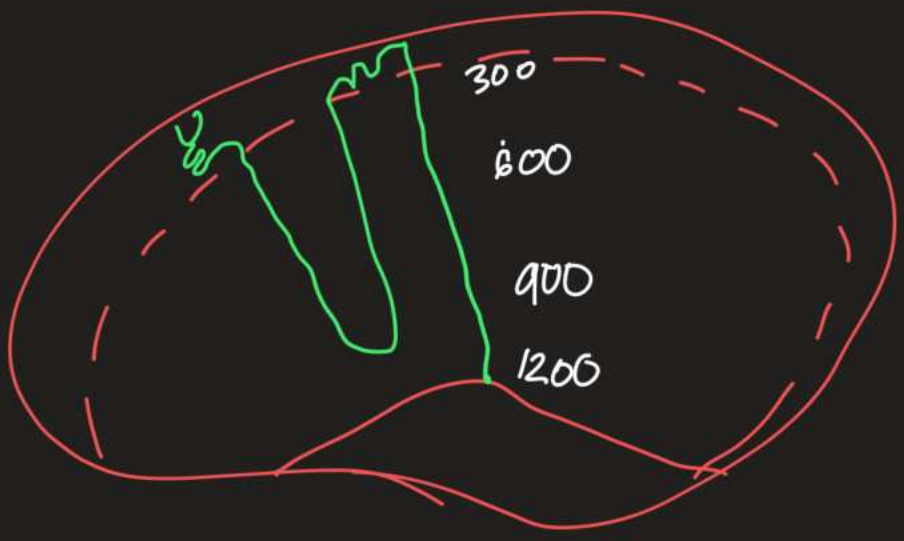
Question 3:

) Explain the role of the collecting duct in controlling the water content of body fluids.

- permeability of collecting duct varies.
- due to ADH
- if blood water potential is low, more water reabsorbed and vice versa

[3]



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Question 4:

(a) Complete the following sentences about osmoregulation.

In mammals, the water potential of the blood is constantly monitored by osmoreceptors in the hypothalamus of the brain.

When the water potential of the blood decreases, the production of a hormone called ADH in the cells of the hypothalamus increases.

This hormone is released into the blood via the posterior pituitary gland

This causes the kidneys to retain more water until the water potential of the blood returns to the set point.

This is an example of a negative feedback mechanism.

[4]

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Question 5 :

(b) Describe the action of ADH on the kidney.

- affects collecting duct
- binds to receptors on cell surface membrane
- activates series of enzyme-controlled reactions
- phosphorylase causes vesicles to move towards cell membrane
- vesicles containing aquaporins fuse
- membrane more permeable to water
- water moves out of lumen
- down water potential gradient.

[5]

(c) Diabetes insipidus is a condition caused by an inability to produce ADH or by the kidneys being unable to respond to ADH.

Suggest symptoms that may be experienced by a person who has diabetes insipidus.

* large volume of urine produced
* dehydration → dry skin
* increased thirst

[2]

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Question 6 :

(c) Describe the roles of the hypothalamus and the posterior pituitary in osmoregulation.

- hypothalamus detects change in water potential by osmoreceptors
- when less water, in blood, ADH released from posterior pituitary gland
- aquaporins
- collecting duct more permeable
- ADH causes more water reabsorption

[5]

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Question 7:

State precisely the name **and** location of the cells where a change in the water potential of the blood would be detected.

osmoreceptors in hypothalamus

..... [1]

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Question 8:

Fig. 3.1 shows the water potential of renal fluid as it passes through the loop of Henle.

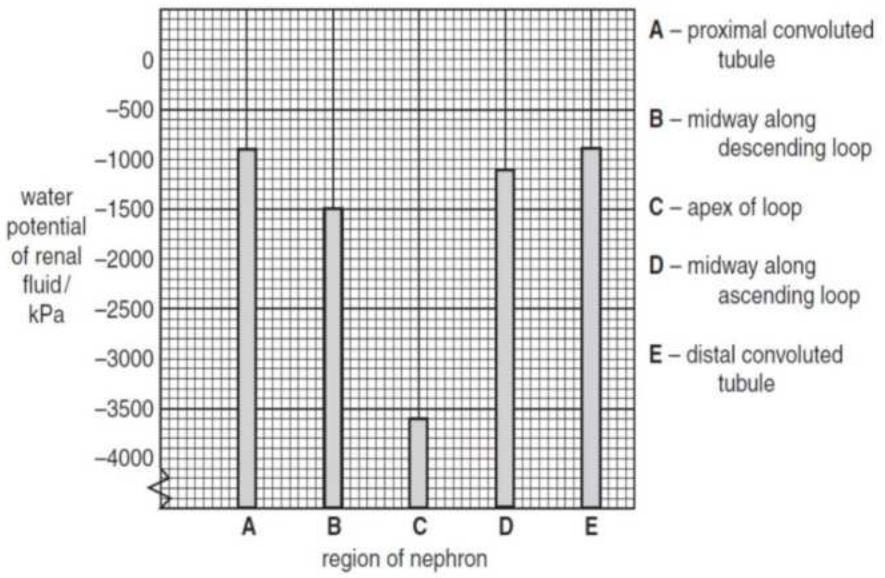

Fig. 3.1

(b) Using the information given in Fig. 3.1, describe and explain what happens to the renal fluid as it passes through the loop of Henle.

- B lower Ψ than A (B = -1500 kPa while A = -900 kPa)
- water moves out through osmosis into medullary tissue
- D higher Ψ than C (D = -1100 kPa while C = -3600 kPa)
- Na^+/Cl^- move out into medulla tissue by active transport [5]

(c) Control systems often work by using negative feedback. These systems require a receptor and an effector. In the process of osmoregulation name the receptor and effector involved.

Receptor hypothalamus (osmoreceptors)

Effector pituitary gland / Collecting duct [2]

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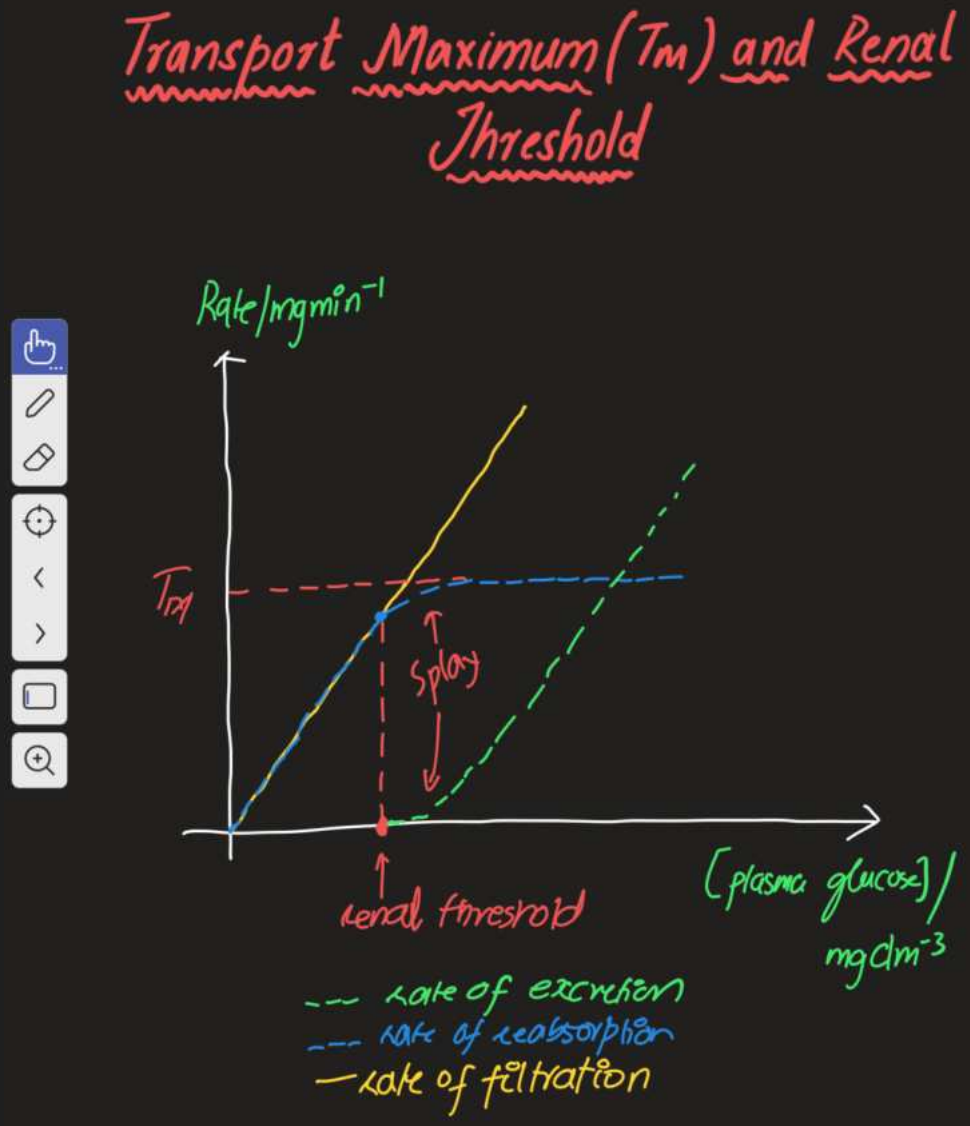
Homeostasis



With

Mohammad Hussham Arshad, MD

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ADVANCED LEVEL BIOLOGY 9700
UNIT 14: Homeostasis

Learning Objectives:

- Transport maximum & renal threshold

Video Lecture 7 Slides

Mohammad Hussham Arshad, MD
Biology Department

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Previously,

* Introduction to negative feedback and osmoregulation
* ADH and it's role in osmoregulation
* Diabetes Insipidus

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Question 9:

Urea is the main nitrogenous waste product in humans. It is made in the liver and excreted by the kidneys in urine.

(a) Define the term *excretion*.

* removal of metabolic waste products which are toxic

[2]

(b) The kidneys regulate the water potential of body fluids. This is known as osmoregulation and involves a negative feedback system.

Outline the role of negative feedback in osmoregulation.

* Homeostatis
* change in water potential detected
* by osmoreceptors
* in hypothalamus
* response via effector
* ADH released
* effect on collecting duct
* return to norm. set point

[4]

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Question 10:

1 **(a)** ADH is a hormone that is released into the blood of a mammal when changes occur in the internal environment.

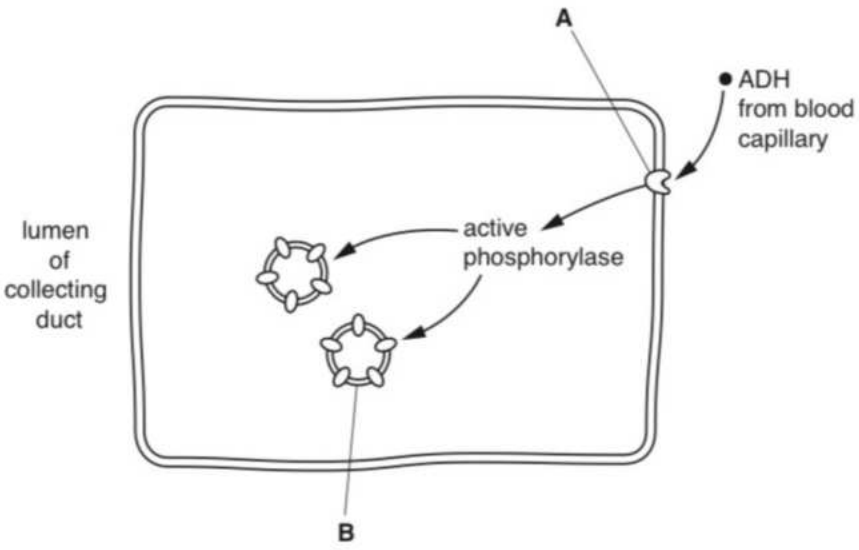
(i) State **one** change in the internal environment of a mammal that leads to the release of ADH.

decrease in water potential of blood plasma ..... [1]

(ii) Name the part of the body that releases ADH into the blood.

posterior pituitary gland ..... [1]

(b) Fig. 1.1 shows a cell of one of the collecting ducts of the kidney.



not to scale

Fig. 1.1

Name membrane protein **A** and cell structure **B**.

A ADH receptor .....

B vesicle ..... [2]

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(c) The phosphorylase enzyme stimulates structure **B**.

Describe the response of structure **B** to this stimulation **and** describe the consequences of this response.

* vesicles fuse with the luminal membrane
* aquaporins attach to the luminal membrane

AND

* this will lead to rapid reabsorption of water into collecting duct cells
* via facilitated diffusion
* water is thereafter reabsorbed into PTC restoring the water potential of blood plasma

[4]

[Total: 8]

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Q.11.

(b) Explain how the collecting ducts in the kidneys may reduce the loss of water from the body. [7]

Q.12.

Describe the role of ADH when the water potential of blood decreases. [7]

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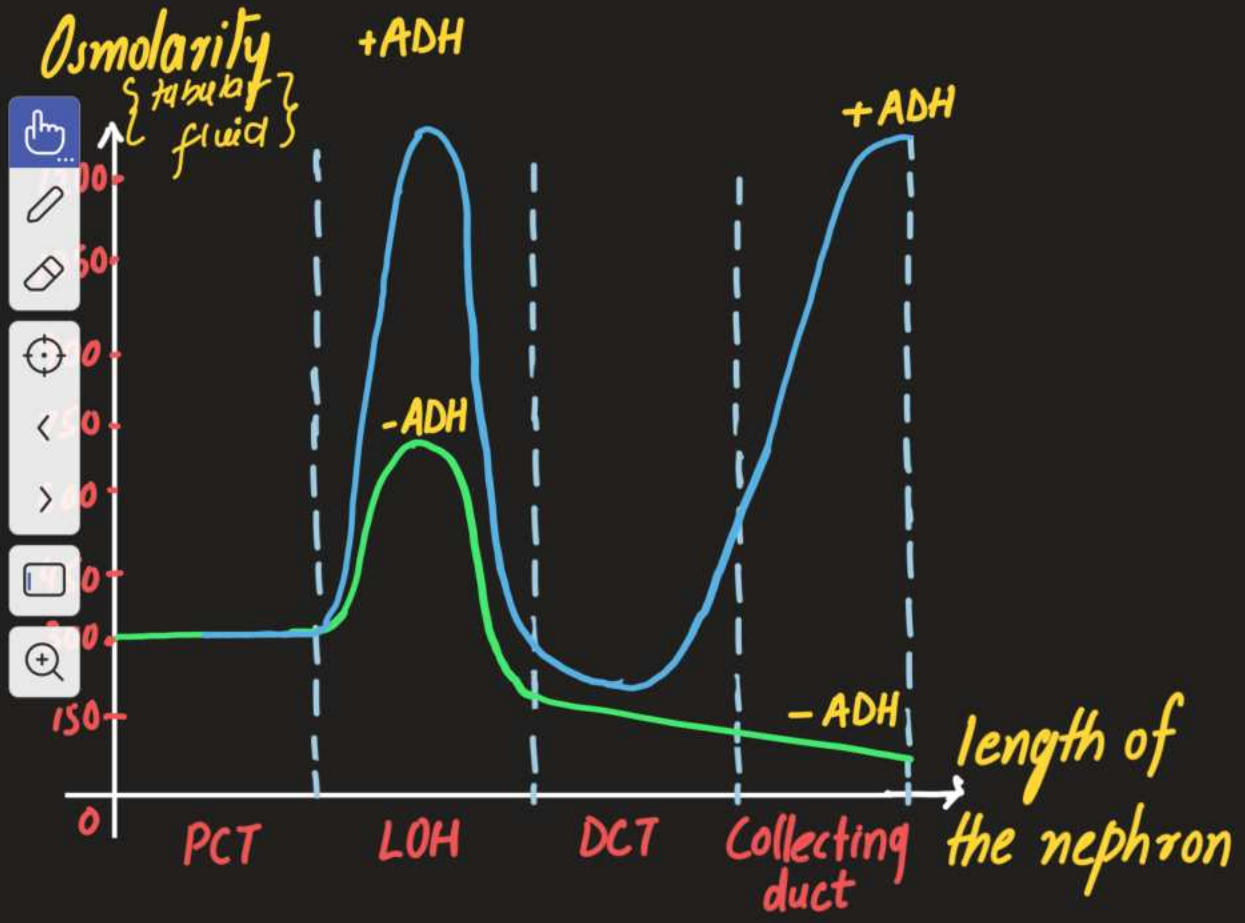
Q13. Use the graph below to answer the following question.



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State and explain the effect of ADH on the osmolarity of the luminal fluid in the DCT and the collecting duct?

Ans: ADH causes a steep rise in the osmolarity of the luminal fluid in the DCT and collecting duct. The rise is more significant in the collecting duct. The results due to upregulation of aquaporins in the luminal membrane of collecting duct cells enabling rapid reabsorption of water via facilitated diffusion.

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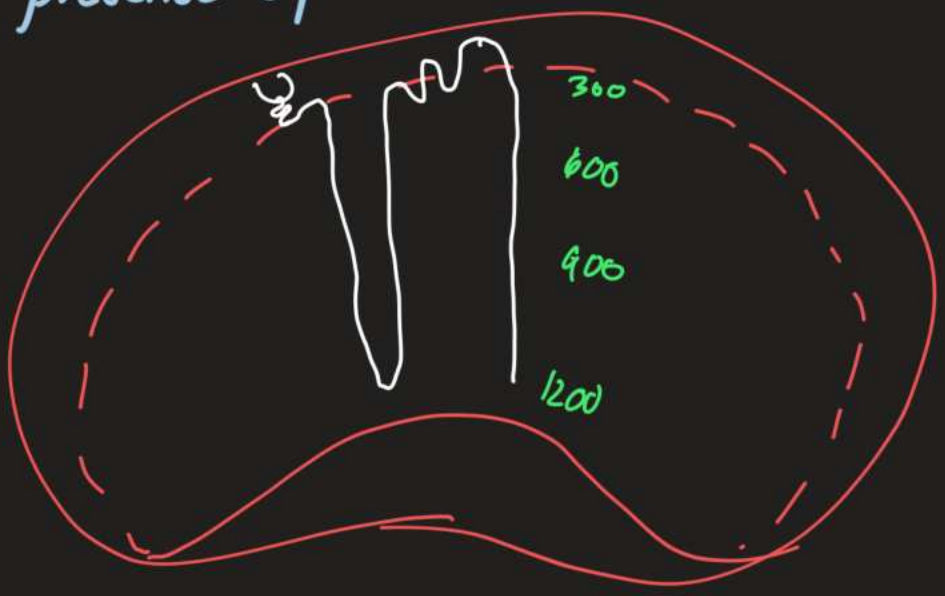
The fluid leaving the collecting duct has an osmolarity of 1200 mOsm/L in the presence of ADH.



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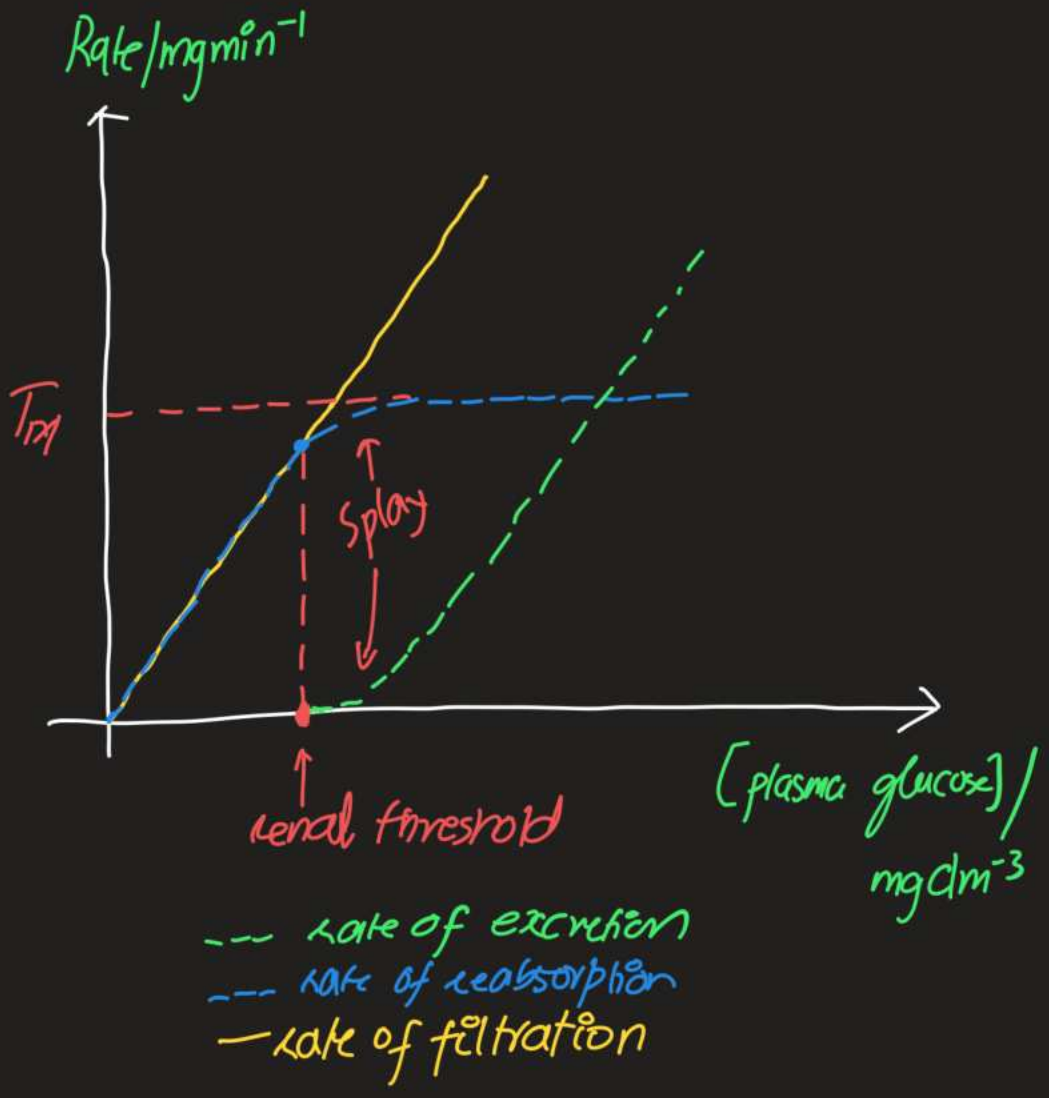
Transport Maximum (Tm) and Renal Threshold



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Transport Maximum (T_M) and Renal Threshold

* T_M is "the maximum rate of reabsorption of a particular solute through transport proteins.

* Renal threshold is the maximum plasma concentration of a particular solute (e.g. glucose) beyond which it starts appearing in the urine.

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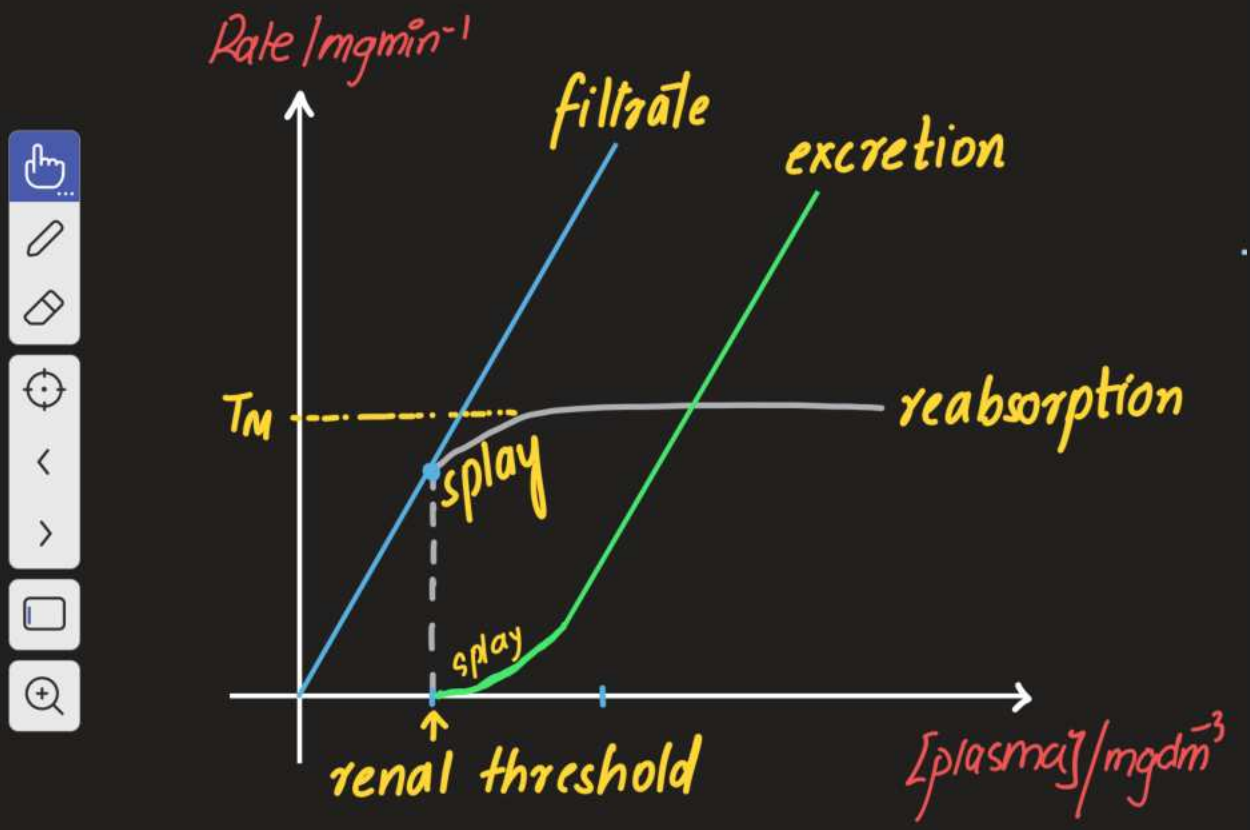
Q14 Use the graph below to answer the following questions.



