VASCULAR SYSTEM
- THE HEMODYNAMICS -

Lecture 1

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Components of the vasculature and their function

1. **Arteries**: highest blood pressure, thick-walled (elastic tissue, smooth mm)
2. **Arteriols**: highest resistance in the CV system, smooth mm innervated by ANS (skin, splanchnic circ.: $\alpha_1$-adren. rec., skeletal mm: $\beta_2$-adren. rec.)
3. **Metarteriols**: 
   - part of their wall surrounded by smooth mm
   - can by-pass capillaries going directly to the venous circulation if precapillary sphincters are constricted
   - allow WBC to circulate from arterioles to venous circulation
4. **Capillaries**: largest total cross-sectional and surface area, thin-walled (one layer of endothelial cells on a basal lamina), exchange area
5. **Venules**: smallest veins formed from merged capillaries
6. **Veins**: low pressure, thin-walled, **capacitance vessels**, contains the highest % of the blood in the CV system, the blood volume contained is called the unstressed volume (blood reservoir), innervated by ANS

**Microcirculation** = network of arterioles, capillaries and venules...
# Morpho-functional diversity of blood vessels

<table>
<thead>
<tr>
<th>VESSEL TYPE</th>
<th>FUNCTION</th>
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<tbody>
<tr>
<td>Aorta</td>
<td>Pulse dampening and distribution</td>
</tr>
<tr>
<td>Large Arteries</td>
<td>Distribution</td>
</tr>
<tr>
<td>Small Arteries</td>
<td>Distribution and resistance</td>
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<td>Arterioles</td>
<td>Resistance (pressure/flow regulation)</td>
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<tr>
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<td>Exchange</td>
</tr>
<tr>
<td>Venules</td>
<td>Exchange, collection, and capacitance</td>
</tr>
<tr>
<td>Veins</td>
<td>Capacitance function (blood volume)</td>
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<td>Vena Cava</td>
<td>Collection</td>
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<th>VESSEL TYPE</th>
<th>MEAN DIAMETER</th>
<th>MEAN WALL THICKNESS</th>
<th>ENDOTHELIUM</th>
<th>ELASTIC TISSUE</th>
<th>SMOOTH MUSCLE</th>
<th>FIBROUS TISSUE</th>
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<tr>
<td>Artery</td>
<td>4.0 mm</td>
<td>1.0 mm</td>
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</tr>
<tr>
<td>Arteriole</td>
<td>30.0 µm</td>
<td>6.0 µm</td>
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<tr>
<td>Capillary</td>
<td>8.0 µm</td>
<td>0.5 µm</td>
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</tr>
<tr>
<td>Veneule</td>
<td>20.0 µm</td>
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</tr>
<tr>
<td>Vein</td>
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Blood distribution through the CV system

84 % — systemic circulation
- 64 % - veins
- 13 % - arterioles
- 7 % - arteriols & capillaris

9 % — pulmonary system
7 % — heart
Systemic Vessels of each type put side-by-side

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Velocity of blood flow is inversely proportional to vascular cross-sectional area, \( \sim 33 \text{ cm/sec} \) in the aorta, but only \( \sim 0.3 \text{ mm/sec} \) in the capillaries (capillaries length of \( \sim 0.3 \div 1 \text{ mm} \) → blood remains in the capillaries for only \( 1 \div 3 \text{ sec} = \) time for diffusion ...)

\[ \text{velocity} = \frac{\text{Flow}}{\text{Area}} \]
Blood pressure in various portions of the circulation

Figure 14-2. Normal blood pressures in the different portions of the circulatory system when a person is lying in the horizontal position.

120-100-80 - 35-17-10 - 0
Ao (Max-Mean-Min)-Capill (a-av-v)-Vc

25-16-8 - 7... (mmHg)

*Left CO = Right CO
Main aspects of the circulatory function

1. Blood flow to most tissues is coupled to the tissue need: 20-30x blood flow local increase possible, but just 3-7x more CO → need for local metabolic and nervous regulatory factors

2. Cardiac Output (CO) is the sum of all the local tissue flows: the heart receives – pump as an automaton – send - receive, etc; extra-control from the Autonomic Nervous System (ANS)

3. Arterial pressure regulation is generally independent of either local blood flow control or CO control: fast by nervous reflexes, delayed by kidneys and humoral factors; significance…
Cardiac output = Total tissue blood flow

Figure 20-6. Experiment in a dog to demonstrate the importance of nervous maintenance of the arterial pressure as a prerequisite for cardiac output control. Note that with pressure control, the metabolic stimulant dinitrophenol increases cardiac output greatly; without pressure control, the arterial pressure falls and the cardiac output rises very little. (Drawn from experiments by Dr. M. Banet.)
Why does blood flow?

