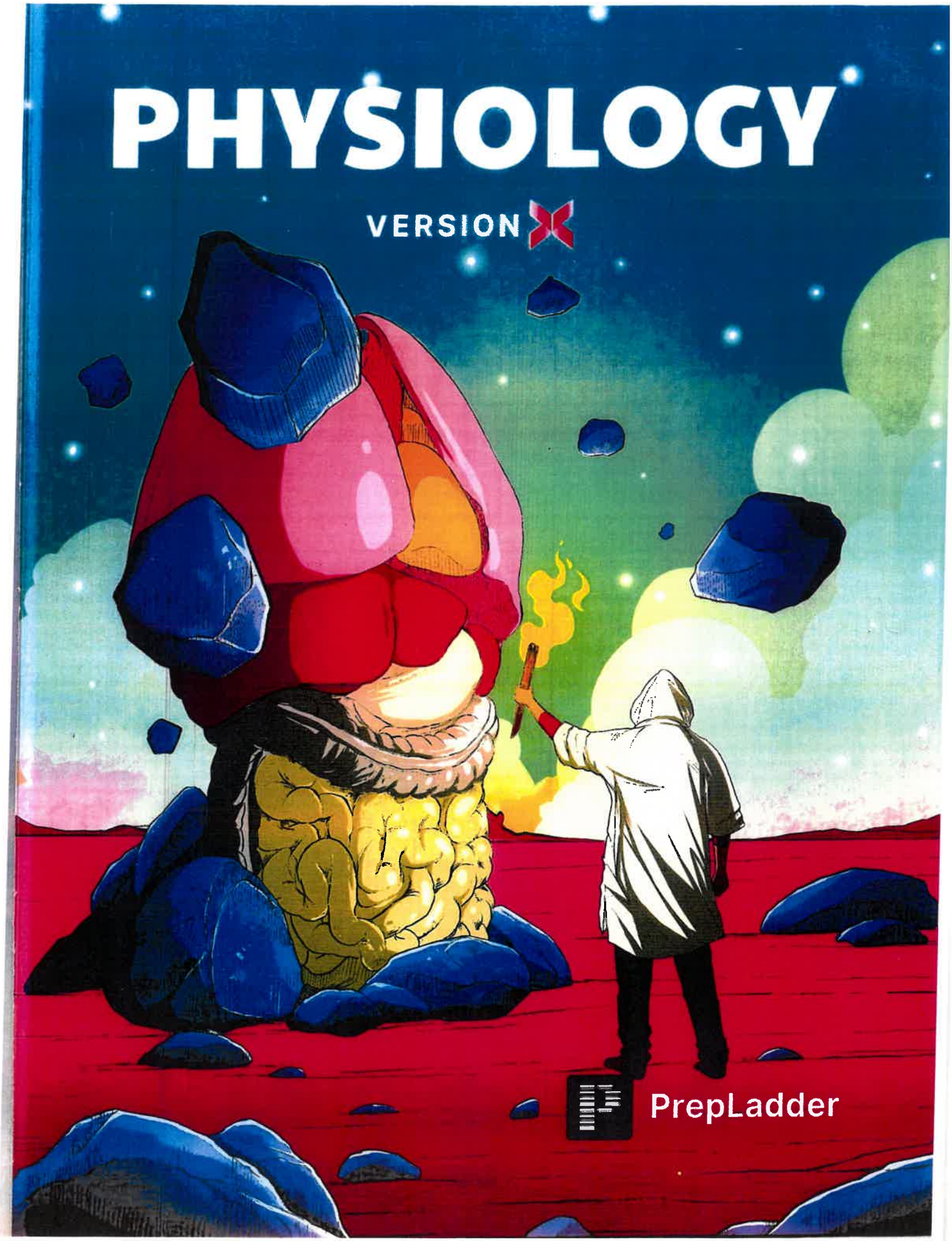
PHYSIOLOGY

VERSION X



PrepLadder

Created by team PrepLadder based on PHYSIOLOGY lectures on the Prepladder app

Revision friendly **Fully Colored Book/Structured Notes**

For Best results, watch the video lectures along with reading notes

CONTENTS

Physiology

1. HOMEOSTASIS

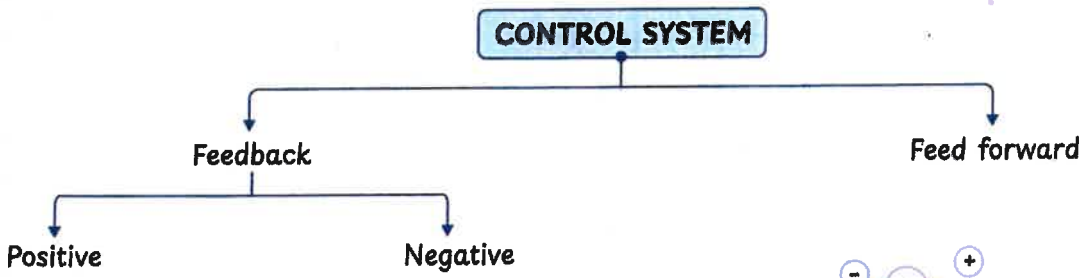
HOMEOSTASIS

00:00:40

- Maintenance of near-constant conditions in the internal environment
- The concept of the "milieu intérieur" (internal environment) was introduced by [redacted]
  - He stated "the stability of the internal environment (milieu intérieur) is the condition for a free & independent life"
- Homeostasis depends on interstitial fluid (ISF), a component of the extracellular fluid (ECF)
- Term "homeostasis" → coined by Walter B Cannon
  - Homeostasis → various physiological arrangements which serve to restore the normal state, once it has been disturbed (According to Walter B Cannon)
- Mechanisms maintaining the internal environment → control systems

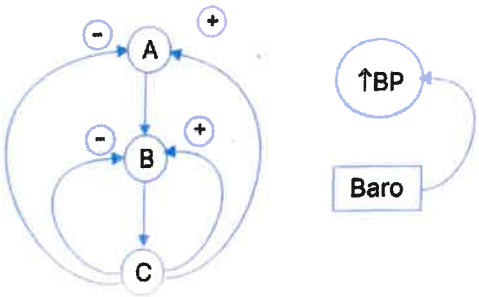
CONTROL SYSTEM

00:05:47



FEEDBACK CONTROL SYSTEM

- If hormone A → stimulates production of hormone B → in turn stimulates production of hormone C (output)
