Pathology

Subject :

Lec no : lec16-

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وَقُل رَّبِّ زِدْنِي عِلْمًا

EDEMA

- 60% of the lean (without fat) body weight is water, with: 2/3 intracellular (within cells); & 1/3 extracellular (out side the cells), mostly as interstitial fluid.
- 5% of total body water only is in the intravascular compartment, i.e. in the blood plasma .
- The term edema refers increased fluid in the interstitial tissue spaces .
  - Fluid collections in different body cavities are refered to as :

Hydrothorax : in pleural cavity.

Hydropericardium : in pericardial cavity.

Hydroperitoneum : in peritoneal cavity also called ascites .

Anasarca : Is a severe generalized edema with a profound subcutaneous swelling .

Edema

- Fluid movement between the vascular & interstitial spaces is governed by two opposing forces, **the vascular hydrostatic pressure and the colloid osmotic pressure produced by plasma proteins .**
- Normally the outflow of fluid produced by hydrostatic pressure at the arteriolar end of the micro circulation is balanced by the inflow due to the slightly elevated osmotic pressure at the venular end , hence , **there is only a small net outflow of fluid into the interstitial spaces,** which is drained by the lymphatic vessels .
- Either increased hydrostatic pressure or decreased osmotic pressure causes increased movement of water into the interstitium .
- Excess edema fluid is removed by the lymphatic drainage & returned to the blood stream by the way of the thoracic duct. .

- Edema can be divided into many types based on the mechanisms causing edema:
  1. increased capillary hydrostatic pressure
  2. decreased plasma oncotic pressure,
  3. enhanced permeability of capillary walls(inflammation)
  4. lymphatic obstruction.
- Each of the types can be further divided into generalized and local forms.