- In the systemic circulation the mean pressure decreases progressively (100 mmHg - aorta, 30 mmHg - end of arterioles, 4 mmHg - vena cava) with increase in resistance to blood flow.
- Largest decrease in pressure occurs across the arterioles.
Interrelationships of pressure, resistance and blood flow

\[ F = \frac{\Delta P}{R} \]  

“Ohms law” for the blood flow

1) *pressure difference* (\( \Delta P \)) of the blood - "pressure gradient" along the vessel, that pushes the blood through the vessel

2) *vascular resistance* (\( R \)) - impediment to blood flow through the vessel

(result of friction between the flowing blood and the intravascular endothelium)
Blood flow: the “Ohm’s Law” for the blood flow

Blood flow means the quantity of blood that passes a given point in the circulation in a given period of time.

\[ F = \frac{\Delta P}{R} = \text{blood flow} = \text{cardiac output (ml/min)} \]

The overall blood flow in the circulation at rest = \( CO = 5 \text{ L/min} \)

\[ \Delta P = \text{pressure gradient} \] that drives the blood flow

\[ = \text{mean arterial pressure (mmHg)} - \text{RA pressure (mm Hg)} \]

\[ R = \text{resistance} = \text{total peripheral resistance (TPR)} \]

\[ (\text{mmHg/ml/min}) \]
Fluids flow from a higher pressure to a lower pressure

Flow ~ $\Delta P$

$P_1 - P_2 = DP$

Flow depends on DP, not absolute P

No pressure gradient, so no flow

100 mm Hg

100 mm Hg

DP = 0, so no flow

Flow

100 mm Hg

Flow

75 mm Hg

DP = 100 - 75 = 25 mm Hg

flow is equal

40 mm Hg

15 mm Hg

DP = 40 - 15 = 25 mm Hg
Laminar vs. turbulent blood flow in the vessels

**Laminar flow** - blood flows in *streamlines*, at a steady rate through a long, smooth blood vessel. Each layer of blood remains at the same distance from the vessel wall. The central most portion of the blood stays in the center of the vessel.

Cause for the **parabolic profile for velocity of blood flow**: the blood near the wall of the vessel flows extremely slowly, whereas that in the middle of the vessel flows extremely rapidly.

![Diagram of laminar flow](image)

**Before flow begins**

**1 sec. after flow begins**
Turbulent flow:

When:
- the rate of blood flow becomes too great
- blood passes by an obstruction in a vessel or over a rough surface
- blood makes a sharp turn
- changes in the blood density and viscosity

Turbulent flow - the blood flows disorderly, both crosswise and along the vessel forming whorls in the blood called *eddy currents* → increase the overall friction of flow in the vessel → **much greater resistance**

Turbulent flow - elements of the fluid moving in a disorderly pattern.
Reynolds' number (Re):
measures the tendency for turbulence to occur

\[
\text{Re} = \frac{\nu \cdot d \cdot \rho}{\eta}
\]

- \( \nu \) - mean velocity of blood flow
- \( d \) - vessel diameter
- \( \rho \) - density (normal for blood \( \sim 1 \))
- \( \eta \) (eta) - viscosity (normal for blood \( \sim 1/30 \) poise)

**Re \( \sim 200 – 400 \) in large arteries**

The type of flow can be predicted by Reynolds’ number:
if Re \( \uparrow (>200 – 400) \) \( \rightarrow \) more turbulence; if Re \( \downarrow \) \( \rightarrow \) less turbulence

**Reynold’s number & turbulence are increased by:**
1. \( \downarrow \) blood viscosity (e.g., \( \downarrow \) hematocrit, anemia)
2. \( \uparrow \) blood velocity (e.g., during ejection, pulsatile flow, narrowing of a vessel)
3. blood making a sharp turn or passing over a rough surface
4. Sudden change into a larger vessel diameter.

