Structured Notes According to

PHYSIOLOGY

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(Author)

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1 HOMEOSTASIS

- Homeostasis means the maintenance of nearly constant conditions in the internal environment of a cell.

MCQ 00:02:00

Q. What does homeostasis of the cell depend on?

Ans. According to Bernard's concept of Milieu Interieur, homeostasis is mainly dependent on the interstitial fluid (ISF).

Explanation

- Claude Bernard introduced the concept of homeostasis and the term "Milieu Interieur". He stated that the cell maintains a constant internal environment, which is dependent on the interstitial fluid (ISF). Therefore, homeostasis is mainly dependent on the ISF.

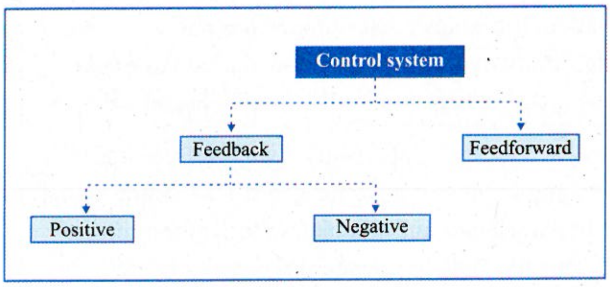
Q. Who was the first person to coin the term Homeostasis?

Ans. Walter Bradford Cannon was the first person to coin the term homeostasis.

Q. How does a Cell maintain Homeostasis? 00:02:36

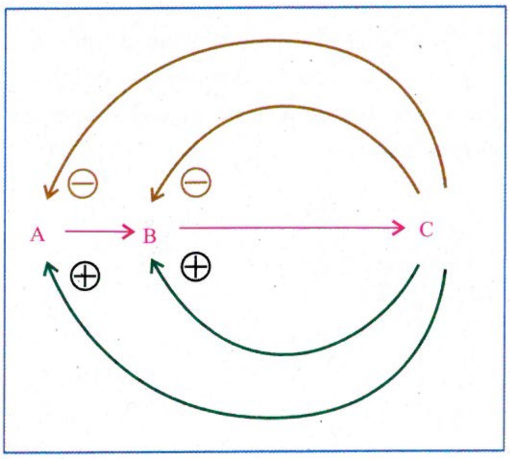
Ans. For the maintenance of homeostasis, our body contains the control system. There are two types of control systems, the feedback control system and the feed-forward control system.

Control System



Feedback Control System

- A produces B, and B produces C, which becomes the output. The feedback control system is a mechanism where the output (C) gives feedback to input (A or B) to alter the subsequent action.



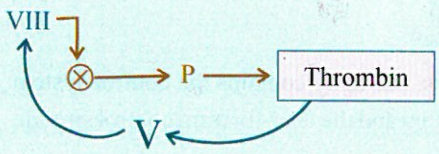
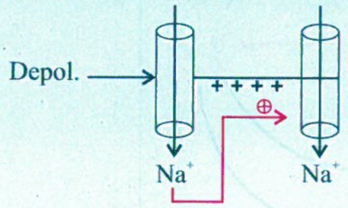
00:03:53

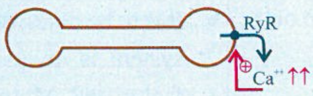
Positive feedback control system	Negative feedback control system
Input that has returned is of stimulatory type. So, if C is stimulating B then again B will produce C, the pathway will move in the same direction. It is a vicious cycle.	The C which has been produced, will give input to B or A, which will be inhibitory in nature so that the next action changes accordingly.
It destabilizes our control system	It stabilizes our control system

- There are certain conditions where positive control feedback systems are beneficial to the body.

Here are a few examples of the positive feedback control system

00:06:35

Examples	Explanation
The process of blood clotting	• Whenever thrombin is generated, it gives positive feedback and activates clotting factors like factor V, and factor VIII. All these clotting factors in turn will activate factor X. This leads to the production of more thrombin. 
A Spike in Oestrogen and LH	• A spike in LH is observed during the follicular phase of the menstrual cycle causing ovulation. It is known that estrogen has positive feedback on LH just before ovulation. Otherwise, during the whole menstrual cycle, estrogen has negative feedback on FSH and LH.
Uterine Contraction During Childbirth	• When uterine contraction occurs, it pushes the fetal head towards the cervix causing stretching of the cervix which generates a neural signal that ascends to the hypothalamus and stimulates the synthesis of the oxytocin hormone. This oxytocin hormone causes more uterine contractions.
Lactation	• When the baby suckles near to the areolar region of the breast, a positive feedback control system is initiated producing oxytocin which causes more ejection of the milk.
Generation of Nerve Impulses/Nerve Action Potential	• Depolarization of the voltage-gated sodium (Na+) channel leads to the channel opening, allowing Na+ ions to enter. This positive-charged sodium will produce more depolarization which will lead to opening of more voltage-gated sodium channels. 