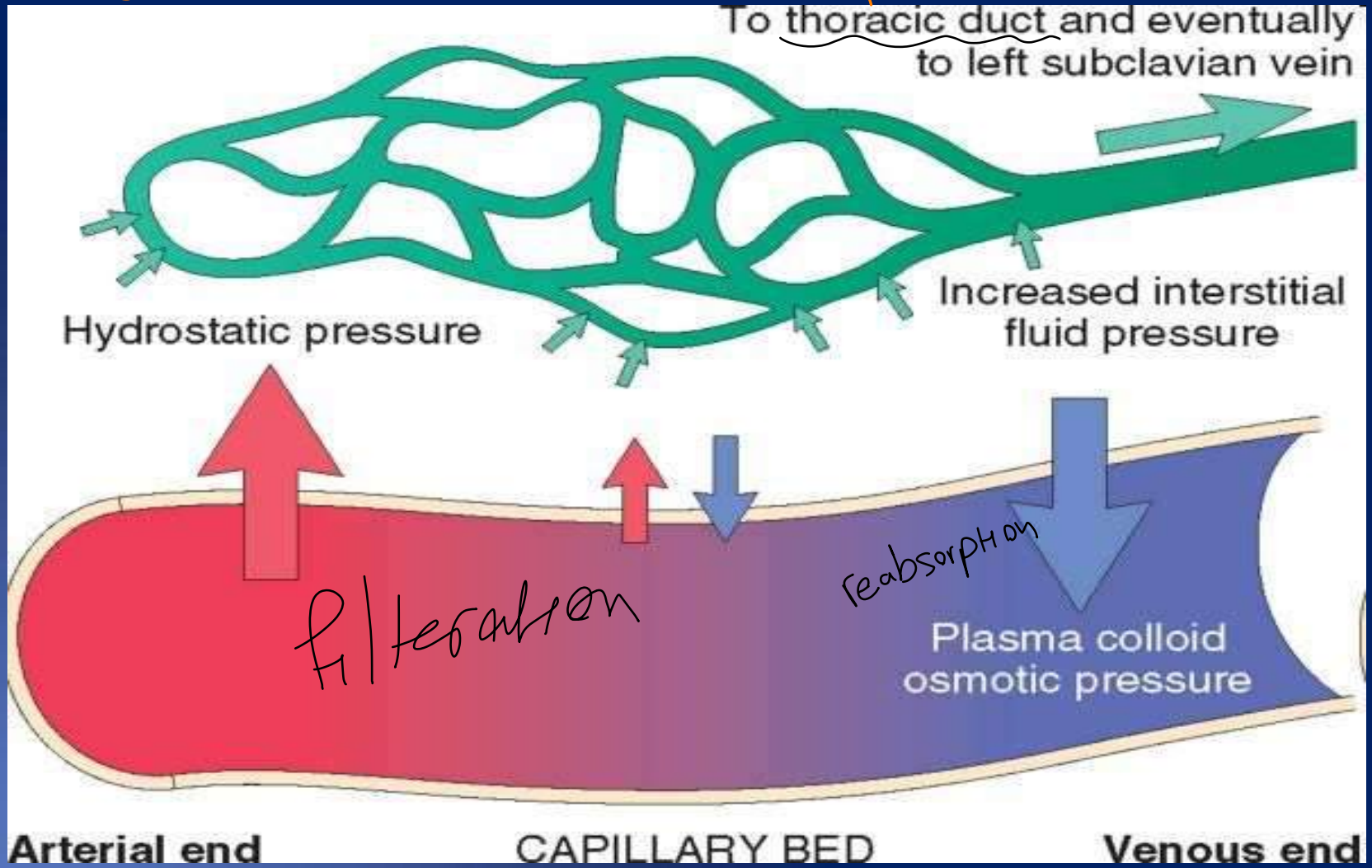
1 2

تقسيم حسب مكان ال edema

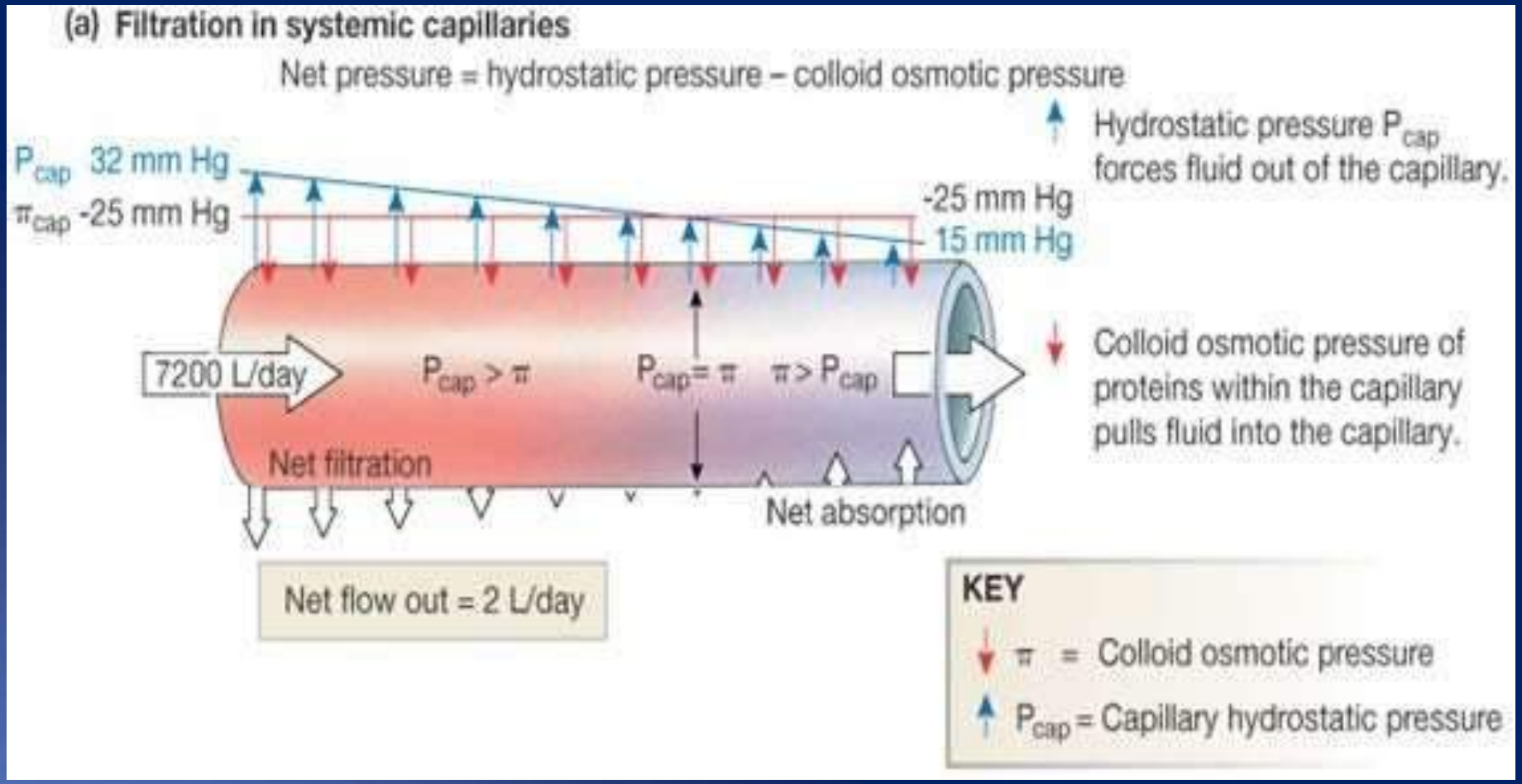
* right lymphatic duct تأخذ ما زاد من السائل right upper limp من الجهة اليمنى للجسم والرأس

Fluid transit

موجوده في lymphatic system ترجع ما زاد من السائل الى الـ Blood



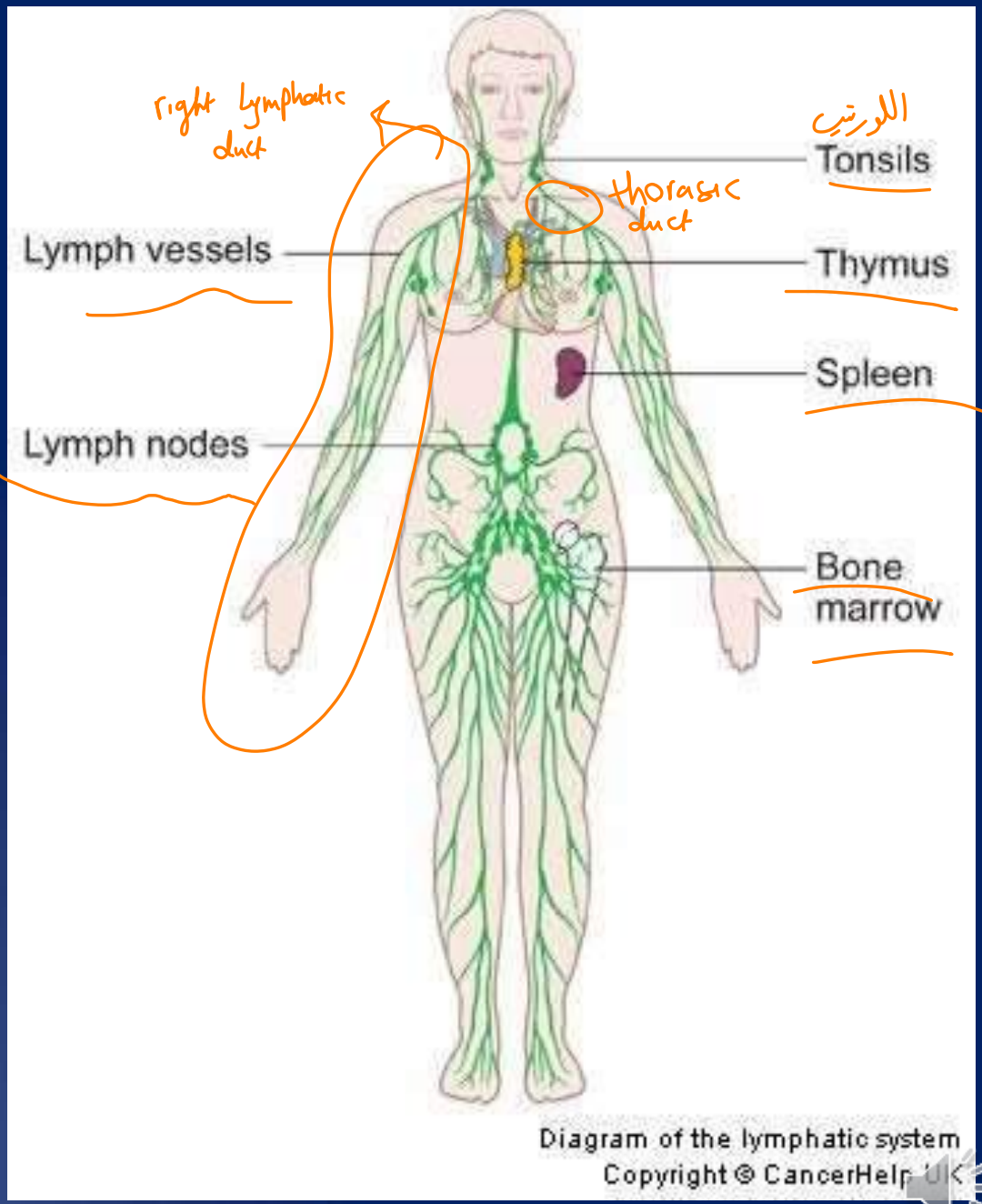
Note: (Wikipedia)- Oncotic pressure, or colloid osmotic pressure, is a form of osmotic pressure exerted by proteins, notably albumin, in a blood vessel's plasma (blood/liquid) that usually tends to pull water into the circulatory system. It is the opposing force to capillary filtration pressure and interstitial colloidal osmotic pressure.



