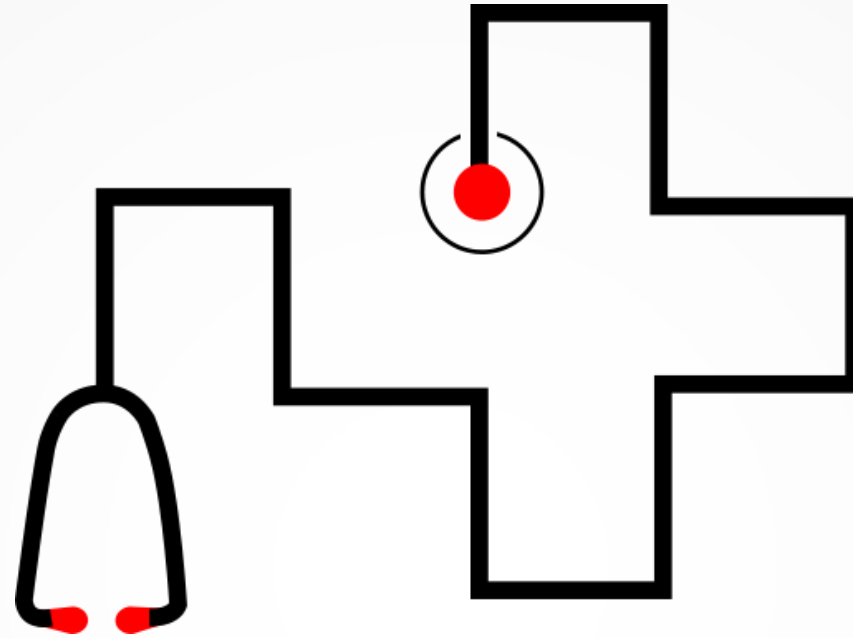
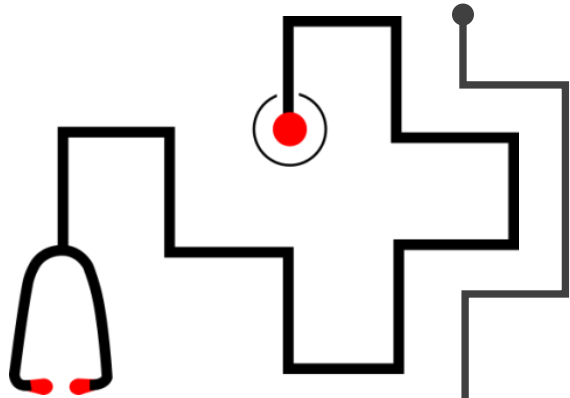




Fluid therapy what is between lines?

Prepared by Dr El Gaeedy Gehad



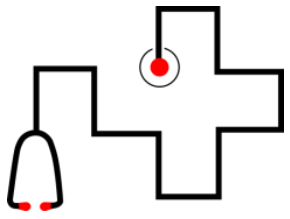
Introduction

Advances in fluid therapy have had a lower profile than other areas of anesthesia (New Drugs & Monitors)

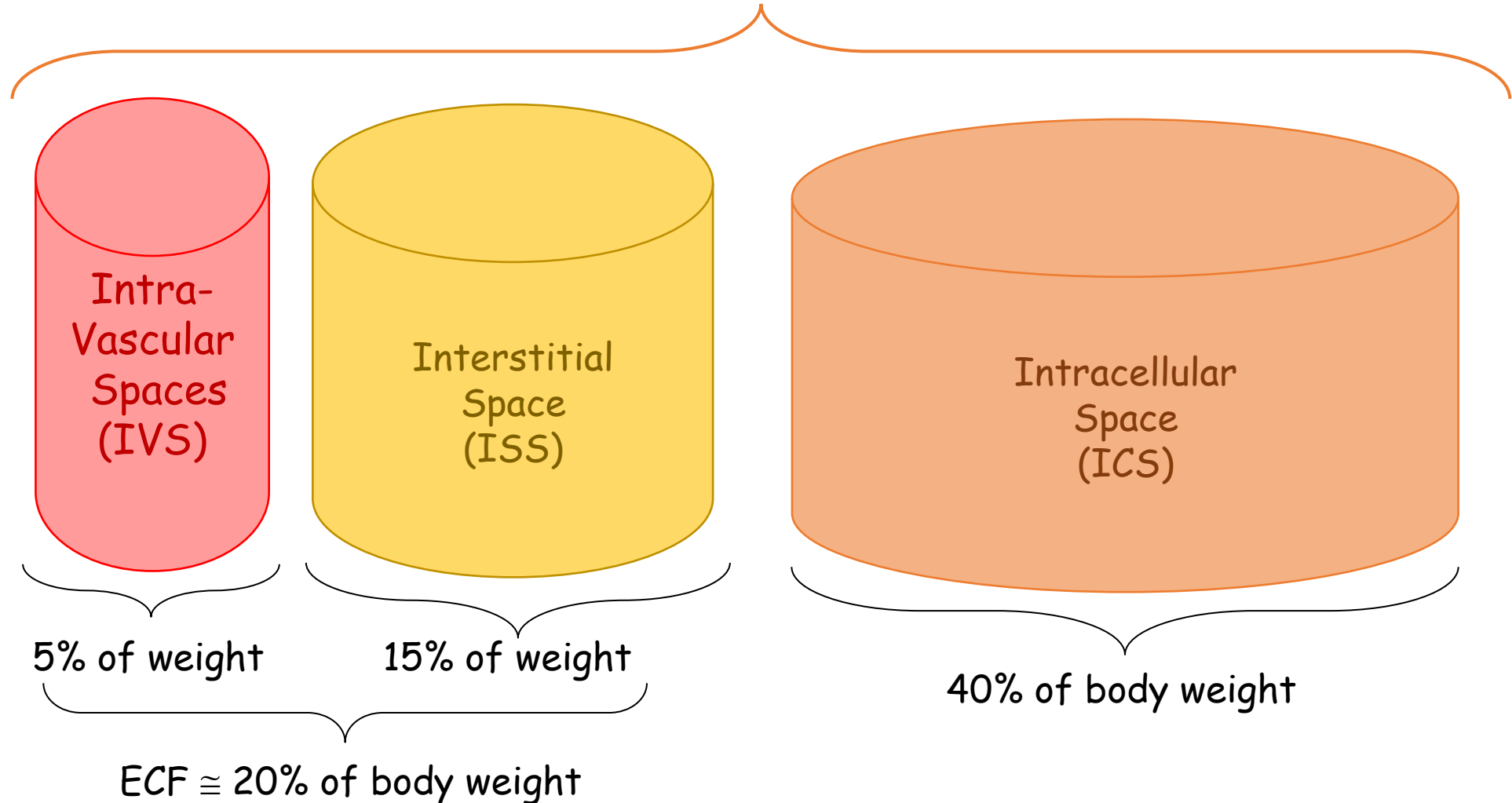
WHY?

- 🍏 Less problems with our routine perioperative use.
- 🍏 Fluids are not confined to specific organ.
- 🍏 Finances

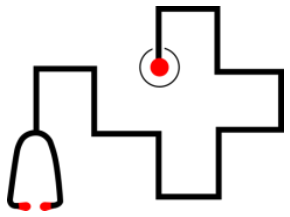
Physiological Considerations



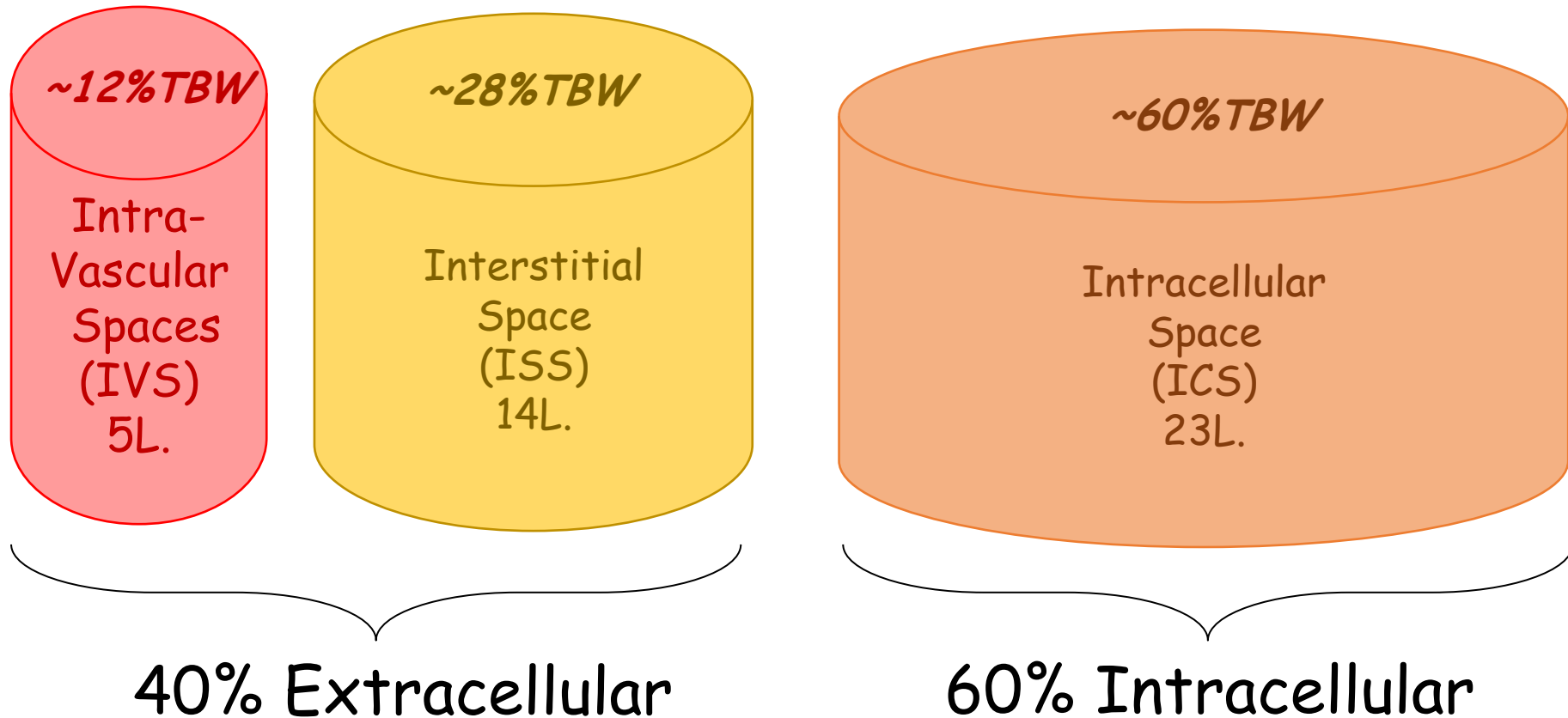
Total Body Water (TBW) $\cong$ 60% of body weight