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a) Why does the rate of reabsorption reach T_M?

Ans: T_M is reached for substances reabsorbed via transport proteins. This implies that all transport proteins are working at their maximum rate.

b) What does the splay signify?

Ans: Splay region signifies that all nephrons do not attain their T_M simultaneously.

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Past Paper Questions

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Question 1:

4 Fig. 4.1 shows a kidney tubule, collecting duct and associated blood vessels.

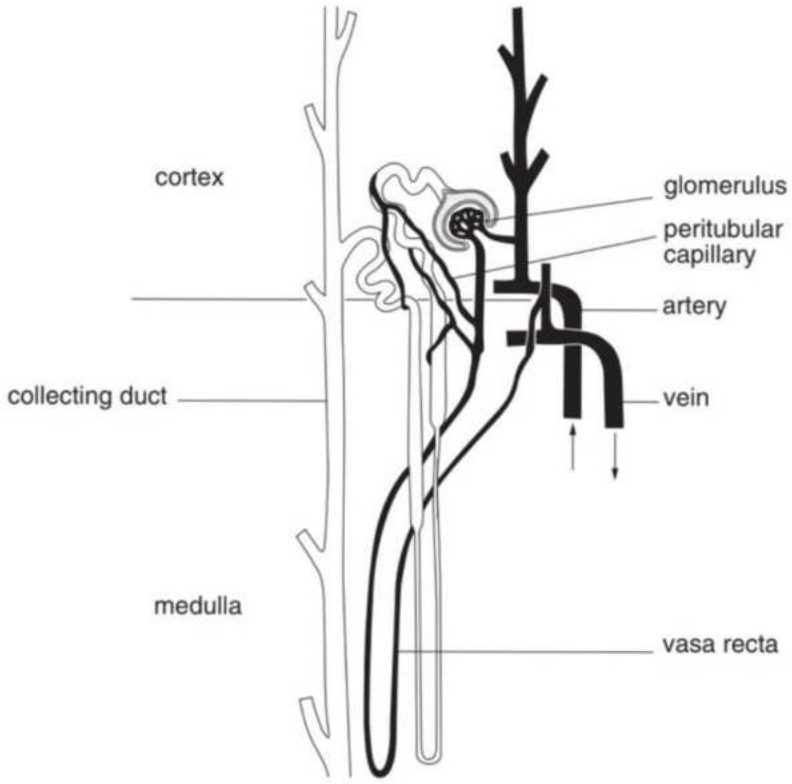

Fig. 4.1

(a) Describe the function of the

(i) glomerulus;

* glomerulus is the site of ultrafiltration
* filters water, glucose, amino acids and other small soluble molecules [2]

(ii) peritubular capillaries;

* removing substances that are selectively reabsorbed
* eg. glucose, amino acids, etc [2]

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(iii) vasa recta.

* collects water reabsorbed by the loop of Henle
* to maintain the medullary conc. gradient [2]

(b) Explain the role of the collecting duct in controlling the water content of body fluids.

* ADH can vary water reabsorption in the CD
* if water potential decreases → more H_2O reabsorbed
* if water potential increases → less water reabsorbed [3]

(c) Suggest **two** disadvantages of the use of dialysis machines in treating kidney failure.

[2]

[Total : 11]

Question 2:

3 Fig. 3.1 is a diagram of a section through the proximal convoluted tubule of a kidney nephron showing details of cell structure, as seen with the electron microscope.

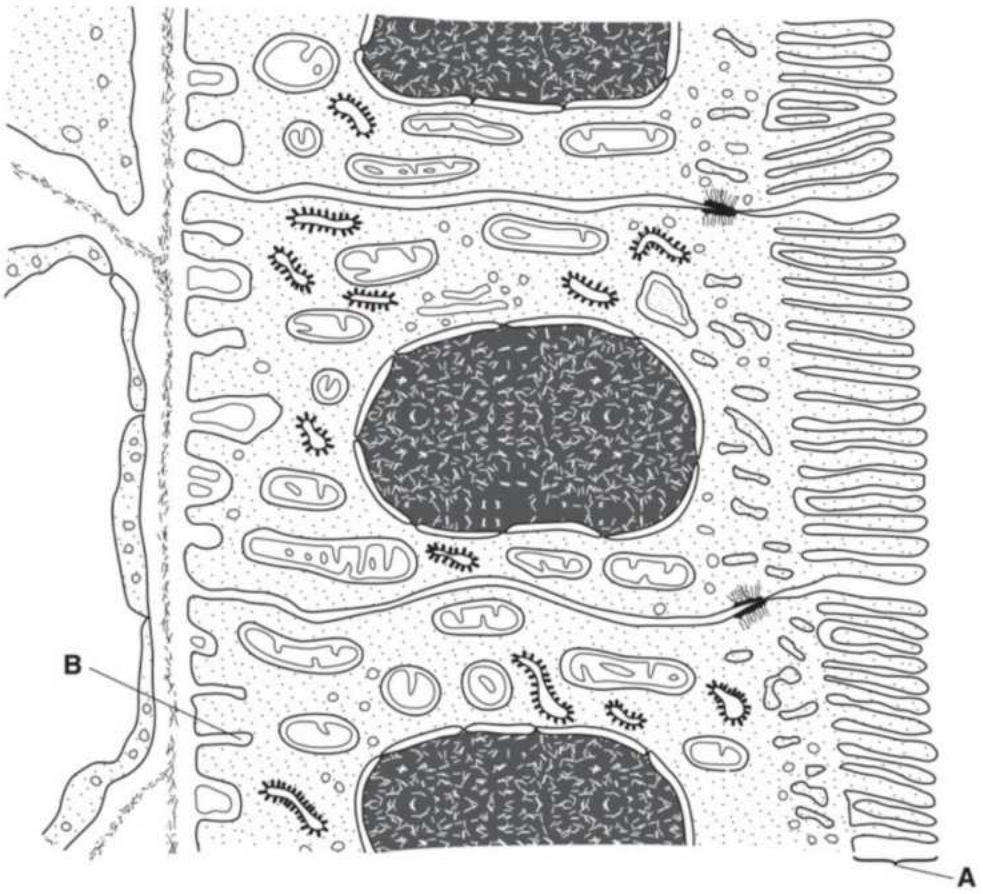

Fig. 3.1

(a) Name the structures **A** and **B**.

A ..microvilli..

B ..invaginations / infoldings..[2]

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(b) Explain three ways in which the cells of the proximal convoluted tubule are adapted for selective reabsorption.

1. microvilli and infoldings ⇒ ↑ S.A to accomodate transport proteins for selective reabs.
2. numerous mitochondria ⇒ to provide energy in the foom of ATP
3. tight junctions ⇒ preventing the LF from mixing coath the ICF [3]

(c) Describe the mechanism of glucose reabsorption into the blood from the lumen of the proximal convoluted tubule of the kidney.

* Na^+-K^+ pump creates a low intracellular [Na^+]
* which (enables) Na^+ and glucose to be cotransported into the PCT via Na^+-glucose cotransporters
* This is secondary active transport
* Glucose is reabsorbed into peritubular cap. via GLUTs [3]

(d) Outline, in terms of water potential, how water is reabsorbed by the cells of the **proximal convoluted tubule**.

* There is low water potential in the PCT cell
* water moves via osmosis into the PCT cell
* down the water potential gradient [2]

[Total: 10]

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Question 3:

3 During the process of the excretion of nitrogenous waste in mammals, blood passes from the renal artery into networks of capillaries called glomeruli.
Fig. 3.1 is an electronmicrograph showing the relationship between the capillaries and the renal capsule cells, called podocytes.

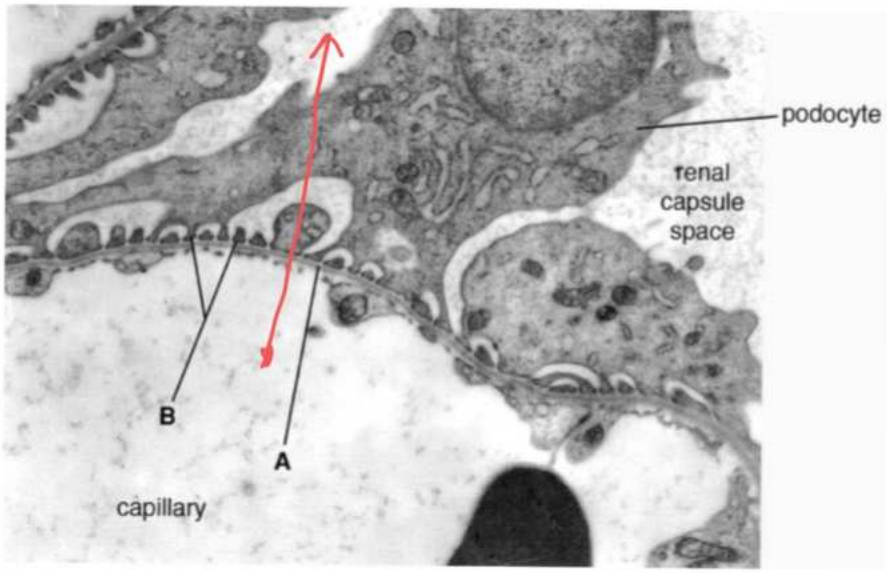

Fig. 3.1

(a) Name structures **A** and **B**.

A ..basement membr.

B ..foot processes [2]

(b) Draw an arrow, on Fig. 3.1, to show the passage of fluid out of the capillary. [2]

(c) (i) Name the fluid that collects in the capsular space.

glomerular filtrate

.....[1]

(ii) Describe how the composition of this fluid differs from blood plasma.

* NO RBCs
* NO large plasma proteins (>68 kDa)

.....[2]

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(d) Ultrafiltration involves the removal of small molecules, including urea, from the blood into the renal capsule. Explain what is required for ultrafiltration to occur.

* hydrostatic pressure of the blood
* increases efferent a. compared with efferent a.
* small soluble molecules pass through the filtration barrier (specifically the basement membrane)

[3]

[Total: 10]

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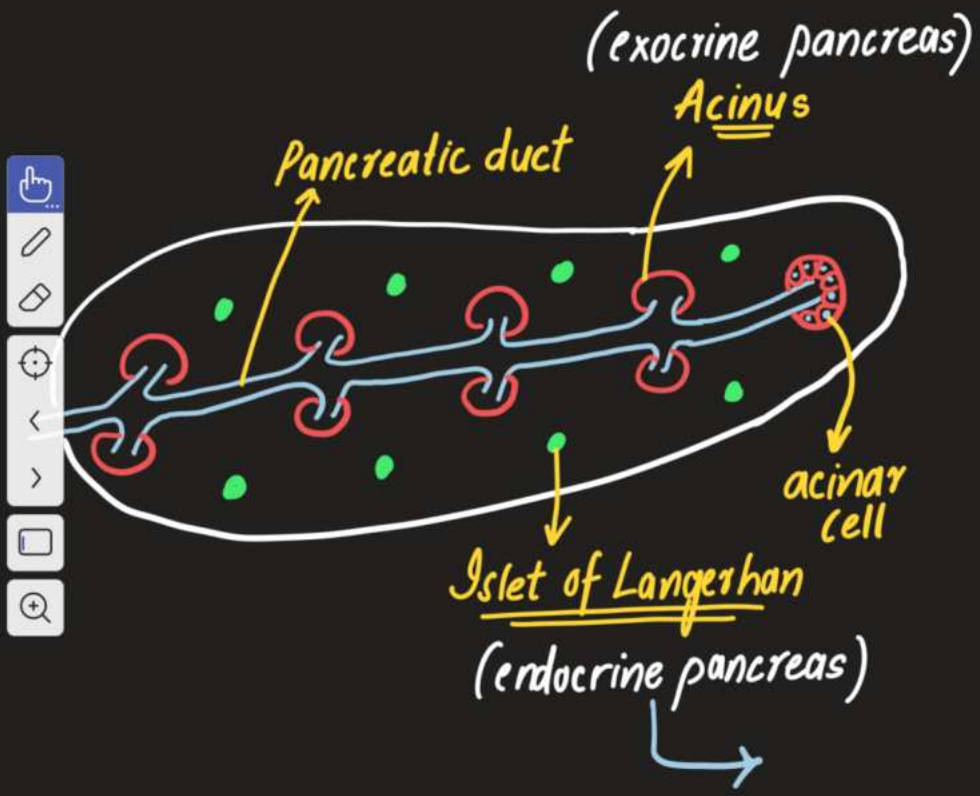
Homeostasis



With
Mohammad Hussham Arshad, MD

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ADVANCED LEVEL BIOLOGY 9700
UNIT 14: Homeostasis

Learning Objectives:

- Structure of pancreas
- Histology of Islet Of Langerhans
- Carbohydrate metabolism in our body
- Insulin & it's role in control of control of blood glucose

Video Lecture 8 Slides

Mohammad Hussham Arshad, MD
Biology Department

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PANCREAS and the control of blood glucose

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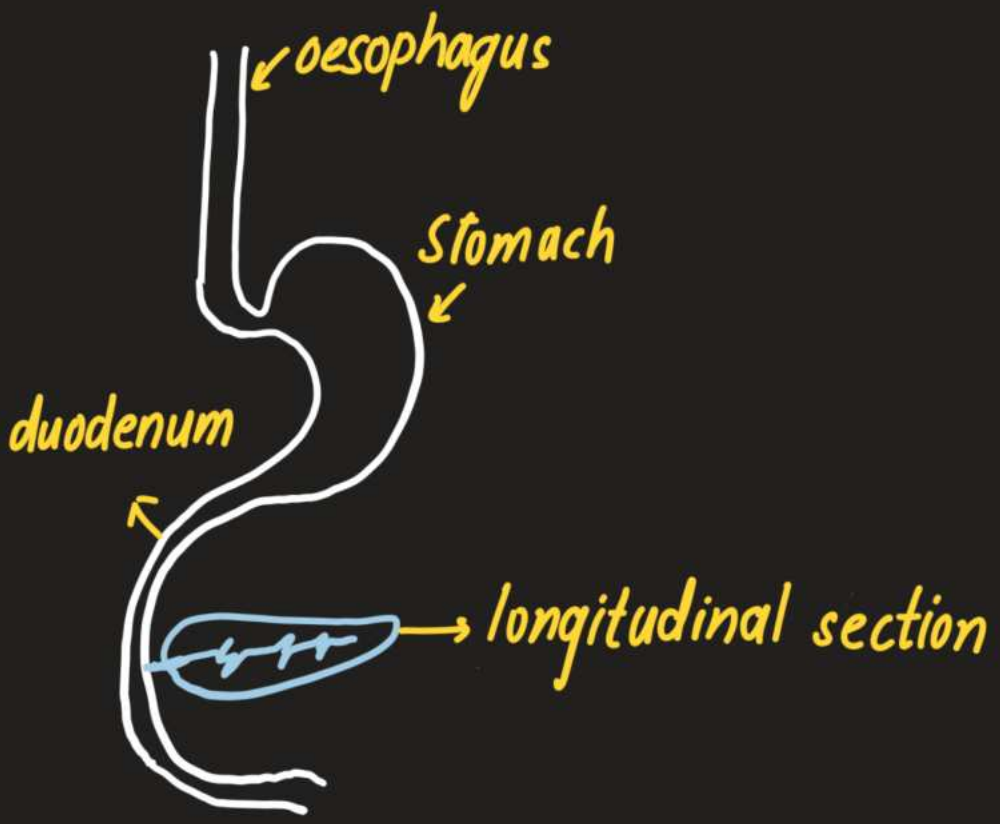
Structure of pancreas



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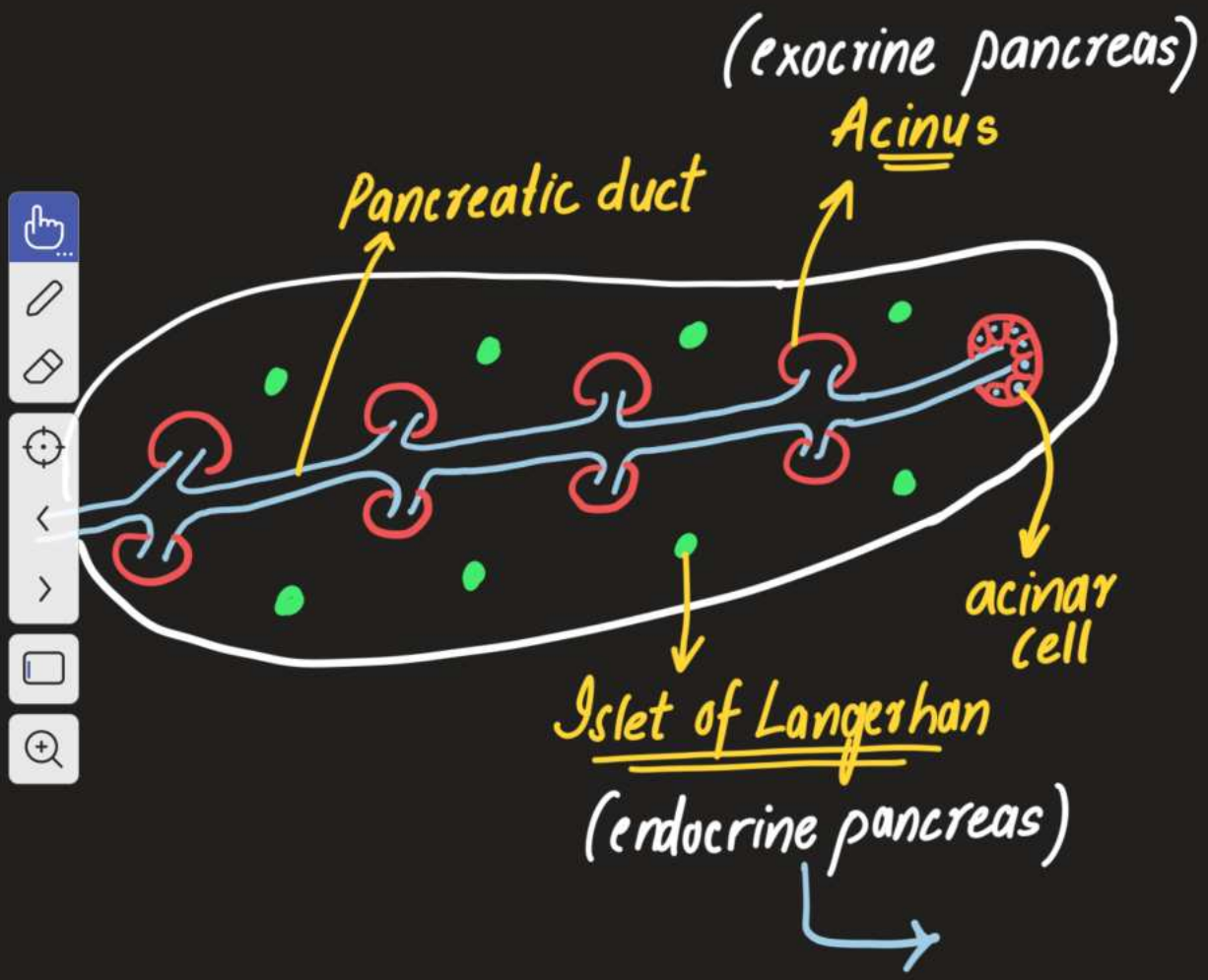
(exocrine pancreas)
Acinus
Pancreatic duct
acinar cell
Islet of Langerhan
(endocrine pancreas)

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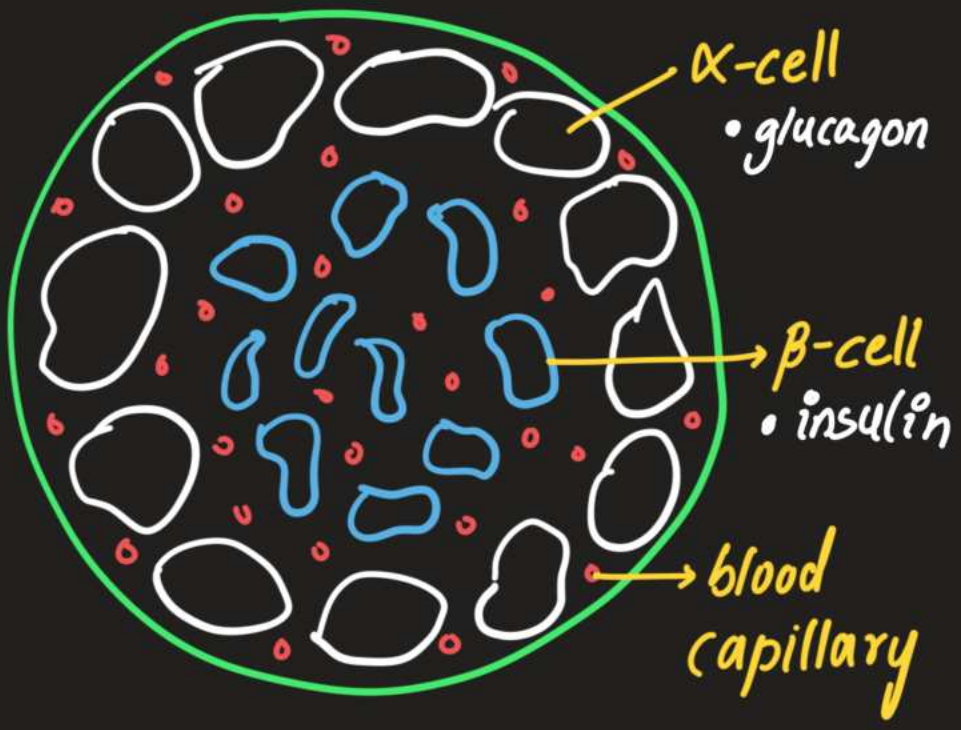
The endocrine pancreas ⇒ "Islet of Langerhans"



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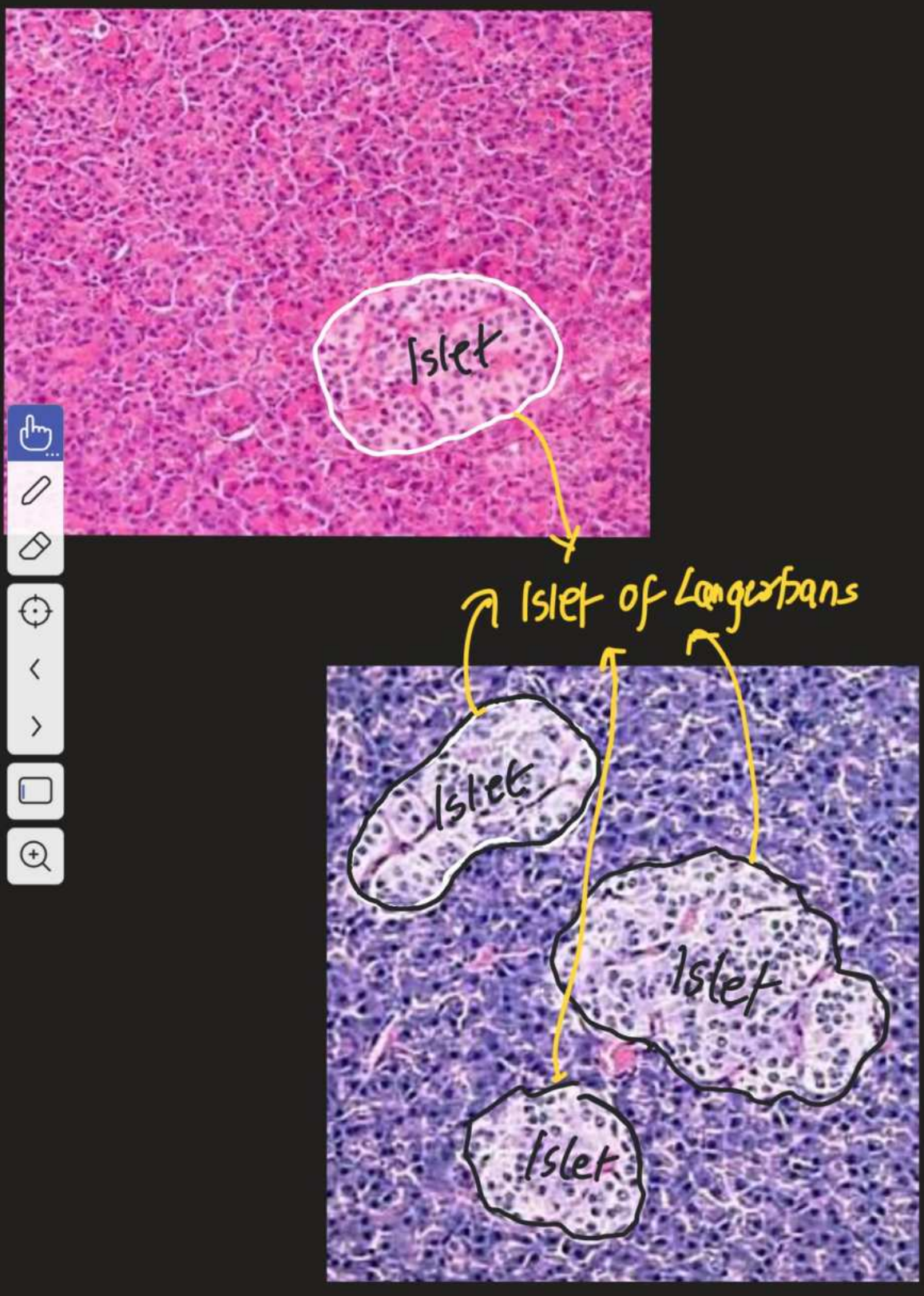

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* Pancreas is a mixed gland.
* A mixed gland is defined as a gland which contains both an endocrine and an exocrine portion.
* The Islet of Langerhans constitute the endocrine portion of the pancreas.
* The acini (singular → acinus) constitute the exocrine portion of the pancreas.
* The endocrine pancreas releases it's secretions directly into the blood vessel.