The movement of water and low molecular weight solutes such as salts between the intravascular and interstitial spaces is controlled primarily by the opposing effect of vascular hydrostatic pressure and plasma colloid osmotic pressure.

http://faculty.pasadena.edu/dkwon/chapter%2015/chapter%2015_files/images/image10.png

- If the movement of water into tissues (or body cavities) exceeds lymphatic drainage, fluid accumulates.
- An abnormal increase in interstitial fluid within tissues is called edema.I



Appearance of edema

- Swollen tissues (not cells—fluid is outside the cells)
- Heavy tissues
- Wet tissues
- Widening of fascial planes or interlobular septa
- Filled cavities

توسعة المسافة بين tissue

effusion

Pathophysiological causes of odema

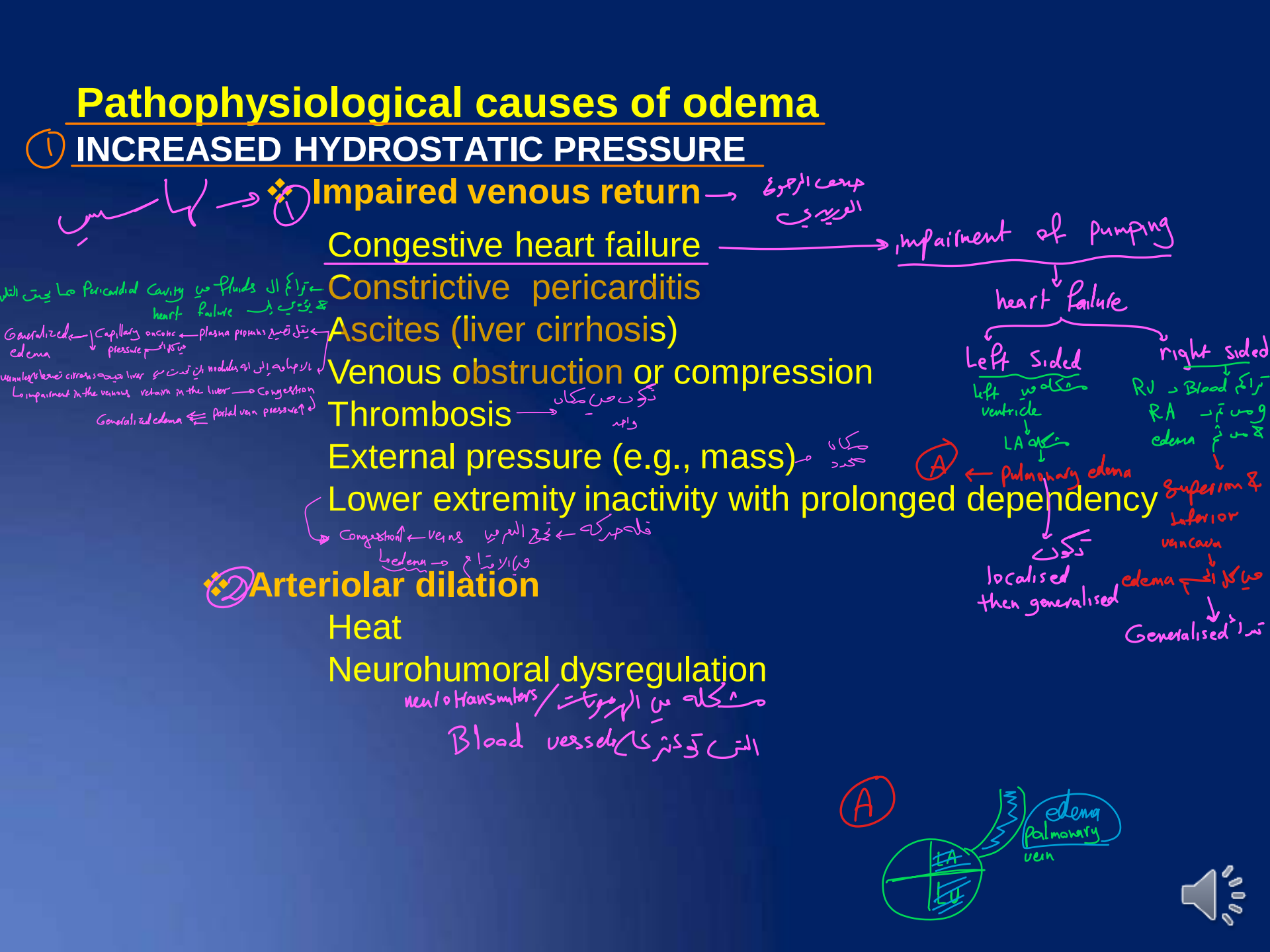
① INCREASED HYDROSTATIC PRESSURE

1. Impaired venous return

- Congestive heart failure → impairment of pumping
- Constrictive pericarditis
- Ascites (liver cirrhosis)
- Venous obstruction or compression
- Thrombosis
- External pressure (e.g., mass)
- Lower extremity inactivity with prolonged dependency