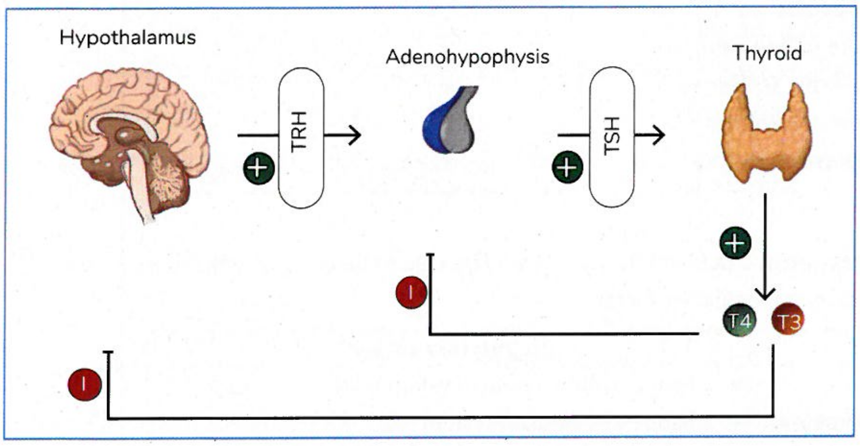
Release of Sarcoplasmic Calcium through Ryanodine Receptors during excitation-contraction coupling in cardiac muscle	• If the ryanodine receptor channel (RyR) is opened, calcium will be released from the sarcoplasmic reticulum into the cytoplasm. This calcium acts as a stimulus for the opening of more RyR channels which in turn will lead to more calcium release and muscle contraction. 

Negative Feedback Control System

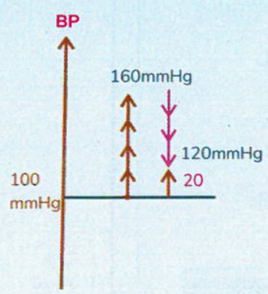
00:12:44

- **Example:** Hypothalamic-Pituitary-Thyroid Axis

PYQ: INICET 2020



00:17:00

Gain of control system	Regulation Factor
• With the gain of control system, we understand the effectiveness of the control system.	• Regulation factor checks the accuracy of the control system
$$\text{Gain} = \frac{\text{Correction}}{\text{Error}}$$	$$\text{Regulation Factor} = \frac{\text{Change with control system}}{\text{Change without control system}}$$
Example	**From the example of BP**
• In a steady state condition, BP is 100 mm Hg. After a blood infusion, it rose to 160 mm Hg. Baroreceptors reduced it to 120 mm Hg, achieving a correction of 40 mm Hg. However, there remains a 20 mm Hg error compared to the initial state of 100 mm Hg.	• The blood pressure rises up to 160 mm Hg, the change without a control system.
• The correction of baroreceptors is in a negative direction; hence the gain of the baroreceptor control system is -2	• The baroreceptors bring back the pressure to 120 mm Hg, which is changed with the control system.
	

$$\text{Gain} = \frac{40}{20} = 2 \text{ (negative)}$$

Gain = -2

- If there was a condition where the correction is 100 percent and the error is 0, then the gain of the control system is known as infinite gain.

$$\frac{\text{Correction}}{\text{Error}} = \frac{\text{Correction}}{0} = \infty$$

- An example of such a control system is the Kidney for the regulation of blood pressure and blood volume. The kidney excretes excess water from the body and the blood pressure will return to 100 mm Hg, which makes the error 0. For regulating blood pressure and volume, the kidney has an infinite gain with zero residual error.
- Now, to calculate R, the change with baroreceptor (20) is placed upon change without the control system (60). This is equal to 1/3.

$$R = \frac{20}{60} = \frac{1}{3}$$

- It is to be noted that the accuracy of the control system is inversely related to the regulation factor, or R. More is the regulation factor, less is the accuracy.

$$\text{Accuracy} \ \alpha \ \frac{1}{R}$$

AIIMS Question

Q. Due to certain reasons, the blood pressure of a person falls by 10 mm Hg. Due to the control system, 8 mm Hg gain takes place. Calculate gain and regulation factor

Gain	Regulation factor
• Correction is 8 and error is 2. • According to the formula, Gain becomes -4.	• Change without control system is 10. • Change with control system is 2. • According to the formula, R becomes 1/5.