- Mechanism: The output (C) is giving input / returning back at the level of A or B to provide input



POSITIVE FEEDBACK CONTROL SYSTEM

- Stimulating / positive feedback
- A stimulates B → B stimulates C → C stimulates A
  - Example of Positive Feedback Control System / Vicious System (cycle)
    → Childbirth (Ferguson Reflex):
    Uterine contractions → Oxytocin release → Stronger contractions → More oxytocin → Cycle continues until delivery
  - Responsible [redacted]

NEGATIVE FEEDBACK CONTROL SYSTEM

- Inhibitory / negative feedback
- **Example:** BP ↑ → Baroreceptors activate to lower BP to normal
- Stability of control system → maintained by Negative Feedback control system

GAIN OF CONTROL SYSTEM

- **Measures the** [redacted]
- **Gain = Correction / Error**
- **Example:**
  - Original / Normal BP: 100 mmHg
  - Raised BP: 160 mmHg
  - Corrected BP (Baroreceptor mediated): 120 mmHg
  - Error: 120-100 = 20 mmHg
  - Correction: 160-120 = 40 mmHg
  - Gain: (40/20) = -2
    - BP is raised → baroreceptor corrects it in opposite direction → Gain is negative
- **Normal gains**
  - Baroreceptor control system: -2
  - Thermoreceptor control system: -33
- **INFINITY GAIN CONTROL SYSTEM:** Control system achieves 100% correction with zero error → infinite gain
  - Eg: Kidney regulating the BP or Blood volume