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* The islet of Langerhans contain two important type of cells besides numerous capillaries:

- α- cells
  - synthesize and secrete glucagon
- β- cells
  - synthesize and secrete insulin

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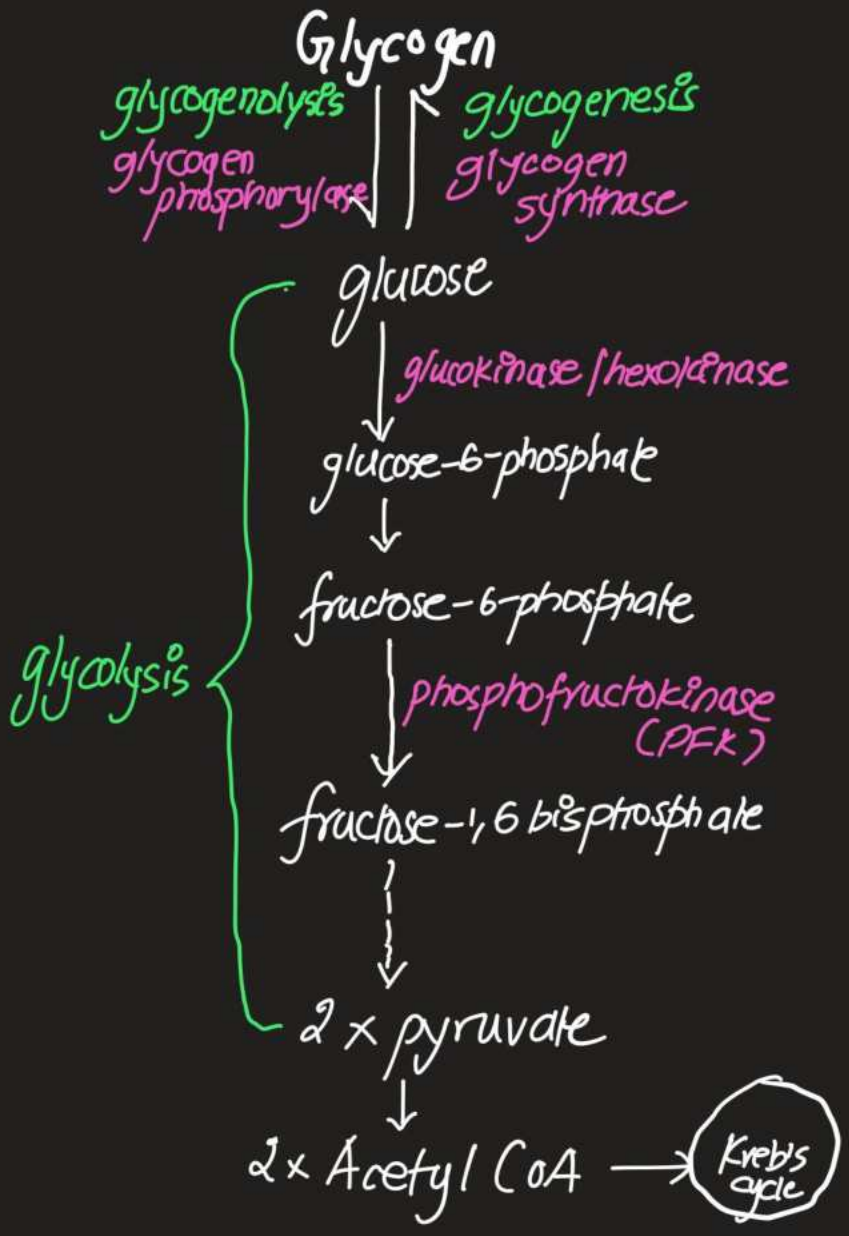
CARBOHYDRATE METABOLISM IN OUR BODY



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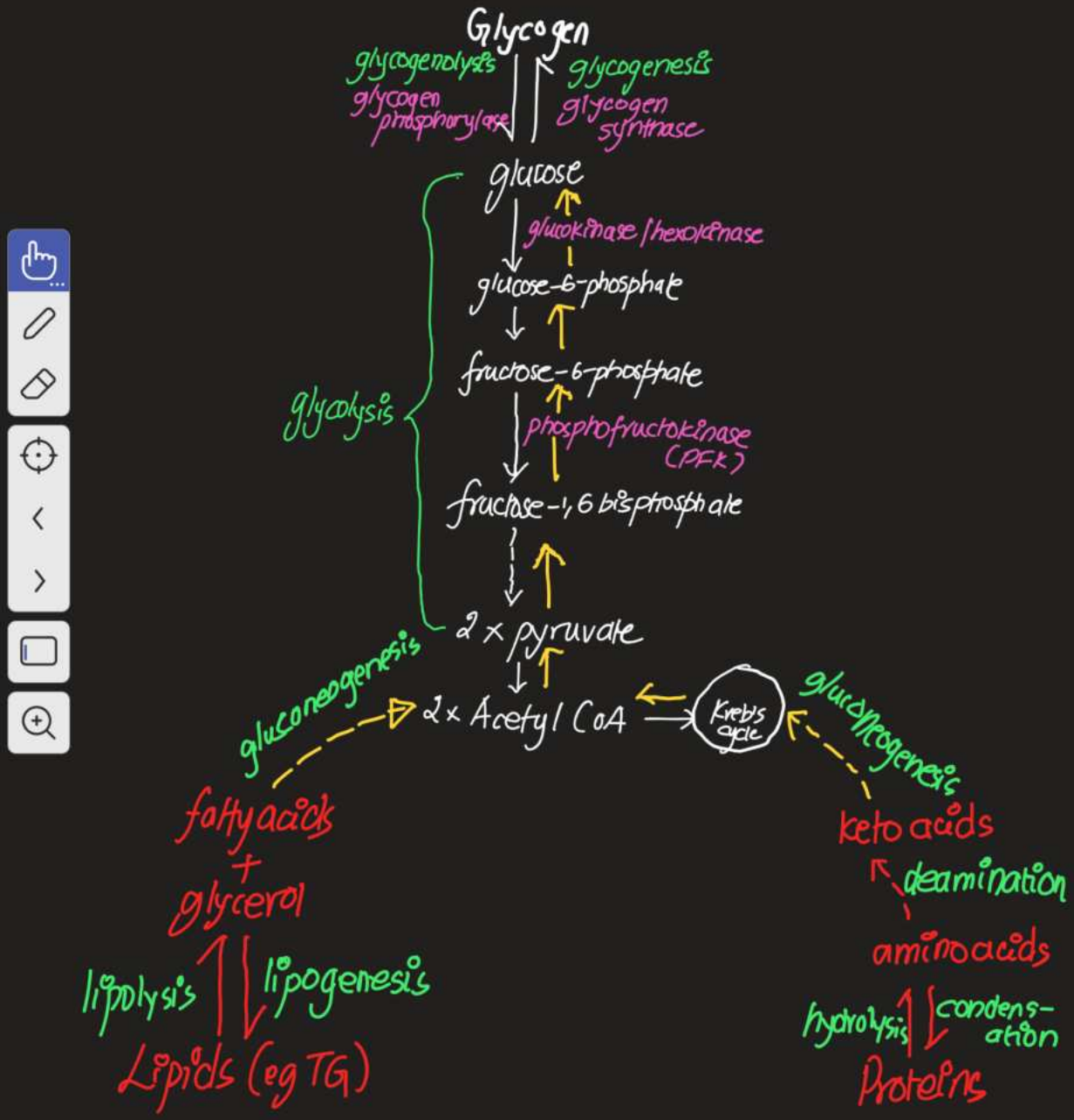
CARBOHYDRATE METABOLISM IN OUR BODY



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Q1: Enlist main features of the following processes: (A) Glycogenesis, (B) Glycogenolysis, (C) Glycolysis, (D) Gluconeogenesis.

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Q1: Enlist main features of the following processes: (A) Glycogenesis, (B) Glycogenolysis, (C) Glycolysis, (D) Gluconeogenesis.

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INSULIN AND GLUCAGON

* Insulin is released by the β-cells of the pancreas when the blood sugar is high.
* Insulin is an anabolic hormone.
* Insulin stimulates the following processes:

① Glycogenesis

② Glycolysis

③ Protein synthesis

④ Lipogenesis

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* Glucagon is released by the α-cells of the pancreas when the blood sugar is low.

- Glucagon is a catabolic hormone.
- Glucagon stimulates the following processes:
  1. Glycogenolysis
  2. Gluconeogenesis
  3. Protein hydrolysis
  4. Lipolysis

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*Insulin and glucagon are antagonistic hormones:

- Glucagon inhibits the processes stimulated by insulin.
- Insulin inhibits the processes stimulated by glucagon.

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* Insulin levels in the body are generally higher after a carbohydrate rich meal/ well fed state.

* Glucagon levels are generally higher during fasting/starvation.

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Insulin and control of blood glucose via negative feedback

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Insulin and the control of blood glucose

* **Stimulus**: high blood plasma glucose concentration (hyperglycaemia)

* Insulin is released by β-cells of the islet of Langerhans within the pancreas.
* Insulin travels in the blood to it's target cells. It's a peptide hormone.
* It's receptors are therefore on the cell surface membrane of it's target cells.

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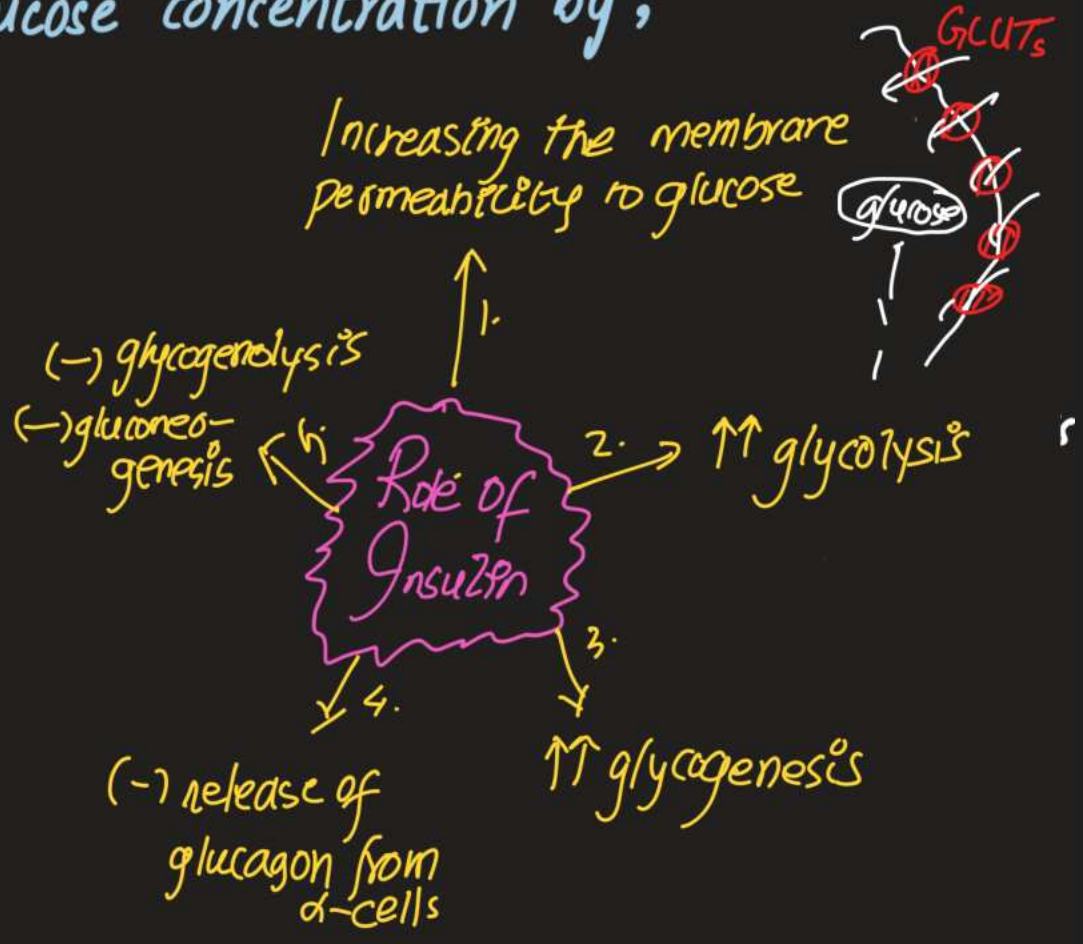
* The target cells of insulin are:
  a) Liver cells
  b) Skeletal muscle cells.
  c) Adipose cells.

* Insulin restores the normal blood glucose concentration by;



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* Insulin restores the normal blood glucose concentration by;

a) increasing the permeability of it's target cells to glucose. It achieves this by upregulation of glucose transporters (GLUTs) on the membrane of target cells. Glucose thereafter enters these cells via facilitated diffusion.

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b) promoting glycolysis due to stimulation of the enzymes glucokinase / hexokinase and phosphofructokinase.

c) promoting glycogenesis due to stimulation of the enzyme glycogen synthase.

d) inhibiting α-cells which release glucagon.

e) inhibiting gluconeogenesis and glycogenolysis.

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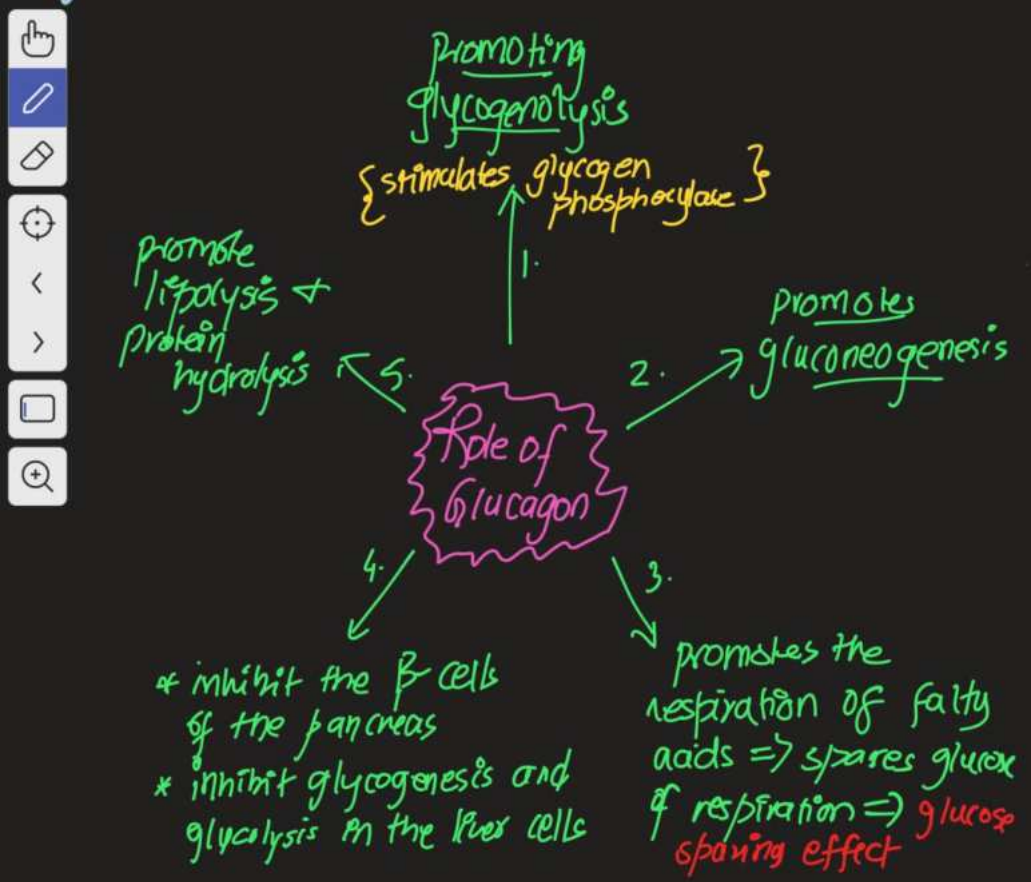
Homeostasis

*The target cells of glucagon are:
a) Liver cells ONLY
*Glucagon restores the normal blood glucose concentration by;



With
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ADVANCED LEVEL BIOLOGY 9700
UNIT 14: Homeostasis

Learning Objectives:

- Glucagon & control of blood glucose

Video Lecture 9 Slides

Mohammad Hussham Arshad, MD
Biology Department

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PANCREAS and the control of blood glucose

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Insulin and the control of blood glucose

* **Stimulus**: high blood plasma glucose concentration (hyperglycaemia)

* Insulin is released by β-cells of the islet of Langerhans within the pancreas.

* Insulin travels in the blood to it's target cells. It's a peptide hormone.

* It's receptors are therefore on the cell surface membrane of it's target cells.

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* The target cells of insulin are:
  a) Liver cells
  b) Skeletal muscle
  c) Adipose cells.

* Insulin restores the normal blood glucose concentration by;

a) increasing the permeability of it's target cells to glucose. It achieves this by upregulation of glucose transporters (GLUTs) on the membrane of target cells. Glucose thereafter enters these cells via facilitated diffusion.

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b) promoting glycolysis due to stimulation of the enzymes glucokinase / hexokinase and phosphofructokinase.

c) promoting glycogenesis due to stimulation of the enzyme glycogen synthase.

d) inhibiting α-cells which release glucagon.

e) inhibiting gluconeogenesis and glycogenolysis.

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* Insulin also promotes protein synthesis in skeletal muscle cells by increasing the uptake of amino acids in these cells.
* Insulin stimulates the synthesis of lipids.
* Since insulin promotes ..... it's termed as an ANABOLIC HORMONE
  - glycogenesis
  - lipogenesis
  - protein synthesis

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Glucagon and control of blood glucose via negative feedback

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Glucagon and the control of blood glucose

* **Stimulus**: low blood plasma glucose concentration (hypoglycaemia)

* Glucagon is released by α-cells of the islet of Langerhans within the pancreas.

* Glucagon travels in the blood to it's target cells. It's a peptide hormone. (globular protein)

* It's receptors are therefore on the cell surface membrane of it's target cells.

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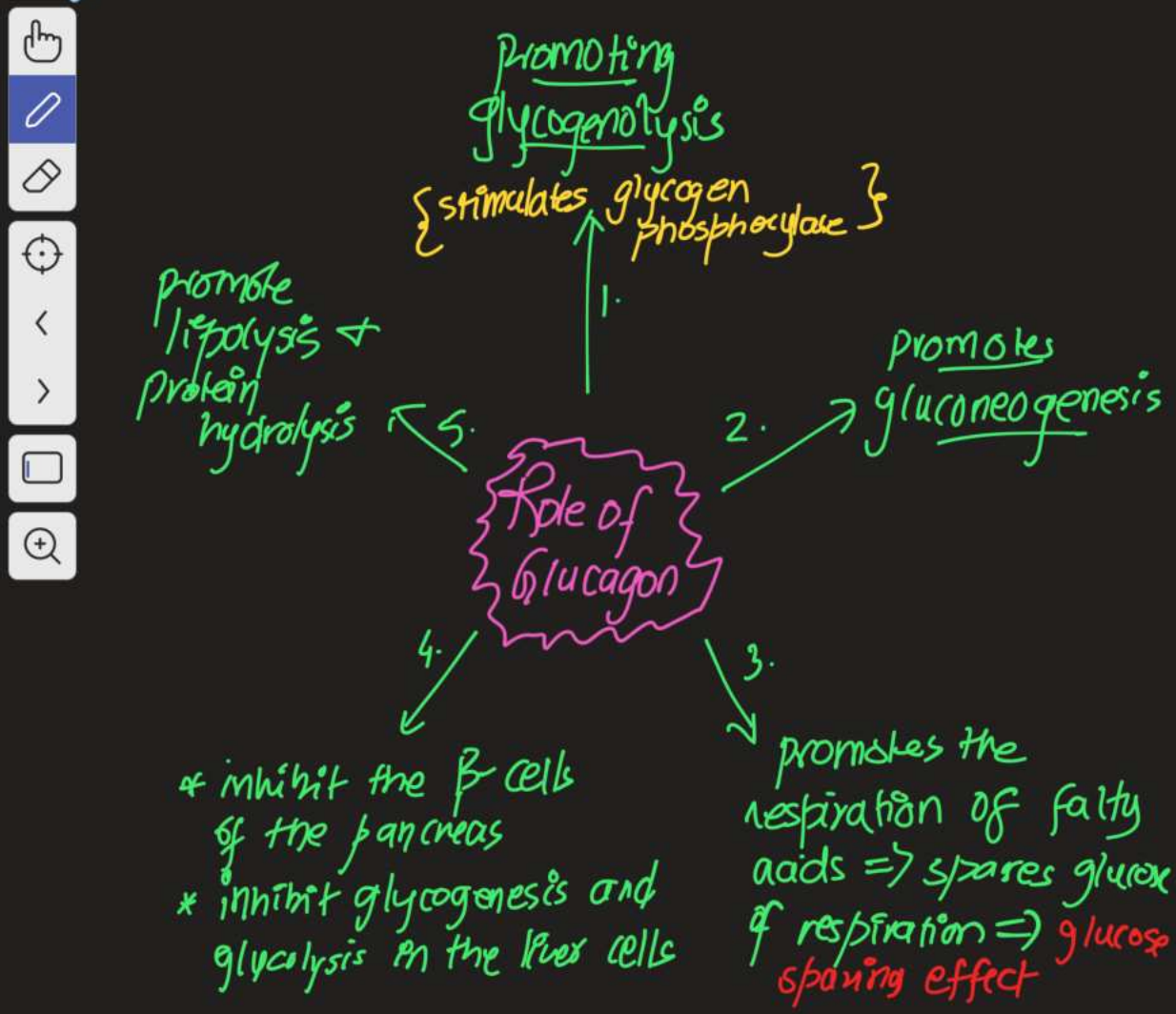
* The target cells of glucagon are:
  a) Liver cells ONLY
* Glucagon restores the normal blood glucose concentration by;



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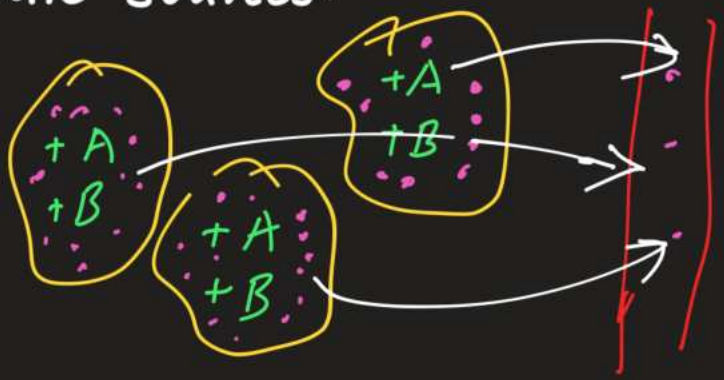
* Glucagon restores the normal blood glucose concentration by;

a) promoting glycogenolysis (A) due To stimulation of the enzyme glycogen phosphorylase

b) promoting gluconeogenesis (B) which involves the formation of glucose from non-carbohydrate sources.