In small vessels Re is normally low and will not cause turbulence. But for Re > 2000, turbulence can occur even in a straight, smooth vessel.
Ventricular contraction

1. Ventricle contracts

2. Semilunar valve opens

3. Aorta and arteries expand and store pressure in elastic walls.

Ventricular relaxation

1. Isovolumic ventricular relaxation

2. Semilunar valve shuts

3. Elastic recoil of arteries sends blood forward into rest of circulatory system.
How is obtained the pressure gradient.

Compressing a fluid raises its pressure

LV systole → the pressure created is transferred to the blood → high-pressure blood displace lower-pressure blood already in the vessels = driving pressure

Volume changes of the heart and blood vessels are major factors that influence blood pressure in the vascular system.

Blood pressure is the force exerted by the blood against any unit area of the vessel wall, measured in mmHg, or cm H$_2$O.

$1 \text{ mmHg} = 1.36 \text{ cm } H_2O$ – as specific gravity of Hg is 13.6 x that of water
Resistance opposes flow

Blood flowing through vessels encounters friction from the walls of the vessels and from cells within the blood rubbing against each other as they flow.

The tendency of the CV system to oppose blood flow is called its resistance (R) to flow.

Blood flow will take the path of least resistance.

Flow $\sim \frac{1}{R}$
Resistance to Blood Flow

**Units of Resistance.**
If the pressure difference between two points is 1 mm Hg and the flow is 1 ml/sec, the resistance is 1 *peripheral resistance unit (PRU)*.

**Total Peripheral Vascular Resistance (TPR):**
Resistance of the entire systemic circulation

\[ \Delta P/F \sim \frac{100 \text{ mmHg}}{100 \text{ ml/sec}} \sim 1 \text{ PRU} \]

For a CO \( \sim 100 \text{ ml/sec} \)

Strong vasoconstriction \( \rightarrow \) TPR up to 4 PRU.

Vasodilation \( \rightarrow \) TPR falls to 0.2 PRU

**Total Pulmonary Vascular Resistance**
Net pressure difference

\[ = \text{mean pulmonary arterial press (16) - mean LA pressure (2)} = 14 \text{ mmHg}. \]

*Total pulmonary vascular resistance* \( \sim \Delta P/F \)

\[ \sim \frac{14 \text{ mmHg}}{100 \text{ ml/sec}} \sim 0.14 \text{ PRU} \]

(1/7 than systemic one)
A simplified model of CV system
Conductance - blood flow through individual blood vessels for a given pressure difference is determined by their resistance

Conductance \sim \frac{1}{\text{Resistance}}
Slight changes in the blood vessels radius by vasodilation or vasoconstriction, can change the conductance.

A. Demonstration of the effect of vessel diameter on blood flow. 
B. Concentric rings of blood flowing at different velocities; the farther away from the vessel wall, the faster the flow.
Role of radius in determining resistance to flow

Resistence $\sim \frac{1}{\text{Radius}^4}$

Conductance $\sim \text{Radius}^4$

<table>
<thead>
<tr>
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<tr>
<td>Tube A</td>
</tr>
<tr>
<td>$R \sim \frac{1}{1^4}$</td>
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<td>$R \sim 1$</td>
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<th>Flow $\sim \frac{1}{\text{Resistance}}$</th>
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Resistance $\sim \frac{1}{\text{Radius}^4}$

Conductance $\sim \text{Radius}^4$
Poiseuille’s Law

\[ F \sim 1/R \text{ and } R \sim 1/r^4 \Rightarrow F \sim r^4 \]

\[ F \sim \Delta P \]

\[ F \rightarrow \frac{\pi \Delta Pr^4}{8\eta l} \]

**R** = resistance

\( \eta \) (eta) = viscosity of blood flow

\( l \) = length of blood vessel

\( r^4 \) = radius of vessel to the 4th power

\( r \sim 4 \div 25 \mu m \) in arterioles, changes up to 4x in response to local or nervous control mechanisms

**Obs.:** ⚠ High \( R \) with increased hematocrit (%RBC...)

⚠ if ‘\( r \)’ increases by a factor of 2, then \( R \) decreases by a factor of \( 2^4 = 16 \), and \( F \) increases by a factor of 16
Resistance

• **A. Resistances in series**: each organ is supplied by a large artery, then smaller arteries, arterioles, capillaries, venules, that merge into veins, collectively *arranged in series* → flow through each sector of vessels is continuous → total resistance to blood flow \( R_{\text{total}} \) is equal to the sum of the resistances of each vessel:

\[
R_{\text{total}} (\text{TPR}) = R_{\text{artery}} + R_{\text{arterioles}}(2/3) + R_{\text{capillaries}}
\]