2. Arteriolar dilation

- Heat
- Neurohumoral dysregulation



2 REDUCED PLASMA OSMOTIC PRESSURE (HYPOPROTEINEMIA)

1. Protein-losing glomerulopathies (nephrotic syndrome)
2. Liver cirrhosis (ascites)
3. Malnutrition
4. Protein-losing gastroenteropathy

3 LYMPHATIC OBSTRUCTION

- Inflammatory
- Neoplastic
- Postsurgical
- Postirradiation

INFLAMMATION

Acute inflammation
Chronic inflammation
Angiogenesis

تكوين الأوعية الدموية

SODIUM RETENTION

زيادة كمية Na+ في الجسم مما يؤدي إلى تراكم الماء ← زيادة Blood volume ← زيادة ضغط

1. Excessive salt intake with renal insufficiency
2. Increased tubular reabsorption of sodium
3. Renal hypoperfusion ← قلة وصول الدم إلى nephrones
4. Increased renin-angiotensin-aldosterone secretion

Increased hydrostatic pressure :

- **Local edema** : increase in intravascular pressure can result from impaired venous return , for example in deep venous thrombosis in the lower extremities can cause edema in the distal part of the affected limb.

- **Generalized edema :** In normal heart , the reduced cardiac output leads to hypoperfusion of the kidneys thus triggering the rennin-angiotensin- aldosterone axis , renin is secreted by specialized cells in renal tubules due to hypoxia renin will stimulate angiotensin that enhances tubular reabsorption of Na & water thus inducing Na& water retention , this will increase the intravascular blood volume & improves the cardiac output to restore the renal perfusion and it is called secondary aldosteronism , .

- **In congestive heart failure** , the heart cannot improve cardiac output and this leads to increased venous hydrostatic pressure and resulting in edema .

Figure; Photographic view of swollen edematous right leg due to deep vein thrombosis (local edema) .

Reduced plasma osmotic pressure:

- Albumin is the serum protein most responsible for maintaining intravascular colloid osmotic pressure
- Reduced osmotic colloid pressure occurs when diffuse albumin is inadequately synthesized as in liver diseases , or in protein deficiency in mal nutrition or is lost from circulation through the glomerular capillaries which become leaky as in nephrotic syndrome .

Lymphatic obstruction :

- Normally , excess interstitial fluid is removed by lymphatic drainage returning it to the blood stream via thoracic duct

(Normally 800 to1000 ml of lymph/per day).

- Impaired lymphatic drainage & consequent lymph edema can result from inflammatory or neoplastic obstruction or post-irradiation scarring .
- Parasitic infestation by ***filariasis*** which involves the inguinal lymphatics causing lymphatic obstruction and lymph nodes fibrosis with resultant progressive edema of the external genitalia and the lower limbs can be so massive to be called ***elephantiasis***

اسم الدودة
Filaria Bancrufti .The parasite that causes Elephantiasis due to lymphadenitis , obstructing the lymphatic drainage resulting in extensive edema in lower limbs & the external genitalia .

Photograph of elephantiasis , sever edema in lower limbs .

Renin Angiotensin Aldoseron System (RAAS)

* مريض حالة heart failure يقل Cordic out put ← يتراكم الدم في RV/LV ← venus return & يقل Impered & Congestion

تقل كمية الدم الواصلة إلى kidney ← فيقل تركيز (Na) الداخل إلى الصوديوم & يتحسس نقصان (Na) (JGA) ① macula densa ② ← ما يجعل (JGA) تفرز مادة (Renin) &

يخرج Renin إلى Blood ثم يدخل (liver) فيلتقي مادة تسمى (Angiotensinogen) & يحولها إلى (Angiotensin I) ← ثم يذهب (Angiotensin I) إلى Palmonary Capilary في الرئة

& يرتبط بـ angiotensin Converting enzyme (ACE) الموجودة على سطح Palmonary Capilary فيتحول إلى (angiotensin II)

له عدة وظائف منها ① يحفز افراز (↑ADH) ← يزيد (H2O) في الجسم

② يعمل (VC) في (Blood vessels)

③ يزود افراز هرمون (↑ aldosteron) الذي يزيد امتصاص Na + H2O إلى (Blood) ← (Na + water retention)

