Edema

Edema is defined as *excess fluid in interstitial compartment.*

1 Fluid Compartments

About 60 % of lean body weight is water. The normal distribution of water:

intracellular compartment
extracellular compartment
intravascular compartment
interstitial compartment

Interstitial fluid is the balance between

- *capillary hydrostatic pressure* which tends to encourage water to enter the interstitium
- *plasma oncotic pressure* which tends to encourage water to leave the interstitium
- *lymphatic drainage* which allows water and proteins to leave the interstitium

2 Mechanisms of Edema

2.1 Increased Capillary Hydrostatic Pressure

Normal situation

- pressure inside the capillary is greater then pressure in the interstitial space
- *water tends to flow out of the capillary into the interstitium*
- fluid leaves the capillary at about 14 ml/min
- capillary hydrostatic pressure is influenced by
  - venous back pressure
  - tissue tone, muscular activity
  - gravity (adds to venous pressure)
  - arterial pressure (of minor influence because precapillary sphincters regulate flow into capillaries)

Edema production

- *increased hydrostatic pressure in the capillary bed leads to increased rate of fluid loss into the intestitium*
- this is most commonly associated with impeded outflow through venous system (increased venous back pressure)
- Examples: congestive heart failure, portal hypertension; localized: venous thrombosis, varicose veins, pressure from outside (tumours)

2.2 Decreased Plasma Oncotic Pressure

Normal situation

- oncotic pressure in plasma leads to an *osmotic reabsorption fo fluid back into the capillary* (small molecules can diffuse freely from intravascular to interstitial spaces while the large molecules (proteins) are normally trapped inside the vascular space)
- fluid is reabsorbed at about 12 ml/min
- the major contributors to plasma oncotic pressure are the plasma proteins, especially *albumin*

- albumin is made by the liver at a rate of about 14 – 18 g/day

Edema production

- *reduced plasma proteins (especially albumin) lead to reduced osmotic reabsorption of interstitial fluid back into capillaries*
- less common than edema due to sodium retention
- generaly not clinically apparent until albunin levels are less than 20 g/l (norma 4 – 5 g/l)
- associated with: *loss of proteins* (nephrotic syndrome, protein losing enteropathies, burns) or *decreased production of albumin* (liver failure, protein malnutrition)

2.3 Lymphatic obstruction

Normal situation

- lymphatic vessels begin as blind ended capillaries in the interstitium
- they collect excess fluid (about 2 ml/min) and the small amount of protein that accumulate in the interstitium; this fluid is returned to the venous circulation via thoracic duct

Edema production

- *obstruction of lymphatics prevents removal of excess interstitial fluid*
- *produces localized edema* depending upon which lymphatic drainage is obstructed
- examples: tumors (esp. metastatic to lymph nodes)
  surgical removal of lymphatics (radical mastectomy)
  fibrosis and scaring (post-inflammatory or post-radiation)
  parasites (filariasis)

2.4 Sodium Retention

Normal situation

- sodium is the major determinant of the osmolarity of extracellular fluid
- *sodium therefore is a major influence in extracellular fluid volume*
- sodium levels are primarily *controlled by renal excretion*, which is influenced by
  - atrial natriuretic factor (increases sodium excretion)
  - renin-angiotensin system (increases sodium retention)
  - sympathetic nervous system (increases sodium retention)

Edema production

- increased sodium → increased extracellular fluid volume; that means
  - *a proportinal increase in interstitial fluid*
  - *increased blood volume → increased hydrostatic pressure*
- usually occurs on the basis of impaired renal excretion of sodium (decreased blood flow to the kidneys, renal disease)

2.5 Increased Capillary Permeability

- leads to loss of fluid and protein into interstitium
- usually produces *localized* edema
- associated with inflammation (blisters, hives), burns, allergic reaction

3 Fluid in Body Cavities

May be associated with any kind of edema.

Transudate fluid of low specific gravity — < 1.012 (protein poor), usually associated with generalized edema (heart failure)

Exsudate high specific gravity, protein rich, usually associated with inflamation or tumors

3.1 Vocabulary

Hydrothorax pleural space; similarly **hydropericardium**

Ascites peritoneal space (liver cirrhosis...)