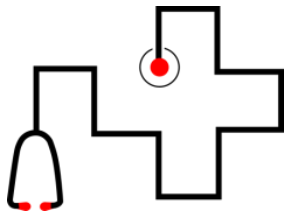
Physiological Considerations



Body Fluid Distribution in a 70 kg Male



Physiological Considerations



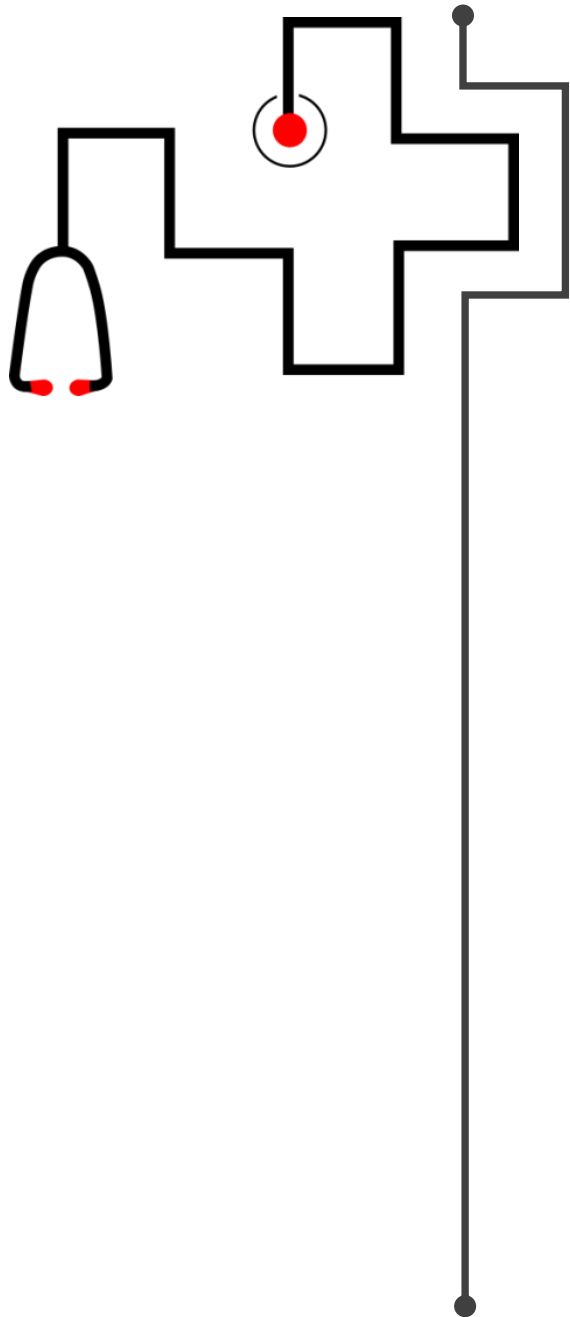
Colloid or Blood



IVS

ISS

ICS



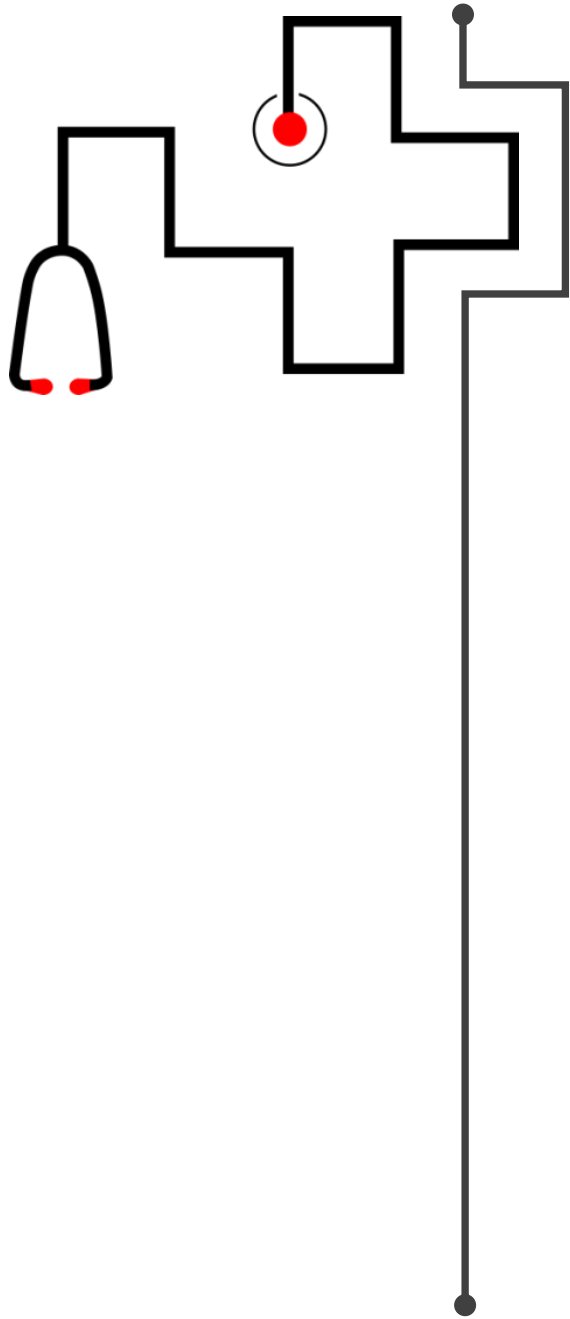
Assessment of Body Fluids

I. Assessment of Intravascular Space

Intravascular Space Is Amenable to estimation through:

- ♪ Pulse rate
- ♪ Blood pressure
- ♪ Peripheral perfusion
- ♪ Urine output
- ♪ CVP ,PCWP
- ♪ COP
- ♪ HCT

*Provided Other Factors Are Fixed
Anesthesia--drugs--diseases*



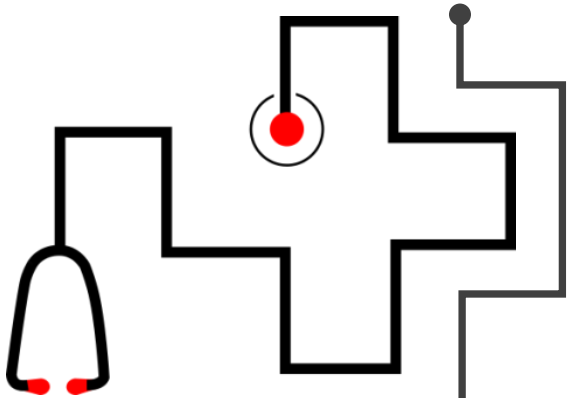
Assessment of Interstitial and Intracellular Space

DIFFICULT

DIFFICULT

DIFFICULT

Assessment of Interstitial and Intracellular Space



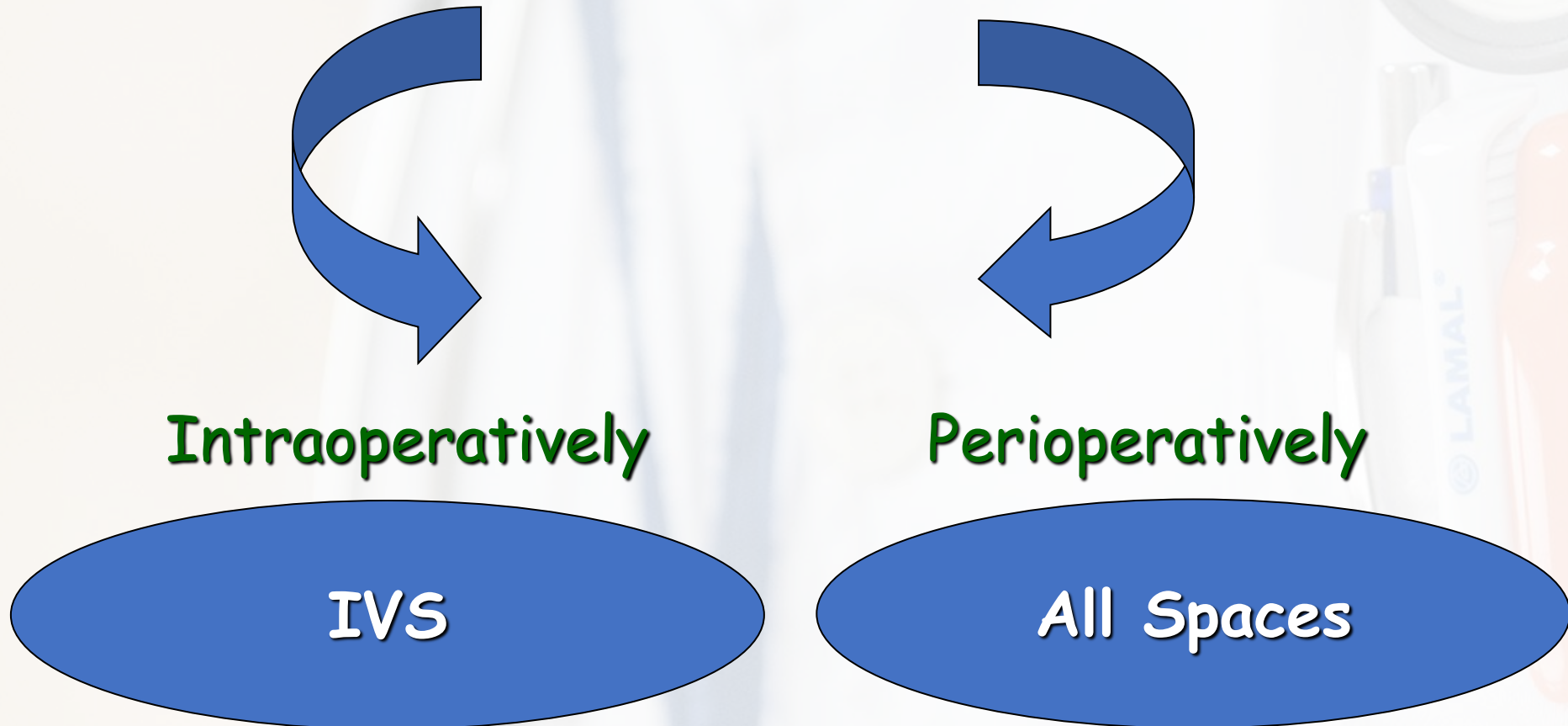
-  Clinical History
-  Skin Turgor
-  Mucous Membrane
-  Fluid Balance Sheet
-  Chest X-ray