ما يؤدي إلى حدوث (Edema) & له اسم اخر Secondary aldoserolism

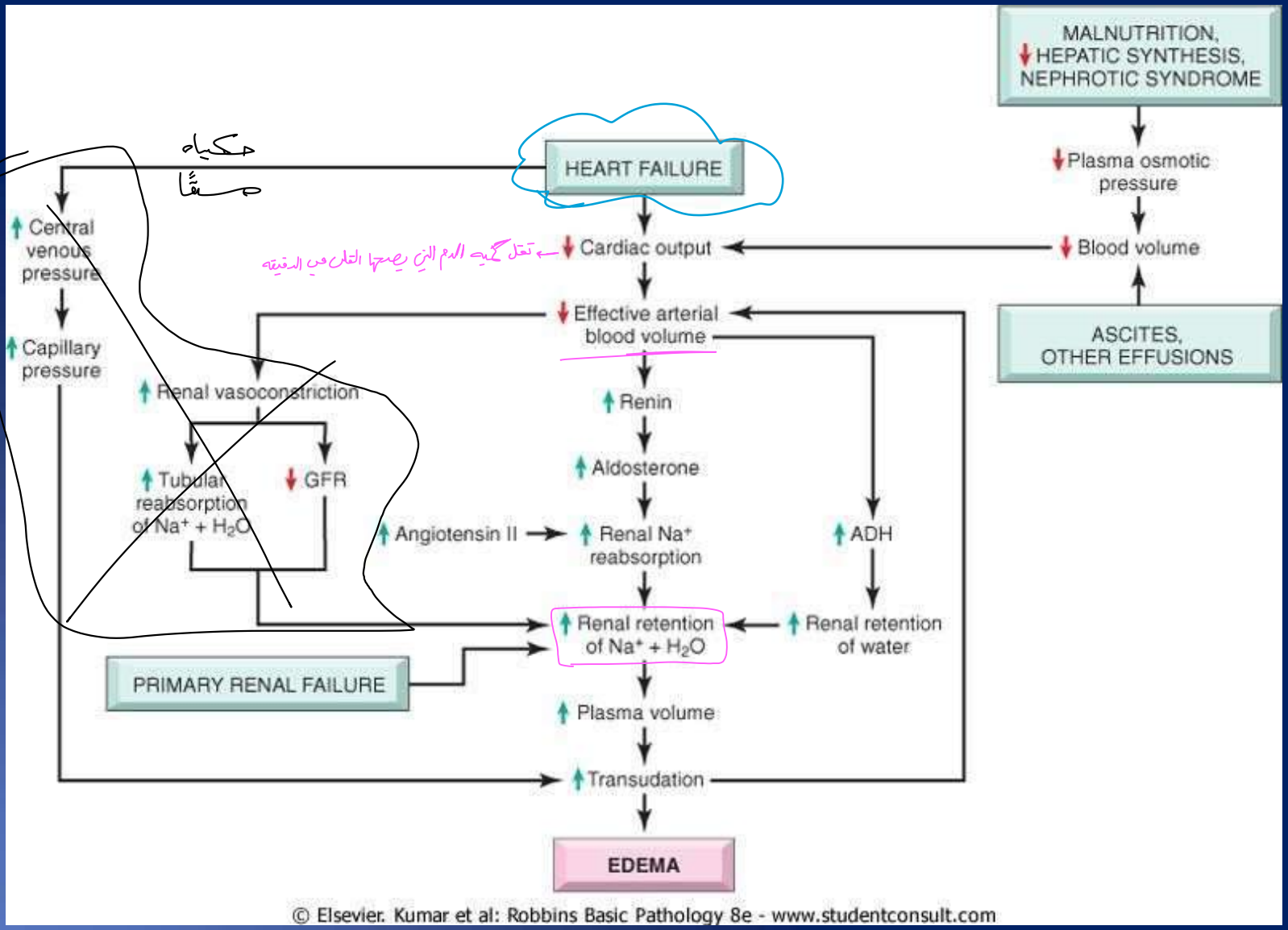


Diagram showing mechanism of edema .

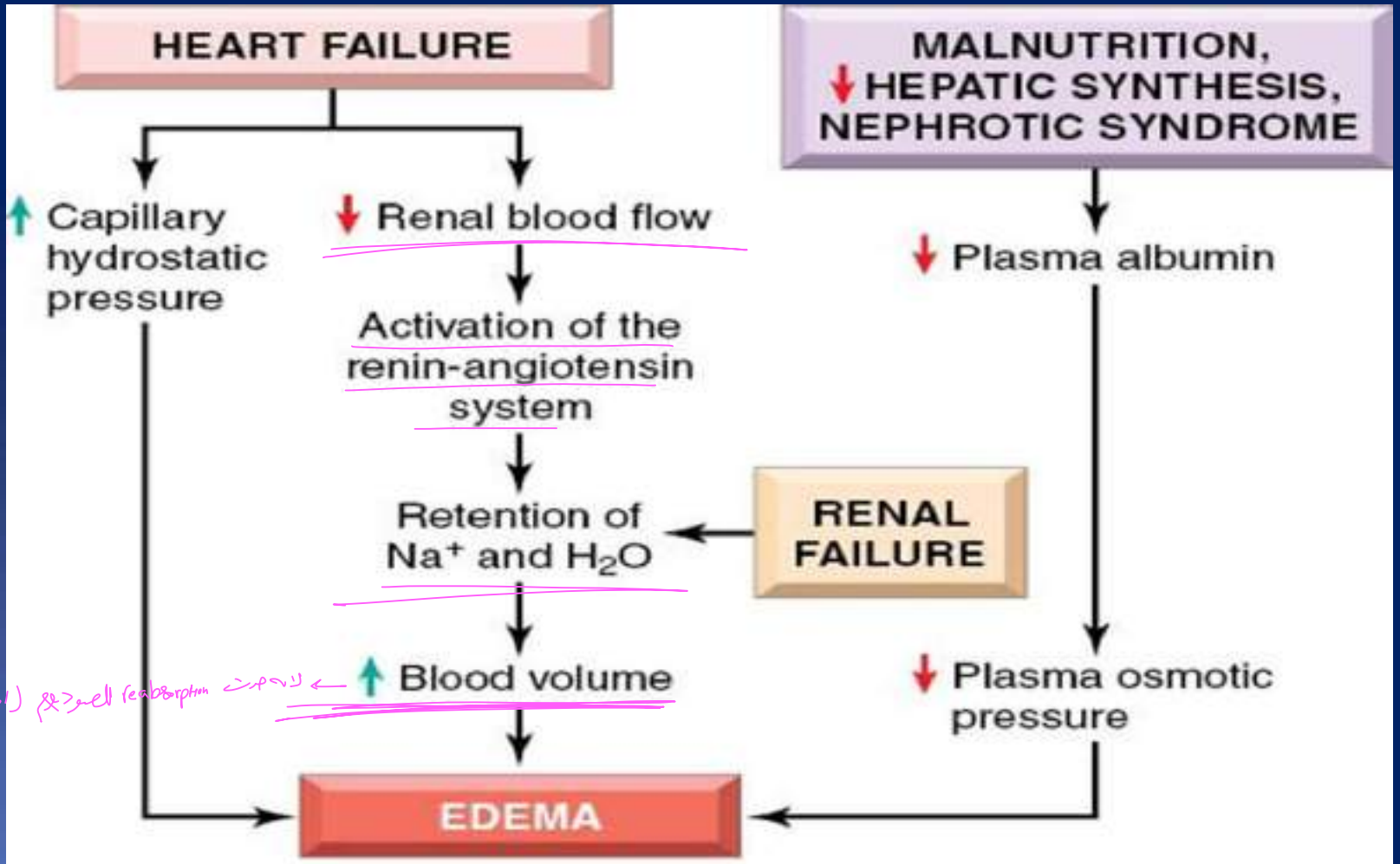


FIGURE 4–2 Pathways leading to systemic edema from primary heart failure, primary renal failure, or reduced plasma osmotic pressure (e.g., from malnutrition, diminished hepatic synthesis, or protein loss from nephrotic syndrome).