The Feedforward Control System

00:25:25

PYQ: AIIMS 2019

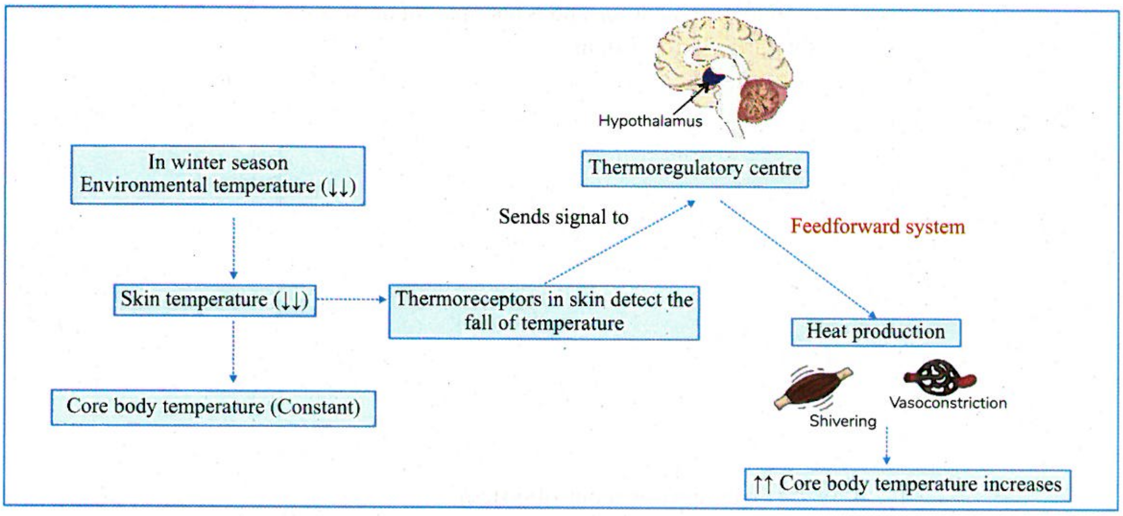
- The feedforward control system is the anticipatory control system. When the control system predicts that some change is about to happen and corrective measures are being taken before the change occurs, that is known as the anticipatory control system.

Examples

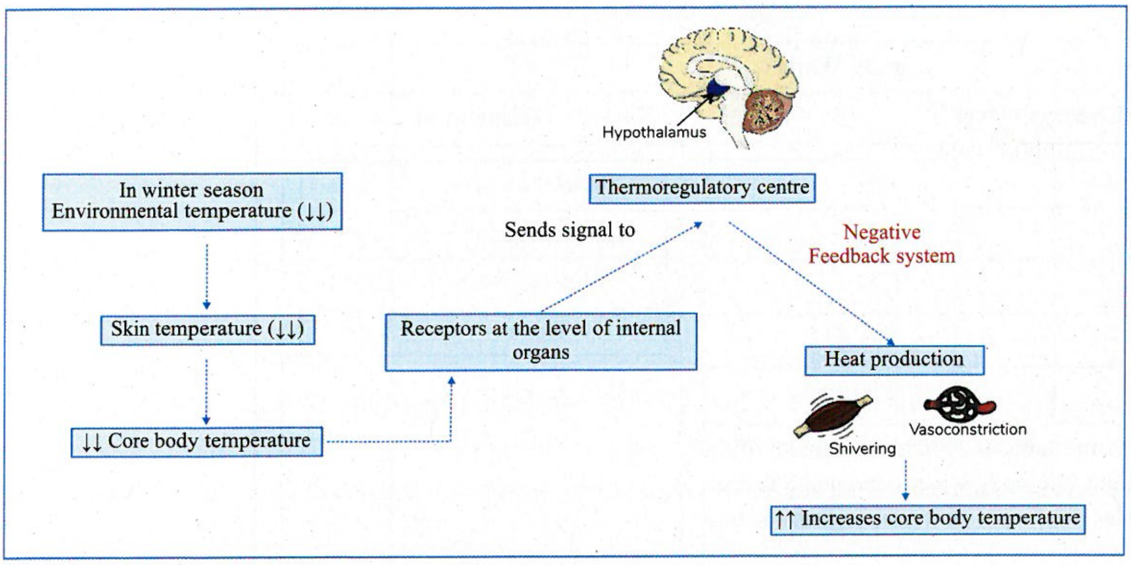
PYQ: INICET 2021

1. **The Thermoregulation System**
   - In this system, the feedforward and the feedback components are present.

For example



- Therefore, the core body temperature rises ahead of fall, this is known as the feedforward loop of thermoregulation.

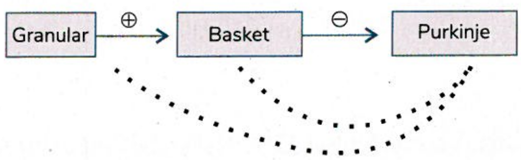


- Thus, when exposed to a very low environmental temperature, the decrease in skin temperature will subsequently decrease the core body temperature.
- Later the core body temperature increases because of the signal received from the thermoregulatory centre which is due to the negative feedback control system.

2. **Increase in Heart Rate and Respiratory Rate even before the start of exercise.**
   - When we start exercising on a treadmill, the thought of exercising activates the system inside the body causing an increase in heart rate and respiratory rate. This is known as psychic stimulation.
3. **Cephalic Phase of Gastric Secretion**
   - The cephalic phase means that the food is at the level of the mouth, or when one is looking at the food when hungry, the acid secretion will start in the stomach as an anticipatory precaution.
4. **Receptive Relaxation of Stomach**
   - Two types of relaxations of the stomach take place,

Receptive relaxation	Adaptive relaxation
When food is at the level of the mouth and one is swallowing it, it enters the upper part of oesophagus first. This in turn relaxes the stomach even before the food reaches. This is known as Receptive relaxation and it is typical of the feedforward control system.	When the food is already inside, the stomach will relax/dilate to adjust the volume of the food. This is adaptive relaxation and is not a part of the feed-forward control system.

5. **Cerebellum**



- The granular cells present at the level of the cerebellum stimulate the basket cells. The basket cells are inhibitory in kind and inhibit the Purkinje cells. The Purkinje cells have no control on the basket cell or on the granular cells. This makes the output unidirectional, from granular to basket and then to purkinje cells. This is an example of the feedforward or anticipatory control system.

