Cardiovascular Physiology II.

42. The function of the aorta and the arteries.
43. The microcirculation: capillary solute exchange and fluid dynamics.
44. The microcirculation: lymphatic circulation and edema formation.
45. The characteristics of the venous circulation.

Ferenc Domoki, November 12, 2019.

THE ARTERIAL SYSTEM

William Harvey
(1578 – 1657)

Harvey’s book on the circulation, the beginning of modern medicine

Exercitatio Anatomica de Motu Cordis et Sanguinis (in Animalibus) (1628)
MABP ≈ P_d + 1/3(P_s - P_d)
Pulse pressure = Systolic pressure - Diastolic pressure
An elastic tube is better when flow is pulsatile!

Windkessel = airtank, transient energy storage of the pump’s energy
During ventricular ejection, the distended aorta store blood and energy of the contraction.

During diastole, the aorta passively contracts and pushes blood forward toward the periphery.

Compliance decreases in the higher blood pressure range.
FACTORS AFFECTING ARTERIAL BLOOD PRESSURE

- **Stroke volume (SV):** its INCREASE will make the pulse larger, so systolic, mean, diastolic pressures all increase AND pulse pressure increases too.
- **Elasticity of the aorta:** its REDUCTION by aging will increase pulsation: mean pressure is UNAFFECTED, systolic pressure is increased, diastolic is decreased and pulse pressure GREATLY increased.
- **Total peripheral resistance (TPR):** its INCREASE will INCREASE the MABP but has no effect on pulsation, so systolic, mean, diastolic pressures all increase BUT the pulse pressure does not change.

SUMMARY OF ARTERIAL BLOOD PRESSURE CHANGES

<table>
<thead>
<tr>
<th>Stroke volume increased</th>
<th>baseline</th>
<th>Stroke volume increased</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>120</td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>90</td>
</tr>
<tr>
<td>reduced aorta elasticity (compliance)</td>
<td>140 60</td>
<td></td>
</tr>
<tr>
<td>increased TPR</td>
<td>120</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>110</td>
</tr>
<tr>
<td>increased TPR + decreased compliance</td>
<td>180 110</td>
<td></td>
</tr>
</tbody>
</table>

Hgmm
CHANGE IN THE PRESSURE PULSE SHAPE DURING PROPAGATION

Towards the periphery:

- Systolic peak increases
- incisura disappears
- diastolic peak appears
- time lag

Causes of changes

- Damping
- interference with reflected waves
- pressure-dependent propagation

PROPAGATION OF PRESSURE PULSE

- Propagation velocity
  - in the aorta: 3-5 m/s;
  - in the little arteries: 15-30 m/s.

- Mean flow velocity is ~20-30 cm/s in the aorta and decreases toward the periphery.

- Velocity of pulse pressure propagation is increased by:
  - decreasing wall elasticity
  - increasing wall thickness
The propagation velocity of the pressure pulse \((Y/t)\) is much faster, than the velocity of blood flow \((X/t)\).
The arterial pulse

- The pressure changes in the aorta during the cardiac cycle are transmitted along the arteries as a pressure pulse - creating a volume pulse that can be palpated by pressing the arteries against a flat hard surface
- The pulse depends on the function of BOTH the heart and the transmitting arteries!

Palpation sites
Arterial pulse qualities (in Latin)

- pulsus frequens
- pulsus altus
- pulsus celer
- pulsus durus
- pulsus regularis
- pulsus aequalis
- pulsus rarus (rate)
- pulsus parvus (amplitude)
- pulsus tardus (rate of rise)
- pulsus mollis (strength)
- pulsus irregularis (rhythmicity)
- pulsus inaequalis (similarity)

Arterial Pulse: examples

- Pulsus celer et altus
- Pulsus frequens, parvus et mollis = pulsus filiformis
- Pulsus irregularis et inaequalis = arrhythmia absoluta
Marcello Malpighi (1628 – 1694)

Italian anatomist and chief physician to Pope Innocent XII. Lectured in Bologna, Pisa, and other places, and wrote works on the anatomy of plants, the physiology of the silkworm, and medical subjects. He discovered capillaries and red blood cells.