Morphology of edema :

- The *edema fluid is typically a protein-poor, called* ***transudate,*** *with a specific gravity below 1012.*
- **In inflammatory edema**, *the increased vascular permeability result in a protein-rich edematous fluid called* ***exudate*** *with*

A specific gravity over 1020.

- **Grossly;** Edema is most easily recognized, causing swelling and increased weight of the affected organ.

- **Histologically :**

Edema is manifest as clearing & separation of the extracellular matrix elements and cell swelling .

Edema is most commonly encountered in subcutaneous tissues can be *diffuse* may affect different locations depending on the cause of edema.

- **Localised edema :** can involve any organ or tissue in the body may be involved the lungs, & brain are especially affected .
- **Glottic or laryngeal edema** may be fatal by obstructing the air passages specially in children.

- **Diffuse systemic edema :**
  - is usually more prominent in certain areas as result of the effect of gravity ,which is called ***dependant edema*** , involving the legs when standing & sacrum when recumbent
  - This is a feature of heart failure especially right ventricular failure.
  - Edema due to renal failure or nephrotic syndrome is generally more sever than cardiac edema tends to affect many parts of the body equally.However, it may be initially appears in tissues with a loose connective tissue matrix, such as the eyelids, causing ***periorbital edema***.

- An important sign of edema is pitting sign If finger pressure is applied over edematous subcutaneous tissue, it displaces the interstitial fluid & leaves a finger- shaped depression so called pitting edema .
- In breast cancer the skin shows a Peau d' orange appearance of the its skin , produced by cutaneous edema causing bulging of the skin (following occlusion of the skin lymphatics by malignant cells around the hair follicles& sweat glands .

14.15 Oedema: skin

Photograph showing pitting edema of skin & subcutaneous tissue .

FIGURE 1. Erythema, edema, and peau d'orange—all classic signs—are seen in a woman with inflammatory breast cancer.

Courtesy of Dr. Eric Strom, M. D. Anderson Cancer Center

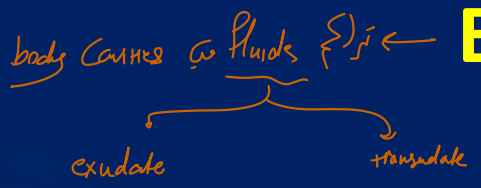
Photograph of breast showing **Peau d' orange appearance** of the breast seen in breast cancer.