2 BODY FLUIDS : DISTRIBUTION AND MANAGEMENT

Body Water

Chemical level

Water	60%
Protein	18%
Fat	15%
Mineral	6%
Glycogen	1%

The percentage given in the table is typical of a male adult person. For a female adult, the body water percentage is less (50% approx.). In females, the fat percentage is higher, and the protein percentage is lower.

Tissue level

Skeletal muscle	36%
Non-skeletal	29%
Adipose tissue	25%
Bone	10%

MCQ

Q. How much is the percentage of protein according to one's body weight?

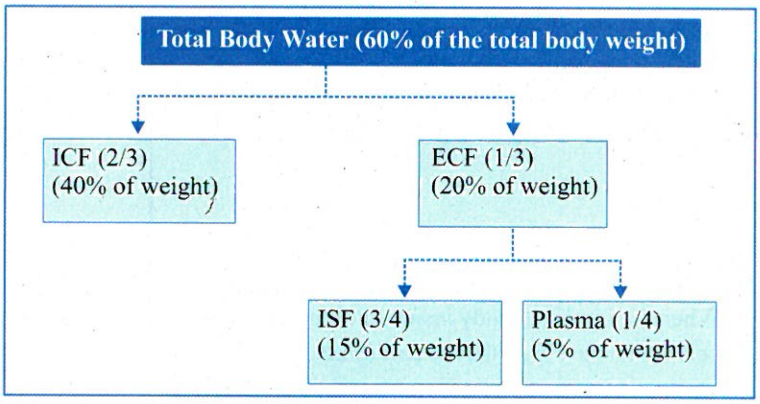
Ans. Protein makes up 18% of one's body weight.

Body Water Percentage in the Body

00:02:21

PYQ: AIIMS 2020

PYQ: NEET PG 2021



- Blood makes up to 8% of body weight (5% plasma and 3% total cell volume - RBC, WBC and Platelets).

MCQ

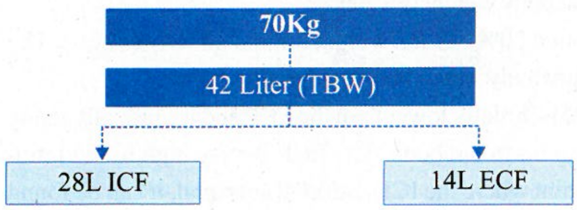
Q 1. ECF is -----------% of the body weight.

Ans: ECF is 20% of the body weight.

Q 2. ECF is -----------% of the total body water.

Ans: As discussed earlier, ECF is 1/3rd of the body water, thus making it 33%. It is to be noted that the percentage here is the percentage of the total body water.

Q 3. When the body weight of the person is known to be 70 kg. What is the total volume of the total body water in this person?



Ans. Our body weight consists of 60% total body water, which for a 70 kg person is 42 litres. This water is divided into 2/3rd (28 litres) for intracellular fluid (ICF) and 1/3rd (14 litres) for extracellular fluid (ECF).

Blood volume calculation

- The total blood volume can be calculated by finding out 8% of the total body weight.
- There is another formula for blood volume calculation based on the hematocrit of the person.
- Blood Volume = $\dfrac{\text{Plasma}}{(1\text{-Htc.})}$

MCQ

Q. The plasma volume of the person is 3 litres, and the hematocrit (packed cell volume/PCV) is 40%, how much is the blood volume?

- Blood Vol. = $\dfrac{\text{Plasma}}{(1\ \text{-Htc.})}$ e.g. Plasma = 3, Htc. = 40% = 0.4

  $= \dfrac{3}{(1\text{-}0.4)} = \dfrac{3}{0.6} = 5$ litres.

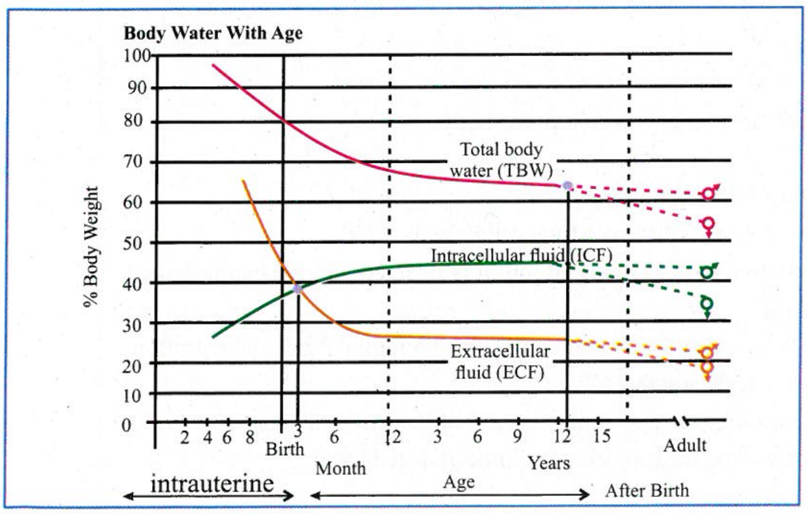
- 5 litres is the blood volume of the person

Transcellular Fluid 00:10:00

- The fluid that is present in certain body cavities.
- For example:
  - Cerebrospinal fluid (CSF) which has a volume of 150 ml approximately.
  - In between the two pleural membranes, the visceral and the parietal pleura, there is an intrapleural fluid of 10-20ml.
  - Pericardial fluid has an approximate volume of 50 ml.
  - Peritoneal fluid has an approximate volume of 0 ml in the case of males and 20 ml in the case of females, particularly in post-ovulatory phases.
  - Synovial fluid which is 1 ml/large joint.