• **B. Resistance in parallel**: in the systemic circulation each organ is supplied by an artery that *branches* off the aorta. This parallel arrangement enable tissue local blood flow regulation independently of flow to other tissues:

\[
1/R_{\text{total}} = 1/R_1 + 1/R_2 + ... + 1/R_n \quad \text{and} \quad F_{\text{total}} = F_1 + F_2 + ... + F_n
\]

\( F = \) flow or conductance (C)
Parallel circulations:
- Brain
- Kidney
- Muscle
- GIT
- Skin
- Coronary

Series & parallel circulations
Effect of Blood Hematocrit and Blood Viscosity on Vascular Resistance and Blood Flow

• *Viscosity of normal blood* ~ 3 x *viscosity of water*, mainly because of large numbers of suspended RBC → increased friction against adjacent cells and vessel wall (three times as much pressure is required to force whole blood as to force water through the same blood vessel)

*Hematocrit (Ht)= % cells from the whole blood*

Normal hematocrit (45%) – blood viscosity ~ 3.

*Increased Ht to 60-70% (polycythemia) → viscosity ~10 x → blood flow greatly retarded.*

• viscosity secondary depends on plasma protein concentration and types of proteins in the plasma.
  Viscosity of blood *plasma* is about 1.5 x that of water.
Effect of hematocrit on blood viscosity. (Water viscosity = 1)
Figure 14-12. Effect of changes in arterial pressure over a period of several minutes on blood flow in a tissue such as skeletal muscle. Note that between pressure of 70 and 175 mm Hg, blood flow is "autoregulated." The blue line shows the effect of sympathetic nerve stimulation or vasoconstriction by hormones such as norepinephrine, angiotensin II, vasopressin, or endothelin on this relationship. Reduced tissue blood flow is rarely maintained for more than a few hours because of the activation of local autoregulatory mechanisms that eventually return blood flow toward normal.
Figure 14-13. Effect of arterial pressure on blood flow through a passive blood vessel at different degrees of vascular tone caused by increased or decreased sympathetic stimulation of the vessel.
Velocity of blood flow

\[ v = \frac{F}{A} \]

\( v \) = velocity of flow (cm/sec) = a measure of how fast blood flows past a point

\( F \) or \( Q \) = blood flow (L or mL/min) or flow rate (blood volume that passes one point in the system /unit time).

\( A \) = cross-sectional area (cm\(^2\)) at a certain level of the cardiovascular system

Obs: \( v \) in aorta vs. capillaries
Flow rate and velocity of flow in a tube:

more narrow the tube, the faster the velocity of flow

\[ \text{Flow rate (Q)} = 12 \, \text{cm}^3/\text{min} \]

- At point X:
  \[ v = \frac{12 \, \text{cm}^3/\text{min}}{1 \, \text{cm}^2} = 12 \, \text{cm/min} \]
- At point Y:
  \[ v = \frac{12 \, \text{cm}^3/\text{min}}{12 \, \text{cm}^2} = 1 \, \text{cm/min} \]

1 cm³ = 1 ml
Systemic Vessels of each type put side-by-side

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Vascular Distensibility

- Normally expressed as the % increase in volume /1mmHg rise in pressure:
  \[
  \text{Vascular distensibility} = \frac{\text{Increase in volume}}{\text{Increase in pressure} \times \text{Original volume}}
  \]

- all blood vessels are *distensible*, but arteries on average are ~ 8 x less distensible than the veins

- arteries distensibility allows them to accommodate the pulsatile output of the heart and to average out the pressure pulsations → smooth, continuous blood flow through the very small blood vessels.