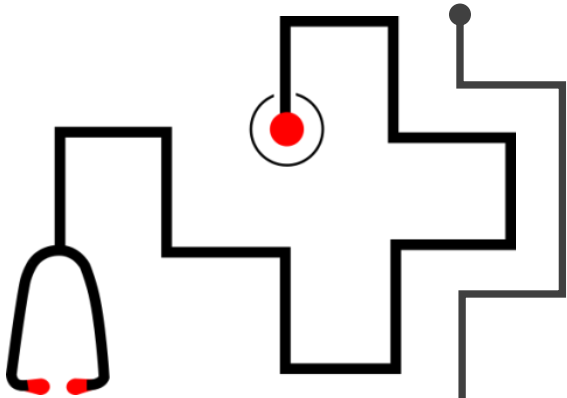
Fluid Replacement



Intracellular dehydration is rarely a life threatening problem

Our Concern





Choice of Fluid Replacement

✧ *Non -Ionic Solutions:-*

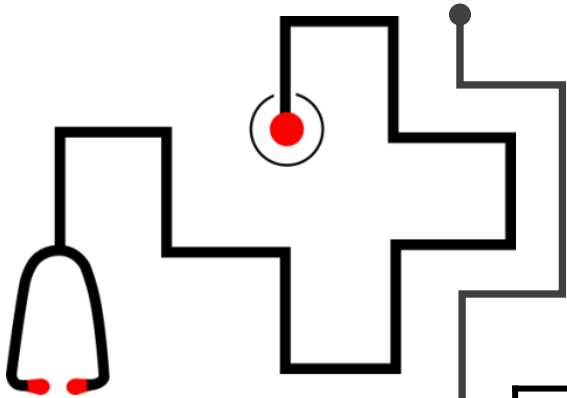
Dextrose 5.0% & Amino-acids solutions.

✧ *Sodium-containing Solutions:- (Ionic Solutions)*

Saline 0.9% Ringer's & Ringer's Lactate.

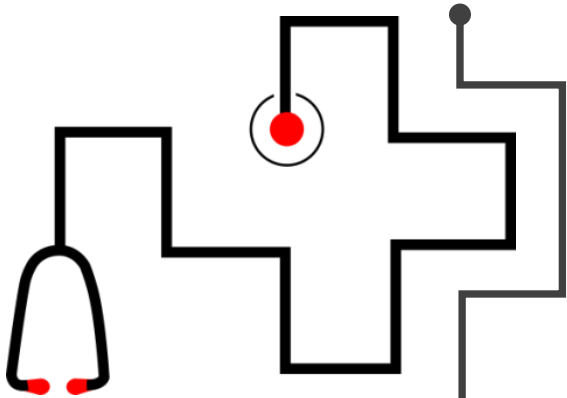
✧ *Blood Products& Colloids :-*

Dextrans & Gelatins & Starch



Composition of Commonly Used I. V. Fluids

Fluid	Na meq/L	Cl meq/L	PH
Saline 0.9%	154	154	??
Ringer's Lactate	131	112	??
Dextrose 5.0%	--	--	??



Manipulation of body fluid spaces

I.V. fluid is distributed to the three fluid spaces according to :-

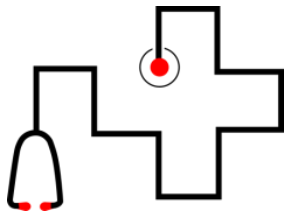


Its sodium concentration.

