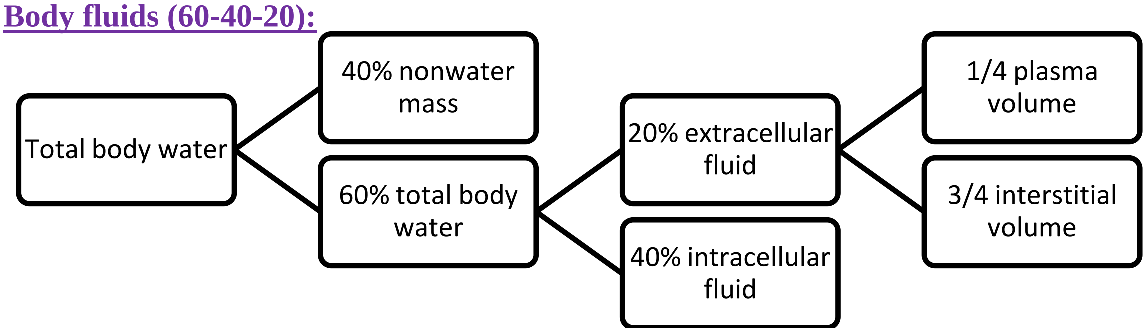
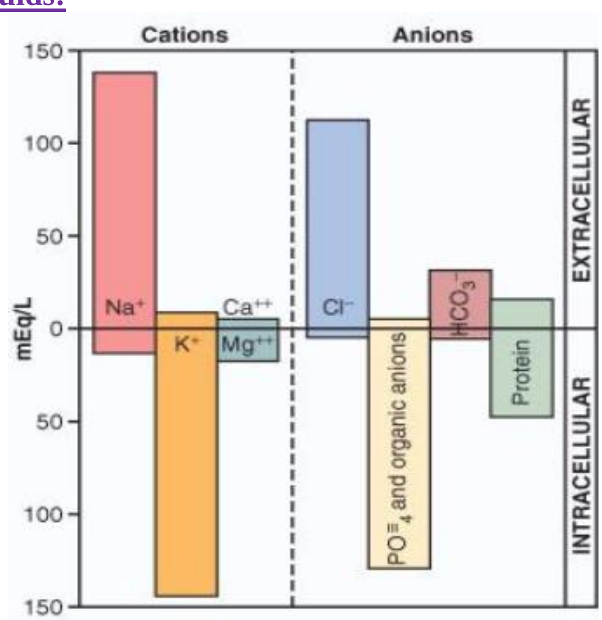
- **The concept of balance (الإتزان):**
  - **Fluid and electrolyte balances are important, in the long-term, to maintain life. This is represented by:**
    - ✓ Fluid loss (regulated mainly by kidneys) = fluid intake (regulated by thirst mechanism).
    - ✓ Electrolyte loss (regulated mainly by kidneys) = electrolyte intake (governed by dietary habits).
  - **Water balance:**
    - ✓ Daily intake is nearly 2.2 L/day.
    - ✓ Metabolic production of water in the body = 0.3 L/day.
    - ✓ Output through (skin, lungs, urine and feces) = 2.5 L/day.

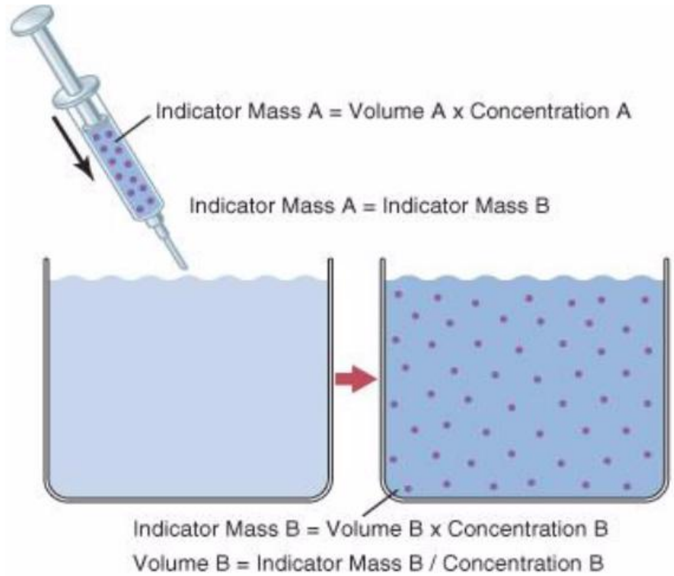
      Notes:
      - ❖ Normally, there is a state of balance (no excessive intake, no excessive output).
      - ❖ Disorders of water homeostasis result in hyponatremia (decreased sodium level in blood) or hypernatremia (increased sodium level in blood).
      - ❖ A minimum urine output of 500 ml/day is needed for neutral solute balance → this is known as obligate water loss.
- **Body fluids (60-40-20):**