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c) promoting lipolysis of triglycerides forming fatty acids and glycerol. These can be respired to release energy in liver cells thereby sparing glucose. This is known as the glucose-sparing effect.

d) inhibiting β-cells which release insulin.

e) inhibiting glycolysis and glycogenesis.

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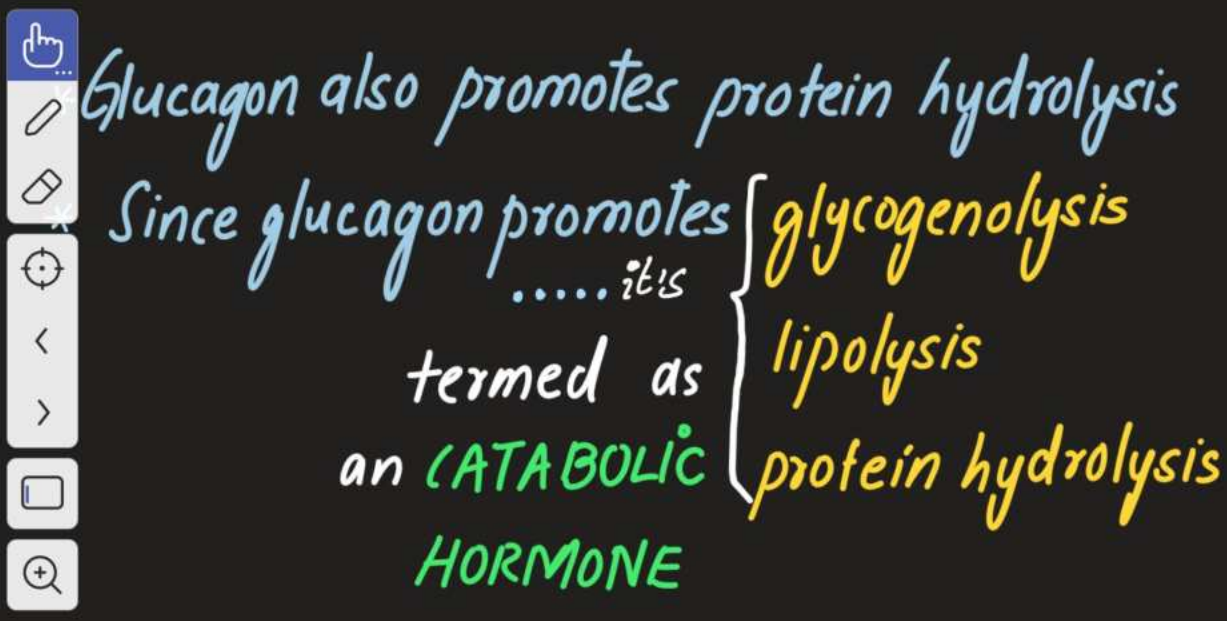
Glucagon also promotes protein hydrolysis
Since glucagon promotes ..... it is termed as an CATABOLIC HORMONE
glycogenolysis
lipolysis
protein hydrolysis

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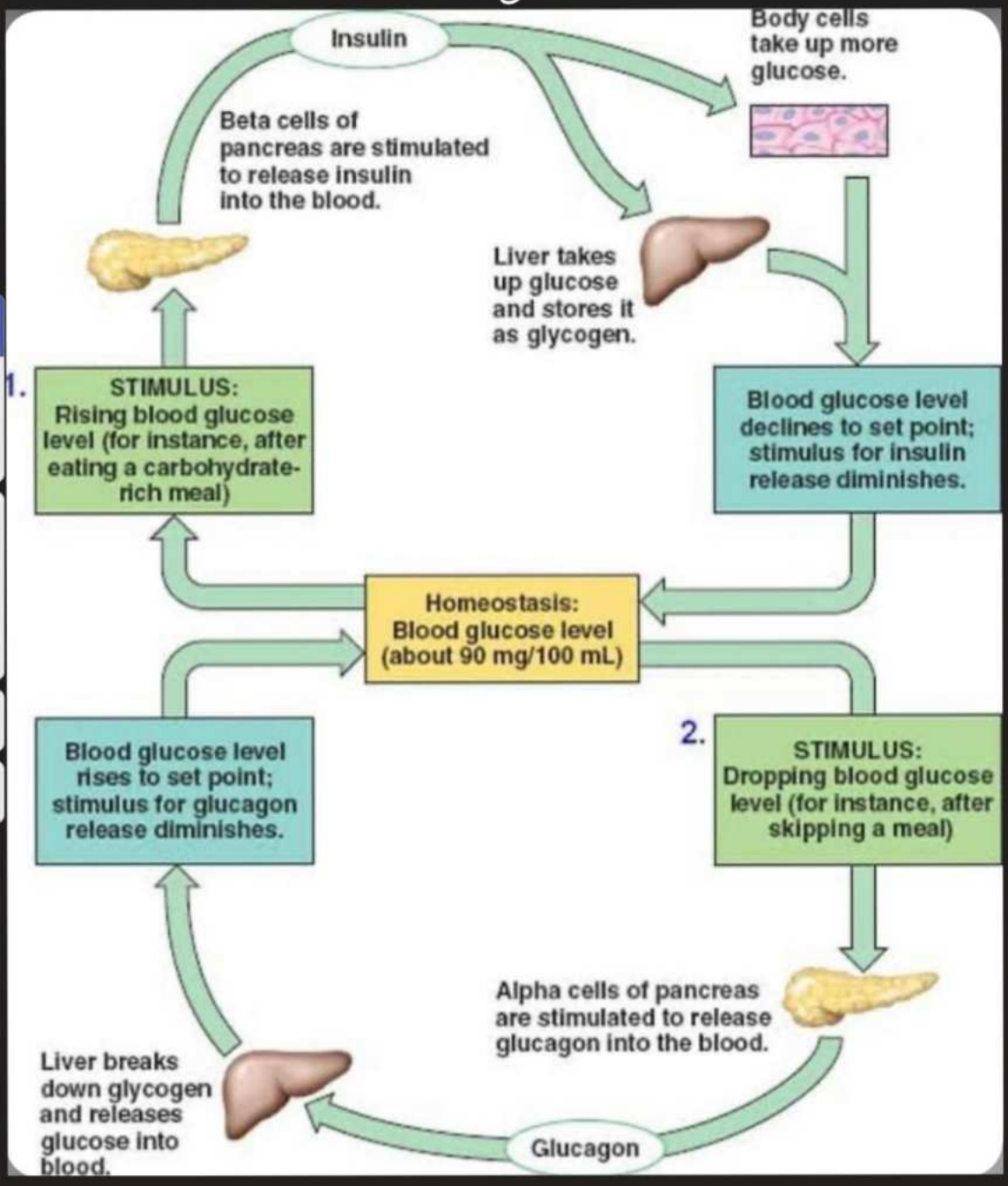
Negative feedback and control of Blood glucose



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Past Paper Questions

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Question 1:

7 **(a)** An important function of control systems in mammals is homeostasis.

Explain what is meant by the term *homeostasis*.

maintenance of a constant internal environment

..... [1]

(b) Insulin plays a part in homeostasis. It affects muscle and liver cells to bring about a decrease in blood glucose concentration, particularly after a meal.

(i) Insulin is composed of two polypeptides which are made in β cells in the pancreas.

State precisely where in β cells polypeptide molecules are synthesised.

rER [1]

(ii) Name the process by which insulin is secreted from β cells.

exocytosis [1]

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(iii) Describe the effects of insulin on muscle cells.

Insulin
1. promotes glycolysis by stimulating the enzymes glucokinase and phosphofructokinase
2. promotes glycogenesis by stimulating glycogen synthase
3. increase the uptake of glucose by muscle cells by increasing it's membrane permeability

[3]

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Question 2:

7 (a) Table 7.1 shows the effect of several events on the blood concentration of g insulin and glucagon in a healthy person.

Complete the table using the words **increase**, **decrease** or **no effect**.

The first row has been done for you.

Table 7.1

event	initial effect of event on blood concentration of		
	glucose	insulin	glucagon
meal containing sucrose	increase	increase	decrease
meal containing only protein	no effect	no effect	no effect
fasting	decrease	decrease	increase
exercising	decrease	decrease	increase
meal containing starch	increase	increase	decrease

[4]

(b) The concentration of glucose in the blood is controlled by the hormones insulin and glucagon.

Describe the part played by **glucagon** in the control of glucose in the blood.

Glucagon → 1. promotes glycogenolysis by stimulating glycogen phospho.
→ 2. promotes gluconeogenesis
→ 3. promotes breakdown of lipids releasing fatty acids which can be used in respiration. This spares the glucose within the cell.

[3]

[Total: 7]

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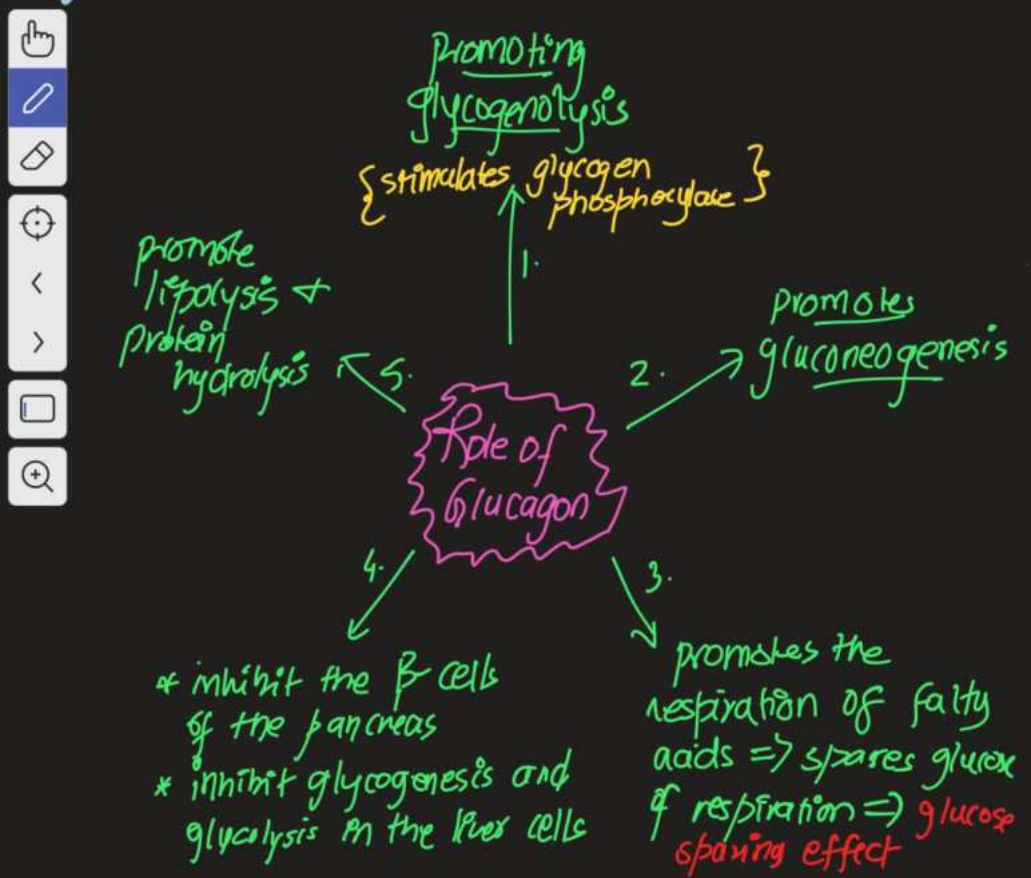
Homeostasis

*The target cells of glucagon are:
a) Liver cells ONLY
*Glucagon restores the normal blood glucose concentration by;



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ADVANCED LEVEL BIOLOGY 9700
UNIT 14: Homeostasis

Learning Objectives:

- Glucagon & control of blood glucose

Video Lecture 9B Slides
Mohammad Hussham Arshad, MD

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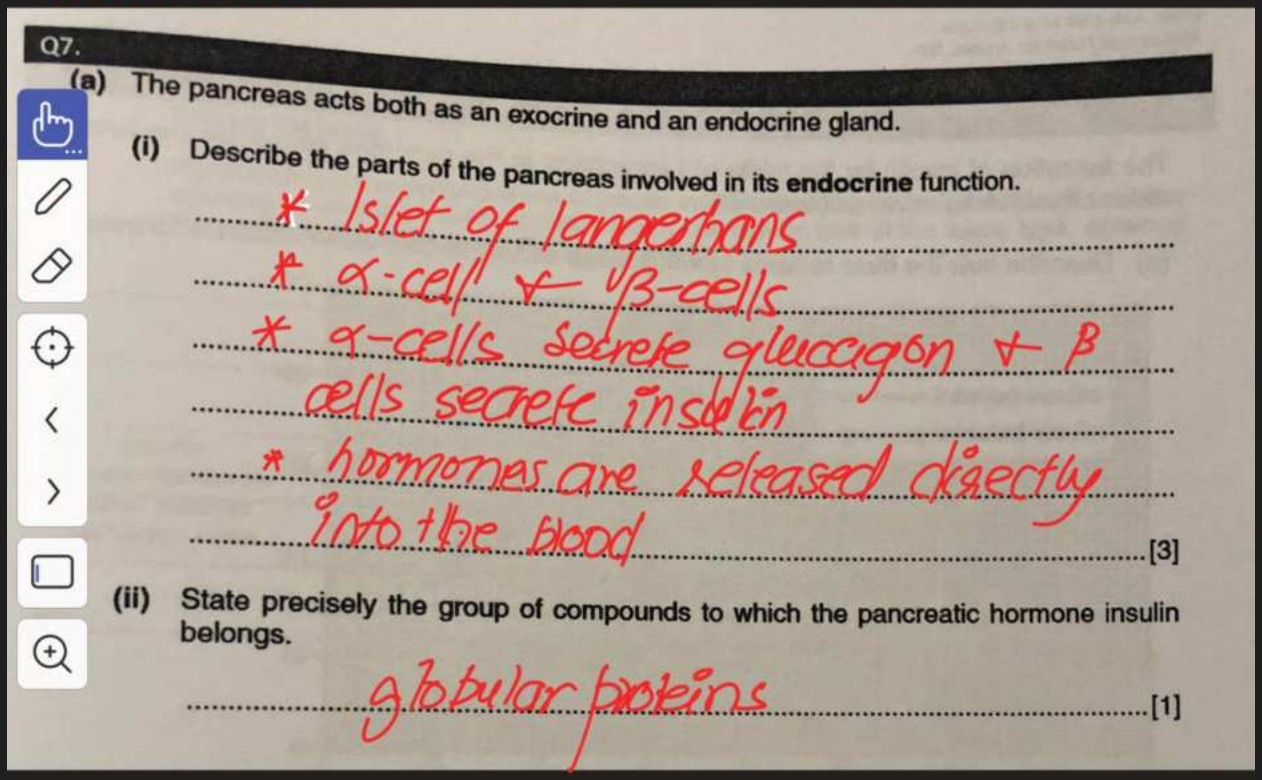
Question 3:



Q7.

(a) The pancreas acts both as an exocrine and an endocrine gland.

(i) Describe the parts of the pancreas involved in its **endocrine** function.

* Islet of langerhans
* α-cell & β-cells
* α-cells secrete glucagon & β cells secrete insulin
* hormones are released directly into the blood

[3]

(ii) State precisely the group of compounds to which the pancreatic hormone insulin belongs.

globular proteins

[1]

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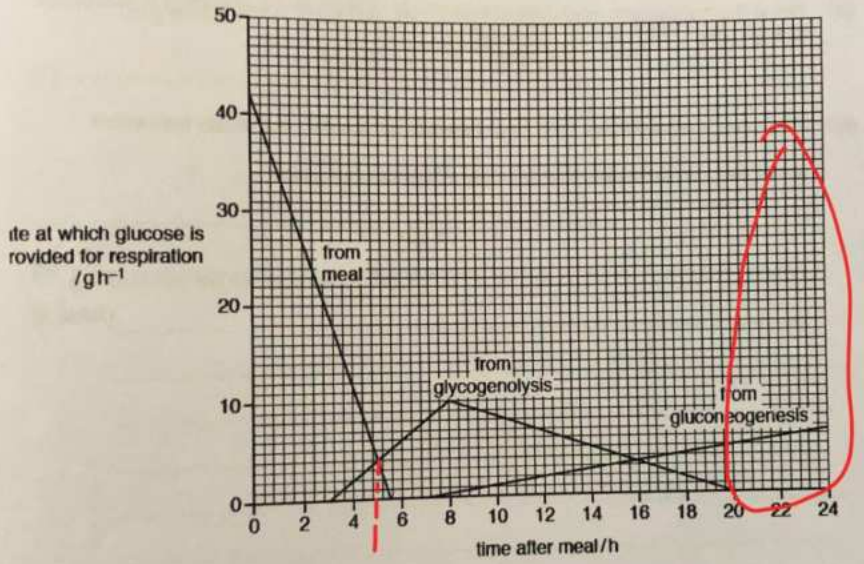
Question 4:

(b) An investigation was carried out to measure the rate at which glucose is provided for respiration from three different sources of glucose:

- a meal
- glycogenolysis – the breakdown of glycogen
- gluconeogenesis – production of glucose from non-carbohydrate molecules.

After a person ate a meal, the rates at which glucose was provided for respiration from the three different sources were measured at regular intervals over a 24-hour period. During this period, no food was eaten.

Fig. 2.1 shows the results of this investigation.



(i) State the time after the meal when the rate at which glucose was provided from the meal for respiration was the same as the rate at which glucose was provided from glycogenolysis for respiration.

5 hrs ..... [1]

(ii) State the first time after the meal when **all** of the glucose for respiration was provided by gluconeogenesis.

20 hrs ..... [1]

(iii) Name the homeostatic mechanism by which blood glucose concentration is maintained at a set point.

negative feedback ..... [1]

(iv) In humans, carbohydrates such as glucose are not the only respiratory substrates.

Name **two** non-carbohydrate respiratory substrates in humans.

* amino acids * fatty acids

..... [2]

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Questions:

Q5.

Figs 3.1 and 3.2 show the concentration of glucose and insulin in blood plasma before and after a glucose drink.

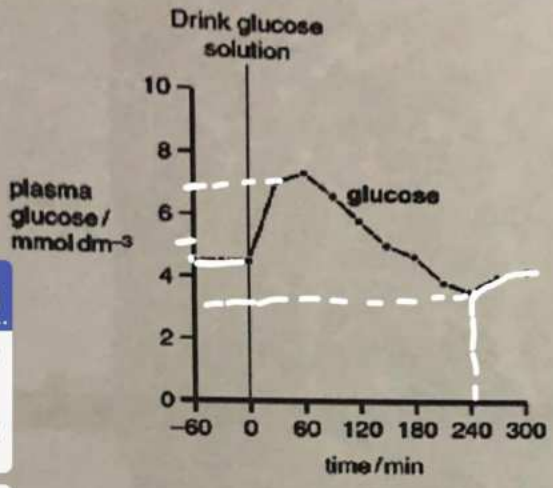

Fig. 3.1

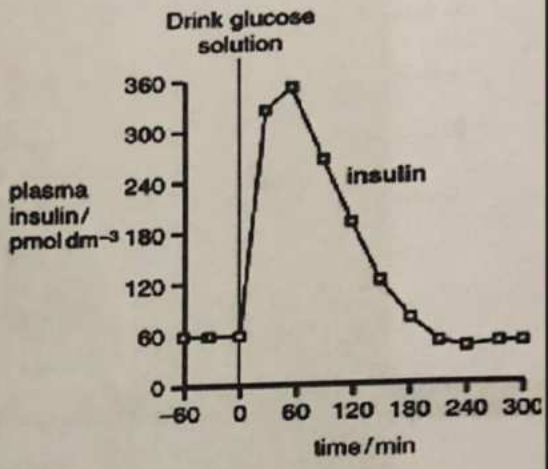

Fig. 3.2

(a) With reference to Fig. 3.1, describe the changes in blood glucose concentration after the glucose drink.

* steep rise in glucose conc. from 4.5 to 7 mmol dm⁻³
* gradual decrease in plasma glucose till it falls below set point
* increases to baseline after 240 min [3]

(b) With reference to Fig. 3.1 and Fig. 3.2, explain how the changes in blood glucose cause:

(i) an increase in the concentration of insulin in the plasma;

* β-cells in the islet of Langerhans stimulated to release insulin due to high plasma glucose [2]

(ii) a subsequent fall in the concentration of insulin in the plasma.

* blood glucose level is restored to normal / set point which decreases the release of insulin * insulin broken down [2]

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Question 6:

Q3.

Fig. 2.1 is a light micrograph of a small part of the pancreas.

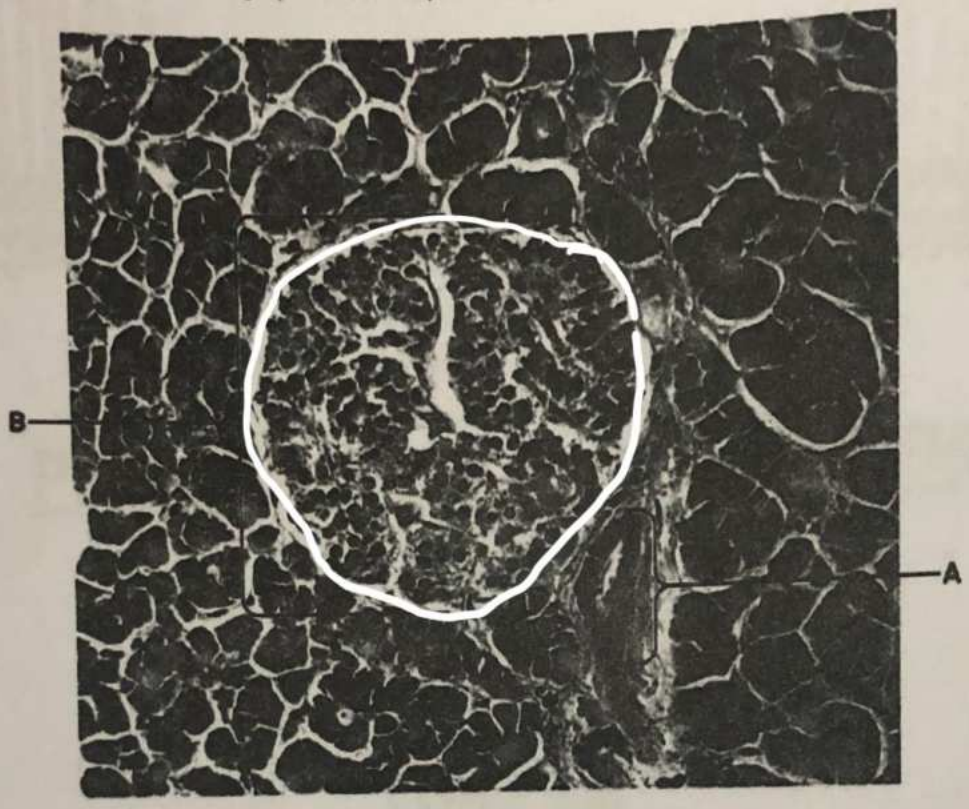

Fig. 2.1

(a) Name structures A and B.

B Islet of Langerhan

A pancreatic duct [2]

(b) With reference to Fig. 2.1, explain why the pancreas is an *endocrine gland*.