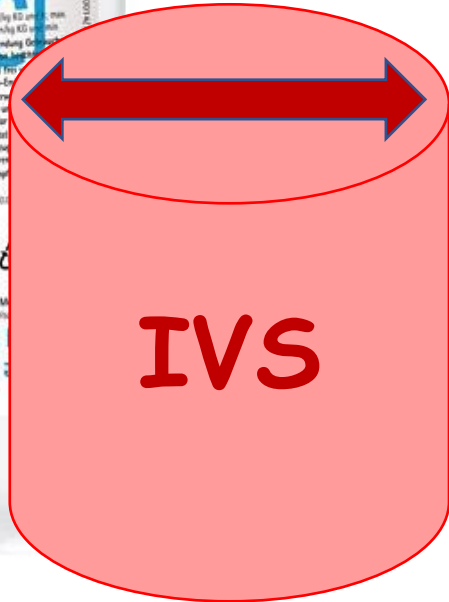


Oncotic pressure

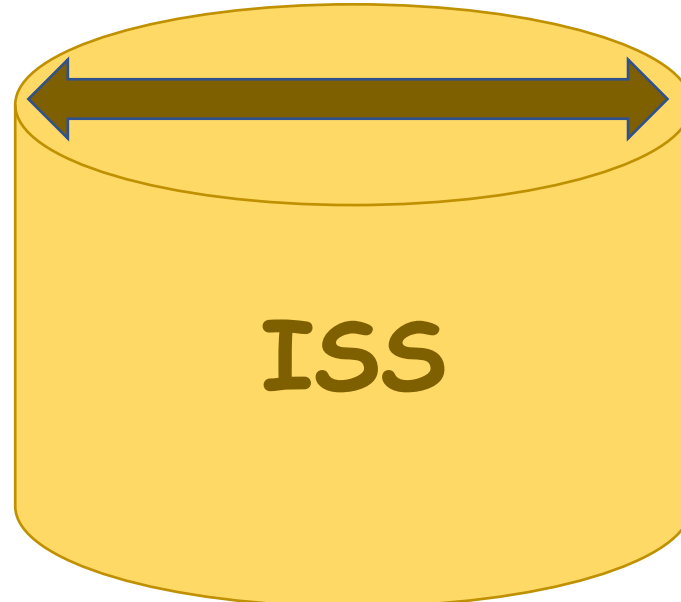
Physiological Considerations



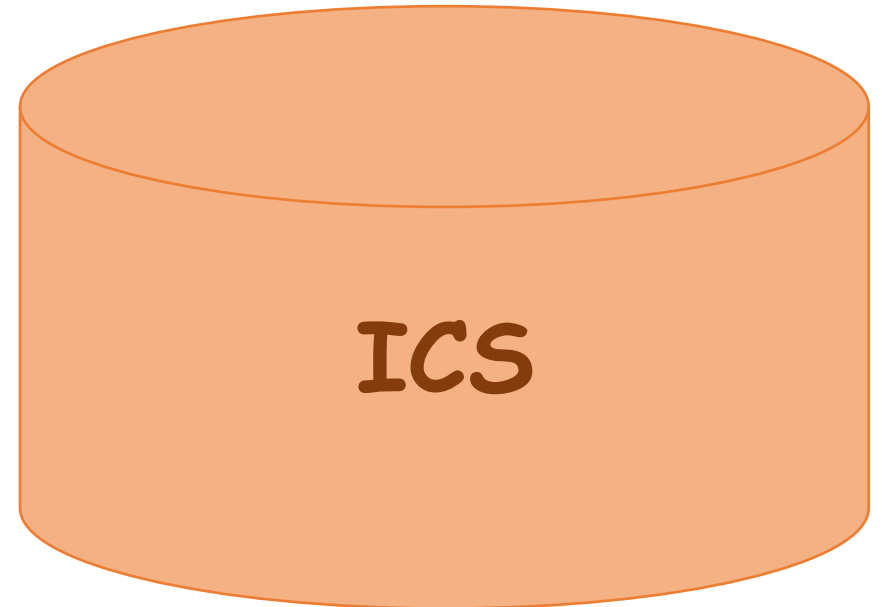
Normal Saline



IVS

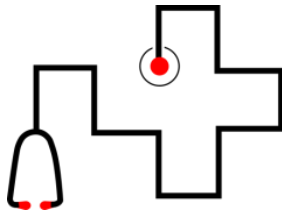


ISS

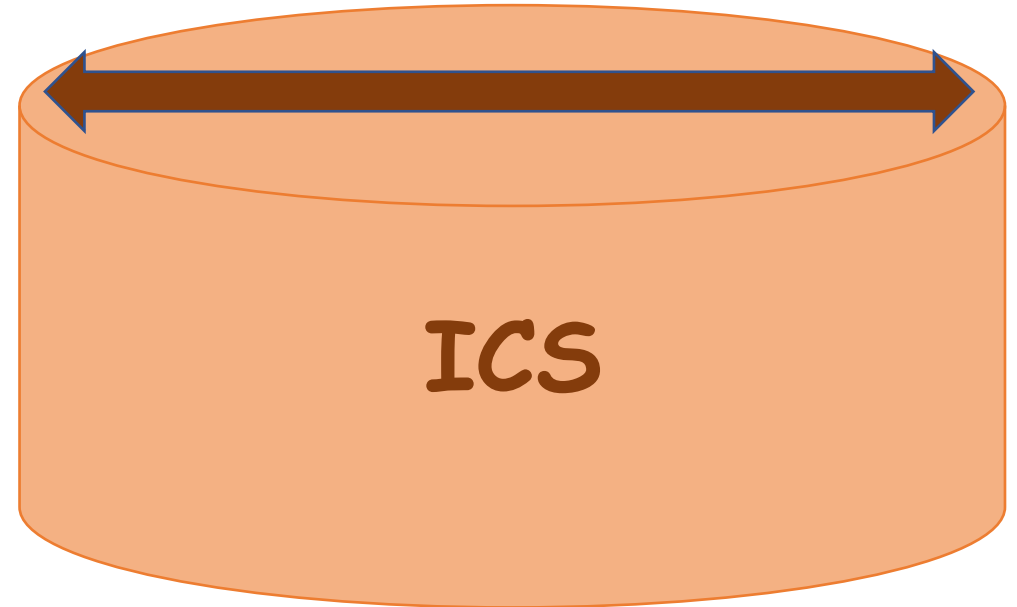
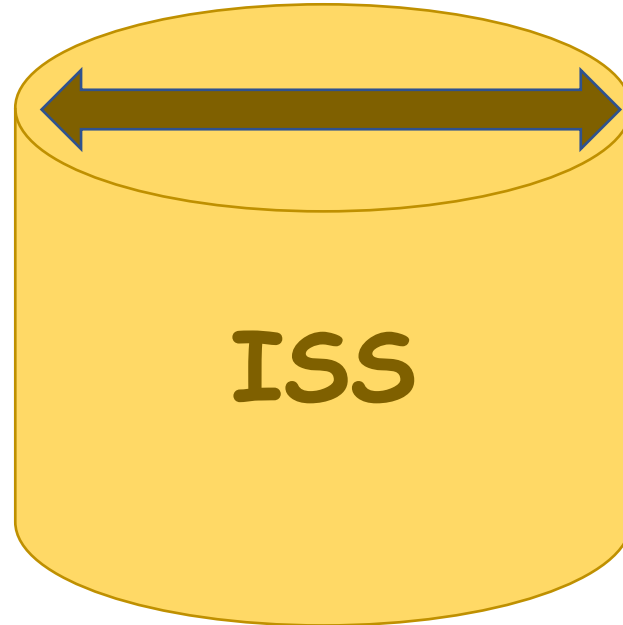
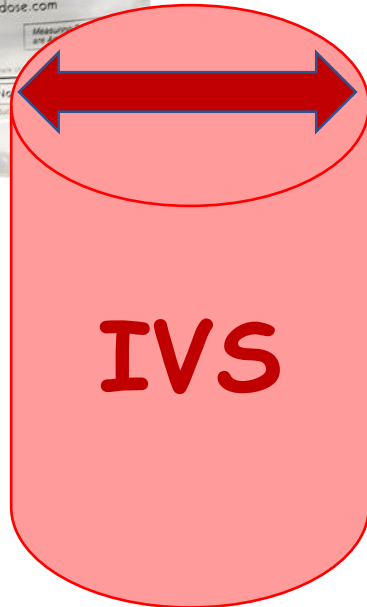


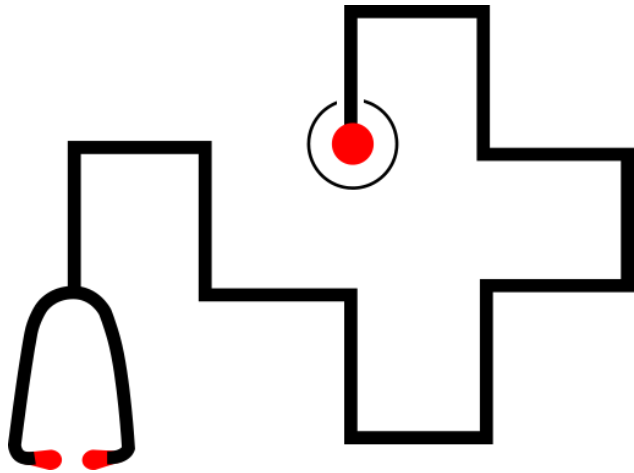
ICS

Physiological Considerations



Dextrose 5% in Water



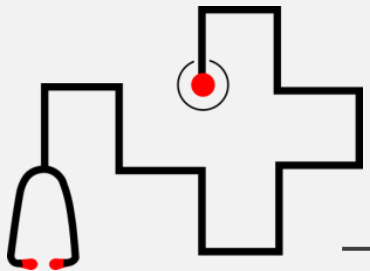


Crystalloid solutions

Crystalloid solutions

Definition

Crystalloids are substances that forms a true solution and is capable of being crystalized



Normal saline

Normal saline

0.9% NaCl

PH 5.7

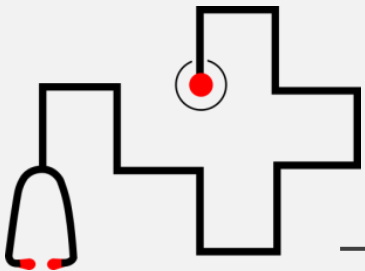
Expansion Volume 10%



Infusion of one liter adds 275 ml to plasma volume and 825 ml to the interstitial space volume.

However the total increase in extracellular volume (1100 ml) Is slightly greater than the infused volume.

This is a result of a fluid shift from the intracellular to extracellular fluid, which occurs because of normal saline is slightly hypertonic to the extracellular fluid (Expansion Volume 10%).



Dextrose 5% in Water

D5%W

The infusion of one liter of D5% results in increase of ECF by 350 ml, which means the remaining 650 ml has moved intracellularly.

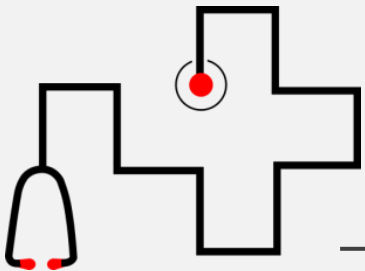


Therefore, the predominant effect of D5% is cellular swelling.

12%(3 parts) and 28% (7 parts)

$350 / 10 \text{ parts} = 35 \text{ ml}$

$35 \text{ ml} \times 3 \text{ parts}(12\%) = 105 \text{ ml D5\%w in IVS}$



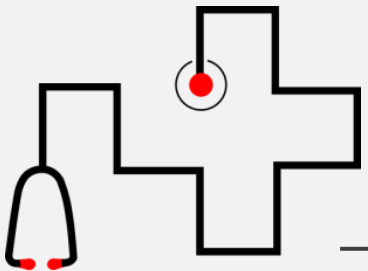
Balanced solutions

Ringers (British physician) 0.9% NaCl + K + Ca

Hartmanns (American pediatrician) added lactate to Ringers solution to provide buffer for treatment of metabolic acidosis, called also **Ringers lactate**.

Ringers acetate; because of concerns that large volume infusions of Ringers lactate solutions could increase plasma lactate levels in patients with impaired lactate clearance from liver disease, the lactate buffer was replaced by the acetate to create Ringers acetate solution.

Acetate metabolized in the muscles rather than liver, which makes Ringers acetate a reasonable alternative in patients with liver failure.



Balanced solutions

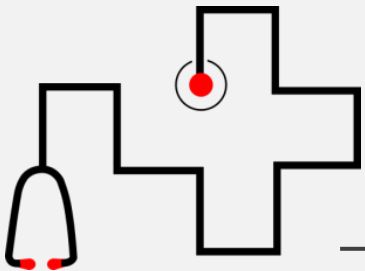
Nb) **lactate**, **acetate** and **citrate** are **bicarbonate precursors** which enters the citric acid cycle.

Changes (increase) in ECF volume is 900 ml and 100 ml in ICF volume.

Lactate 28 or Acetate 28



	Na	Cl	K	Ca	PH	Osm
Ringers	147	155	4	4	5.8	310
Ringers Lactate	130	109	4	3	6.5	274
Ringers Acetate	130	112	5	3	6.7	276



Other Balanced Salt Solutions

Two of the crystalloid fluids:

☆☆ Normosol

☆☆ Plasma-Lyte

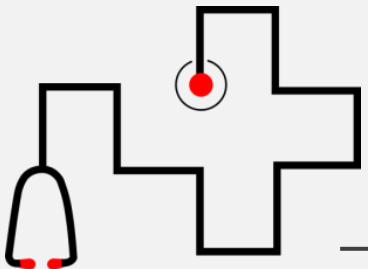


Contain

Magnesium instead of **Calcium**, and contain **both Acetate** and **Gluconate** buffers to achieve a pH of 7.4

These fluids are not as popular as isotonic saline or Ringer's lactate, but the absence of calcium makes them suitable as diluents for RBC transfusions, and

Plasma-Lyte has shown less of a tendency to promote interstitial edema when compared with isotonic saline.

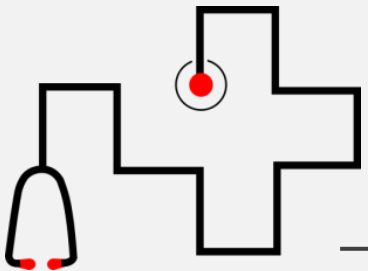


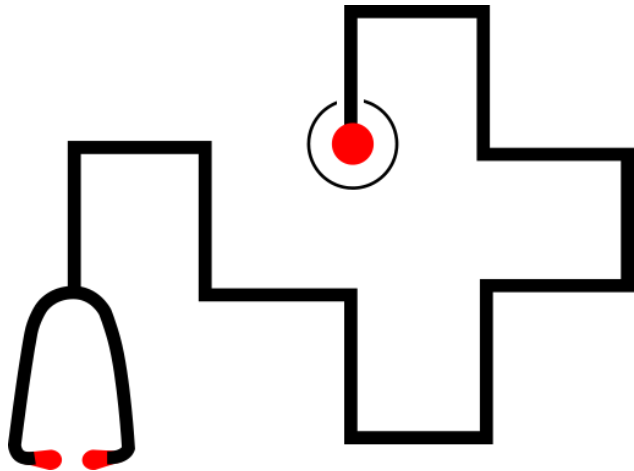
Hypertonic Saline

Hypertonic saline solutions like 7.5% NaCL (which has an osmolality 8-9 times greater than plasma) are much more effective at expanding the extracellular volume than isotonic crystalloid fluids.