REGULATION FACTOR

00:16:33

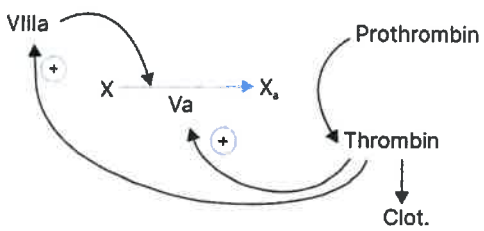
- Measures how much a system reduces the deviation from normal
- Regulation factor (R) = $\frac{\text{Change with regulation}}{\text{Change without regulation}}$
- Example:
  - Original / Normal BP: 100 mmHg
  - Raised BP: 160 mmHg
  - Corrected BP (Baroreceptor mediated): 120 mmHg
  - Change in BP without regulation / control system: 160 - 100 = 60 mmHg
  - Change in BP with regulation / control system: 120 - 100 = 20 mmHg
  - Regulation factor (R): (20/60) = 1/3
- Accuracy of a control system is inversely related to the regulation factor

POSITIVE FEEDBACK CONTROL SYSTEM

00:19:00

- Conditions where positive control feedback systems are beneficial to the body:

EXAMPLES	EXPLANATION
Process occurring during blood clotting	• Thrombin generated → positive feedback to factor Va, VIIIa → activate factor X (to factor Xa) → Converts prothrombin to thrombin → clot formed

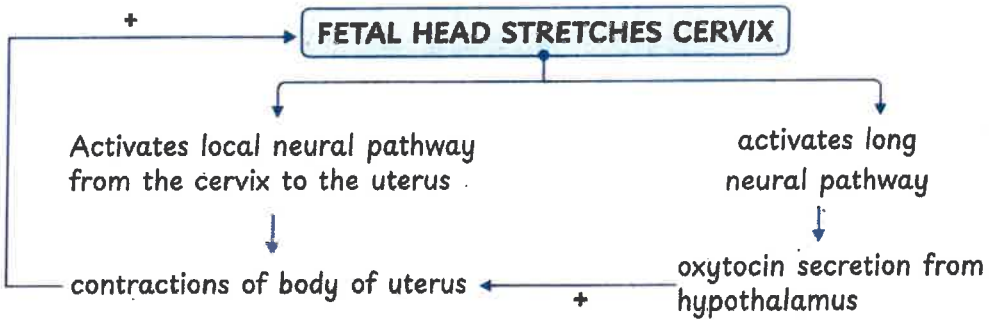


LH surge just before ovulation

- On menstrual cycle (normally)
  - Estrogen exerts a negative feedback effect on LH secretion
- Just before ovulation
  - Estrogen switches to a positive feedback effect → LH surge → ovulation

Uterine Contraction During Labor (Ferguson reflex)

- ↑ contractions → pushing the fetal head further → childbirth



Lactation

- Baby suckles near nipple & areolar region of the breast → Activates long neural pathway → secretion of oxytocin, → milk ejection

Generation of Nerve Action Potential

- Influx of positively charged sodium ions → depolarization of cell membrane → opening of additional voltage-gated sodium channels → further depolarization → further opening of channels

Important Information

- Potassium channel opening → negative feedback mechanism
  - Opening of K^+ channels → efflux of K^+ → Hyperpolarization → closure of K^+ channels

FEEDFORWARD CONTROL SYSTEM

00:29:10

- Anticipatory control system
  - When a control system predicts an impending change → corrective measures are being taken before the change occurs

EXAMPLES

1. Thermoregulation System

- Both, feedback and feedforward components are present
- Thermoreceptors present on:
  - Skin: Peripheral receptor
  - Hypothalamus (Anterior): Central receptors
- A decrease in ambient temperature leads to a decrease in skin temperature, activating peripheral receptors, which send input to the hypothalamus, triggering the heat production system and increasing core body temperature

2. ↑in Heart Rate & Respiratory rate occurs even before the start of exercise

- Cause: Psychic stimulation of the brain

3. Cephalic Phase of Gastric Secretion

- The sight, smell, or thought of food triggers acid secretion in the stomach as an anticipatory response

4. Receptive Relaxation of Stomach

- Food in the mouth that begins to be swallowed → triggers relaxation/dilation of the stomach

5. Cerebellum

Granular cells (cerebellum) $\xrightarrow{+}$ basket & stellate cells (stomach) $\xrightarrow{-}$ Purkinje cells (cerebellum)

- Purkinje cells have no effect at the level of basket or granular cells
- Unidirectional signal → moving forward
- Controls various movements of the body