* Islet of Langerhans produces and releases the hormones insulin / glucagon
* hormones released into blood [2]

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c) Insulin and glucagon are involved in the control of blood glucose concentration. When blood glucose concentration rises, secretion of insulin increases.

Outline two ways in which insulin affects the activity of cells in the liver.

1. increase in membrane permeability to glucose

2. increase in the rate of glycogenesis

[2]

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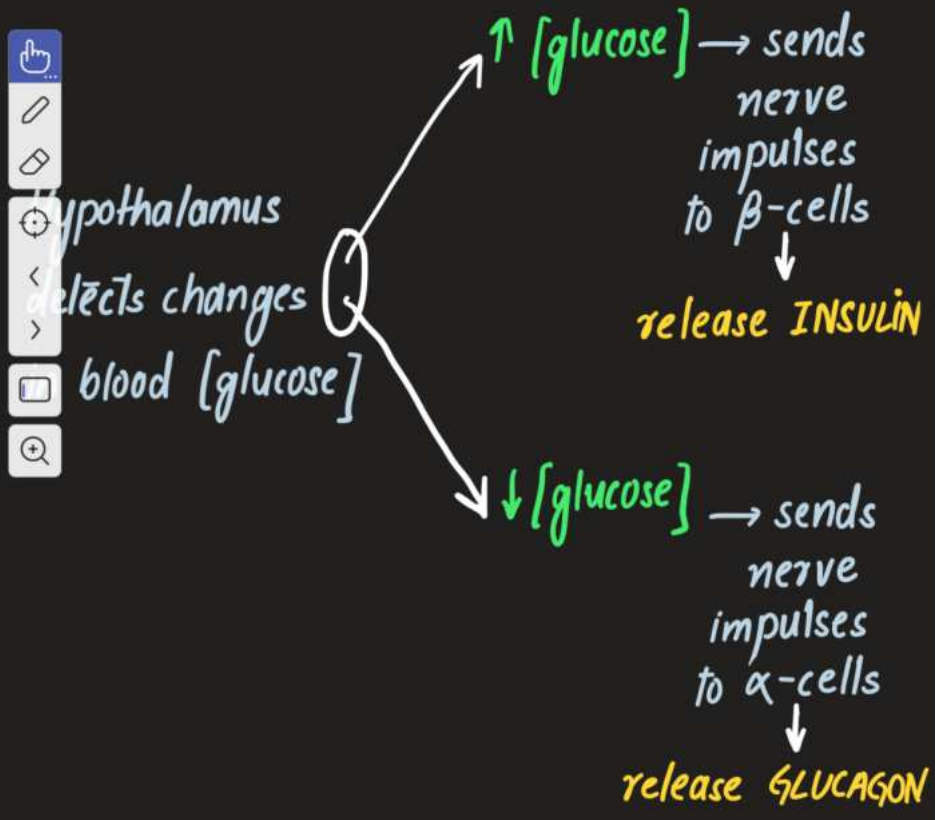
Homeostasis

Nervous control of blood glucose



With
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ADVANCED LEVEL BIOLOGY 9700

UNIT 14: Homeostasis

Learning Objectives:

- Summary of hormonal & nervous control of blood glucose
- Similarities & differences between insulin & glucagon
- Diabetes Mellitus
- Urine Analysis

Video Lecture 10 Slides

Mohammad Hussham Arshad, MD
Biology Department

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Previously:

* Structure of pancreas
* Endocrine and exocrine pancreas
* Endocrine pancreas → Islet of Langerhans
* Control of blood glucose via negative feedback
* Role of insulin and glucagon

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Summary of hormonal control of blood glucose

Regulation of blood glucose is achieved via negative feedback effect.

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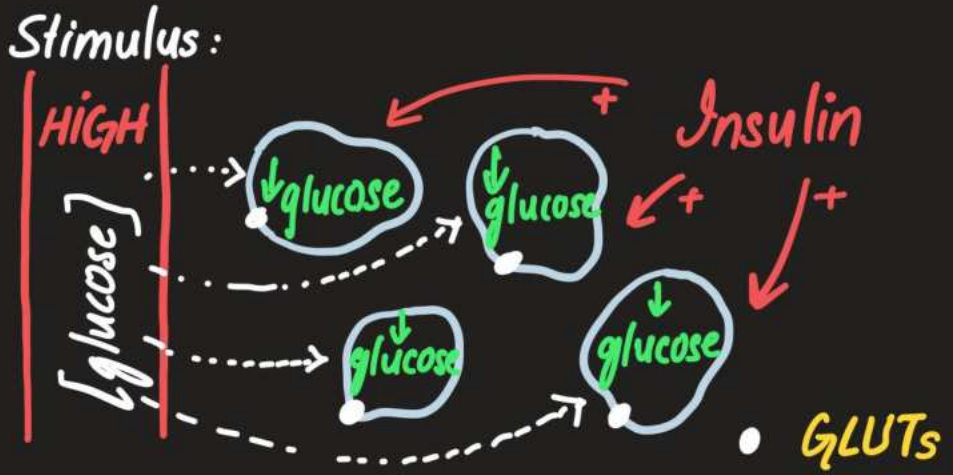
* Effects of insulin:



* Insulin lowers intracellular glucose to allow glucose to move from blood to the target cells ⟹ thus restoring plasma [glucose]

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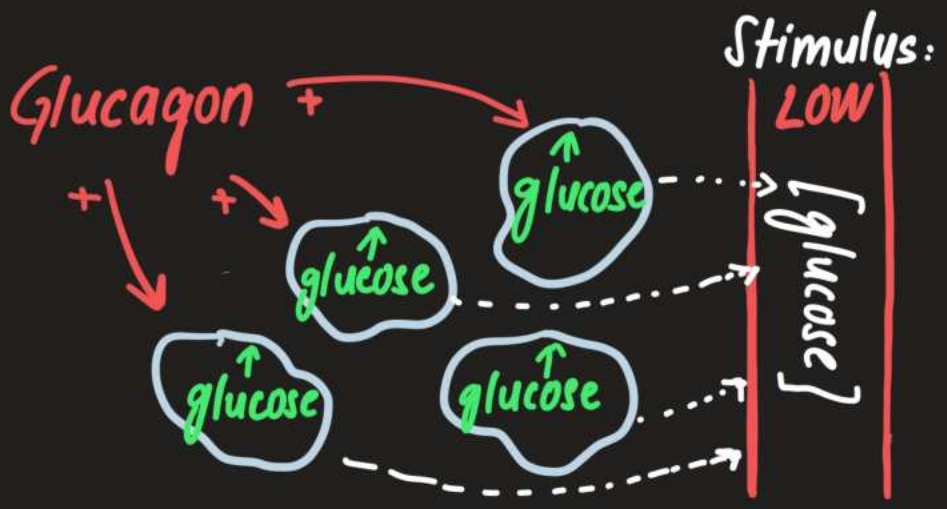
* Effects of glucagon :



* Glucagon raises intracellular glucose To allow glucose To move from target cells into the blood ⟹ thus restoring plasma [glucose]

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Q: Compare and contrast the structure and functions of insulin and glucagon.

SIMILARITIES:

1. Peptide hormones released by Islet of Langerhans.
2. Receptors on cell surface membrane.
3. Receptors work via second messenger

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DIFFERENCES :

INSULIN	GLUCAGON
① Released by β-cells due to hyperglycaemia	① Released by α-cells due to hypoglycaemia
② Target tissues → liver, skeletal muscle, adipose	② Target tissue → liver
③ Promotes glycolysis and glycogenesis	③ Promotes gluconeogenesis & glycogenolysis
④ Promotes protein synthesis and lipogenesis	④ Promotes protein breakdown and lipolysis.
⑤ Anabolic hormone	⑤ Catabolic hormone

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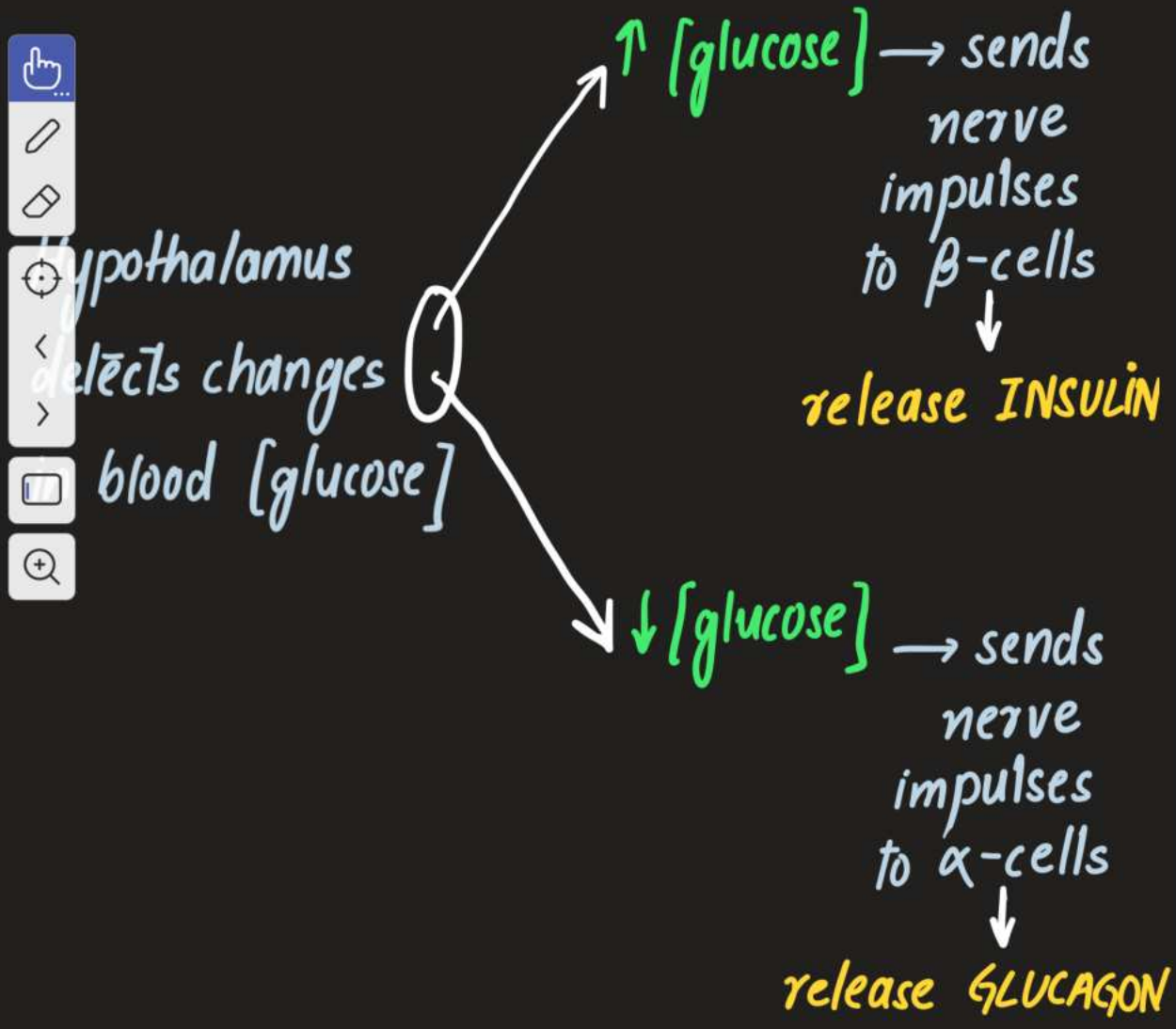
Nervous control of blood glucose



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Diabetes Mellitus

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DIABETES MELLITUS (DM)

* Diabetes Mellitus is a disease characterised by high blood glucose levels.

* There are two Types of DM:

① Type I Diabetes Mellitus

② Type II Diabetes Mellitus

* Type I DM results due to autoimmune destruction of β-cells.

=> decreased insulin production

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* Type II DM results due to INCREASED insulin resistance. It's more common in obese individuals with a family history of the disease.

* Management :

(A) Type I → Insulin
- subcutaneous injections
- intravenous injection
- nasal spray

(B) Type II
- Diet control
- Excercise
- Medications
- Insulin

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* Signs and symptoms:

- excessive frequency of urination (polyuria). WHY?

Due to excretion of glucose in urine as it takes water along with it.

- excessive thirst (polydipsia). WHY?

Excessive production of urine.

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- excessive hunger (polyphagia) WHY?

Glucose cannot enter the cells in diabetes mellitus (insulin increases glucose uptake in cells). This reduces the aerobic respiration of glucose decreasing the rate of formation of ATP. The reduced energy production leads to polyphagia.

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- weight loss. WHY?
  - → There is ↓ uptake of glucose
  - → Breakdown of fat
  - → Loss in body mass.
- Long-Term complications:
  - → diabetic retinopathy
  - → diabetic nephropathy
  - → diabetic neuropathy
  - → diabetic vascular disease

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Urine Analysis

↓

Urine DR

detailed report

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URINE ANALYSIS

* Urine analysis refers to the detection of certain chemical substances that may be present in urine.

* Given below are the features of a normal urine sample:

i) Urine is usually transparent.

ii) Urea levels in a sample of urine are usually high.

iii) Sodium ions, chloride ions, potassium ions and bicarbonate ions are usually

excreted in minimal amounts in urine.

iv) A normal urine sample contains no proteins, glucose, ketones, RBCs, WBCs or bacteria.

An abnormal urine sample may contain the following chemical substances:

a) Glucose:

* Excretion of glucose in urine is referred to as glucosuria.

* Glucosuria occurs when the plasma glucose level exceeds the renal threshold for glucose.

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* High blood plasma glucose levels are usually found in individuals who have diabetes mellitus.

b) Ketones

* Excretion of ketones in urine is referred to as ketonuria.
* Ketonuria occurs in individuals who have diabetes mellitus.
* Glucose uptake into cells reduces in people who have diabetes because insulin is required for the entry of glucose into the cells.

*This decreases the availability of glucose within the cells for respiration.

* Cells, therefore break down fats which leads to production of ketone bodies.

c) Proteins

*Excretion of proteins in the urine is referred to as proteinuria.

* Proteins that are larger in size than 68kDa do not get filtered through the filtration barrier. Smaller proteins that are filtered are taken up via

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endocytosis by the PCT cells.

* Presence of protein in urine may imply a physiological response to:

i) High intensity exercise
ii) Pregnancy
iii) High fever

Or it may indicate kidney damage secondary to the following disease conditions:

i) Diabetes Mellitus
ii) Hypertension
iii) Glomerular Damage
iv) Nephrotic Damage

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d) RBCs

* Presence of RBCs in urine is termed as Haematuria.
* Haematuria may be classified as microscopic (not visible To the naked eye) or macroscopic (visible to the naked eye)
* RBCs usually don't cross the filtration barrier, therefore, presence of RBCs in urine usually signifies a disease condition

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* Presence of RBCs in urine may occur due to :

i) Kidney damage, for example, in cases of Kidney Stones, Nephritic syndrome, Renal Carcinoma or Trauma.

ii) Damage to the ureters, such as, Uretic Cancer.

iii) Bladder, for example, in case of Bladder Cancer

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c) WBCs and Bacteria

* Presence of WBCs in urine may imply infection or inflammation.

* Presence of bacteria in urine signifies infection.

* Usually if a urine sample has bacteria, a urine culture is done to identify the bacteria so that an appropriate antibiotic could be given.

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Homeostasis

Applications of immobilized enzymes

* Immobilized enzymes are frequently used in medicine for diagnostic purposes. One application of the immobilized enzymes to delect glucose concentration in:

i) Urine — using the Urine Dipstick
ii) Blood plasma — using Glucose Biosensor

With
Mohammad Hussham Arshad, MD

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ADVANCED LEVEL BIOLOGY 9700
UNIT 14: Homeostasis

Learning Objectives:

- Applications of immobilised enzymes
- Urine dipstick
- Glucose biosensors

Video Lecture 11 Slides

Mohammad Hussham Arshad, MD
Biology Department

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Earlier

* Pancreas → structure
* Insulin, glucagon and control of blood glucose
* Diabetes Mellitus → Type I / Type II
* Urine Analysis

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Applications of immobilized enzymes

* Immobilized enzymes are frequently used in medicine for diagnostic purposes. One application of the immobilized enzymes To delect glucose concentration in:

i) Urine — using the Urine Dipstick
ii) Blood plasma — using Glucose Biosensor

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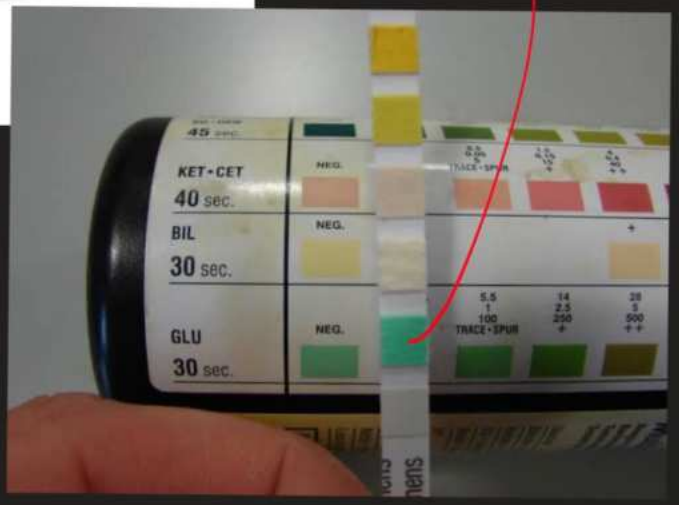
Urine dipstick

* Urine dipstick may be used to analyse a sample of urine for various substances, such as glucose, proteins, ketones and pH.

*cellulose

- glucose oxidase
- peroxidase
- AH_2 (chromogen) ← reduced



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* Each substance is detected through a different pad on the dipstick.

* The pad that is used for detection of glucose is made up of cellulose and contains the following immobilised enzymes:

i) Glucose oxidase

ii) Peroxidase

* The cellulose pad also contains a colourless reduced chromogen (AH_2), which changes colour when it gets oxidised.

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* The cellulose pad is coated with a layer of cellulose acetate which serves the following functions:

a) it prevents the immobilized enzymes and the reduced chromogen from leaking through the pad.

b) it only allows glucose molecules to pass through so that other substances, such as proteins present inside the urine does not interfere with the results.

* A urine sample is taken and the dipstick is inserted into the sample.

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* Following reactions take place with the dipstick if glucose is present in the urine:

$$\text{Glucose} + O_2 \xrightarrow{\text{glucose oxidase}} \text{Gluconic acid} + H_2O_2$$

$$H_2O_2 + AH_2 \xrightarrow{\text{peroxidase}} A + H_2O$$

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* In the first reaction, glucose gets oxidised in the presence of the enzyme glucose oxidase to produce gluconic acid and H_2O_2.

* In the second reaction, H_2O_2 oxidizes reduced chromagen to produce a coloured oxidised chromagen in the presence of enzyme peroxidase.

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* The intensity of the colour produced is proportional to the concentration of glucose present in urine.

Advantages of urine dipstick

- Easy to use and safe
- Produces rapid results
- It can be used on individuals who have needle phobia.
- It is relatively inexpensive.

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Disadvantages of urine dipstick

- It measures the glucose concentration in the urine and will therefore give a positive test only when plasma glucose concentration exceeds the renal threshold.
- The results are not very accurate.
- The urine dipstick is discarded after use and therefore cannot be re-used.
- The estimation of glucose concentration is made through colour standards that are given which make it difficult at times to determine the accurate [glucose].

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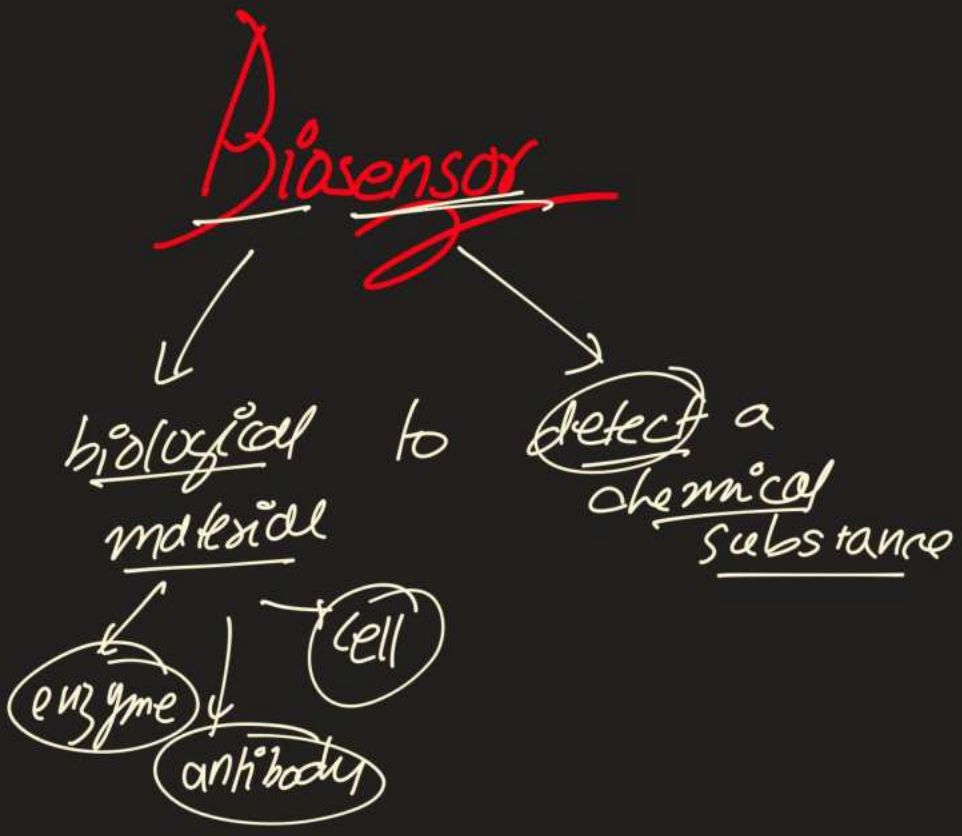
Biosensor
biological material
to
detect a chemical substance
enzyme
cell
antibody

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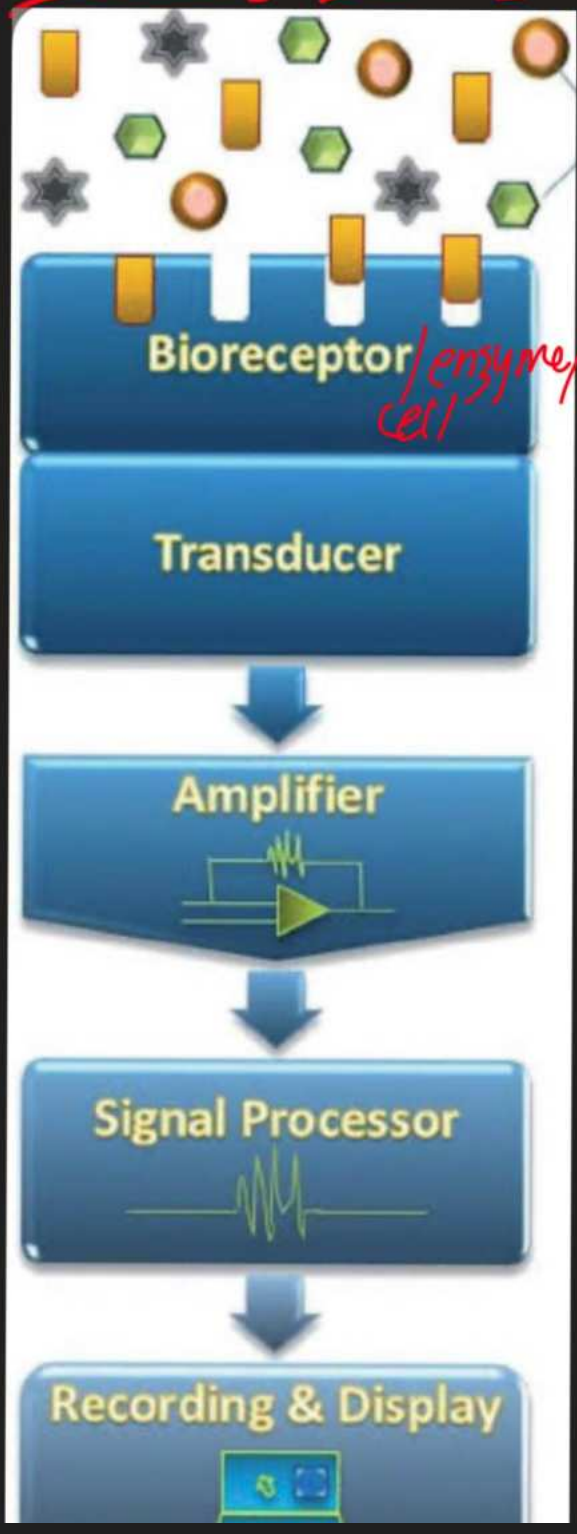
Biosensor - mechanism



chemical reaction produces a chemical change

(enzyme/cell)

transducer

electrical signal

amplifier

amplification

digital display

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BIOSENSORS

* Biosensors are electronic monitoring devices which make use of a biological material, such as a cell, an antibody or an enzyme to detect a chemical substance.
* A biosensor works through the following mechanism:

A chemical reaction takes place between the biological material and the chemical substance being detected, which produces a chemical change

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ii) The chemical change is transduced via a transducer to produce a small electrical signal. The electrical signal produced is proportional to the concentration of the chemical substance being delected.

iii) The electrical signal is then amplified using an amplifier.

iv) The amplifier signal is then used to produce a digital output

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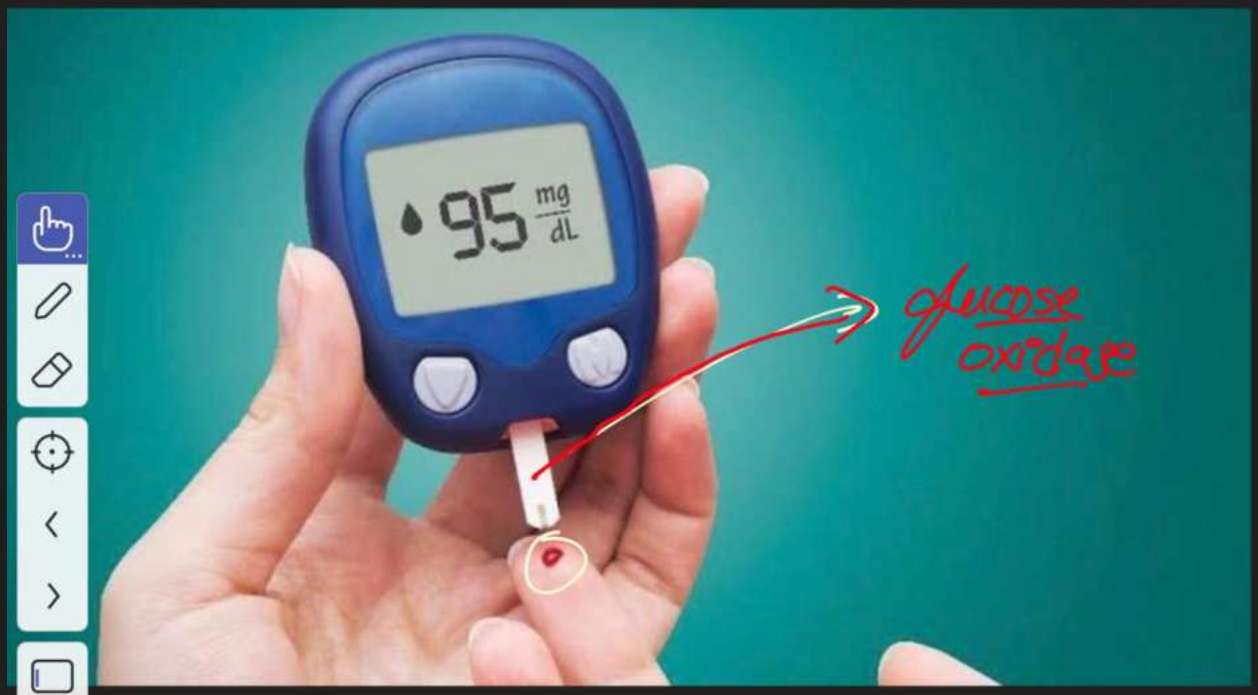
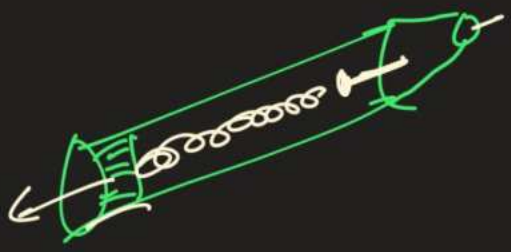
Glucose Biosensor





glucose + O_2 ⟶ gluconic acid + H_2O_2

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GLUCOSE BIOSENSOR:

- A glucose biosensor is an analytical device that is used for measuring plasma glucose concentration.
- The glucose biosensor works in the following way:

i) It contains a layer of immobilized enzyme, known as **glucose oxidase**

ii) The enzyme glucose oxidase binds with glucose in the presence of oxygen To produce gluconic acid and H_2O_2.

iii) This reaction, therefore, produces a drop in oxygen concentration dissolved within the plasma.

iv) This drop in oxygen concentration is measured by platinum electrodes which transduce this chemical change to produce an electrical signal.

v) The size of the electrical signal is proportional to the concentration of glucose in the blood.

vi) The electrical signal is then amplified to give a digital readout for [glucose].

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Advantages of Glucose biosensor

i) Glucose biosensors are very specific for detecting glucose, which implies that they can detect glucose within a complex mixture of substances.

ii) Glucose biosensors are very sensitive which signifies that only a small sample of blood is required to detect the glucose concentration as the blood plasma. It also implies that glucose biosensors can detect a very low [glucose] in blood.

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iii) Glucose biosensors produce a rapid response.

iv) Glucose biosensors are safe to use.

v) Glucose biosensors produce very accurate results.

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Disadvantages of glucose biosensor

i) Glucose biosensors cannot be used on people who have needle phobia.

ii) The electronic device is not sterilizable

iii) The electronic device is not very robust and can produce incorrect reading of glucose concentration if device malfunctions.

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7 (a) Some people have a condition called diabetes. In type 1 diabetes the pancreas does not produce enough insulin.

Fig. 7.1 shows the blood glucose concentrations of a type 1 diabetic person and a non-diabetic person, at regular intervals after drinking a glucose drink.

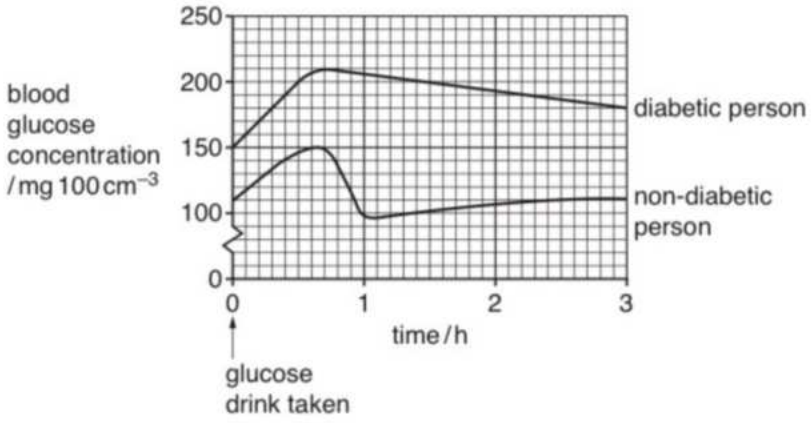

Fig. 7.1

(i) Describe the results shown in Fig. 7.1.

* [glucose] increases in both individuals after glucose drink
* the peak [glucose] is higher in diabetic than non-diabetic
* [glucose] falls slowly in diabetic

[3]

(ii) Name the location of the receptors in a non-diabetic person that detect a change in blood glucose concentration.

islet of Langerhans / β-cells [1]

(iii) Name the homeostatic mechanism by which blood glucose concentration is maintained.

negative feedback [1]

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(b) The urine of a non-diabetic person does not contain glucose. A person with type 1 diabetes will excrete glucose in urine.

A reading of the concentration of glucose in the urine can be estimated using a dipstick.

Fig. 7.2 outlines how a dipstick works.

glucose in urine —(enzyme **A**)→ gluconic acid + hydrogen peroxide

hydrogen peroxide + colourless chromogen —(enzyme **B**)→ water + coloured chromogen

Fig. 7.2

The higher the concentration of glucose in the urine, the darker the colour on the dipstick.

(i) Name enzymes **A** and **B**.

A glucose oxidase

B peroxidase

[2]

(ii) An electronic biosensor can be used to measure the glucose concentration in a drop of blood.

Suggest **one** advantage of using a biosensor and **one** advantage of using a dipstick to measure glucose concentration.

biosensor rapid

dipstick non-invasive / cheap

[2]

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(c) Describe the role played by insulin in the control of blood glucose concentration.

.....

.....

.....

.....

.....

.....

.....

.....

.....

..... [5]

[Total: 14]

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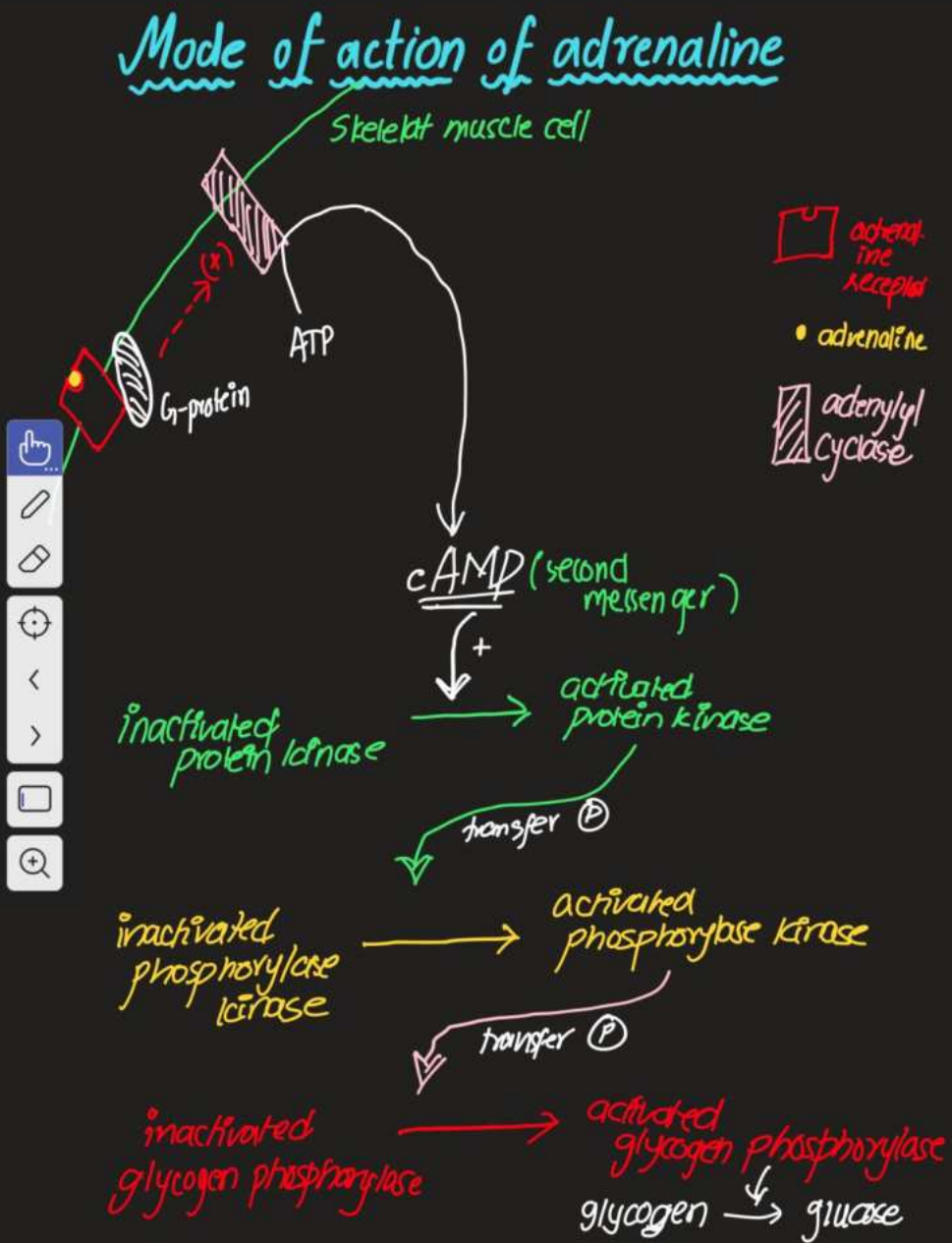
Homeostasis



With
Mohammad Hussham Arshad, MD

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ADVANCED LEVEL BIOLOGY 9700
UNIT 14: Homeostasis

Learning Objectives:

- Adrenaline, glucagon and their second messengers
- role of cAMP
- first messengers and second messengers

Video Lecture 12 Slides

Mohammad Hussham Arshad, MD
Biology Department

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Earlier

* Pancreas → structure
* Insulin, glucagon and control of blood glucose
* Diabetes Mellitus → Type I / Type II
* Urine Analysis
* Applications of immobilised enzymes;
  - Urine dipstick
  - Biosensors

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skeletal muscle cells

liver cells

liver cells

Adrenaline, glucagon and their second messenger

Adrenaline & Glucagon

(+) glycogen phosphorylase

glycogenolysis

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Adrenaline

* Adrenaline is a peptide hormone which is produced by the adrenal gland.
* It serves to increase the basal metabolic rate within the body.
* Adrenaline promotes the process of glycogenolysis in both the liver cells and the skeletal muscle cells, unlike glucagon which only acts on the liver cells.

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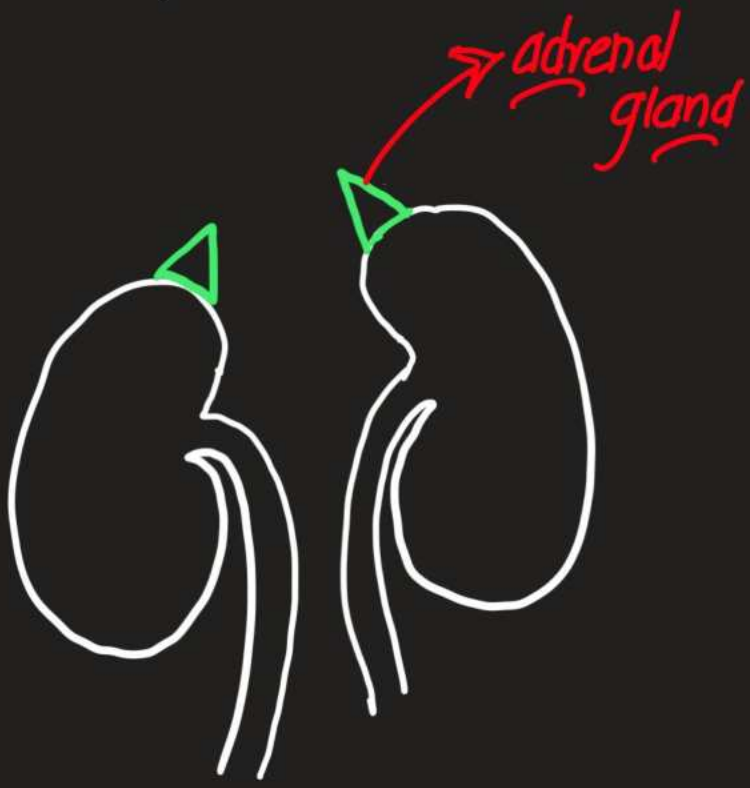
* Being a hydrophilic molecule it sends its message within the cell through second messenger.



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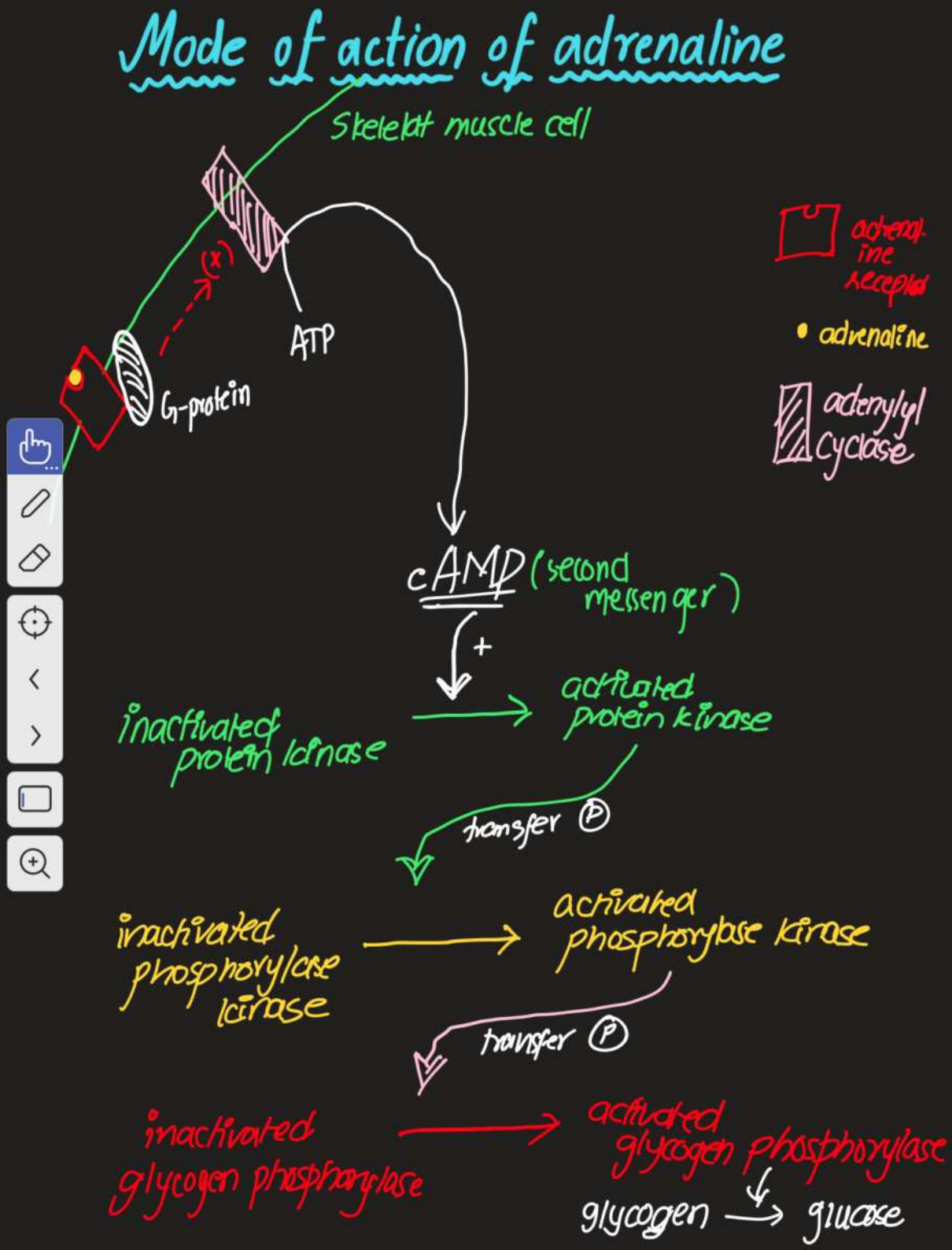
Mode of action of adrenaline
Skeletal muscle cell
(x)
ATP
G-protein
adrenergic receptor
adrenaline
adenylyl cyclase
cAMP (second messenger)
+
inactivated protein kinase
activated protein kinase
transfer P
inactivated phosphorylase kinase
activated phosphorylase kinase
transfer P
inactivated glycogen phosphorylase
activated glycogen phosphorylase
glycogen → glucose

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Mode of action of adrenaline

* Adrenaline binds to its receptors on the target cell's cell surface membrane which leads to activation of a protein termed as the G-protein.

* Activated G-protein binds to an enzyme on the cell surface membrane known as Adenylyl Cyclase, thereby, activating it.

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* The enzyme Adenylyl Cyclase is responsible for converting ATP to cyclic AMP.

* Cyclic AMP binds and activates a protein kinase.

* The activated protein kinase phosphorylates an inactivated phosphorylase kinase enzyme, thereby, activating it.

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* The activated phosphorylase kinase enzyme again transfers a phosphate group to the enzyme glycogen phosphorylase to activate it.

* Glycogen phosphorylase is responsible for catalyzing the breakdown of glycogen to produce glucose.

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* Small amounts of the hormone adrenaline are able to stimulate large copies of the enzyme Adenylate Cyclase which in turn produces large numbers of the molecule cyclic AMP.

* These cyclic AMP molecules which serve as second messengers are able to activate large number of the enzyme protein kinases, which thereby activates numerous phosphorylase kinase enzymes.

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*This phenomenon where a small amount of the initial hormone produces an amplified response within the cell is known as 'Cascade effect' { sequence of events triggered by the activation of the G-protein }

The hormone glucagon produces its intracellular effects through a similar second messenger system as adrenaline but has a different receptor on the cell surface membrane.

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Therefore the mechanism of action of adrenaline can be summarized as:

1) Adrenaline binds to its receptors on the cell surface membrane of the target cells.

2) This leads to the formation of cyclic AMP which binds to protein kinases, thereby, activating them.

3) Activation of protein kinases produces an enzyme cascade involving activation of enzymes by phosphorylation to amplify the signal.

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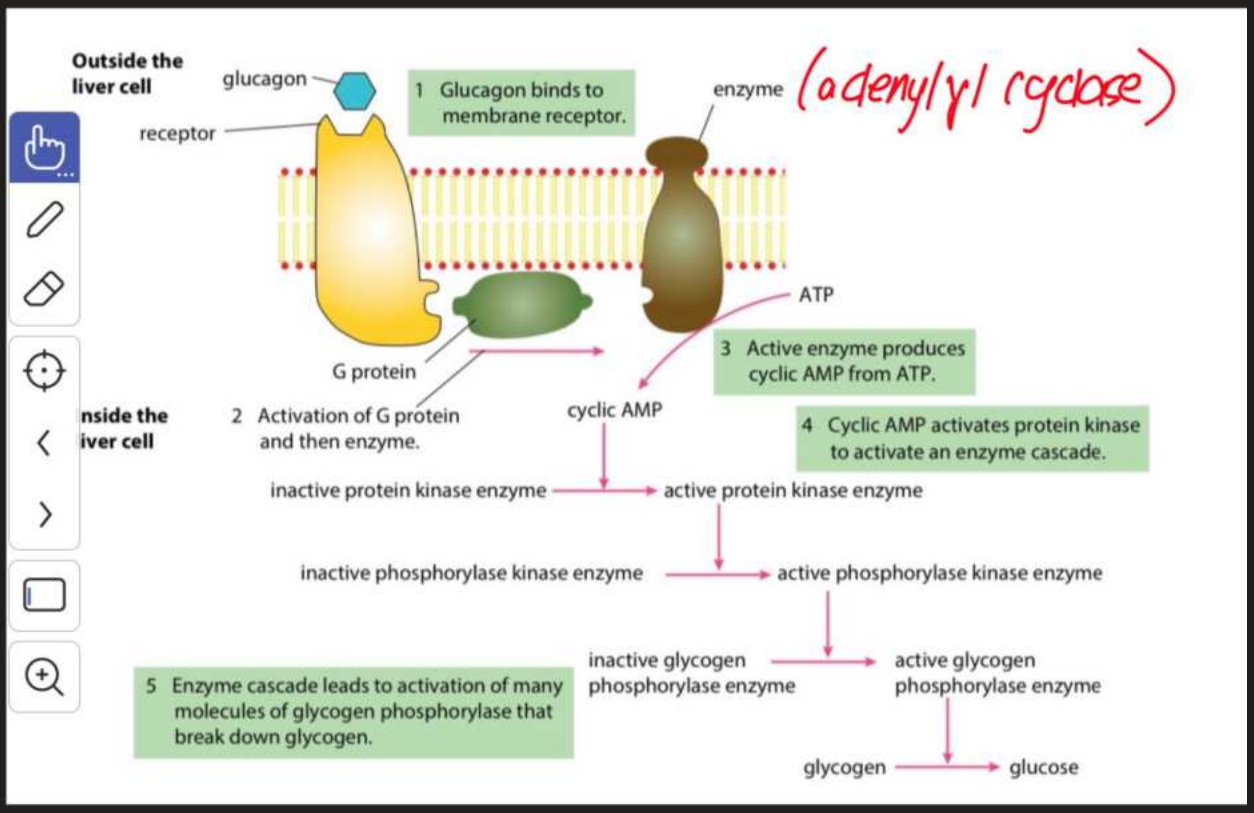
Outside the liver cell
glucagon
receptor
1 Glucagon binds to membrane receptor.
enzyme
(adenylyl cyclase)
ATP
3 Active enzyme produces cyclic AMP from ATP.
G protein
2 Activation of G protein and then enzyme.
cyclic AMP
4 Cyclic AMP activates protein kinase to activate an enzyme cascade.
inactive protein kinase enzyme
active protein kinase enzyme
inactive phosphorylase kinase enzyme
active phosphorylase kinase enzyme
inactive glycogen phosphorylase enzyme
active glycogen phosphorylase enzyme
5 Enzyme cascade leads to activation of many molecules of glycogen phosphorylase that break down glycogen.
glycogen
glucose

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Cyclic AMP and its role as a second messenger

* Cyclic AMP is a small non-protein water soluble molecule derived from ATP.
* The enzyme adenylate cyclase (also termed as **adenylyl cyclase**) which is present on the cell surface membrane is responsible for producing cyclic AMP from ATP.