- **Major cations (positively-charged) and anions (negatively-charged) of intra-cellular and extra-cellular fluids:**



- **Measuring volumes of body compartments (see the image in next page):**
  - **Example**: if 1ml of a solution containing 10 mg/ml of dye is dispersed into chamber B and the final concentration in the chamber is 0.01 mg/ml, the unknown volume of the chamber can be calculated as follows:
    - ✓ Volume B = $\frac{Indicator\ \ mass\ \ B\ (Volume\ \ B\ x\ Concentration\ \ B)}{Concentration\ \ B} = \frac{1\ x\ 10}{0.01}$ = 1000 ml

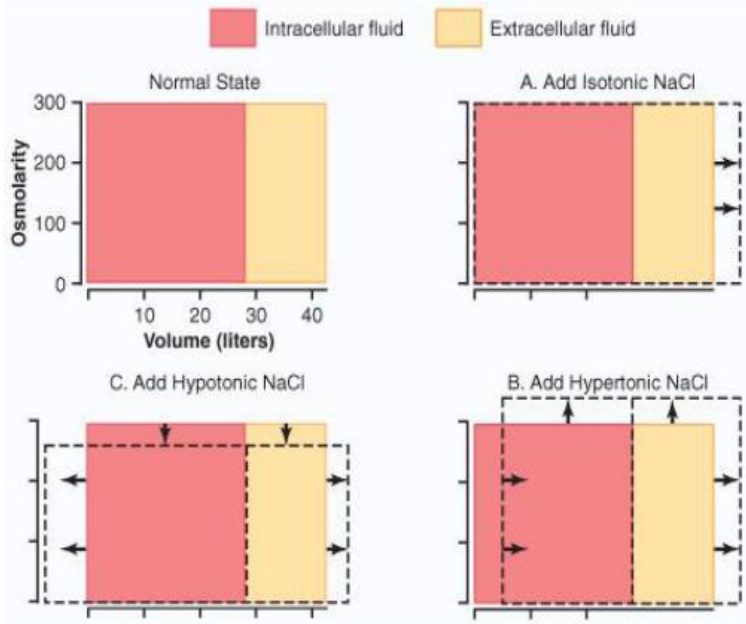


- **Total body water is measured by**: radioactive water ($^{3}H_2O$).
- **Extraceullar fluid volume is measured by**: inulin.
- **Intraceullar fluid volume** = total body water – extracellular fluid volume.
- **Plasma volume is measured by:** radiolabeled albumin (^{125}I-albumin).
- **Intestitial fluid volume** = extracellular fluid volume – plasma volume.
- **Blood volume**: 51 Cr-labeled red blood cells.

- <u>**Basic principles of osmolarity:**</u>

- Osmolality describes the total concentration of all particles that are free in a solution.
- All body fluids have the same osmolality.
- Particles bound to macromolecules do not contribute at all to osmolality.
- **Osmolarity**: osmoles expressed as per liter of solution.
- **Calculated osmolality = 2[Na$^+$] +** $\frac{BUN\ (\frac{mg}{dl})}{2.8} + \frac{glucose\ (\frac{mg}{dl})}{18}$
- **Normal osmolality** = 290 mOsm/kg of water.
- **Antidiuretic Hormone (ADH: which is also known as vasopressin) release:**
  - ✓ <u>When osmolality is increased</u> → this will be sensed via osmoreceptors which are found in the hypothalamus → hypothalamus will send signals to release the stored ADH from posterior pituitary gland → ADH will result in absorption of free water from collecting tubules in kidneys → therefore, correcting osmolality.
- **Aldosterone:**
  - ✓ <u>When blood volume is reduced</u> → renin-angiotensin-aldosterone system will be activated → aldosterone will released from zona glomerulosa of adrenal cortex resulting in absorption of water and sodium, secretion of potassium and secretion of [H$^+$].
- **Atrial Natriuretic Peptide (ANP):**
  - ✓ <u>When blood volume is increased</u> → cardiac atria will be stretched → resulting in the secretion of ANP → which will increase sodium excretion by kidneys → leading to diuresis.
- **Control of body fluid distribution:**
  - ✓ Distribution across cell membranes: it is determined by osmotic forces (mainly from electrolytes).
  - ✓ Distribution across capillaries: it is determined by hydrostatic (pushing fluid outside capillaries) and colloid osmotic forces (pushing fluid inside capillaries).