- *pulmonary circulation*:
  - pulm *veins* distensibility similar to those of the systemic circulation.
  - pulmonary *arteries* normally operate under 6 x lower press.  
  → 6 x greater *distensibility* than the one in the systemic arteries.
Capacitance / Compliance

- Compliance (C) = *total quantity of blood* stored in a given portion of the circulation / 1 mmHg pressure rise

\[
\text{Vascular compliance} = \frac{\text{Increase in volume}}{\text{Increase in pressure}}
\]

\[C \text{ (ml/mm Hg)} = \Delta V/\Delta P\]

Compliance = distensibility \(\times\) volume

- \(C_{\text{veins}} \gg C_{\text{arteries}} \rightarrow \) unstressed vol. (veins) \(\gg\) stressed vol. (arteries)

- Changes with age: arteries become stiffer and less distensible (\(\downarrow C\))
A simplified model of CV system

Elastic recoil
Continuous driving pressure for blood flow

High-resolution outlet for arterial blood flow and distribution to individual tissues

Blood flow through all the systemic capillaries equal the cardiac output (5 l/min)

A simplified model of CV system
Microcirculation

- Main function:
  - transport of nutrients…
  - removal of cellular excreta…

- Arterioles (highly muscular, their diameters can change manifold)
- Metarterioles/terminal arteriole (do not have a continuous muscular coat, but smooth muscle fibers encircle the vessel at intermittent points)
- Precapillary sphincters (smooth mm cell, local control of blood flow)
- Capillaries
An artery branches 6-8 x until becoming arterioles; these are branching further 2-5 x towards capillaries.
Capillaries

- diameter = 4-9 μm, 10 billions, surface = 500 - 700 m²
  Capillary no, distance capill-cells (20-30 μm)~ metabolic activity of the tissue

- “pores” in the capillary membranes:
  1. **intercellular cleft / gap**: 6-7 nm, S~1/1000 of the total capillaries surface, allow the thermal motion of only small molecules
  2. **plasmalemmal / transcytosis vesicles** = caveolae: role in endocytosis, transcytosis (coalesce to form vesicular channels/pores)
  3. **special types** of pores:
     - large clefts in intestinal membranes, larger in liver capillaries (endothelial discontinuity...)
     - fenestrae in glomerular capillaries (20 to 100 nm), that appear to be sealed by a thin diaphragm, but they are permeable to larger molecules
     - no pores, but tight junctions, in brain capillaries (BBB)

- permeability is not uniform along the whole capillary:
  arterial end < venous end < venules (greater no of pores/clefts)
Structure of the capillary wall. Note especially the *intercellular cleft* at the junction between adjacent endothelial cells; it is believed that most water-soluble substances diffuse through the capillary membrane along the clefts. Small membrane invaginations, called *caveolae*, are believed to play a role in transporting macromolecules across the cell membrane. Caveolae contain caveolins, which are proteins that interact with cholesterol and polymerize to form the caveolae.
“Pores” in the capillary membranes

Exchange between blood & interstitial fluid takes place in the capillaries by diffusion, filtration, pinocytosis (transcytosis).
Cerebral endothelium: Tight-junction epithelium & blood-brain barrier

- Nutrients (especially glucose)
- Oxygen
- Carbon dioxide
- Waste products
- Tight junction
- Astrocyte
- Interstitial fluid
- Capillary lumen
- Endothelial cell
Pericytes

• Capillary walls are closely associated with elongated, highly branched cells = pericytes

• Mesh-like outer layer between endothelium and interstitial fluid, more developed at the capillary venous end and venules level

• Functions: exchange, growth & repair processes, local control of blood flow at microcirculation level
Average function of the capillary system

- For the billions of capillaries which operate intermittently in response to the local conditions in the tissue, there are...
  - average rate of **capillary blood flow**
  - average **capillary pressure**
  - average rate of **transfer of substances**
Blood flow in the microcirculation

- **Vasomotion**
  = intermittent contraction/relaxation of the metarteriols and precapillary sphincters (5-10/min)
  - partly an intrinsic contractile behavior of the vascular smooth muscle
  - depends on local and humoral factors, mostly on O$_2$ conc.
  - influenced by sympathetic tone
Blood flow in the microcirculation

Blood flows intermittently/randomly or it may oscillate rhythmically at different frequencies as determined by contraction and relaxation (vasomotion) of the precapillary vessels.

Changes in \textit{transmural pressure} = \textit{intravascular press.} \textit{extravasc. press} affect the contractile state of the precapillary vessels:

- increase of transmural pressure $\rightarrow$ terminal arteriole/precapillary constriction

$\rightarrow$ CHANGES IN CAPILLARY DIAMETER ARE PASSIVE AND ARE CAUSED BY ALTERATIONS IN PRECAPILLARY AND POSTCAPILLARY RESISTANCE.

Average velocity of capillary blood flow $\sim$1 mm/sec (zero-several mm/sec).