Important Information

Adaptive Relaxation of stomach

- Once the food enters the stomach, → stomach stretches & dilates → accommodates increased volume
- Not feedforward control system

Negative feedback control system - Thermoregulatory system

- ↓↓↓ in ambient temperature → ↓↓↓ Core body temperature → ↓↓↓ Blood temperature → Central receptors activated → activate heat production system → ↑ core body temperature

MCQ's

Q. In negative feedback, feedback gain is infinity in which of the following? (AIIMS 2020)

a. Temperature control in hypothalamus
b. Blood volume control by kidney
c. Blood pressure control by baroreflex
d. Infinite feedback gain is not possible

Ans (b)

Q. A patient's SBP decreased by 10 mm of Hg upon standing and recovered by only 8 mmHg With an error of 2 mmHg, what was the gain? (AIIMS 2020)

a. 2
b. 4
c. 8
d. 10

Ans (b)

2. BODY FLUID COMPARTMENTS

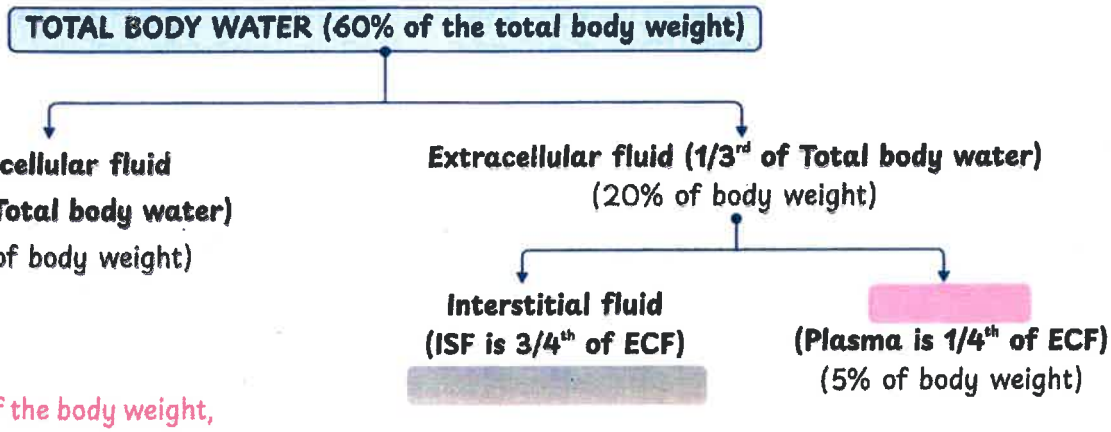
HUMAN BODY COMPOSITION

00:00:56

CHEMICAL LEVEL		TISSUE LEVEL	
Water		Skeletal muscle	
Protein		Non-skeletal	
Fat		Adipose tissue	
Mineral		Bone	
Glycogen			

DISTRIBUTION OF BODY FLUID

00:02:19



- Blood - 8% of the body weight,
  - 5% plasma + 3% total cell volume

TRANSCELLULAR FLUID

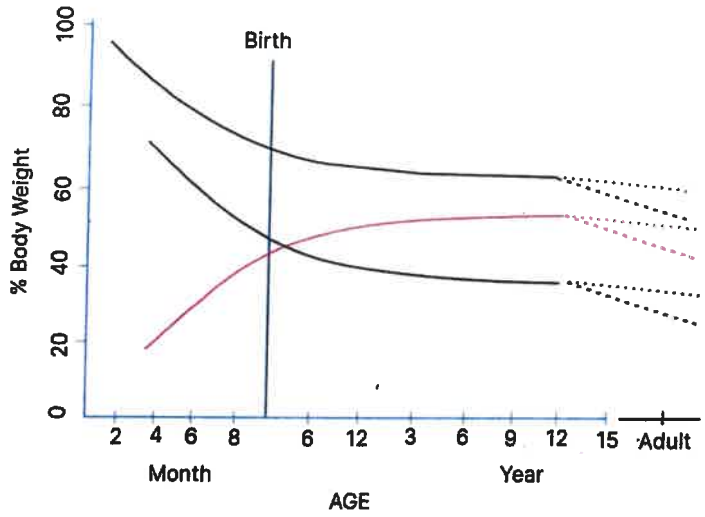
00:08:00

- Fluid present in certain body cavities

Cerebrospinal fluid (CSF)	150 ml
Intra pleural fluid	10-20 ml
Pericardial fluid	50 ml
Peritoneal fluid	Males: 0 ml Females: 20 ml, (after ovulation)
Synovial fluid	1 ml/large joint