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* Being a small polar molecule cyclic AMP can rapidly diffuse throughout the cell.
* Cyclic AMP binds to the enzyme protein kinase within the cell, thereby, activating it.
* Activated protein kinases initiate a cascade of phosphorylation steps which eventually activates the enzyme glycogen phosphorylase.

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* Glycogen phosphorylase catalyses the hydrolysis of glycogen to glucose.

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Q: Compare and contrast the role of first and second messengers within the body?

Ans: Similarity:

* Both of them are chemical messengers.
* Both of them are polar water soluble molecules.

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Differences:

First Messenger	Second Messenger
• First messengers are large protein molecules.	• Second messengers are small non-protein molecules.
• First messengers are produced extracellularly and bind to receptors on the cell surface membrane.	• Second messengers are produced within the cells and bind to enzymes activating or inhibiting them.

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First Messenger	Second Messenger
• First messengers are produced in small amounts.	• Second messengers are produced in large amounts.
• First messengers stay in the bloodstream for a longer time.	• Second messengers are rapidly broken down within the cells for e.g. cAMP is broken down by the enzyme phosphodiesterase.
* Examples of first messengers: insulin, glucagon, adrenaline, etc.	* Examples of second messengers: cAMP, Ca^{2+}, etc

Q1 : Compare and contrast between glucagon and adrenaline?

Ans:

SIMILARITIES

1) Adrenaline and glucagon are peptide hormones.
2) Their receptors are located on the cell surface membrane.
3) Adrenaline and glucagon have G- protein coupled receptors.
4) These hormones increase the rate of glycogenolysis by stimulating glycogen phosphorylase.

DIFFERENCES

1) Adrenaline binds to skeletal muscle cell and liver cell, glucagon only binds to liver cells.
2) Adrenaline is produced by adrenal glands, glucagon is produced by the alpha- cells within the islet of Langerhans.

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Q2: Describe the role of glucagon in regulating blood glucose levels ? [8 marks]

Ans : Glucagon is released by the alpha-cells of the pancreas in response to low blood glucose levels. It travels in the blood to reach its target liver cells where it binds to its receptors on the cell surface membrane. Glucagon regulates the blood glucose by :

a) stimulating glycogenolysis which involve the breakdown of glycogen to glucose . It achieves this effect by stimulating the enzyme glycogen phosphorylase .
b) stimulating the lipid breakdown to form fatty acids. Fatty acids are used in respiration to release energy in the form of ATP. This lessens the need to use glucose for respiration (glucose sparing effect).
c) stimulating gluconeogenesis which involve the formation of glucose form non-carbohydrate sources such as fatty acids , lactate and amino acids.

All these processes enable glucose to diffuse from the liver cells into the blood thereby normalising the blood glucose concentration. Glucagon also inhibits the release of the hormone insulin from the Beta- cells of the pancreas. This slows down the rate of glycolysis and glycogenesis . Glucagon regulates blood glucose via negative feedback.

Q3: Describe the role of hormone insulin in regulating blood glucose levels ? [8 marks]

Ans : Insulin is released by the beta-cells of the pancreas in response to high blood glucose levels. It travels in the blood and it binds to its receptors on the cell surface membrane of liver cells, skeletal muscle cells and adipose cells.Insulin regulates the blood glucose by :

a) increasing the permeability of the cell surface membrane to glucose. It achieves this effect by upregulation of GLUTs which allows glucose to enter the cell via facilitated diffusion.
b) stimulating glycolysis which involve the oxidation of glucose to pyruvate. Insulin achieves this effect by stimulating hexokinase and phosphofructokinase.
c) stimulating glycogenesis which involves synthesis of glycogen using glucose monomers. Insulin favours glycogenesis by stimulating the enzyme glycogen synthase.

All these processes enable glucose to diffuse from the blood into the liver cells and skeletal muscle cells thereby normalising the blood glucose concentration. Insulin also inhibits the release of the hormone glucagon from the alpha-cells of the pancreas. This slows down the rate of glycogenolysis and gluconeogenesis .Insulin regulates blood glucose via negative feedback.

Q4: Describe how an enzyme can be immobilised using alginate and discuss the advantages of using immobilised enzyme? [8 marks]

Ans: An enzyme is said to be immobilised if it's attached to an inert insoluble material. One way of achieving enzyme immobilisation is through alginate beads. The enzyme (for example lactase) is mixed with the solution of calcium alginate, the mixture is drawn into a syringe and introduced drop by drop into a beaker containing calcium chloride solution. Insoluble alginate beads are formed with the enzyme lactase entrapped within them. These beads are separated from the calcium chloride solution and rinsed with water before use. The advantages of immobilising an enzyme are ;

a) the enzyme does not contaminate the product.
b) the enzyme can be reused which saves cost.
c) the enzyme is more stable to external pH and temperature changes . This stability is due to enzymes being less exposed to external pH and temperature.
d) the reaction catalysed by immobilised enzyme have a higher yield.

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Q5: Explain how a dipstick can be used to measure glucose concentration? [8 marks]

Ans : A urine dipstick contains the enzyme glucose oxidase and peroxidase , immobilised using cellulose fibres. The dipstick is lowered into a sample of urine which contain glucose. Glucose reacts with oxygen in the presence of glucose oxidase to form gluconic acid and hydrogen peroxide.

$$\text{glucose} + O_2 \xrightarrow[\text{glucose oxidase}]{} \text{gluconic acid} + \text{hydrogen peroxide}$$

Hydrogen peroxide reacts with the reduced chromogen in the presence of peroxidase to produce a coloured compound.

$$H_2O_2 + \underset{\text{reduced chromogen}}{AH_2} \xrightarrow{\text{peroxidase}} \underset{\text{coloured}}{A} + 2H_2O$$

The intensity of the colour change produced is proportional to the concentration of glucose in urine. This colour change is compared with known colour standards to estimate the glucose concentration.

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Q6: Briefly outline how a glucose biosensor work ?

Ans : A glucose biosensor is an electronic monitoring device which detects the glucose concentration using the immobilised enzyme glucose oxidase . Glucose in blood reacts with oxygen in the presence of enzyme glucose oxidase to form gluconic acid and hydrogen peroxide. This reaction produces a chemical change in the form of drop in oxygen concentration . This chemical change is transduced into an electric signal using platinum electrodes . The intensity of the electric signal produced is directly proportional to the blood glucose concentration . The electric signal is amplified to give a digital output.

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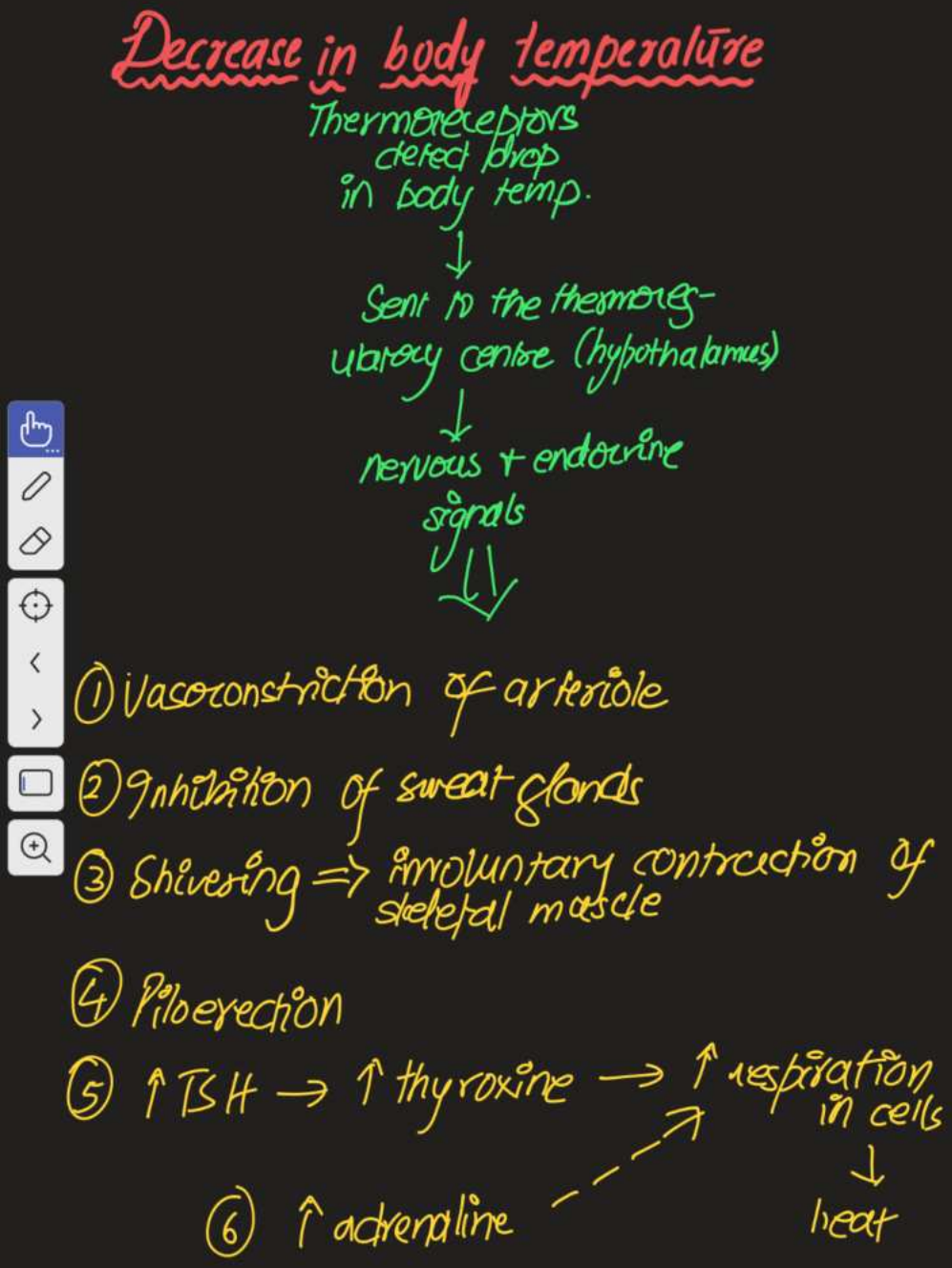
Homeostasis



With
Mohammad Hussham Arshad, MD

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ADVANCED LEVEL BIOLOGY 9700
UNIT 14: Homeostasis

Learning Objectives:

- Thermoregulation

Video Lecture 13 Slides

Mohammad Hussham Arshad, MD
Biology Department

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Earlier

* Pancreas → structure
* Insulin, glucagon and control of blood glucose
* Diabetes Mellitus → Type I / Type II
* Urine Analysis
* Applications of immobilised enzymes;
  - Urine dipstick
  - Biosensors
* Adrenaline, glucagon and their second messenger
* First and second messengers

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Thermoregulation

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Thermoregulation

* Thermoregulation refers to the active maintenance of the core body temperature through negative feedback control mechanism.
  - ⇒ deviation from the set-point
  - ⇒ detection by receptors
  - ⇒ information received by the control center
  - ⇒ endocrine + nervous coordination
  - ⇒ information sent to effectors → corrective action
* It is essential to maintain the core body temperature for optimal activity of the enzymes which are required for metabolic reactions.

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* The receptors responsible for detecting changes in skin temperature and core temperature are termed as thermoreceptors. Thermoreceptors are located within the skin and the hypothalamus.

* These thermoreceptors send signals to the thermoregulatory centre which is located in the hypothalamus. The thermoregulatory control centre coordinates the

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information coming from different thermoreceptors to initiate nervous and endocrine signals which are sent to the effectors.

* The effectors then carry out the required response to bring the body temperature back to the set point.

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Elevation in body temperature

Thermoreceptors

↓

Thermoregulatory control centre (hypothalamus)

↓

nervous & endocrine signals

(1) vasodilation of the arterioles supplying blood to the skin → ↑ blood supply to capillaries → increase heat loss through radiation & connection

(2) Stimulation of sweat glands → ↑↑ sweat → evaporation from the skin surface → remove latent heat of vaporisation

(3) pilorelaxation

(4) ↓ the secretion of
- ↓ TSH → ↓ thyroxine
- → Adrenaline
- ↓

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Elevation in body temperature

* When the body temperature elevates above the set point, the thermoreceptors in the skin and the hypothalamus send signals to the thermoregulatory centre within the hypothalamus.

* The thermoregulatory centre co-ordinates the information received to produce the following changes;

HEUSER

a) It causes vasodilation of the arterioles supplying blood to the skin which promotes heat loss via radiation and convection currents.

b) It stimulates the sweat gland to increase the production of sweat. Evaporation of sweat from the skin surface serves to remove heat from the body.

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c) It causes pilorelaxation which refers to relaxation of arrector muscles. This causes flattening of the hair/fur, which therefore, thins the layer of air that acts as an insulator above the skin surface.

d) It causes the anterior pituitary gland to decrease secretion of the hormone TSH (Thyroid Stimulating Hormone)

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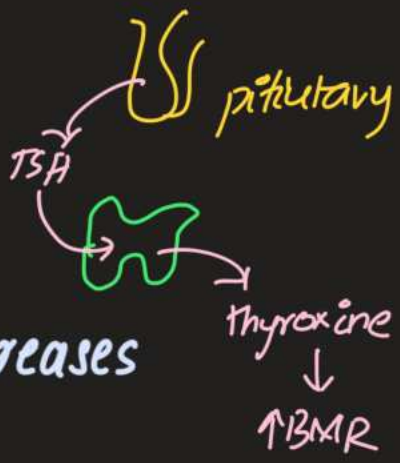

which, therefore, decreases the production of thyroxine causing a decrease in Basal Metabolic Rate (BMR)

e) It causes reduction in the levels of adrenaline in the blood which also serves to reduce the BMR.

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Decrease in body temperature

Thermoreceptors detect drop in body temp.

↓

Sent to the thermoregulatory centre (hypothalamus)

↓

nervous + endocrine signals

1. Vasoconstriction of arteriole
2. Inhibition of sweat glands
3. Shivering => involuntary contraction of skeletal muscle
4. Piloerection
5. ↑ TSH → ↑ thyroxine → ↑ respiration in cells → heat
6. ↑ adrenaline → ↑ respiration in cells → heat

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Decrease in body temperature

* When the body temperature drops below the set point, the thermoreceptors in the skin and the hypothalamus send signals to the thermoregulatory centre within the hypothalamus.

* The thermoregulatory centre co-ordinate the information received to produce the following changes;

HEUSER

a) It causes vasoconstriction of the arteriole. supplying blood to the skin which minimises heat loss via radiation and convection currents.

b) It inhibits the sweat gland which decrease the production of sweat.

c) Causes involuntary contraction of the skeletal muscles which produces heat that can be distributed throughout the body.

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d) It causes piloerection which results due to the contraction of arrector muscles. This causes the hair/fur to rise thereby trapping a layer of air that serves as a good insulator.

e) Increase in the secretion of TSH and hence thyroxine which increases BMR.

f) Increased production of adrenaline from adrenal glands → increases BMR (by increasing the rate of respiration).

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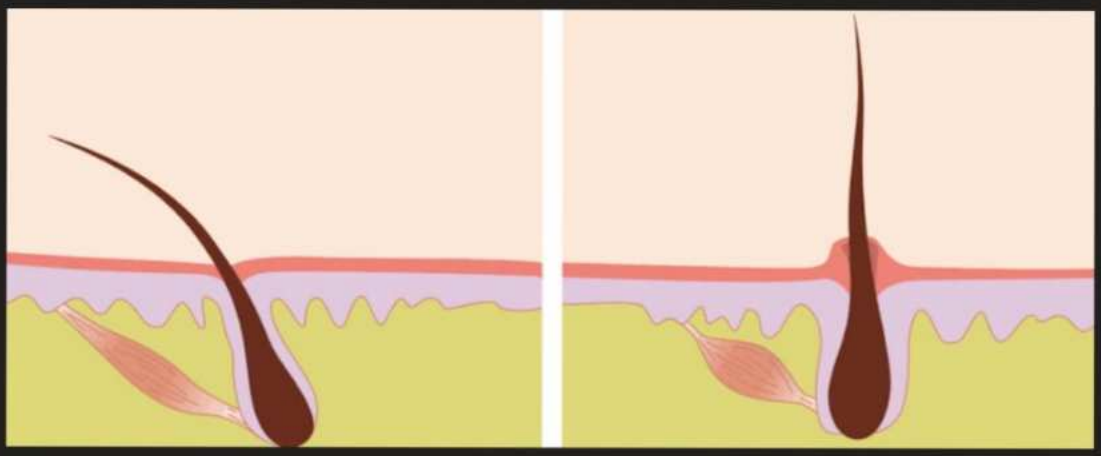

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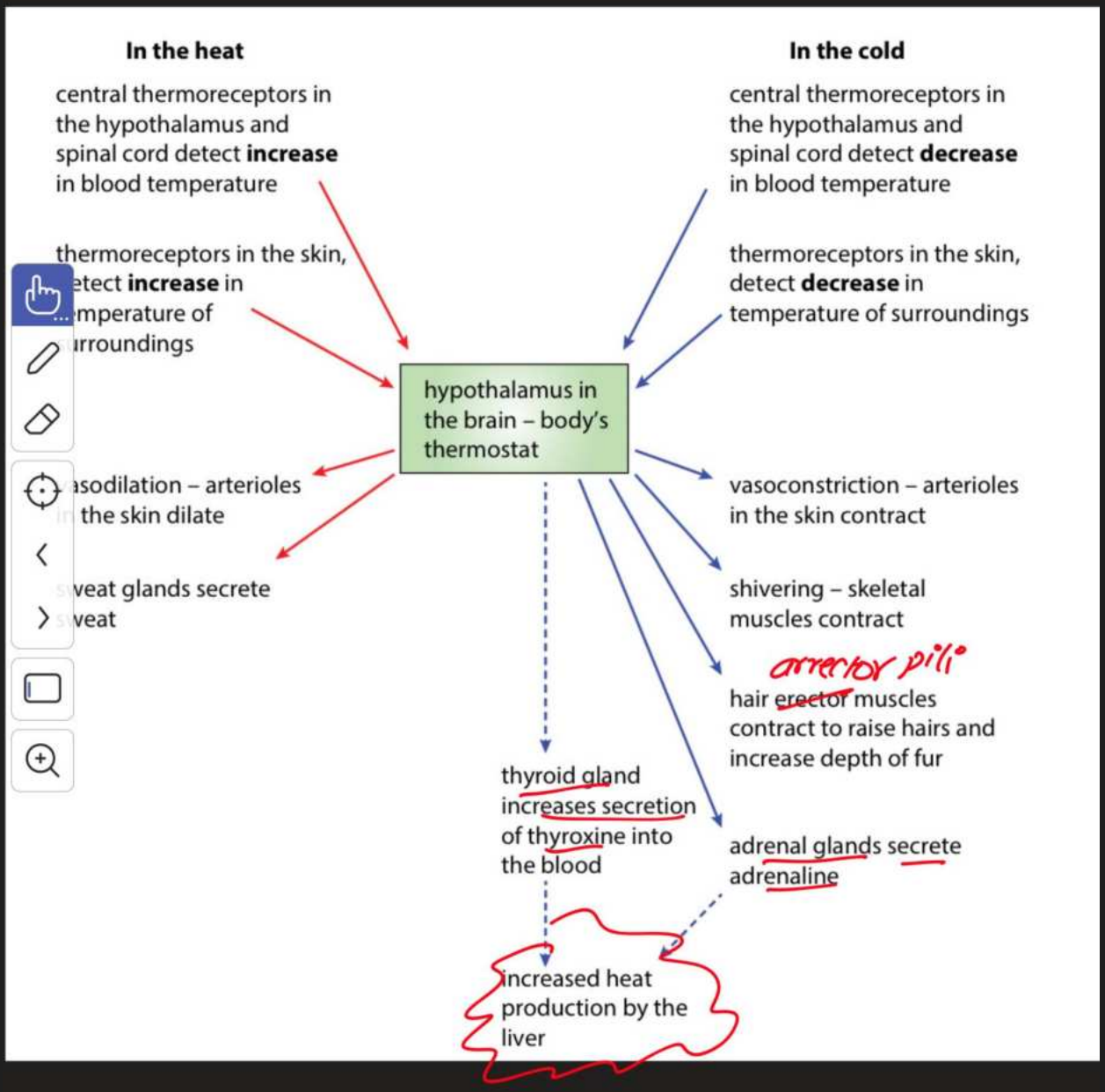
In the heat
central thermoreceptors in the hypothalamus and spinal cord detect **increase** in blood temperature
thermoreceptors in the skin, etect **increase** in mperature of rroundings
hypothalamus in the brain – body's thermostat
asodilation – arterioles the skin dilate
veat glands secrete veat
In the cold
central thermoreceptors in the hypothalamus and spinal cord detect **decrease** in blood temperature
thermoreceptors in the skin, detect **decrease** in temperature of surroundings
vasoconstriction – arterioles in the skin contract
shivering – skeletal muscles contract
arrector pili
hair erector muscles contract to raise hairs and increase depth of fur
thyroid gland increases secretion of thyroxine into the blood
adrenal glands secrete adrenaline
increased heat production by the liver

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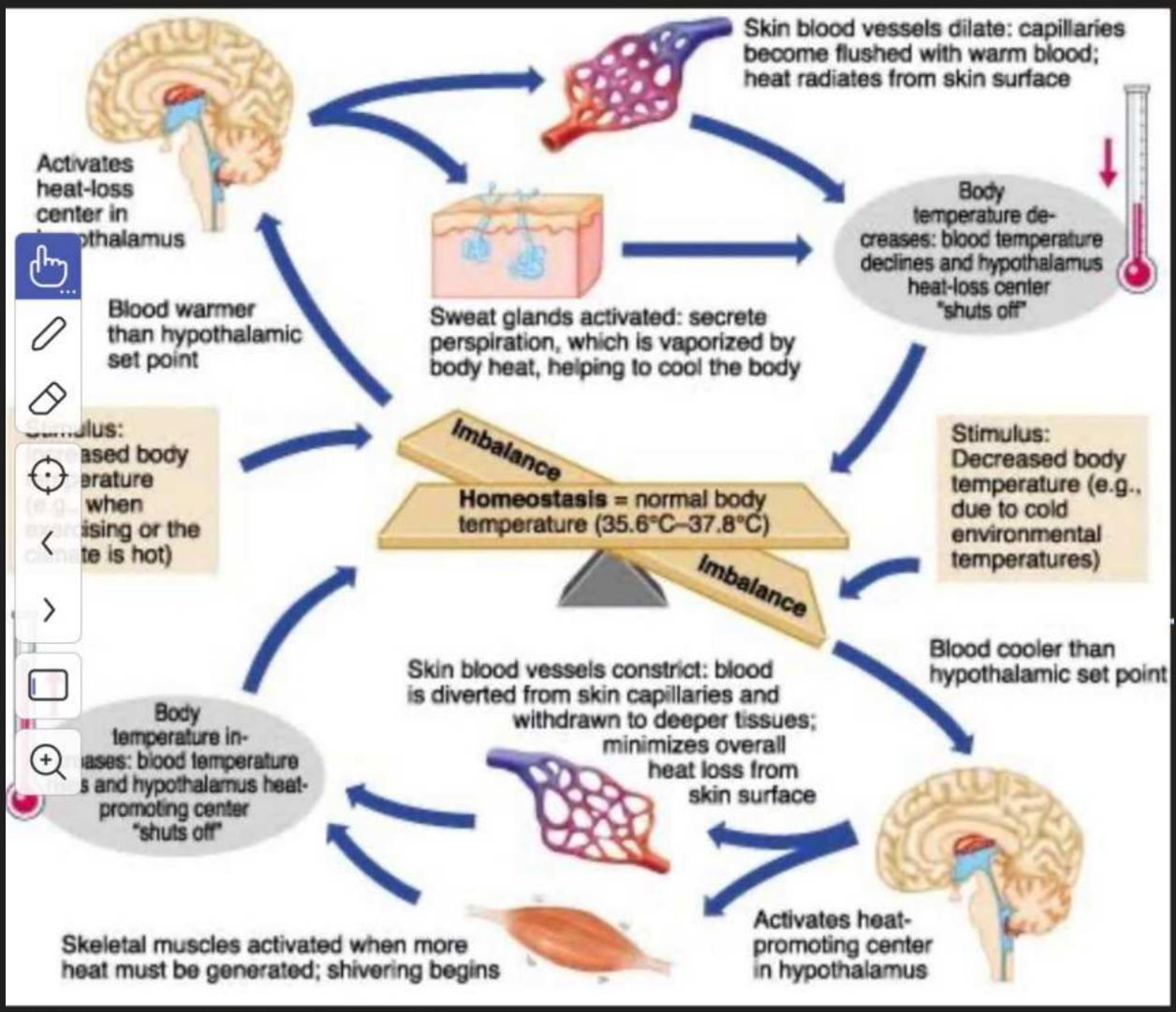
Skin blood vessels dilate: capillaries become flushed with warm blood; heat radiates from skin surface
Activates heat-loss center in hypothalamus
Body temperature decreases: blood temperature declines and hypothalamus heat-loss center "shuts off"
Blood warmer than hypothalamic set point
Sweat glands activated: secrete perspiration, which is vaporized by body heat, helping to cool the body
Imbalance
Homeostasis = normal body temperature (35.6°C–37.8°C)
Imbalance
Stimulus: Decreased body temperature (e.g., due to cold environmental temperatures)
Blood cooler than hypothalamic set point
Skin blood vessels constrict: blood is diverted from skin capillaries and withdrawn to deeper tissues; minimizes overall heat loss from skin surface
Activates heat-promoting center in hypothalamus
Skeletal muscles activated when more heat must be generated; shivering begins
Body temperature increases: blood temperature and hypothalamus heat-promoting center "shuts off"

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Question 1:

4 (a) The body temperature of a human is maintained at its set point of approximately 37 °C. If it rises above this temperature, physiological responses begin to return the temperature to its set point. Two of these responses are vasodilation and sweating.