THE MICROCIRCULATION

Arteries

Arteriole

Precapillary sphincters

Metarteriole

Capillaries

Arteriovenous bypass

Precapillary sphincters

Vein

Venule

Small venule

Microcirculation
Resistance vessels of the microcirculation

- Arterioles + metarterioles + precapillary sphincters
- They are the most important vessels for the REGULATION of the circulation:
  Contraction/relaxation of their vascular smooth muscle regulates vessel diameter, total peripheral resistance, systemic blood pressure, local blood flow, and local capillary pressure.
- Vascular smooth muscle in these vessels has a resting tone (baseline contraction state) that can be modified in both direction to induce vasoconstriction (increasing the tone) or vasorelaxation (decreasing the tone).
Quantitative facts on the human microcirculation

- ~ 10,000,000,000 perfused capillaries at rest
- ~ 300 m² surface area for exchange
- In tissues with large metabolic activity (myocardium, brain) up to 4000 capillary/mm² tissue

Types of capillaries

- All capillaries service the tissues to meet metabolic demands
- In many organs the capillaries show special features to meet the function of the organ (see next slide)
- The description of the „average“ capillary refers to the the so-called continuous capillaries that are most numerous in the body. The special capillaries will be discussed with the circulation of the respective organs!
In the continuous capillaries, almost exclusively simple **DIFFUSION**, the respiratory gases in the transcellular path, the water soluble solutes between the cells, in the PARACELLULAR pathway according to Fick's law of diffusion. The reflexion coefficient of the small molecules is effectively $\sigma=0$ (freely permeable)

- In contrast, the capillary wall is effectively impermeable for plasma proteins ($\sigma=1$), proteins are transported in part by vesicular transport. There is a large concentration gradient between the protein concentration of the plasma (60-80 g/l), and the interstitial fluid (15-20 g/l).
**FLUID filtration in the capillaries: Starling’s near-equilibrium**

- Frank-Starling law of the heart
- Starling’s theory on capillary fluid exchange
- Bayliss-Starling law of the gut

Ernest Starling (1866-1927)

**FLUID filtration in the capillaries: Starling’s near-equilibrium**

- The capillary wall forms a semipermeable membrane dividing two compartments with different protein concentration: osmotic water movement is expected.
- There is also a pressure difference between the two compartments suggesting pressure-driven filtration.
- Starling’s theory: the forces are in a complete balance.
- This proved to be false, but the correctly recognized forces driving fluid movement are still called “Starling forces”.

Ernest Starling (1866-1927)
1. **Capillary hydrostatic (blood) pressure**: drives fluid out.

   - 25-40 mmHg
   - 10-15 mmHg
   - Mean: 15-25 mmHg

2. **Interstitial hydrostatic pressure**

   - Varies with tissues between – 4 and + 8 mmHg, but its magnitude is *always small* compared to \( P_c \).

   - Positive \( P_i \) drives fluid into capillaries.
   - Negative \( P_i \) sucks fluid into interstitium.

3. **Plasma colloid osmotic pressure**: the only significant force that drives the fluid back to the capillaries.

   - \( \sim 5000 \) mmHg total plasma osmotic pressure

<table>
<thead>
<tr>
<th>Protein</th>
<th>g/L</th>
<th>mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>45</td>
<td>21.8</td>
</tr>
<tr>
<td>Globulin</td>
<td>25</td>
<td>6.0</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>3</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>73</strong></td>
<td><strong>28.0</strong></td>
</tr>
</tbody>
</table>

   - The colloid osmotic pressure is higher than calculated from the number of protein molecules. The colloid osmotic pressure is resulted from the *protein anions + associated cations*.

4. **Interstitial colloid osmotic pressure**: small force driving fluid out.