CHANGE IN BODY FLUID WITH AGE

00:09:55



TBW

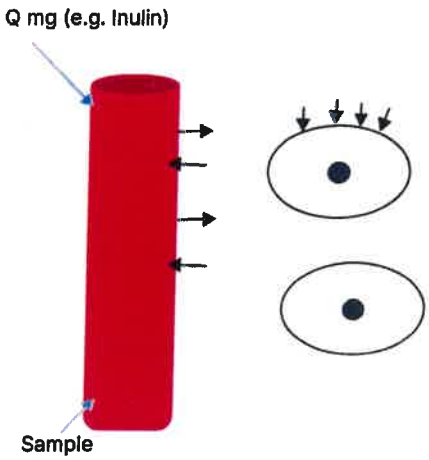
- **Intrauterine life** → 95% of total body weight; Decreases with age
- **Preterm infants** → 90% of birth weight
- **Term infants** → 75% of birth weight

- ICF and ECF
  - Intrauterine life: initial intracellular fluid (ICF) < extracellular fluid (ECF)
  - ICF gradually increases due to organogenesis, while ECF decreases
  - 3-4 months after birth → ICF and ECF become equal, (ratio of 1:1)
  - By 1 year of age - ICF and ECF approach adult levels
  - At puberty, percentage and distribution of body fluids = adult proportions

MEASUREMENT OF BODY WATER

00:17:56

- To measure the exact amount of body water (TBW)
- Principle - Indicator dilution principle or volume of distribution method
- Diagram shows a capillary along with body cells
  - Water inside the cell: Intracellular fluid (ICF)
  - Water outside the cell: Interstitial fluid (ISF)
  - Water inside the capillary: Plasma
  - Plasma + ISF = Extracellular fluid (ECF)
- To measure body water, a substance like inulin (Q mg) is injected into the capillary,
  - Distributed in plasma → penetrate capillary → enter interstitial fluid
  - Inulin impermeable to cell membrane



- Resulting in inulin distributed throughout the entire ECF
  - Equilibrium reached between the plasma and ISF concentrations,
  - Inulin concentration is measured in the plasma using a specific formula

$$\text{Volume of distribution} = \frac{Q}{C}$$

Q- total amount injected;

C- concentration in plasma

- However, for substances that are easily metabolized, both metabolism and excretion must be considered, → requiring a modification of the formula

$$\text{Volume} = \frac{Q-e}{C}$$ e → excreted or, metabolized part of injected substance

- When injected substance is permeable to capillaries → reaches interstitial fluid (ISF)
- Injected substance is also permeable to the cell membrane → reaches intracellular fluid (ICF)
  - This substance measures total body water (TBW)
- If substance is impermeable to the capillary, → only measure Plasma volume

VARIOUS INDICATORS FOR BODY FLUID MEASUREMENT

00:25:30

COMPARTMENT	INDICATOR USED
Total body water	• D_2O, tritium oxide, Antipyrine (Freely permeable to capillary and cell membranes)
ECF volume	• Inulin (Best), Sucrose, ^{22}Na, ^{125}I-iothalamate, mannitol (Freely permeable to the capillary, impermeable to the cell membrane)
ICF volume	• ICF volume is typically determined by subtracting the extracellular fluid (ECF) from the total body water (TBW) ICF volume = (TBW - ECF) • Requires 2 substances: 1 for TBW & 1 for ECF
Plasma	^{125}I-albumin (Best), Evans' blue (Impermeable to capillaries)
ISF (Interstitial fluid)	ISF =
RBC	^{51}Cr, ^{59}Fe tagged RBC
Blood Volume	Plasma volume / (1-Hematocrit)