- Infusion of 250 mL of 7.5% NaCL results in a 1,235 mL increase in extracellular fluid, which is about 5 times greater than the infusion volume. (The added volume comes from the intracellular fluid.)

Animal studies have shown that hypertonic saline is effective for limited-volume resuscitation of hemorrhagic shock, which shows that hypertonic saline can restore and maintain cardiac output with 1/5 the volume required with isotonic saline.





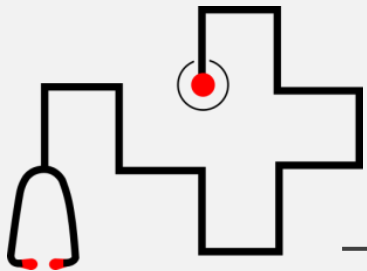
Colloid solutions

Definition

A colloid is defined as a high molecular weight (MW) substance that largely remains in the intravascular compartment, thereby generating an oncotic pressure.



Colloids are considered to have a greater intravascular persistence when compared to crystalloids. This property is lost, however, when capillary membranes are altered in a diseased state.



Types

 **Natural** i.e., human albumin

Albumin **4% iso-oncotic** with a degree of **volume expansion 80%**,

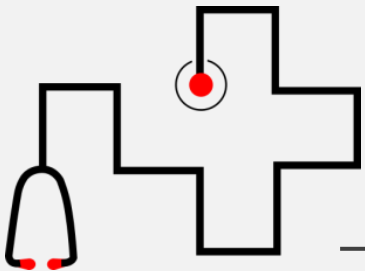
whereas

 Albumin **25% hyperoncotic** with a degree of **volume expansion 200-400%**.

The effect of infused albumin persists 16-24 h.

Molecular weight 69000 Dalton.

Albumin normally comprising 50-60 % of all plasma proteins and contributes to 80% of the normal oncotic pressure.



Types

✳ Artificial,

i.e., Gelatin and Dextran solutions, Hydroxyethyl Starches (HES).

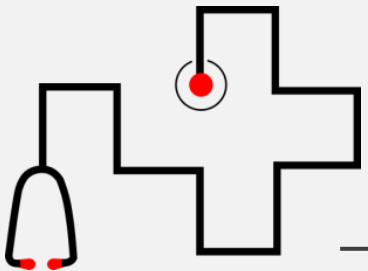


Acid Base Composition:

Albumin and Gelatins have physiological PH,

while

Other solutions tend to have acidic PH.

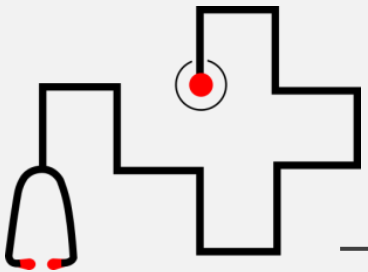


Dextran

Two dextran solutions are now most widely used,

• a 6% solution with an average molecular weight of 70,000 (Dextran 70) and

a 10% solution with an average weight of 40,000 (Dextran 40, low-molecular-weight dextran).



Metabolism & Excretion

Kidneys primarily excrete dextran solutions.

Smaller molecules (14000-18000kDa) are excreted in 15 minutes,

whereas

larger molecules stay in circulation for several days.

- Up to 40% of dextran-40 and 70% of dextran-70 remain in circulation at 12 h.

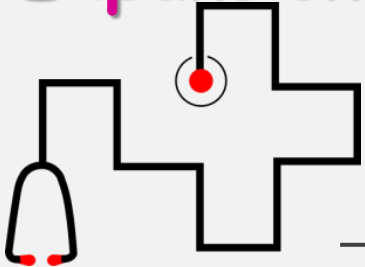
The duration lasts for 6-12 hours

Dextran-40 (200%),

Dextran-70 (120%).

Maximal daily Infusion: **1.5 g/kg.**

Volume Expansion



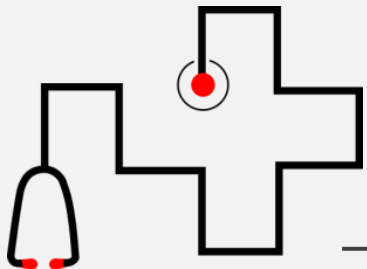
Indications

- ⌘ Dextran-40 is used mainly to improve micro-circulatory flow in microsurgical re-implantations.
- ⌘ Extracorporeal circulation: It has been used in extracorporeal circulation during cardio-pulmonary bypass.



Advantages

- Ω Volume expansion: Dextran leads to 100-150% increase in intravascular volume.
- Ω Microcirculation: Dextran 40 helps in improving microcirculatory flow by two mechanisms, i.e., by decreasing the viscosity of blood by haemodilution and by inhibiting erythrocytic aggregation.



Disadvantages

✳️ Anaphylactic reactions:

Causes more severe anaphylactic reactions than the gelatins or the starches.

✳️ Coagulation abnormalities:

- Decreased platelet adhesiveness
- Decreased factor VIII
- Increased fibrinolysis
- Associated with significant bleeding complications.

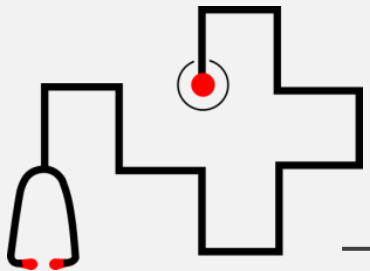
✳️ Interference with cross-match:

Coats the surface of RBCs and can interfere with the ability to cross-match blood.

Increases erythrocyte sedimentation rate.

✳️ Precipitation of acute renal failure:

A possible mechanism for this is the accumulation of the dextran molecules in the renal tubules causing tubular plugging.



Gelatins

Gelatin is the name given to the proteins formed when the connective tissues of animals are boiled.

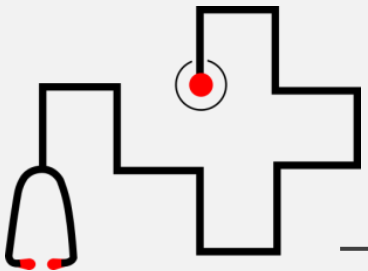
They have the property of dissolving in hot water and forming a jelly when cooled.

 Gelatin is thus a large molecular weight protein formed from hydrolysis of collagen.

Gelatin solutions were first used as colloids in man in 1915.

The early solutions had a high molecular weight (about 100,000). This had the advantage of a significant oncotic effect but the disadvantages of a high viscosity and a tendency to gel and solidify if stored at low temperatures.

Several modified gelatin products are now available; they have been collectively called the New-generation Gelatins.



New-generation Gelatins

There are 3 types of gelatin solutions currently in use in the world:

❧❧❧ Succinylated or modified fluid gelatins

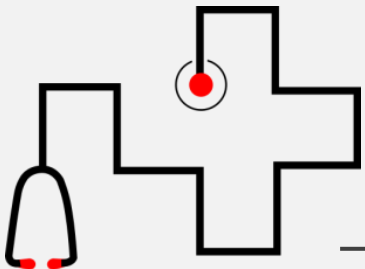
Gelofusine
Plasmagel
Plasmion

❧❧❧ Urea-crosslinked gelatins

Polygeline {Haemaccel}

❧❧❧ Oxypolygelatins

Gelifundol



Physiochemical properties:

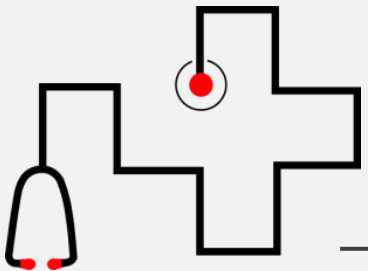
Both succinylated and Urea-crosslinked gelatins are supplied as preservative-free, sterile solutions in sodium chloride.

● Succinylated gelatin

Is supplied as 4% solution with electrolytes
(Na⁺ 154, K⁺ 0.4, Ca⁺⁺ 0.4 and Cl⁻ 120 mmol/l).

As it contains low chloride it is helpful for fluid resuscitation in patients with hyperchloremic acidosis.

Also succinylated gelatins are compatible with blood transfusions due to low calcium content.



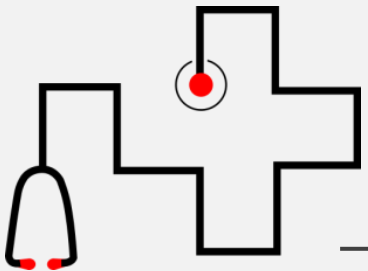
Polygeline

Is supplied as a 3.5% solution with electrolytes
(Na⁺ 145, K⁺ 5.1, Ca⁺⁺ 6.25 & Cl⁻ 145 mmol/l).

As polygeline contains calcium ions it can lead to increase in serum calcium concentration following large volume resuscitation.

Polygeline also contains potassium ions: beneficial to those patients who are hypokalaemic.

It is sterile, pyrogen free, contains no preservatives and has a recommended shelf-life of 3 years when stored at temperatures less than 30°C.



Metabolism & Excretion

It is rapidly excreted by the kidney.

Following infusion, its peak plasma concentration falls by half in 2.5 hours.

Distribution (as a percent of total dose administered) by 24 hours is 71% in the urine, 16% extravascular and 13% in plasma.

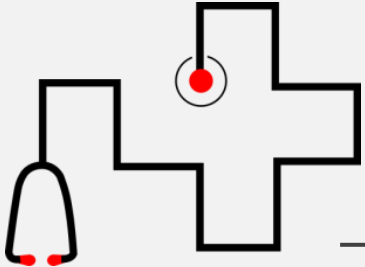


The amount metabolized is low: perhaps 3%.

Gelatins lead to 70 to 80% of volume expansion. But duration of action is shorter in comparison to both albumin and starches.