   - \( 2 \text{ g} \% \) protein \( \sim 8 \) mmHg

   \[ \text{g} \% = \frac{g}{100\text{ml}} \]
STARLING’S (NEAR) EQUILIBRIUM

<table>
<thead>
<tr>
<th>Forces</th>
<th>Filtration force</th>
<th>Absorption force</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean capillary pressure</td>
<td>17.3</td>
<td></td>
</tr>
<tr>
<td>Negative interstitial pressure</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>Interstitial colloid osmotic pr.</td>
<td>8.0</td>
<td></td>
</tr>
<tr>
<td>Plasma colloid osmotic pr.</td>
<td></td>
<td>28.0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>28.3</td>
<td>28.0</td>
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BALANCE: 0.3 mmHg net filtration pressure!

The Starling equation

\[ J = K \left[ (P_c - P_i) - \sigma(\pi_c - \pi_i) \right] \]

- J – filtration rate (ml/min)
- K – filtration coefficient (ml/min/mmHg)
- \( \sigma \) – reflection coefficient (ideally 1)
- \( P_c, P_i, \pi_c, \pi_i \): the Starling forces, capillary and interstitial hydrostatic (P) and colloid osmotic (\( \pi \)) pressures
- With average K value, the net filtration pressure produces ~2 ml/min filtrate that is less than 0.1% of the ~3000 ml/min plasma flow. So the equilibrium is ALMOST fulfilled, still this would mean 3-4 liters fluid in a day. This fluid is returned to the circulation with the LYMPH FLOW!
LYMPHATIC CAPILLARIES ARE INTEGRAL PART OF THE MICROCIRCULATION

LYMPHATIC SYSTEM

Functional morphology:
• Lymphatic capillaries originate as blind sacs.
• Lymphatic capillary endothelial cells form valves allowing interstitial fluid to enter.
• Larger lymphatic vessels contain smooth muscle displaying intrinsic pumping activity, and valves to direct lymph flow toward the circulation
Functions of lymphatic system:

1. **Drainage of interstitial proteins**: fundamental, vital function!
2. Return of excess filtrate.
3. Absorption of lipids.
4. Traffic of lymphocytes.

Lymph vessels always flow through regional lymph nodes. Any foreign substance, infectious organism, metastatic cancer will likely be transferred to the regional lymph nodes. Therefore, their functional anatomy is of high importance in medicine!
STRUCTURE OF THE INTERSTITIUM

The interstitial fluid is in GEL, water is bound to macromolecules.

INTERSTITIAL COMPLIANCE AND LYMPH FLOW

- When filtration increases, the increase in interstitial pressure will increase lymph flow. If this compensation becomes saturated, the excess fluid will quickly accumulate in the interstitium (interstitial compliance increases), the gel structure is disrupted: edema develops. The edema fluid can compress the lymph vessels, starting a vicious circle.
EDEMA: INCREASED INTERSTITIAL VOLUME DUE TO A FILTRATION – REABSORPTION IMBALANCE

\[ J = K \left[ (P_c - P_l) - \sigma(\pi_c - \pi_i) \right] \]

1. Increased intracapillary hydrostatic pressure (\(P_c\))
   - increased venous pressure e.g.
     - heart failure, local venous compression
     - (pregnancy), varicosity
2. Decreased plasma colloid osmotic pressure, \((\pi_c)\) e.g.
   - kidney diseases (albumin loss)
   - liver diseases (albumin synthesis deficiency)
   - starvation (protein catabolism)
3. Increased permeability (\(K\)), increased (\(\pi_i\)), decreased (\(\sigma\))

INFLAMMATION

4. Lymphatic obstruction, e.g.
   - surgical removal of lymph nodes and vessels
   - blockade by cancer or inflammation-induced fibrosis (elephantiasis)
+1. Increased deposition of interstitial matrix proteoglycans
   - hypothyroidism (myxedema) – not a true edema, the „gel” increases!