COMPOSITION OF BODY FLUIDS

00:28:58

Component	Plasma (mOsmol/L)	Interstitial Fluid (mOsmol/L)	Intracellular Fluid (mOsmol/L)
Na^+	142	139	14
K^+	4.2	4	140
Ca^{++}	1.3	1.2	0
Mg^{++}	0.8	0.7	20
Cl^-	106	108	4
$HCO3^-$	24	28	10
Phosphate	-	2	11
Protein	7 g/dl	1 g/dl	30 g/dl
Others	-	-	-
Total Osmolality (mOsmol/L)	299	300	301
Corrected Osmolar Activity	282	281	281

- Major ions in ICF: K^+, Mg^+, Phosphate
- Major ions in ECF: Na^+, Cl^-
- Plasma has slightly more positively charged ions than ISF
  - Because of more protein, (negatively charged)
    → Donnan effect
  - Interstitial fluid has slightly more negatively charged ions than plasma
- Total osmolarity - sum of all osmotically active substances = Corrected osmolarity
- Corrected osmolarity is slightly lower than total osmolarity
  - Due to interactions between positively and negatively charged osmotically active molecules forming complexes
- Osmotic pressure of 1 mOsmol/L impermeable substances = 19.3mmHg
  - Total osmotic pressure of the plasma = 19.3 x 282 = 5441mmHg (~approx. 5500mmHg)

OSMOLAR GAP

00:37:12

- Total osmolarity measured with Osmometer
  - Principle: Freezing point depression
- Calculation of osmolarity

$$\text{BUN} = \frac{\text{urea}}{2.14} \qquad \text{Osmolarity} = 2x\,[\,Na^+ \text{ mmol/L}] + \frac{\text{Glucose (mg\%)}}{18} + \frac{\text{BUN (mg\%)}}{2.8}$$

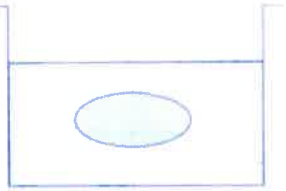
  - If all units are given in mmol/L, → **2x [Na^+] + Glucose + BUN**

- Measured osmolality > calculated osmolality
- Osmolar gap=
  - Normal- 10
  - Increased osmolar gap seen in
    → Alcohol poisoning
    → Sorbitol
    → Huge amount of protein
    → Hyperlipidaemia

OSMOLARITY AND TONICITY

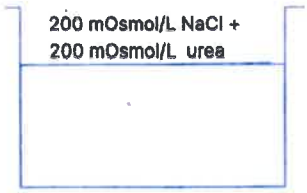
00:43:00

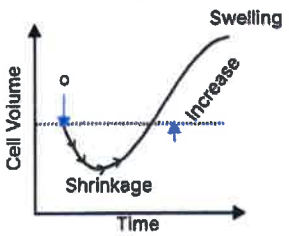
- Osmolarity → Concentration of osmotically active particles (osmoles) in one liter of solution
- Osmolality → Osmoles per kilogram of water
- Difference between Osmolarity and Osmolality → 1%
- Tonicity of a solution predicts the effect of the solution on cell volume at equilibrium (depends on impermeant solutes)



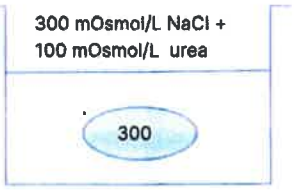
  - **Cell osmolarity is 300 mOsm/L, solution is 500 mOsm/L**
    → Solution is hyperosmotic (compared to the cell)
    → However, without knowing the concentration of impermeable solutes, → difficult to determine whether the solution is hypertonic / hypotonic / isotonic
  - **Solution - 200 mOsmol/L NaCl (impermeable) and 300 mOsmol/L urea (permeable)**
    → Solution is hyperosmotic but hypotonic in comparison to cell
    → Hypotonic solution → increase in cell volume at equilibrium
  - Solution - 300 mOsmol/L NaCl (impermeable) and 200 mOsmol/L urea (permeable)
    → Solution is Isotonic (in comparison to the cell) → cell volume will remain the same