- **Calculation of intracellular and extracellular fluid volumes and osmolarities after fluid administration:**
  - ✓ The image below shows the effect on body fluid compartments of infusing different solutions:



  - ✓ Assume the standar 70 kg male, in whom the original osmolality of extracellular fluid is 290 mOsm/kg water. Consider addition of 2L of distilled water to the extracellular fluid. Describe in words the shifts that take place, and calculate the effect of this addition on the volumes and osmolality of the extracellular fluid and intracellular fluid.
    - ❖ Addition of water to the extracellular fluid increases its volume and reduces its osmolality.
    - ❖ We assume there are no significant movements of solutes across the cell membrane.
    - ❖ The cell membranes are permeable to water, and the increased water concentration in the extracellular fluid causes water to enter cells, increasing the volume of the intracellular fluid and reducing the extracellular fluid volume (but not returning it to its initial volume).
    - ❖ The shift of water results in re-establishment of osmotic equilibrium between extracellular fluid and intracellular fluid, with both having increased volumes and decreased osmolalites.
    - ❖ Initial conditions:

Total body water	0.6 x 70 = 42 liters
Intracellular fluid volume	0.4 x 70 = 28 liters
Extracellular fluid volume	0.2 x 70 = 14 liters
Total body osmoles	Total body water volume x osmolality = 42 x 290 = 12180 mOsm
Intracellular fluid osmoles	Intracellular fluid volume x osmolality = 28 x 290 = 8120 mOsm
Extracellular fluid osmoles	Extracellular fluid volume x osmolality = 14 x 290 = 4060 mOsm

    - ❖ Final conditions:

Final osmolality	Total body osmoles/ new total body water volume = 12180/(42+2) = 277 mOsm/kg water
Final intracellular fluid volume	Intracellular fluid osmoles/ new osmolality = 8120/277 = 29.3 kg water = 29.3 liters

Final extracellular fluid volume	Extracellular fluid osmoles/ new osmolality = 4060/277 = 14.65 kg water = 14.65 liters

- ✓ Summary of common body fluid disturbances:

Condition	Example	EC Fluid		IC Fluid	
		Osmolality	Volume	Osmolality	Volume
Hyposmotic expansion	excessive water intake	↓	↑	↓	↑
Hyposmotic contraction	salt wasting (Loss by kidneys)	↓	↓	↓	↑
Isosmotic expansion	IV infusion, edema	↔	↑	↔	↔
Isosmotic contraction	hemorrhage, burns	↔	↓	↔	↔
Hyperosmotic expansion	drink conc. saline	↑	↑	↑	↓
Hyperosmotic contraction	severe sweating	↑	↓	↑	↓

- **Abnormalities of extracellular fluid Na^+ concentration (notice that normal plasma level of Na^+ = 140-145 mmol/L):**
  - ✓ Hypernatremia: increased sodium concentration leading to shrinkage of the cell:
    - ❖ *Water loss through:*
      - ➢ Increased water loss.
      - ➢ Excessive sweat loss.
      - ➢ Central (e.g. no production of ADH) or nephrogenic (e.g. ADH is produced but not acting on its receptors in kidneys) diabetes insipidus.
    - ❖ *Sodium excess through:*
      - ➢ Excessive secretion of aldosterone.
  - ✓ Hyponatremia: decreased sodium concentration leading to swelling of the cell:
    - ❖ *Water excess through:*
      - ➢ Large water ingestion.
      - ➢ Syndrome of Inappropriate ADH Secretion (SIADH).
    - ❖ *Sodium loss through:*
      - ➢ Diarrhea and vomiting.
      - ➢ Overuse of diuretics.
      - ➢ Addison's disease (due to the decreased secretion of aldosterone).
    - ❖ *The image shows effects of acute and chronic hyponatremia on the brain.*