Body Water Changes Along with Age

0012:00



- During intrauterine life, around 90% of the total body weight is water.
- Body water decreases with age & reaches around 60% of total weight around puberty (12yrs). The curve after this point shows that males have more body water than females after puberty.
- During intra-uterine life, the ICF volume curve is initially lower than the ECF and is gradually rising due to organ growth and cell generation going on in the body. The ECF is very high in the intra-uterine life but is gradually decreasing. At a point where the ICF and ECF are equal, it can be found after birth, at 3-4 months of age, the ECF: ICF = 1:1.

Total Body Water: Points to Remember

00:18:57

- More content of body water is seen in pre-term life. 75% of the birth weight of a term infant is body water. In the case of pre-term, it is 90%.
- By the age of 3-4 months, postnatal life ICF and ECF volume become equal, with their ratio being 1:1.
- By the age of 1 year, ICF and ECF approach towards adult levels.
- By 12 years of age, the percentage distribution is equal to the adult percentage distribution.
- At puberty, body fluid % and distribution becomes equal to adult percentage.

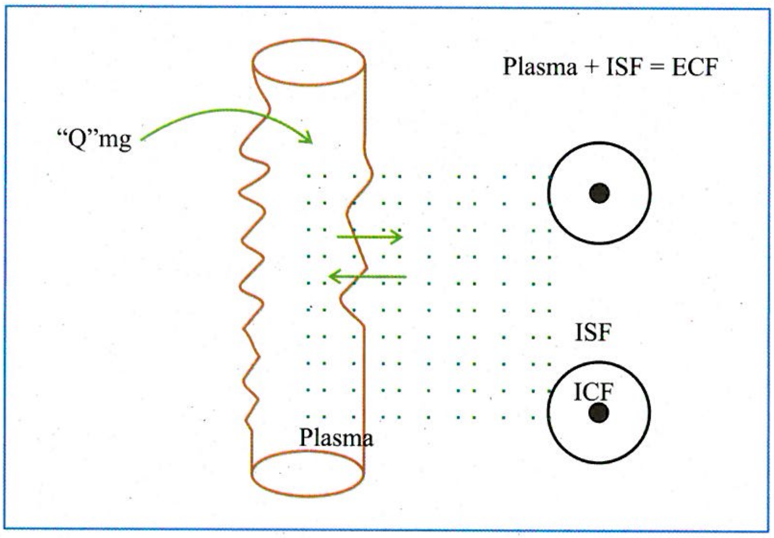
Measurement of Body Water

00:21:11

PYQ: AIIMS 2019

- Approximate calculation of the body water can be estimated according to the body weight.
- To measure the exact amount of body water, the formula of volume of distribution is to be used.

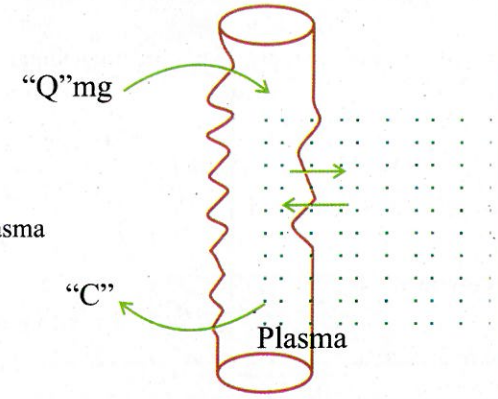
The formula of volume of distribution concept is integrated with the pharmacology.



- Here, a capillary is depicted in the diagram along with cells of the body.
  - Water present inside the cell - ICF
  - Water present outside the cell - Interstitial fluid (ISF)
  - Water present inside the capillary - plasma. (Plasma + Interstitial fluid = ECF)
- When measuring body water, a substance such as Q mg of inulin is injected into the capillary and evenly distributed in the plasma and ISF.
- An equilibrium is reached between the plasma concentration and the interstitial fluid concentration, resulting in inulin being distributed inside the whole ECF.
- After this distribution has reached equilibrium, the concentration of the inulin is measured in the plasma of the person's blood sample by using the formula of volume of distribution.