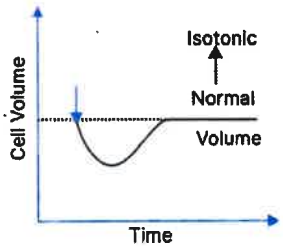
Hyperosmotic but Hypotonic solution



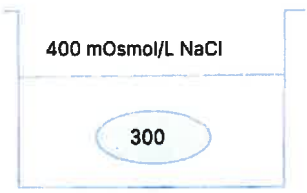


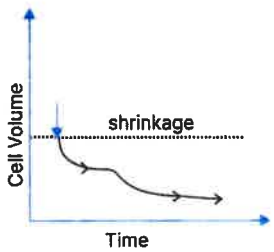
Hyperosmotic but isotonic solution





Hyperosmotic and Hypertonic solution





ISOTONIC SOLUTIONS

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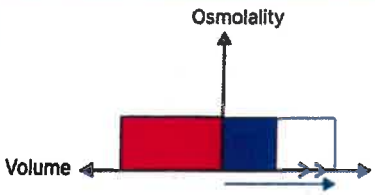
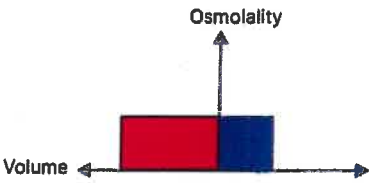
ISOTONIC SOLUTIONS

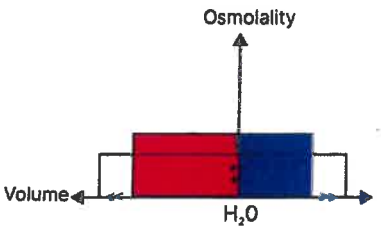
- 5% mannitol
- 5% Dextrose - isotonic in vitro
- 0.9% NaCl (normal saline)
  - Once infused into the plasma, glucose is rapidly taken up by cells (leaving behind water) making it hypotonic
- Ringer's lactate solution/ lactated Ringer's/ Hartmann's solution
- Ringer's solution
  - Same constituents as plasma but does not contain sodium lactate

DARROW-YANNET DIAGRAM

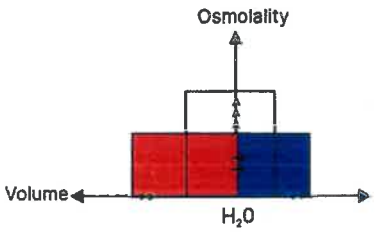
00:59:35

- Change in ECF & ICF volume on administration of solutions of different tonicity (infusion)
- At equilibrium, the osmolality of ICF and ECF are equal
  - 280mOsmol/L

Gains/Losses of Fluids	D-Y Diagram	Explanation
Gain of Isotonic Fluid		• When isotonic solution is administered, → ECF volume without any change in osmolarity • Example: 0.9% NaCl infusion
Loss of Isotonic Fluid		• In cases of hemorrhage, urinary loss, acute vomiting, or diarrhea → isotonic fluid loss from the body→ ↓ in extracellular fluid (ECF) volume without altering osmolarity

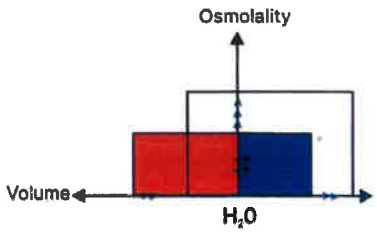
Gain of Hypotonic Fluid		• Examples: 0.45% NaCl, Polydipsia, SIADH
		• Extracellular fluid (ECF) volume expansion → ↓ECF osmolarity
		• Since intracellular fluid (ICF) osmolality remains higher, the condition is not in steady state
		• Hypotonic ECF moves into the ICF by osmosis → ICF volume expansion and ↓ osmolarity
		• Hypotonic fluid therapy is dangerous, → swelling of brain tissue can occur → herniation of brain tissue
		• If 1 liter of hypotonic fluid is infused
		  ○ 1/3rd will enter ECF - 333ml
		  ○ 2/3rd will enter ICF - 667ml