Maximal daily Infusion: **No limits.**

Degree of volume expansion



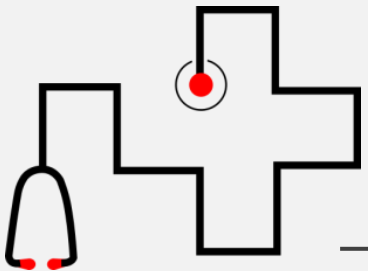
Indications

- ♪ Hypovolemia due to acute blood loss
- ♪ Acute normovolaemic haemodilution
- ♪ Extracorporeal circulation - cardiopulmonary by-pass
- ♪ Volume pre-loading prior to regional anaesthesia



Advantages

- ♪ **Cost effective:** *It is cheaper as compared to albumin and other synthetic colloids.*
- ♪ **No limit of infusion:** *Gelatins do not have any upper limit of volume that can be infused as compared to both starches and dextrans.*
- ♪ **No effect of renal impairment:** *Gelatins are readily excreted by glomerular filtration as they are small sized molecules. Gelatins are associated with lesser renal impairment as compared to HMW HES.*



Disadvantages

✳ **Anaphylactoid reactions:**

Gelatins are associated with higher incidence of anaphylactoid reactions as compared to natural colloid albumin.

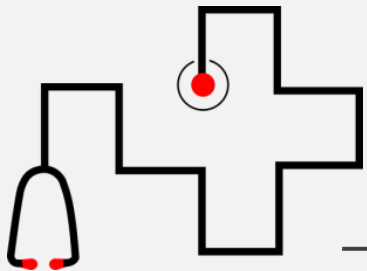


✳ **Effect on coagulation:**

The effect of gelatins on coagulation is not clear.

✳ **Circulatory disturbance:**

Gelatins are associated with occurrence of circulatory dysfunction marked by increased plasma renin activity and aldosterone in patients with ascites undergoing large volume paracentesis.



Hydroxyethyl starches (HES)

HES are derivatives of amylopectin, which is a highly branched compound of starch.

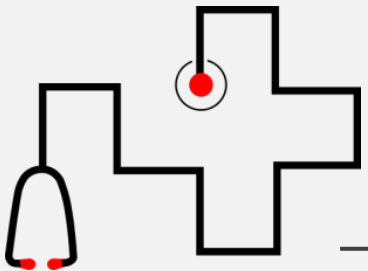
Amylopectin structurally resembles glycogen.

Amylopectin is rapidly hydrolyzed with a $\frac{1}{2}$ life of about 20 min.

In order to make the amylopectin molecule more stable, anhydroxyethyl glucose residues are substituted with hydroxyethyl groups mainly at positions C2 and C6 .

The first HES product, Hespan, was made available in the United States in the 1970s.

Since then, further generations of HES have been developed, differing in their mean molecular weight (MW), molar substitution (MS), and C2/C6 ratio.



HES are identified by three numbers, e.g.,

10% HES 200/0.5

or

6% HES 130/0.4



 **The first number**

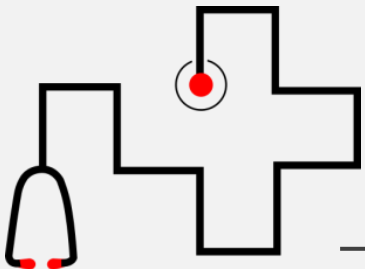
Indicates the concentration of the solution

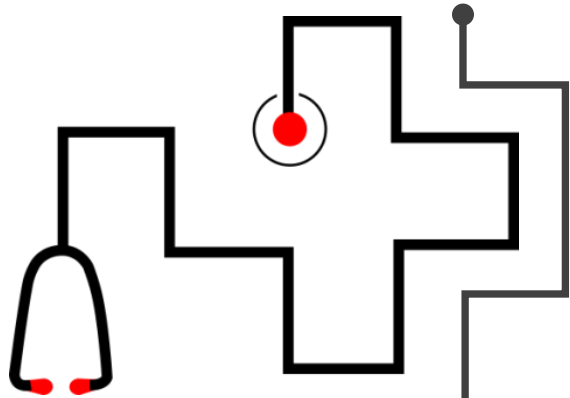
 **The second number**

Represents the mean MW expressed in kiloDalton (kDa)

 **The third number**

The most significant one is MS.

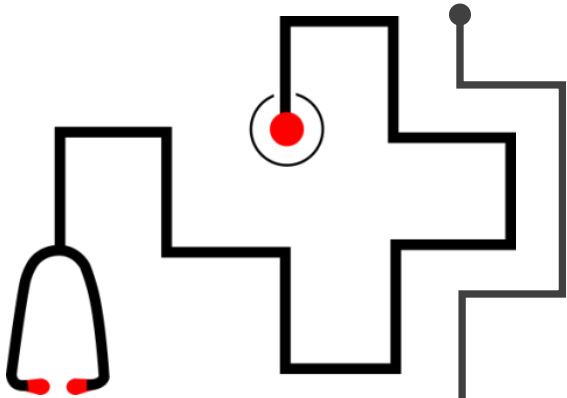




Average Molecular Weight (MW)

- ♪ Low (≈ 70 kDa)
- ♪ Medium (200 kDa)
- ♪ High (≈ 450 kDa)

In common with all of the synthetic colloids, HES are **polydisperse** systems containing particles with a wide range of molecular mass.



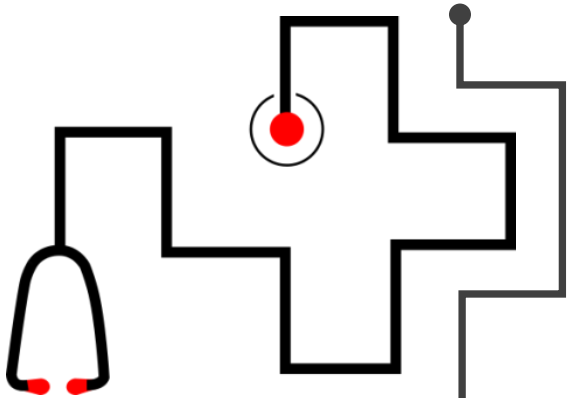
The **ratio M_w/M_n** gives an index of the **degree** of **polydispersity** in the system.

When a polydisperse colloid is infused into the circulation, **small molecules** below the renal threshold (45 to 60 kDal) are **rapidly excreted**,

whereas

the **larger molecules** are **retained** for varying periods of time *depending on their **size** and **ease of breakdown**.*

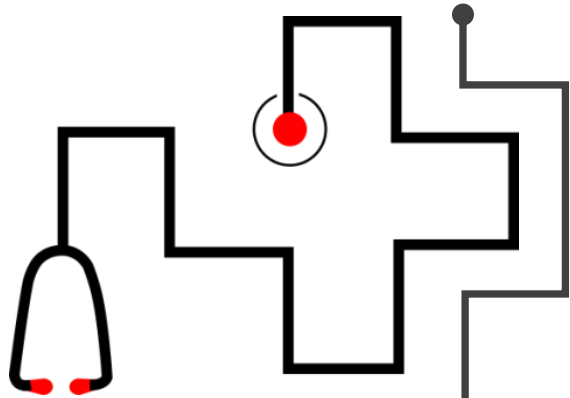
However, **osmotic effectiveness** depends on the **number** of **particles**, and **not** the molecular **size**;



therefore, the excretion of the smaller particles continuously reduces the osmotic effectiveness of the infused solution.

This is compensated for by the continuous supply of oncotically active molecules arising from degradation of larger fragments.

Mean MW of the available products ranges from over 670 kDal to 70 kDal.

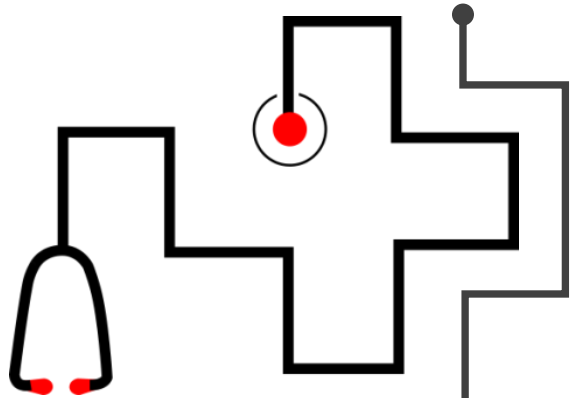


Molar substitution (MS)

Low (0.45-0.58) or **high** (0.62-0.70)

The **higher** the **degree** of **MS**, the **greater** the **resistance** to **degradation**, and consequently, the **longer** its **intravascular persistence**.

This **substitution increases** the **solubility** of the **starch** in **water** and, to a varying degree, **inhibits** the rate of **destruction** of the **starch** polymer by amylase.

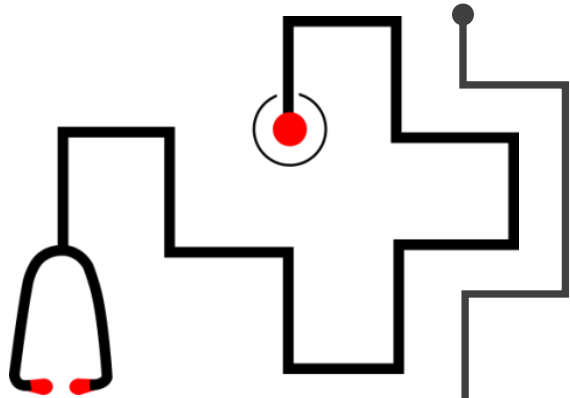


MS is thus the average number of hydroxyethyl residues per glucose subunit.

The figure 0.7 in the description of a HES preparation indicates that there are seven hydroxyethyl residues on average per 10 glucose subunits.

Starches with this level of substitution are called *Hetastarches (MS 0.7)*, and similar names are applied to describe other levels of MS: *Hexastarch (MS 0.6)*, *Pentastarch (MS 0.5)*, and *Tetrastarch (MS 0.4)*.

Unsubstituted anhydroglucose units are *more prone* to *enzymatic degradation* by alpha-amylase; *therefore, hydroxyethylation slows* down the rate of *enzymatic breakdown* of the HES molecule and *prolongs intravascular retention* time.



C2/C6 ratio

Low (<8) or high (>8).

The C2/C6 ratio refers to the site where substitution has occurred on the initial glucose molecule.

The higher the C2/C6 ratio, longer the half-life and hence, longer persistence in the blood.

Hydroxyethyl groups at the position of the C2 atom inhibit the access of alpha-amylase to the substrate more effectively than do hydroxyethyl groups at the C6 position. Hence, HES products with high C2/C6 ratios are expected to be more slowly degraded.