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

Q-total amount injected; C - concentration in plasma



- Inulin is inert, there is a little chance of it being metabolized by the body. However, some substances are easily metabolized by the body, in such cases both the metabolism and the excretion of such substances must be taken into consideration. The formula for such cases is modified.

  $$\text{Volume} = \frac{Q-e}{c}$$

  e → excreted or metabolized

Must Know Topic

- Here are a few substances used to measure different fluid compartments :

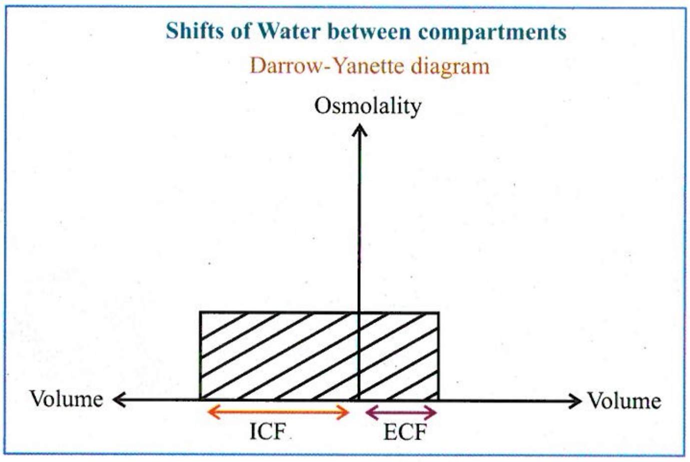
Compartment	Indicator used
Total body water	D_2O, tritium oxide, Antipyrine (freely permeable to capillary and cell membranes)
ECF volume	Inulin (Best), sucrose, ^{22}Na, ^{125}I-iothalamate, mannitol (freely permeable to the capillary and impermeable to cell membrane)
ICF volume	To measure ICF volume, a substance that only distributes within cell fluid should be used. Injecting such a substance into the capillary won't allow it to bypass the ISF to enter the cell directly. Therefore, ICF volume is measured by determining TBW and ECF, and then subtracting ECF from TBW. ICF volume = (TBW - ECF)
Plasma	Evans' blue, ^{125}I-albumin (Impermeable to capillaries)
ISF (Interstitial fluid)	ISF = (ECF – Plasma volume)
RBC	^{51}Cr, ^{59}Fe tagged RBC

The Shift of Body Water Between Different Compartments

00:33:29

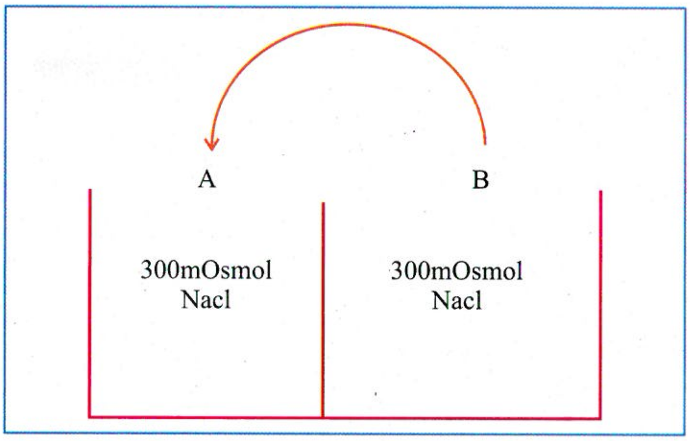
PYQ: AIIMS 2018

- Discussion on how an extra amount of different fluids enter the ICF or ECF based on the Darrow-Yanette diagram.
- Darrow – Yanette Dias illustrates the correlation between volume and osmolality. Total body water is at the center, divided into extracellular fluid (ECF) on the right and intracellular fluid (ICF) on the left. In a steady state, both ECF and ICF have the same osmolality, typically within the normal range of 280-290 mOsmol/l. Changes in osmolality due to fluid administration can alter the diagram accordingly.

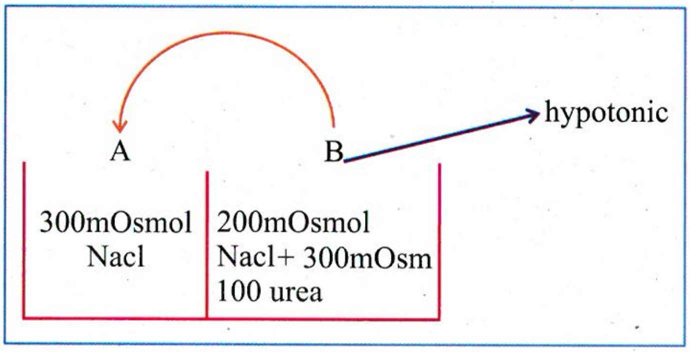


Tonicity

00:37:11



- Tonicity means two compartments separated by a semi-permeable membrane. If both compartments contain 300 mOsmol NaCl, then they become iso-osmolar and isotonic to each other. Tonicity is a way of comparing two solutions' effective osmolality separated by a semi-permeable membrane.
- In medical field, tonicity means the effective osmolality of a solution in comparison to plasma osmolality.
- The osmolality of 0.9% NaCl solution is around 300 mOsmol/l, which is the same as the osmolality of plasma. **This solution is known as an isotonic solution since its effective osmolality is nearly equal to plasma osmolality.**
- Adding 200 mOsmol of NaCl and 100 mOsmol of Urea to compartment B makes it iso-osmolar with compartment A. However, Urea can easily move through the cell membrane, making compartment B hypotonic eventually. Thus, iso-osmolar does not always mean iso-tonic, it may be hypotonic or hypertonic.