12.11 Carcinoma: breast

Peau d'orange and **post-mastectomy lymphedema**

بعد استئصال الثدي + upper lymph nodes

EFFUSION

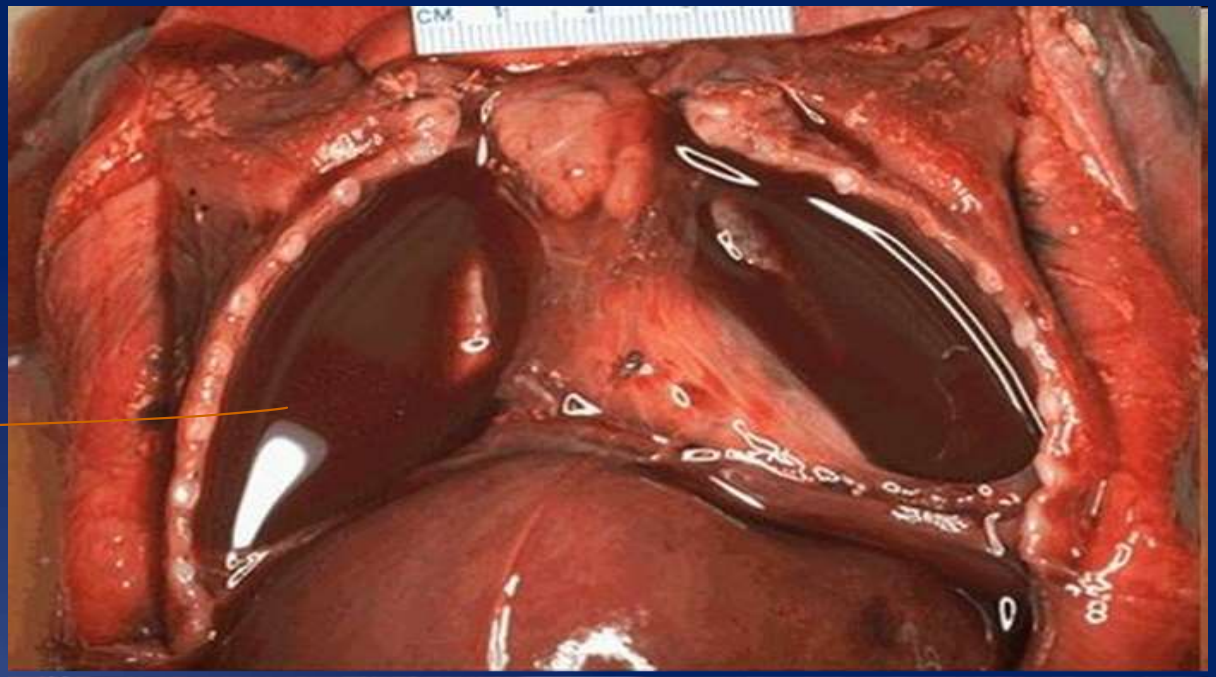


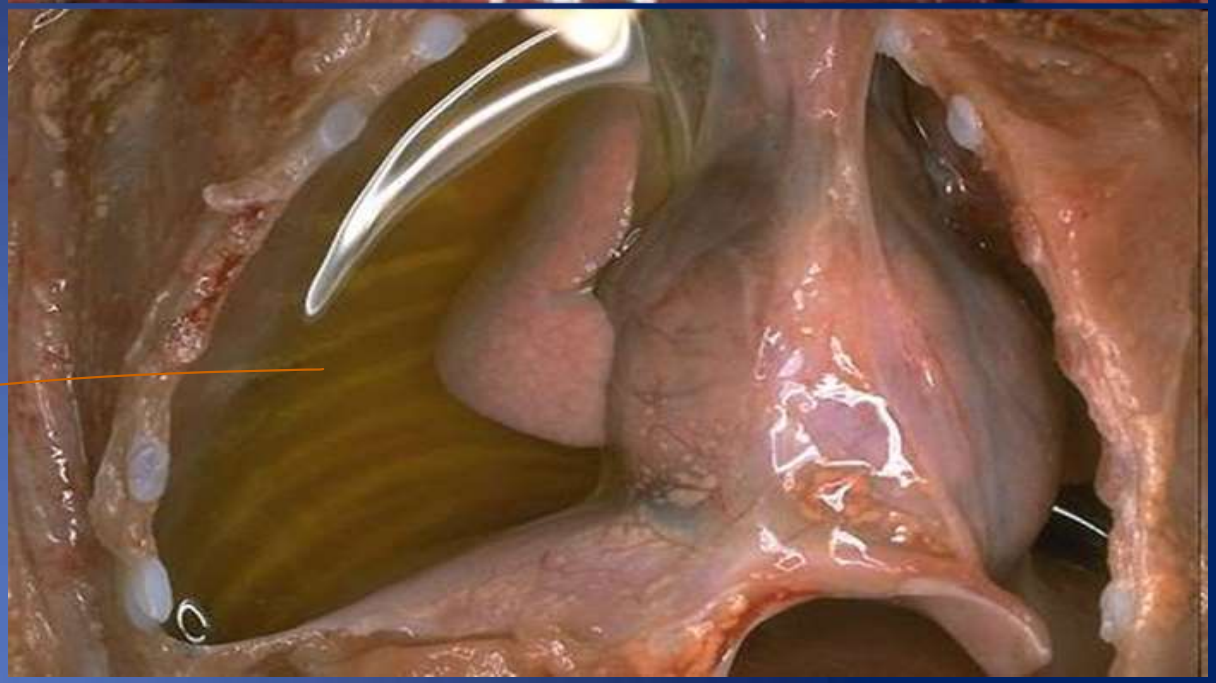
- Extravascular fluid collections can be classified as follows:
  - Exudate: extravascular fluid collection that is rich in protein and/or cells.Fluid appears grossly cloudy. سائل عكر
  - Transudate: extravascular fluid collection that is basically an ultrafiltrate of plasma with little protein and few or no cells. Fluid appears grossly clear. سائل صافي
- Effusions into body cavities can be further described as follows:
  1. Serous: a transudate with mainly edema fluid and few cells. + little proteins
  2. Serosanguinous: an effusion with red blood cells. transudate + (RBC) كمية دم
  3. Fibrinous (serofibrinous): fibrin strands are derived from a protein-rich exudate. → fibrin مرقة
  4. Purulent: numerous PMN's are present. Also called "empyema" in the pleural space. ↳ تراكم (صديد) في pleural cavity

polymer of nuclear cells (Neutrophils)