Postcapillary venules

- Important immune function: during inflammation, endothelial cells produce adhesion molecules that promote rolling, adhesion, and migration (by diapedesis) of white blood cells (special HEV venules in lymph nodes contiously express these proteins, lymphocyte patrol)
- The increased protein permeability during inflammation will destroy the colloid osmotic pressure gradient leading to edema.
THE VENOUS SYSTEM

GENERAL CONSIDERATIONS

- From the venous end of the capillaries to the right atrium only ~10 mmHg pressure gradient maintains flow – low venous resistance
- Because of high compliance, 2/3 of blood volume resides in the venous system, feature of stress-relaxation (delayed compliance)
- Because of the thin distensible walls, and low blood pressure, transmural pressure and thus blood flow will be affected by a variety of external factors.
- The upright posture of humans challenges the venous circulation
Venous smooth muscles adapt to increased volumes, by active relaxation in response to stretching. They share this feature with other organs’ smooth muscle (bladder, stomach etc).

**STRESS RELAXATION:** a feature of venous smooth muscle

![Graph showing stress-relaxation](image)

Volume → Pressure + radius → TENSION → Relaxation

**EFFECT OF POSTURE ON VENOUS PRESSURE**

- Blood pressure is reduced above the heart, and pressure is elevated below the heart.
- Arteries do not dilate much, and pressure gradient does not change, but veins considerably dilate, when hydrostatic pressure is elevated. For instance, when standing up venous volume increases by 500 ml, decreasing venous flow to the heart (venous return).
VENOUS COMPRESSION ELEVATES VENOUS RESISTANCE

Veins can be compressed easily at vulnerable points, elevating resistance. Venous resistance is the third largest (after arteriolar and capillary resistances)

FACTORS PROMOTING VENOUS RETURN

1. THE HEART ACTIVITY
   maintaining the pressure gradient by
   – pumping (vis a tergo)
   – sucking (vis a fronte)

2. MUSCLE PUMP+ VALVES

3. CONTROL OF COMPLIANCE by
   SYMPATHETIC VENOCONSTRICTION

4. Respiratory pump
MUSCLE PUMP: EFFECT OF WALKING ON VENOUS PRESSURE

In dilated, varicose veins valves fail →
Muscle pump is insufficient.
EDEMA is frequent.
CONTROL OF COMPLIANCE

• Systemic veins are innervated by sympathetic noradrenergic vasoconstrictor fibers. Noradrenaline contracts venous smooth muscle via $\alpha_1$-adrenergic receptors

• VENOCONSTRICTION will affect resistance little but will reduce compliance ie venous volume at a given blood pressure. Thus it will promote venous blood flow to the heart, and mobilize blood from the venous „stores” toward the other parts of the circulation.

BLOOD RESERVOIRS

BLOOD may be mobilized from:
1. Venous system (64%)
2. Pulmonary circulation (9%)
3. Heart (7%) by increased ejection

SPECIFIC VENOUS STORES IN HUMANS:
1. Cutaneous venous plexuses (300-500 ml)
2. Great abdominal veins (300 ml)
3. Liver (200-300 ml)
4. Spleen (150 ml)

Mobilization is primarily governed by sympathetic stimulation!
Respiratory pump

INSPIRATION

EXPIRATION

CHANGES:

Intrathoracal pressure

Left ventricular stroke volume

Right ventricular stroke volume

Venous return (to right atrium)

More negative

Increased pulmonary compliance

Less negative

Decreased pulmonary compliance

Increased Venous return

Decreased venous return

RESPIRATORY PUMP

Intrathoracal pressure

Left ventricular stroke volume

Right ventricular stroke volume

Venous return

Inspiration

Expiration
WHAT is the mechanism of the beat-to-beat adaptation of the ventricles to respiratory-induced changes in diastolic filling?

The Frank-Starling mechanism.

VALSALVA maneuver: forced expiratory effort with closed glottis: whenever we use our thoracohumeral muscles or want to remove something from the pelvis.

The VALSALVA-maneuver evokes complex cardiovascular reflexes.
The large fluctuations in venous flow may dislocate thrombi. Going to the restroom with a deep venous thrombosis is risky business!