*Transmural pressure is essentially equal to intraluminal pressure because extravascular pressure is usually negligible.*
Laplace's law

\[ T = P \times r \]

in which **P**, intravascular pressure; **r**, radius of the vessel; **T**, wall tension as the force per unit length tangential to the vessel wall (a force that tends to pull apart a theoretical longitudinal slit in the vessel).

**r of resistance vessels** \( \sim \) contractile force of the vasc. smooth muscle

\( \sim \) distending force produced by the intraluminal pressure.

Intravascular pressure diminished \( \rightarrow \) vessel diameter and tension in the vessel wall decreased (Laplace's law) \( \rightarrow \) terminal arteriole response: vasodilation

When perfusion pressure is progressively reduced, a value of the transmural pressure = **critical closing pressure** is reached; at this pressure the vessel is occluded and blood flow ceases even though a positive pressure gradient from the afferent to the efferent end of the vessel may still exist.

Also, small arterioles may be occluded because of **infitling** of the endothelium.
Vascular Remodeling in Response to Chronic Changes in Blood Flow or Blood Pressure

- Inward eutrophic remodeling
- Hypertrophic remodeling
- Outward remodeling
- Outward hypertrophic remodeling
Consequences of Laplace's law: \( T = p \times r \)

Even the capillaries are thin-walled, they can withstand high internal pressures without bursting because of their narrow lumens.

At normal aortic (100 mm Hg) and capillary (25 mm Hg) pressures, the wall tension of the aorta is about 12,000 times greater than that of the capillary:

\[ 100 \text{ mmHg} \times r \text{ of 1.5 cm for the aorta vs. 25 mmHg} \times r \text{ of } 5 \times 10^{-4} \text{ cm for the capillary} \]

In a person standing quietly, capillary pressure in the feet may reach 100 mm Hg. Under such conditions, capillary wall tension increases to a value that is only 0.003 that of the wall tension in the aorta at the same internal pressure.

According to Laplace's equation, **wall tension increases as vessels dilate**, even when internal pressure remains constant \((T = p \times r)\).

In aneurysm (local widening) of the aorta, the wall tension may become high enough to rupture the vessel.
Endothelium synthesize substances that affect the contractile state of the arterioles:

1. *Endothelium-derived relaxing factor (EDRF) - nitric oxide (NO)*, vasodilator formed and released in response to stimulation of the endothelium by various agents (e.g., acetylcholine, ATP, serotonin, bradykinin, histamine, substance P); NO can also interfere with platelet aggregation.

2. *Endothelium-derived hyperpolarizing factor (EDHF) - vasodilator*

3. *Prostacyclin*, a vasodilator that also inhibits platelet adherence to the endothelium and platelet aggregation, aiding in the prevention of intravascular thrombosis.

4. Endothelin, a 27-am.ac. powerful vasoconstrictor substance, require just ng for vasoconstr., released in large quantities in lesioned endothelium.

5. Also, synthesize structural components: glycocalyx, basal lamina endoth. enzymes: AG converting enz, carbonic anhydrase (lungs) thromboxane, von Willebrand factor (f VIII) adhesive molecules involved in cell migration during inflammation.
Prostacyclin (PGI$_2$) is formed from arachidonic acid (AA) by the action of cyclooxygenase (Cyc-Ox) and prostacyclin synthetase (PGI$_2$ Syn) in the endothelium and elicits relaxation of the adjacent vascular smooth muscle via increases in cAMP. Stimulation of the endothelial cells with acetylcholine (Ach) results in the formation and release of an EDRF (NO). EDRF stimulates guanylyl cyclase (G Cyc) to increase cGMP in the vascular smooth muscle to produce relaxation. The vasodilator agent nitroprusside (NP) acts directly on the vascular smooth muscle. Substances such as adenosine, H$^+$, CO$_2$, and K$^+$ can arise in the parenchymal tissue and elicit vasodilation by direct action on the vascular smooth muscle.
Vasomotion is influenced by sympathetic tone

**Arterioles** - A, before and B, after the microinjection of norepinephrine. **Right inset** - capillary with red cells during a period of complete closure of the feeding arteriole.
Angiogenesis creates new blood vessels

Relation angiogenesis — growth, development, wound healing — endurance exercise training

Angiogenic vs. antiangiogenic factors/cytokines:
mitogens like VEGF, FGF vs. angiostatin and endostatin

Therapeutic role: cancer, coronary artery disease/myocardial ischemia