These parameters are highly relevant to the pharmacokinetics of HES.

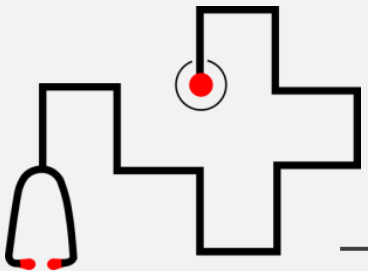
Physiochemical Properties:

- Concentration mainly influences the initial volume effect:

6% [low] HES solutions are **iso-oncotic** in vivo, with 1 L replacing about 1 L of blood loss

whereas

10% [High] HES solutions are **hyperoncotic**, with a volume effect considerably exceeding the infused volume (about 145%).





HES	Expansion V	Daily Max
Hextend (670/0.75)	100%	20 mL/kg
Hetastarch (450/0.7/5)	100%	20 mL/kg
Pentastarch (260/0.45)	100-150%	33 mL/kg
Elohes (200/0.62/10)	110%	20 mL/kg
Hesteril 6% (200/0.5/6)	100%	33 mL/kg
Lomol 10% (200/0.5/6)	145%	20 mL/kg
Tetrastarch (Voluven) (130/0.4/9)	130%	50 mL/kg

Indications

Duration of volume expansion is usually 8-12 h

🎵 **Stabilization of systemic haemodynamics.**

🎵 **Anti-inflammatory properties:**

● HES has been shown to preserve intestinal microvascular perfusion in endotoxaemia due to their anti-inflammatory properties.

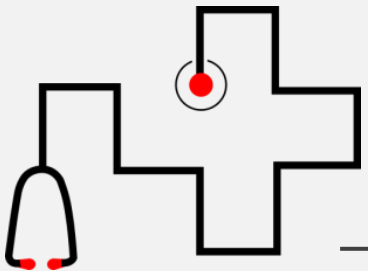
Advantages

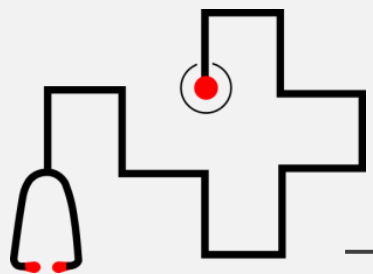
🎵 **Cost effectiveness:**

HES is less expensive as compared to albumin and is associated with a comparable volume of expansion.

🎵 **Maximum allowable volume:**

Max volume which can be transfused of medium weight HES (130 kDa) with medium degree of substitution (0.4) is 50 ml/kg. This is greater as compared to other synthetic colloids like dextrans.





1st & 2nd Generation HES Disadvantages



Coagulation:

- Reduction in circulating factor VIII and von Willebrand factor
- Impairment of platelet function:
- Prolongation of activated partial thromboplastin time
- Increases bleeding complications

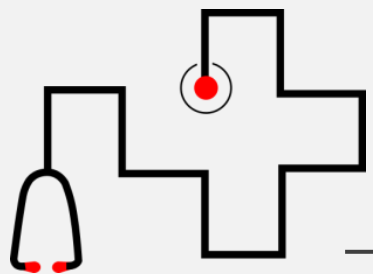


Accumulation:

High molecular weight (HMW) HES are associated with greater degree of accumulation in

- ✓ Interstitial spaces
- ✓ Reticulo-endothelial system
- ✓ Skin, Liver, Muscle, Spleen, Intestine, and Placenta.

Such depositions have been associated with pruritus.



1st & 2nd Generation HES Disadvantages



Anaphylactoid Reactions:

HES is associated with higher incidence of anaphylactoid reactions as compared to other synthetic colloids as well as albumin.



Renal impairment:



HMW HES has been found to be associated with

- increased creatinine levels
- oliguria
- acute renal failure

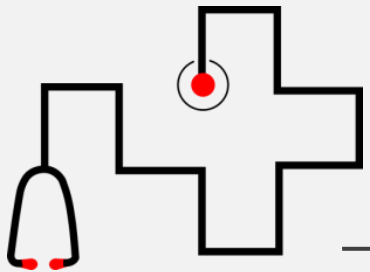
in patients who were critically ill with existing renal impairment.



Increase in amylase levels:

HES infusion is an occasional elevation of the serum amylase levels. But this has no clinical implication.

3rd Generation HES



✿ Effects on Coagulation and Platelet Function:

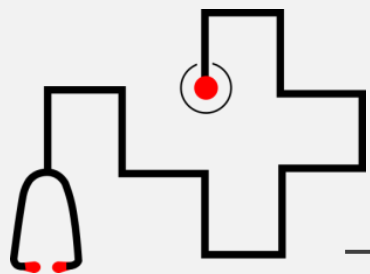
No adverse effects on coagulation have been reported

✿ Accumulation and Tissue Storage:

Due to the more rapid clearance of the latest generation of tetrastarches, it is expected that tissue accumulation and its clinical manifestations will not be observed with the same frequency as compared to older starches.

✿ Effects on Plasma Bilirubin:

Waxy maize-derived HES 130/0.4 has been extensively studied in a large number of clinical trials. None of these reports suggests that it is associated with deterioration of liver function. However, *Potato-derived* HES 130/0.42 is the only tetrastarch to be absolutely contraindicated in patients with severe hepatic impairment.



3rd Generation HES



Effects on Renal Function:

A number of earlier reports suggest that HES products may have adverse effects on renal function.

However, more recent studies using third-generation products have not reported unfavorable effects, suggesting that the lower tendency of these products to accumulate may improve their profile with regard to renal function.

In summary,

the published data suggest that there are differences between the older and newer generations of HES and that ***the reports of adverse effects on renal function should not be extrapolated to newer HES products.***

Colloid versus crystalloid controversy



LET US HAVE A CONSENSUS.

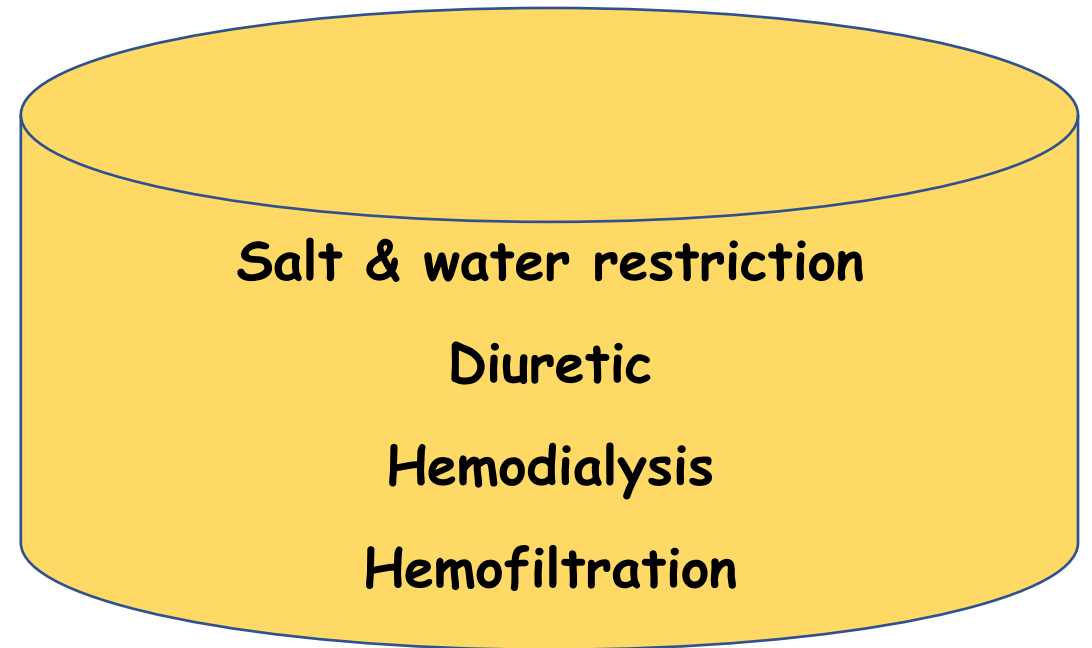
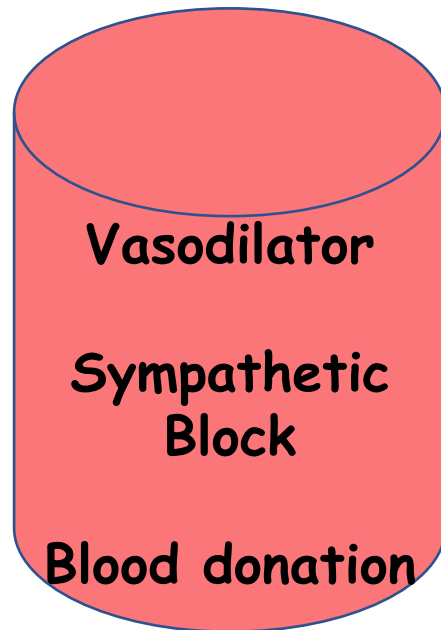
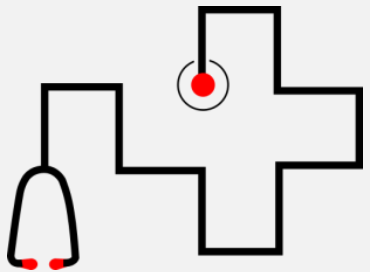
- ⚡ Crystalloids, when given in sufficient amounts can be as effective as colloids in restoring intravascular volume.
- ⚡ When fluid replacement exceeds 3-4 L. use of colloids in conjunction with crystalloids is recommended.
- ⚡ Severe intravascular volume deficits can be more rapidly corrected using colloids.