How is Plasma osmolality Calculated? (00:43:03)

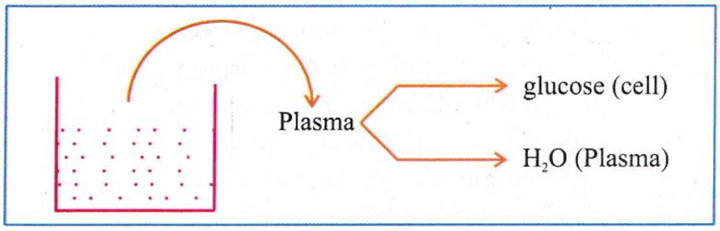
PYQ: FMGE 2023

Plasma Osmolality	
Calculated Osmolality	**Measured Osmolality**
Plasma Osmolality = $2 \times Na+ + \frac{Glu.\ (mg\%)}{18} + \frac{BUN\ (mg\%)}{2.8}$ (or) Plasma Osmolality = $2 \times Na^+ + Glu. + BUN$ (mmol/L) (As per Harrison Internal Medicine) $BUN = \frac{Urea}{2.14}$	• The Freezing Point Depression Technique which is used to measure the actual osmolality of the plasma in the lab, is known as measured osmolality.
• Calculated osmolality takes sodium, glucose and blood urea nitrogen into consideration.	• Measured osmolality takes into consideration all the osmoles present in the plasma.

- Measured Osmolality – Calculated Osmolality = 10 (Osmolar Gap)
- When measuring plasma osmolality (MO), it's essential to note that the value obtained will always be slightly higher than the calculated osmolality (CO). The difference between the two is typically around 10 and should not exceed this limit.
- Increased osmolar gap is noticed in conditions such as:
    - Alcohol poisoning
    - Certain types of sugar can also increase this osmolar gap. For instance, in sorbitol, when its concentration increases in the plasma, the plasma osmolality by calculation will remain the same, but the measured osmolality will be higher.
    - Hyperproteinaemia or hyperlipidemia

Examples of Isotonic Solutions (00:50:38)

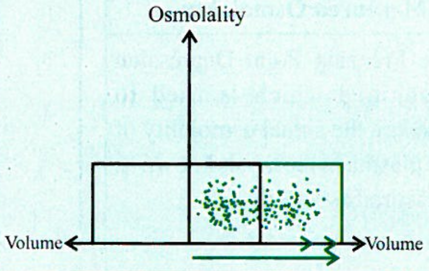
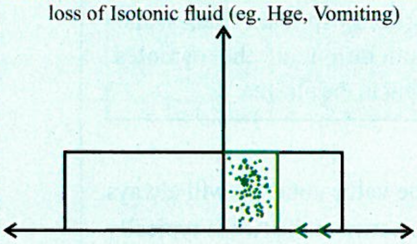
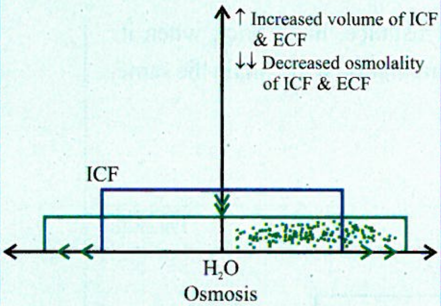
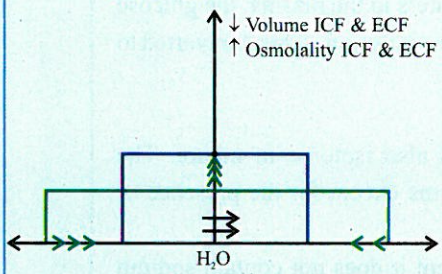
- 5% mannitol is an isotonic solution

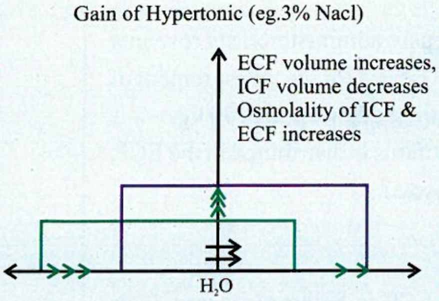
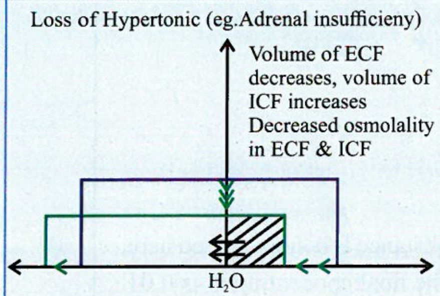


- 5% dextrose is isotonic (in-vitro). This means that if a solution is made of 5% dextrose in a bottle, it will have a tonicity of 290-300 mOsmol/l. But when this solution enters in the plasma, the glucose will be taken out by the cells, and only water will remain. This dextrose solution is then converted to only water, which is hypotonic.
- 0.9% NaCl is isotonic.
- Ringer's lactate solution/lactated Ringer's/Hartmann's solution is also isotonic in nature. The composition of this solution is exactly the same as that of the plasma except for the presence of magnesium.
- The Ringer's solution is the same as Ringer's lactate solution except it does not contain sodium lactate.