Explain how vasodilation and sweating help to return the body temperature to its set point.

vasodilation arterioles supplying blood to the skin widen ⇒ more blood flow to the capillaries ⇒ more heat loss from the skin surface

sweating increased production of sweat ⇒ increased evaporation from the skin surface ⇒ removing latent heat of vaporisation

[4]

(b) Diabetes mellitus is a disease where the pancreas is not able to secrete sufficient insulin.

The symptoms of diabetes mellitus include a tendency to drink a lot of water and a loss of body mass.

Suggest why these symptoms occur.

thirst * blood glucose concentration rises ⇒ water potential of the blood decreases ⇒ osmoreceptors stimulated ⇒ more thirst

↓ body mass * decreased uptake of glucose by cells ⇒ increased fat breakdown ⇒ loss in body mass

[4]

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(c) A person with diabetes mellitus can use a biosensor to measure the concentration of glucose in their blood.

(i) Outline how a glucose biosensor works.

* strip contains glucose oxidase which will
* oxidise glucose (in blood) to form gluconic acid
* the drop in O_2 conc. is detected and transduced to generate an electric signal
* electric signal is amplified to
* give a digital numerical output

.....[3]

(ii) Suggest **one** advantage of using a biosensor rather than a dip stick.

* readings are accurate

.....[1]

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Question 2:

(c) During periods of stress or extreme exercise more glucose needs to be released into the blood. The hormone adrenaline is released and binds to receptors on the cell surface membranes of liver cells.

Describe how the effect of adrenaline on liver cells results in an increase in blood glucose concentration.

* Adrenaline binds to its receptors which change shape → activation of the G-protein
* G-protein activates adenylyl cyclase which
* converts ATP → cAMP → second messenger
* cAMP binds to and activates protein kinases which transfer Ⓟ groups to phosphorylase kinases → thereby activating them
* phosphorylases will activate glycogen phosphorylase which breaks down glycogen to glucose
* glucose diffuses out via GLUTs thereby increasing blood glucose concentration. [5]

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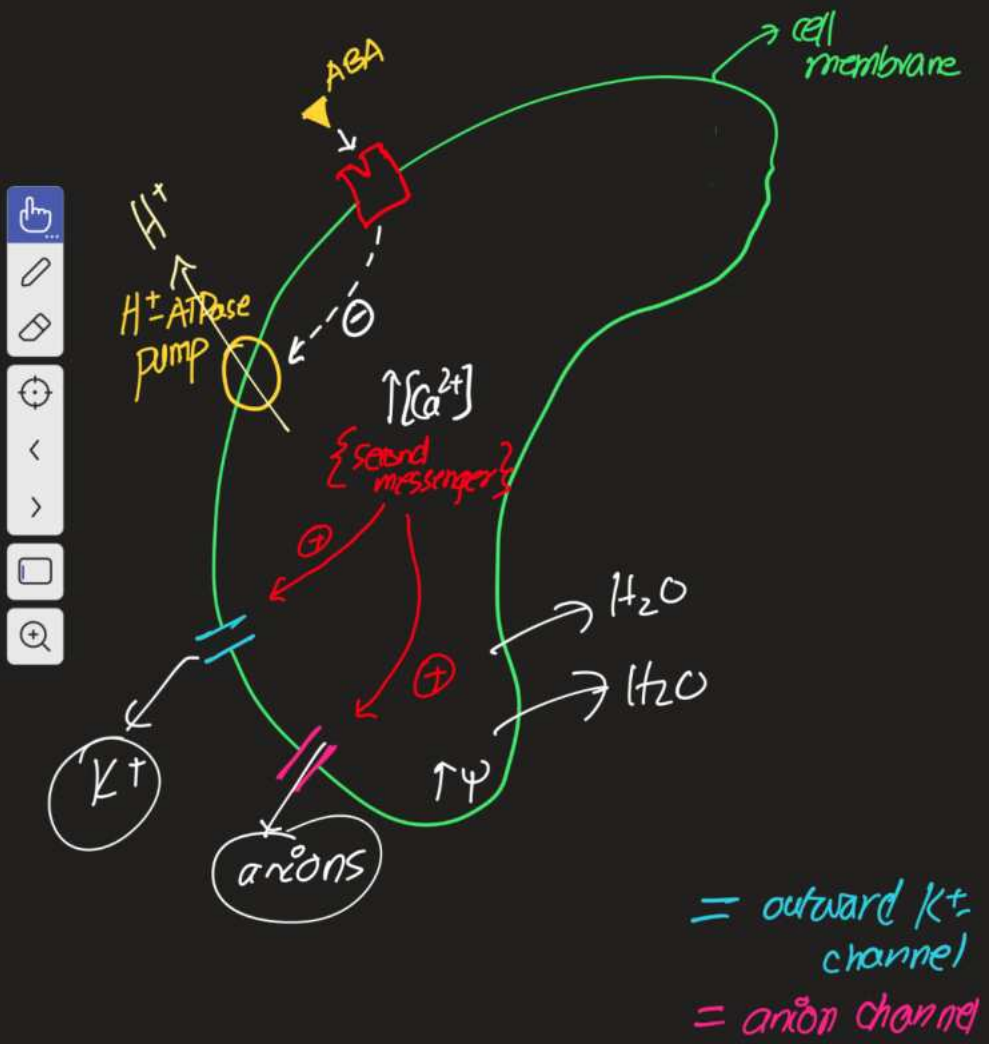
Homeostasis

Mechanism of action of ABA



With
Mohammad Hussham Arshad, MD

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ADVANCED LEVEL BIOLOGY 9700
UNIT 14: Homeostasis

Learning Objectives:

- Overview of Plant Growth Regulators (PGRs)
- - Abscisic acid & stomatal closure

Video Lecture 14 Slides

Mohammad Hussham Arshad, MD
Biology Department

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Earlier

* Pancreas → structure
* Insulin, glucagon and control of blood glucose
* Diabetes Mellitus → Type I / Type II
* Urine Analysis
* Applications of immobilised enzymes;
  - Urine dipstick
  - Biosensors
* Adrenaline, glucagon and their second messenger
* First and second messengers

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Question 3:

(a) Homeostasis in mammals involves negative feedback mechanisms.

Outline how a negative feedback mechanism works.

* deviation of a factor from it's set point
* detected by receptors
* information sent to the control centre which coordinates and sends out nervous and/or endocrine signals
* to the effector
* which carry out corrective actions
* this restores the set-point

[4]

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(b) Fig. 8.1 is a diagram summarising the role of the nervous and endocrine systems in the control of blood glucose concentration.

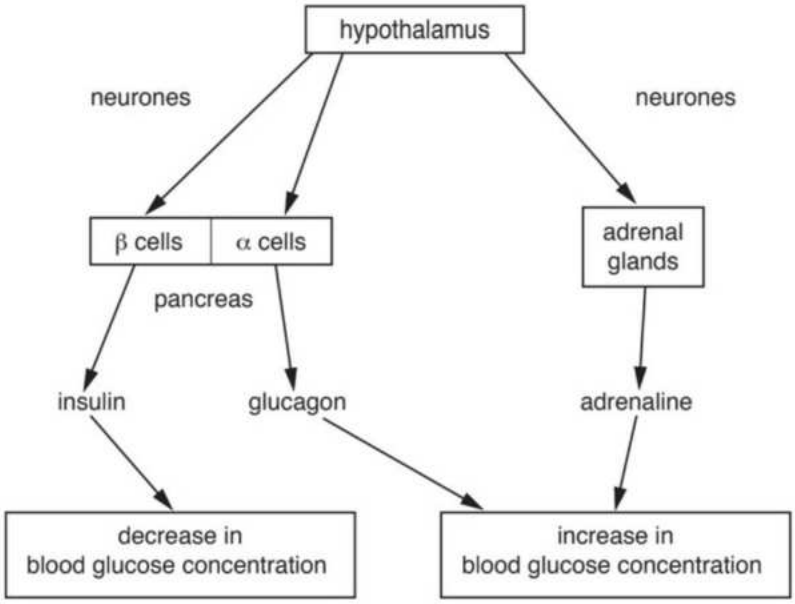

Fig. 8.1

With reference to Fig. 8.1, describe the role of the **nervous system** in the control of blood glucose concentration.

* hypothalamus detects changes in blood glucose concentration
* sends nerve impulses to
  - β-cells which secrete insulin when the blood glucose increases
  - α-cells which secrete glucagon when blood glucose decreases
* hypothalamus sends nerve impulses to adrenals to secrete adrenaline when blood glucose decreases [4]

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(c) If the core temperature of the human body falls, the hypothalamus sends impulses to activate several physiological responses, some of which are listed below.

For each one, state how it would help to bring the core temperature back to normal.

vasoconstriction ... arterioles supplying blood to the skin narrows → less blood flow to the capillaries → less heat loss to the surrounding ...

shivering ... involuntary skeletal muscle contraction which releases energy in the form of heat ...

increasing secretion of adrenaline ... increases the rate of cellular respiration → which releases energy in the form of heat ... [4]

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Question 4:

2 (a) The hormone glucagon is an example of a cell signalling molecule. Table 2.1 lists the main events that occur when the blood glucose concentration decreases below the set point.

The events are **not** listed in the correct order.

Table 2.1

event	description of event
A	adenylyl cyclase enzyme is activated
B	cyclic AMP activates an enzyme cascade
C	glycogen stored in liver cells is broken down to glucose
D	blood glucose concentration increases
E	glucagon is secreted by α cells in the pancreas
F	conformational change to glucagon receptor causes G-protein activation
G	active adenylyl cyclase acts on ATP to produce second messenger
H	glucagon signal is amplified
I	glucose diffuses out of liver cells through GLUT transporter proteins
J	glucagon binds to receptors in the cell surface membranes of liver cells
K	cyclic AMP is formed

1 E *
2 J
3 F
4 A
5 G
6 K
7 B
8 H
9 C
10 I
11 D **

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Complete Table 2.2 to show the correct order in which these events occur.

Three of the events have already been placed in their correct order.

Table 2.2

correct order	letter of event
1	E
2	
3	
4	
5	
6	K
7	
8	
9	
10	
11	D

[4]

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Plant Growth Regulators

* Abscisic Acid

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Plant Growth Regulators (PGRs)

* PGRs are chemical substances required for growth and development of plants.

* PGRs are chemical messengers in plants like hormones in animals.

* Common PGRs include:

(A) Abscisic Acid (ABA)

(B) Gibberellins (GA)

(C) Auxins

(D) Cytokinins

(E) Ethylene

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* We will be discussing ABA as a part of the current section.

* ABA is considered as the PGR released under stressful conditions in plants.

* ABA has a role to play in stomatal closure besides other functions.

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Normal opening of the stoma during daylight

Light

↑↑ rates of photosynthesis

↑↑ production of sugars

↓

↓

H^+ pumped out of guard cell via H^+-ATPase on the membrane of guard cells

K^+ enters guard cells via inward K^+-channels

water potential in the guard cells lower

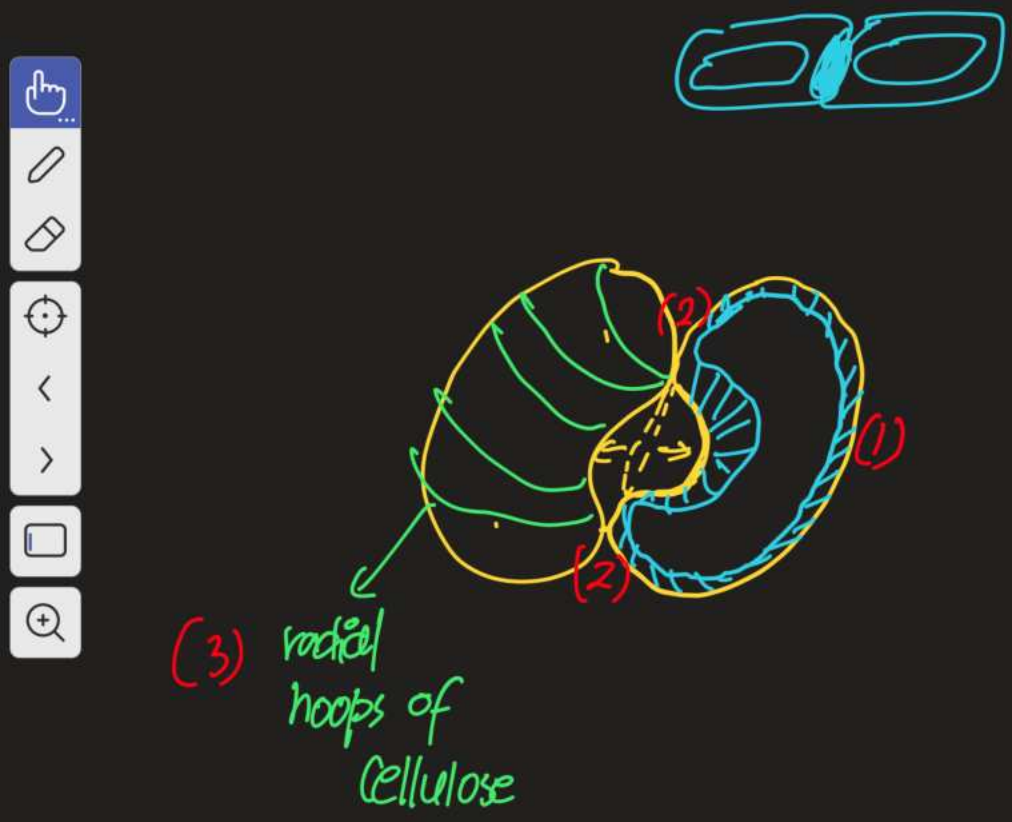
water enters via osmosis

guard cells become turgid

STOMA OPENS

HEUSER

Features of guard cells that assist in stomatal opening



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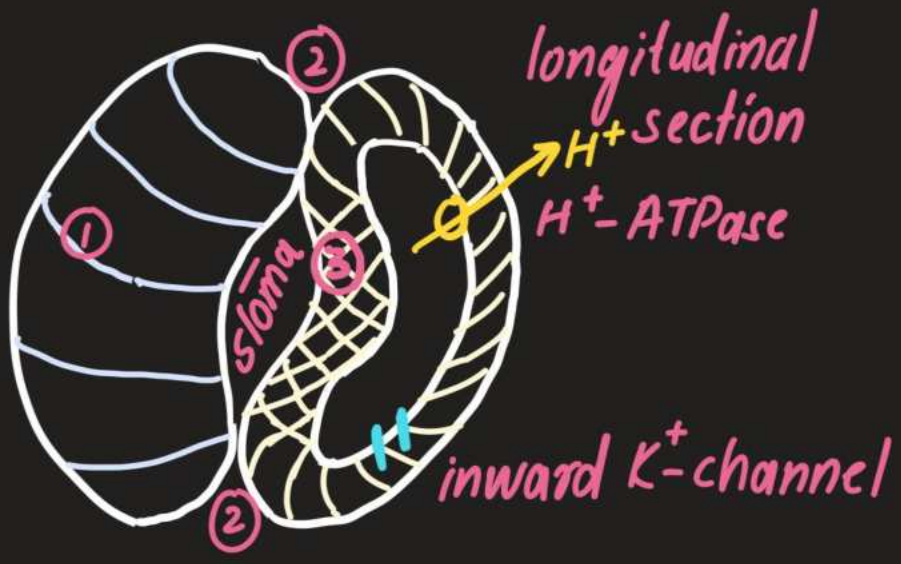
Features of guard cells that assist in stomatal opening



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① Radial hoops of cellulose microfibrils around the surface of guard cells.

② The ends of the guard cells are always joined together.

③ The cell wall facing the stoma is thicker than the cell wall away from the stoma.

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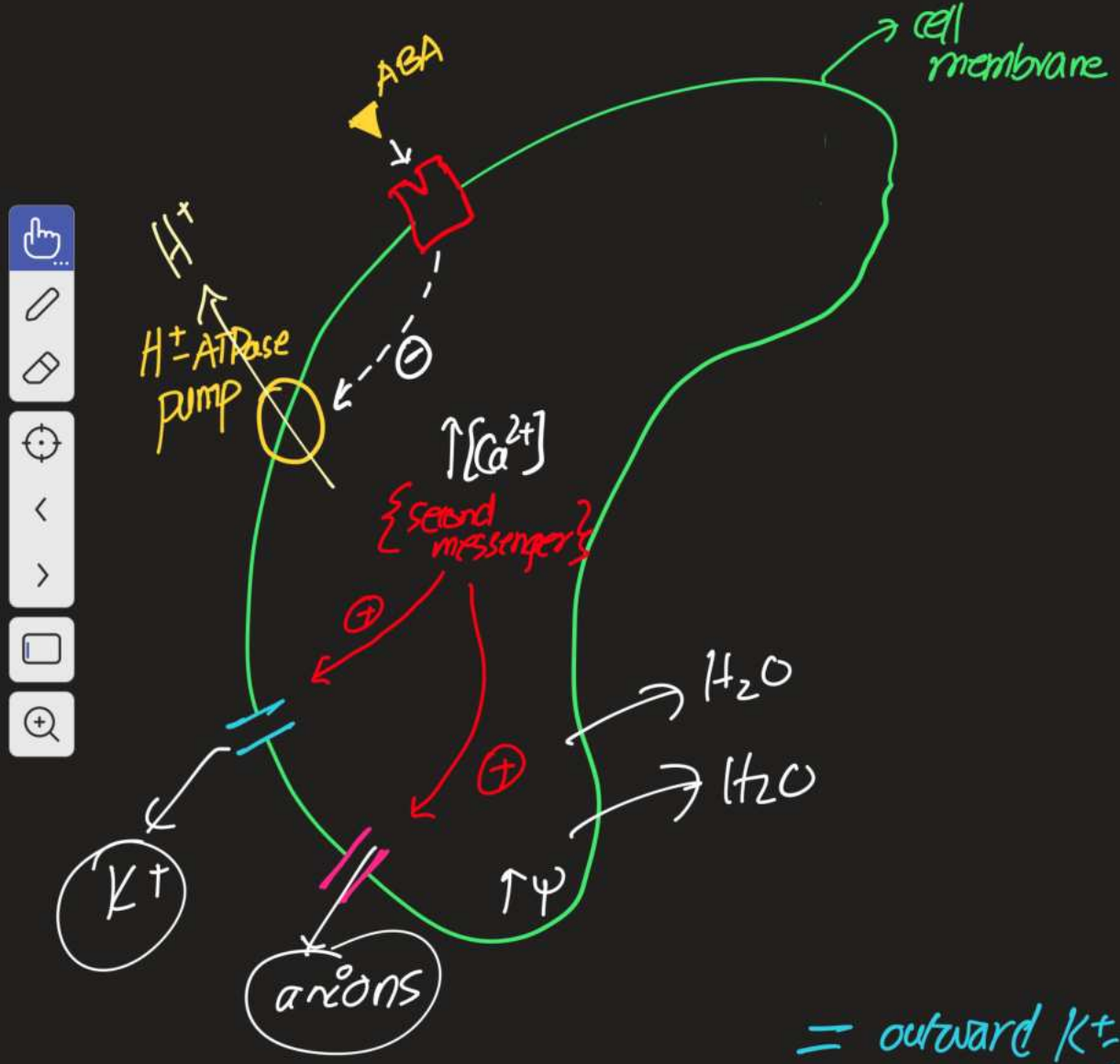
Mechanism of action of ABA



= outward K+ channel

= anion channel

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Mechanism of action of ABA

* Site of production: root cells and buds
* Target site: guard cells
* Role: stomatal closure
* ABA is translocated from it's site of production towards the guard cells in leaves.
* ABA is a hydrophilic chemical → thus has its receptors on the cell surface membrane of guard cells. Ca^{2+} are the second messengers of ABA.

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ABA is released under the following stressful conditions in plants:

- drought
- extremely high Temperature
- dormancy
- abscission (shedding of leaves, fruits — thus the name)
- high salinity in soil ?? Why?

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ABA binds to its receptors on the cell surface membrane of guard cells.

↓

Blocks H^+-ATPase.

↓

Increases intracellular $[Ca^{2+}]$ which serves as the second messenger.

↓

Ca^{2+} stimulate the opening of outward K^+-channels and anion channels.

↓

Loss of K^+ and anions from guard cells.

↓

Water flow via osmosis.

↓

Flaccidity of guard cells.

↓

Stomatal closure

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Stomatal closure

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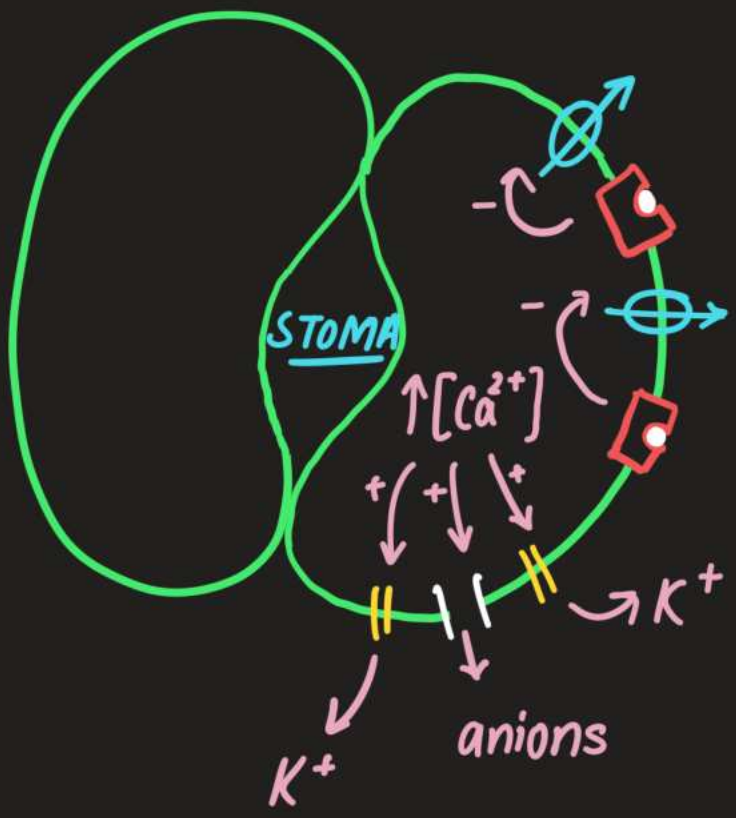

= outward K^+ - channel

H^+ - ATPase

• ABA

ABA receptor

anion channel

\+ stimulate

\- inhibit