Anasarca extreme generalized edema especially of subcutaneous tissues

Effusion edema fluid accumulation in a body cavity

Pitting edema subcutaneous tissues show transient „pit“ where examining finger has compressed the tissue and pushed aside the fluid

Urticaria, hives smooth, elevated patches of skin due to localized edema, usually associated with inflammation

3.2 Morphology

- Gross:
  - organ is enlarged, heavy
  - pale
  - capsule is tense
  - sometimes pitting is present (skin)
- Microscopic:
  - separation of cells and structures by empty spaces
  - eosinophilic extracellular precipitate (protein)

4 Congestive Heart Failure

A syndrome that occurs when the heart does not pump an adequate volume of blood to meet the needs of the body (decreased cardiac output).

4.1 Pathogenesis

1. decreased cardiac output is *percieved as decreased blood volume*
2. this percieved decreased blood volume stimulates mechanisms which
   - compensate for decreased blood volume by decreasing efective vascular volume — *vasoconstriction*
   - increase blood volume by *sodium retention*
   - increase pumping efficiency of the heart

   However...
   while they may initially be effective in restoring cardiac output, these mechanisms *increase the workload of a failing heart*
3. Edema production is associated with:
   - sodium retention, which leads to
   - increased blood volume
   - increased venous back pressure due to inability of the heart to effectively pump the blood that is returned to it

4.2 Pathologic Features of Congestive Heart Failure

4.2.1 Left sided heart failure

- pulmonary edema and congestion
- dyspnea
- orthopnea (shortness of breath when lying down)
- paroxysmal nocturnal dyspnea (awakening by sudden episodes of shortness of breath)
- hypoperfusion of kidneys

4.2.2 Right sided heart failure

- congestion of viscera and soft tissues
- generalized edema (usually sparing the face), pleural effusions, ascites
- pitting edema of dependent regions (lower extremities, presacral)
- distension of jugular veins

5 Renal disease

5.1 Decreased renal blood flow

and some intrinsic renal diseases lead to *sodium retention* and thus production of edema.

5.2 Nephrotic syndrome

Massive loss of protein in urine, accompanied by hypoproteinemia, hyperlipidemia and generalized edema. Associated with *glomerular damage.*

5.2.1 Mechanism of edema in nephrotic syndrome

1. increased glomerular capillary permeability to proteins
2. loss of protein (especially albumin) in urine ($> 3.5\,\mathrm{g/day}$)
3. hypoalbuminemia (and hyperlipidemia and hyperlipiduria)
4. decreased colloid osmotic pressure
5. movement of fluid from intravascular space to interstitium leads to decreased blood volume
6. that leads to activation of renin-angiotensin system
7. results in retention of sodium and water

5.2.2 Manifestations

Generalized soft tissue edema, ascites, effusion. The edema typically does not spare the face and eyelids.

6 Cirrhosis of the Liver

6.1 Pathogenesis of edema in cirrhosis

1. Scarring and reorganization of liver architecture obstructs blood flow through the liver; the synchronization of mixing of arterial and portal blood in liver sinuses is lost and high arterial pressure is transmitted into portal system. This mechanisms lead to *increased hydrostatic pressure in portal system.* Ascites is formed.
2. Loss of functioning hepatocytes → decreased production of albumines and other plasma proteins → decreased oncotic pressure of the plasma.
3. Sodium retention — decreased effective intravascular volume of possible decreased clearance of aldosterone by failing liver.

7 Pulmonary Alveolar Edema

Features protecting the lung from edema:

- low perfusion pressure in lung capillaries
- increased effectivness of lymphatic drainage
- tight cellular junctions between endothelial cells

Causes of pulmonary edema:

- Increased capillary pressure (most common); usually associated with left ventricular failure or mitral valve disease
- Increased capillary permeability; most often associated with acute lung injury (shock lung)

Eosinophilic edema fluid fills alveoli. Clinical features:

- dyspnea
- increased sputum production
- hypoxemia, cyanosis
- crackly breath sounds (rales)

8 Cerebral edema

Caused either by excess fluid *between* the cells or excess fluid *inside* the cells (cellular swelling). Causes increased intracranial pressure and displacement of brain structures — *herniations*, accompanied by altered brain function or death. This topic will be covered later (Special Pathology, CNS).