Darrow-Yanette Diagram (00:54:26)

- Variations of D-Y diagram due to fluid loss/gain will be discussed :

Gain / Loss of fluids	D-Y Diagram	Explanation
Gain of Isotonic Fluid	**D – Y Diagram** Gain of Isotonic (eg. 0.9% Nacl) 	• When the isotonic solution is given, **ECF volume increases without any change in osmolality**. • Isotonic fluid therapy is safe because only ECF volume increases, which leads to an increase in blood pressure controlled by baroreceptors. However, if ICF volume expands, it can lead to problems.
Loss of Isotonic Fluid	loss of Isotonic fluid (eg. Hge, Vomiting) 	00:57:26 • In cases of hemorrhage or vomiting, there is a loss of isotonic fluid from the body that leads to a **decrease in the volume of ECF without any change in osmolality**.
Gain of Hypotonic Fluid	Gain of Hypotonic (eg. SIADH, Drinking) 	00:59:06 • SIADH causes excess water absorption from the kidneys resulting in hypotonic fluid gain. • Psychogenic polydipsia occurs when one drinks too much water, resulting in hypotonic fluid gain. • There is **ECF volume expansion and the ECF osmolality will fall**. This is not a steady state condition because the ICF osmolality is higher than the current ECF. • Hypotonic ECF solution by osmosis moves to the ICF, **leading to the expansion of ICF volume and a decrease in osmolality**. • Hypotonic fluid therapy is not a good option because it causes cell volume to expand causing intracellular edema.
Loss of Hypotonic Fluid	Loss of Hypotonic (eg.DI) 	01:05:07 • In diabetes insipidus, excess water is excreted due to lack of ADH. • **ECF volume decreases** due to the loss of fluid but since only the water is going out and the solute remains, the **net osmolality and tonicity of ECF increases**, making ECF hypertonic in comparison to ICF. • Water flows via osmosis, **decreasing ICF volume** because the water is going from the cell to ECF, and the **osmolality of the ICF will also start increasing.**

Gain of Hypertonic Fluid		01:08:11 • Infusing 3% NaCl solution (hypertonic solution) in a patient causes **ECF volume to expand and ECF tonicity to increase.** • ECF is now hypertonic in comparison to ICF, and water will now move out of the cell **decreasing ICF volume and increasing ICF tonicity.**
Loss of Hypertonic Fluid		01:10:25 • Conditions such as adrenal insufficiency, the solute is lost from the body with excess of water. • ECF volume will decrease due to hypertonic fluid loss, making it hypotonic compared to cell volume. Water will move from ECF to ICF, leading to a slight increase in cell volume. This will cause a decrease in **ECF volume, an increase in ICF volume, and a decrease in the tonicity of both compartments,** achieving a new steady-state condition.

MCQ

01:12:53

Q1. The volume of distribution of intravenously administered sucrose in a healthy 70-kg man is about

A. 3.5 L
B. 10.5 L
C. 14 L
D. 28 L

Q2. 100 mg of sucrose is injected into a 70 kg man. The plasma level of sucrose after mixing is 0.01 mg/ml. If 5 mg has been metabolized during this period, then what is the ECF volume?

A. 9.5 liters
B. 14 liters
C. 17.5 liters
D. 10 liters

Q3. Total body water differences between male and female is not seen at the age of

A. Above 60 years
B. 40 – 60 years
C. 10-18 years
D. 18 – 25 years

Q4. There is loss of 1 L of water (hypotonic) from body. Calculate decrease in ICF volume

A. 1 L
B. 333 ml
C. 667 ml
D. No loss from ICF

Question 1 Explanation

- The first question deals with the volume of distribution of intravenously administered sucrose in a healthy man of 70 kg. The first catch in this question is sucrose, which is used for the measurement of ECF. So, the question here is asking the volume of ECF in a person with a body weight of 70 kg.
- 70 Kg of weight means that there is 42 liters of total body water. 1/3rd of this is distributed in the ECF, making it 14 litres. Thus, the correct answer is 14 litres (answer is option c).

Question 2 Explanation

- In this question since there is sucrose, it can be understood that ECF is being measured. This question is based on the volume of distribution principle.
- $V = \frac{Q - e}{C}$

  $= \frac{100-5}{0.01} = \frac{95}{0.01} = 9500 \text{ nU}$

- So, V = Q – e upon C, this formula is being applied here. 100 mg of substance is being injected here, making the Q 100. 5 mg of substance is metabolized, making e 5. The final concentration is 0.01. Thus, it is calculated to be 9500 ml, which is 9.5 litres (the answer is option a).

Question 3 Explanation

- The third question deals with the total body water difference between males and females. The difference is not seen until in and around puberty. This difference continues for lifelong after that. Thus, the age group here will be 10-18 years (the answer is option c).

Question 4 Explanation

- Here, there is a loss from both compartments. 2/3rd is lost from ICF, and 1/3rd is lost from ECF. So, 1/3rd of 1 litre is 333 ml is lost from ECF, and 667 ml is lost from ICF (the answer is option c).