Rate of replacement depends on rate of loss

Manipulation of body fluid spaces

Removing transfused fluid is difficult

IVS < ISS and ICS

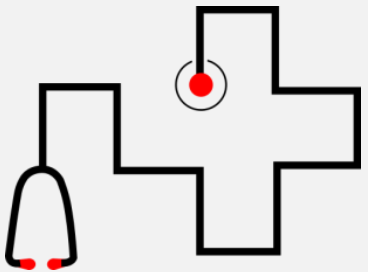


Complications of fluid therapy

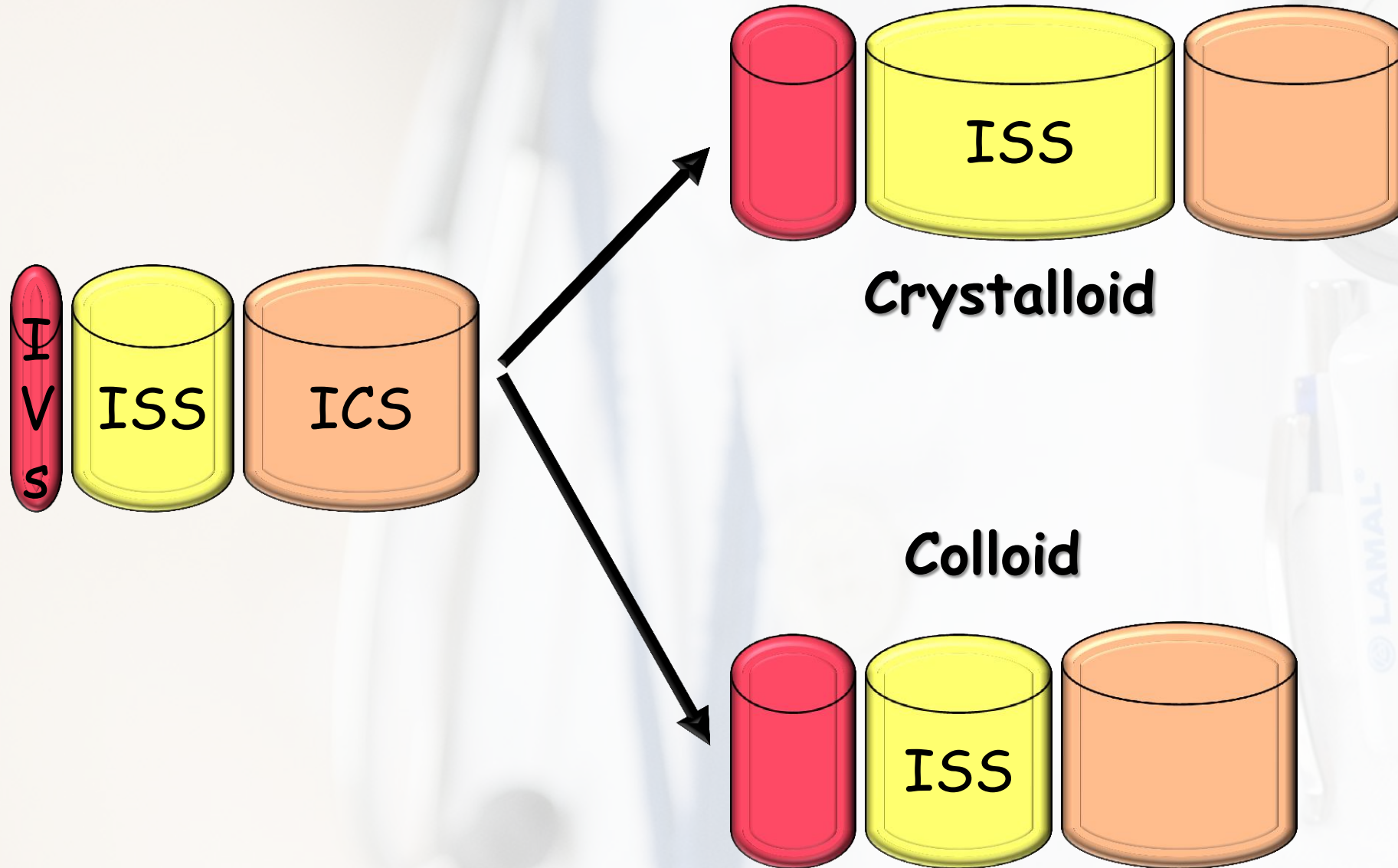
😊 Under-infusion.

😊 Over-infusion.

😊 Expansion of ISS
(inevitable with crystalloids)

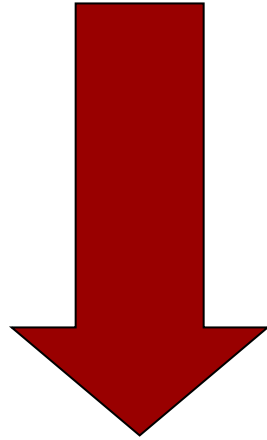


Complications of fluid therapy

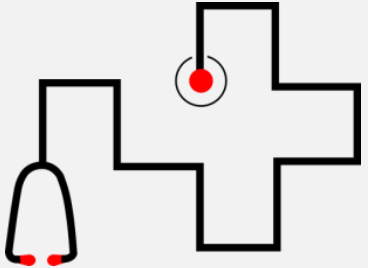


Complications of expansion of ISS

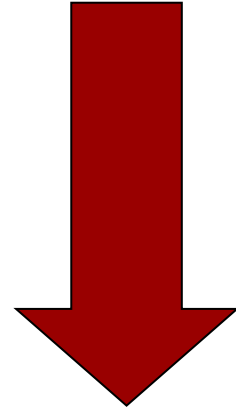
I. Disruption of lymph drainage



edema

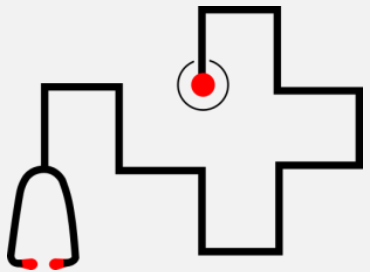


II. Capillary Occlusion

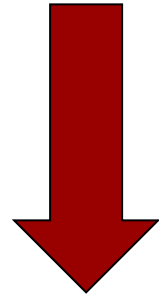


TISSUE ISCHEMIA

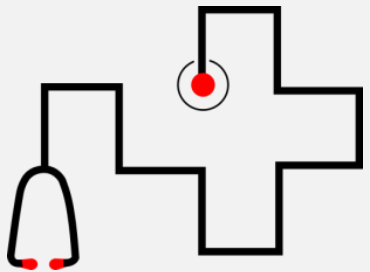
BAD HEALING



III. Interstitial Lung Edema



HYPOXIA



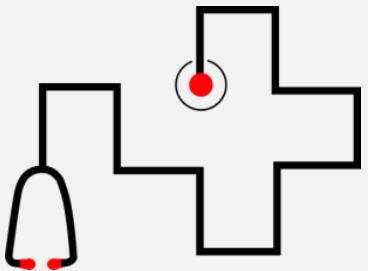
Does ISS Expansion Matter ?

It depends on 2 main factors :-

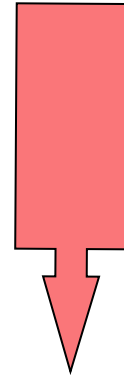
1. Body homeostatic mechanisms.

- a-Renal function.
- b-Efficient lymphatic.
- c-Intact capillary membrane.
- d-Intact G I T.

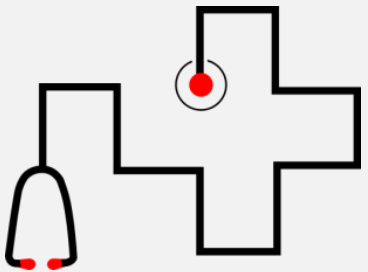
2. Amounts of fluids used.



With efficient homeostatic mechanisms in a healthy patient

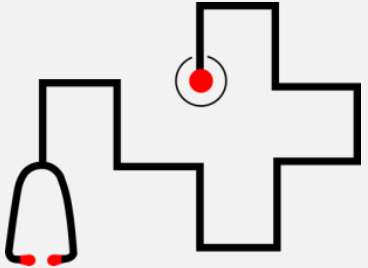


*ISS Expansion Is Not
Clinically Significant*



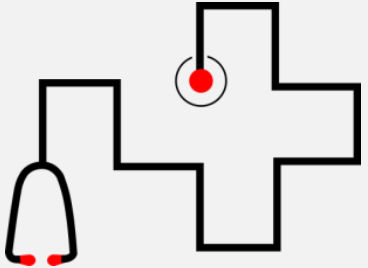
ISS EXPANSION MIGHT BE HAZARDOUS IN THE FOLLOWING:-----

- ✓ Critically ill patient
- ✓ Major trauma
- ✓ Major surgery (great amounts of crystalloids)

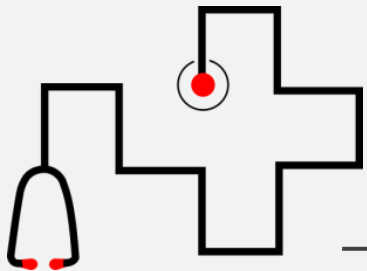


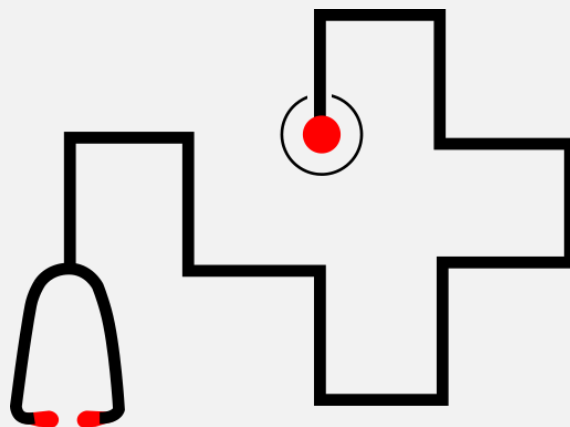
Summary and Conclusions

- 🍏 Priority is for IVS resuscitation.
- 🍏 Rate of replacement depends on rate of loss.
- 🍏 While using crystalloids be careful:-
 - 🍏 In critically ill patients.
 - 🍏 when you give great amounts .
- 🍏 Colloids are useful, however they have side effects and are more expensive.



**Sound knowledge
of the
physiology,
techniques and drugs
that facilitate
fluid removal and redistribution
is vital for handling fluids with
confidence and safety**





Thank you
Any question !