pyogenic bacteria ← تكون

Serosanguinus





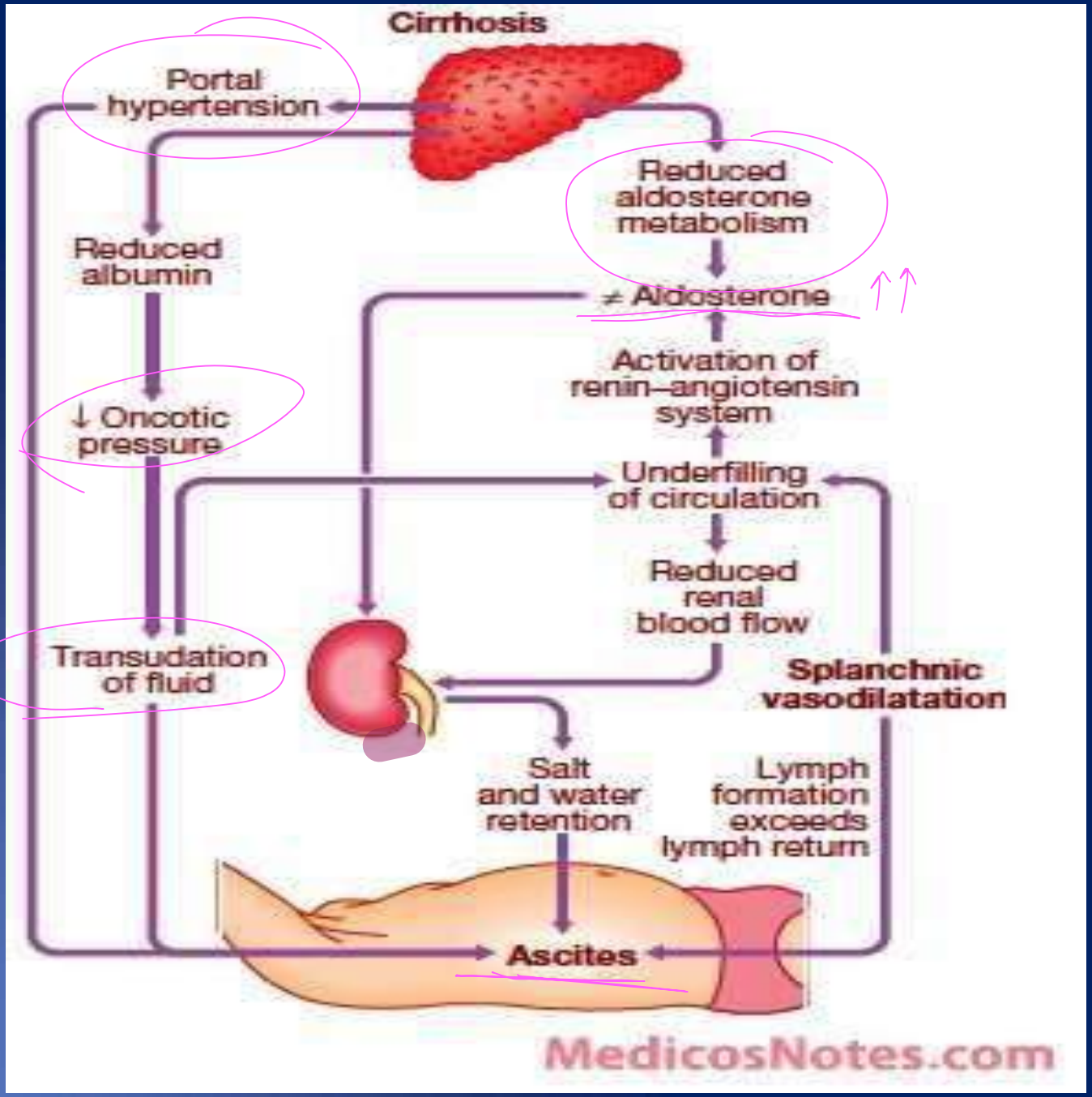
Serus

ASCITIS

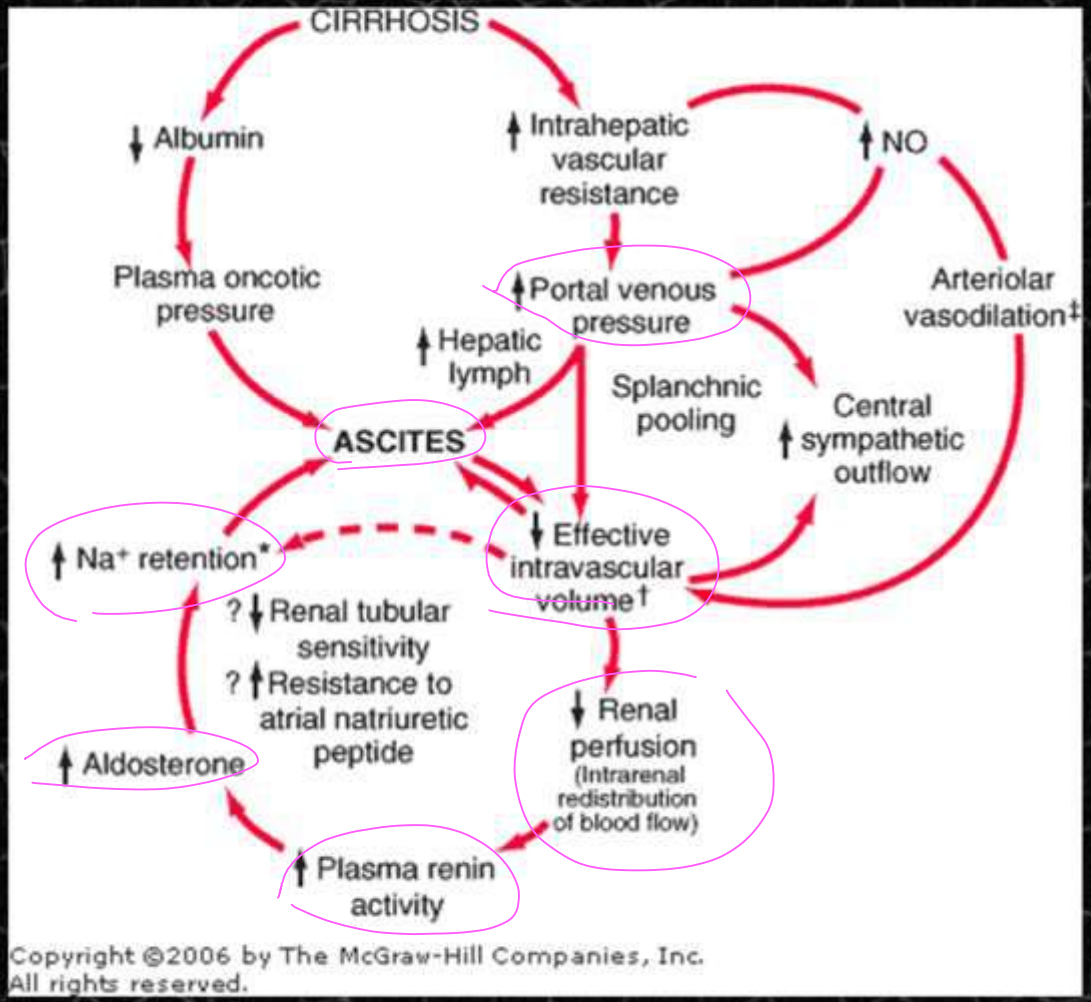
❖ Ascites is the excess accumulation of fluid in the peritoneal cavity. The fluid can be defined as transudate or exudate

❖ Cirrhotic Ascitis :

- The main pathophysiology of ascites in cirrhotic patients consists of three interrelated mechanisms, include:
  1. Portal hypertension
  2. Vasodilation
  3. Hyperaldosteronism
- There is a nitric oxide overload in cirrhotic patients from an unknown source. Therefore, they involved in hypovolemia secondary to the systemic vasodilation.
- The vasodilation induced by nitric oxide would trigger the stimulation of juxta-glumerular system to upregulate antidiuretic hormone (ADH) and sympathetic drive. Excess ADH causes water retention and volume overload.
- Despite the normal physiology of vessels, angiotensin would not cause vasoconstriction in cirrhotic patients and vasodilation becomes perpetuated.
- Portal hypertension leads to more production of lymph, to the extend of lymphatic system overload. Then, the lymphatic overflow will directed into to peritoneal cavity, forming ascites.


Cirrhosis
Portal hypertension
Reduced aldosterone metabolism
Reduced albumin
≠ Aldosterone
Activation of renin–angiotensin system
↓ Oncotic pressure
Underfilling of circulation
Reduced renal blood flow
Transudation of fluid
Splanchnic vasodilatation
Salt and water retention
Lymph formation exceeds lymph return
Ascites
MedicosNotes.com

Ascites



The accumulation of ascitic fluid represents a state of total- body sodium and water excess, but the event that initiates this imbalance is unclear.

Cirrosis ما ليس

Non-Cirrhotic Ascites

1. ❖ **Peritoneal malignancy** produces some protein factors into the peritoneum, which may lead to osmotic drainage of water and fluid accumulation.
2. ❖ **Tuberculosis** and other forms of ascites are induced through the same mechanism and osmotic fluid shift.
3. ❖ **Pancreatic and biliary ascites** are induced through leakage of pancreatic secretions or bile into the peritoneal cavity, which may lead to inflammatory fluid shift and accumulation

مشكلة من السكريتس أو القنوات الصفراوية

Tumor Cells → produce factors → ↑ osmotic pressure / ↑ osmolarity in the peritoneum → سبب تراكم الـ Fluids في الـ peritoneal Cavity → edema