Loss of Hypotonic Fluid



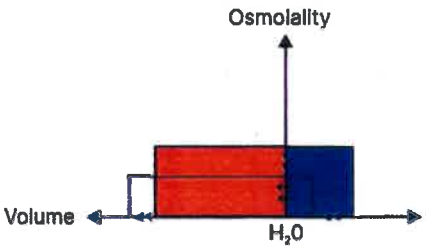
- In conditions like diabetes insipidus or inadequate water intake → excess water is excreted (insufficient ADH)
- Decrease in extracellular fluid (ECF) volume
- Since only water is lost and solutes remain, ECF osmolarity and tonicity , making it hypertonic compared to intracellular fluid (ICF)
- Water moves from ICF to ECF, ↓ ICF volume and ↑ its osmolarity
- Volume of ICF and ECF ↓, and Osmolarity of both compartments ↑

Gain of Hypertonic Fluid



- Infusing 3% NaCl (hypertonic solution) expands ECF volume and its osmolarity
- The ECF becomes hypertonic relative to the ICF, causing water to move out of cells, ↓ in ICF volume and increase in ICF osmolarity

Loss of Hypertonic Fluid



- In adrenal insufficiency, solute is lost in excess of water
- Hypertonic fluid loss ↓ ECF volume, making it hypotonic relative to ICF
- Water moves from ECF to ICF, ICF volume slightly
- This results in reduced ECF volume, ICF volume, and ↓ tonicity in both compartments, reaching a new steady state

MCQ's

Q. A research fellow was studying the volume and electrolytes in different body water compartment. During his experiment, he took a sample and measured the electrolytes as Na^+: 10 mEq/L and K^+: 140 mEq/L. The analysis indicates which of the following compartment: (NEET 2021)

a. ECF
b. ICF
c. ISF
d. Plasma

Ans (b)

Q. Calculate the blood volume with the followings: Weight of the patient 60kg, Hematocrit 45% (JIPMER 2019)

a. 4.8 L
b. 5.0 L
c. 5.45 L
d. 6 L

Ans (c)

Q. 100mg of sucrose is injected into a 70Kg man. The plasma level of sucrose after mixing is 0.01mg/ml. If 5 mg has been metabolized during this period, then what is the ECF volume? (AIIMS 2020)

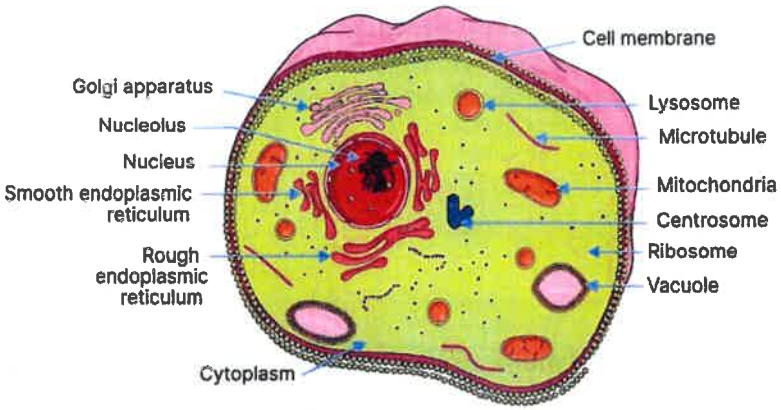
a. 9.5L
b. 14 L
c. 17.5 L
d. 10 L

Ans (a)

3. CELLULAR PHYSIOLOGY

CELL

00:00:10



CELL MEMBRANE

00:00:51

CELL MEMBRANE

- Lipid bilayer (Phospholipid)
- Thickness of the cell membrane - 7.5 nm
- Proteins are embedded in these layers
  - Fluid Mosaic Model (1972) by Singer and Nicolson
  - Proteins present in fluid phase
- Structure of Phospholipid:
  - Hydrophilic phosphate head: present outward
  - Two hydrophobic tails: present inward

COMPOSITION OF CELL/ PLASMA MEMBRANE

00:03:58

Lipid (42%)	• Phospholipids (25%) • Cholesterol (13%) • Triglyceride (0%)	
Protein (55%)	Integral or • Spanning throughout the cell membrane	Peripheral or Extrinsic Membrane protein • Attached either to intrinsic membranes or to the surface of the cell membrane
Carbohydrates (3%)	• Form of glycoprotein or glycolipid	