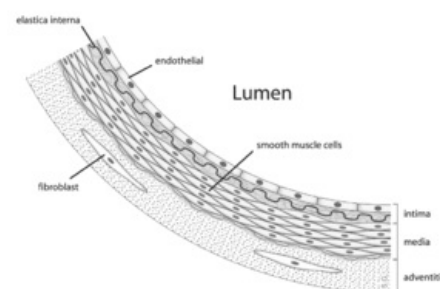


Vascular endothelial cells

Endothelium under the microscope (<https://mikroskop.wikiskripta.eu/?idx=>



Description of an artery

20143%2B&link=1&cx=613&cy=438&n=32&m=5&q=65&f=0&r=0&annot=2079) **Endothelial cells** (endothelium, *endothelium*) form a simple layer of cells lining the inside of a vessel. They are not considered true epithelium because they arise from mesenchyme. They have an elongated polygonal shape, contain numerous pinocytotic vacuoles and form complex connections with neighboring cells. They also contain Weibel-Palade bodies ($0.1 \times 3 \mu\text{m}$), which store **von Willebrand factor**. The structural and functional integrity of endothelial cells is a basic prerequisite for homeostasis of the vessel wall and blood circulation.

Function of endothelium

- The semipermeable membrane of the endothelium controls the transfer of small and large molecules into the wall of arteries and further through the wall of capillaries and venules. In most regions of the human body, intercellular junctions are normally impermeable to these molecules, but the relatively labile junctions between endothelial cells can be expanded by hemodynamic factors (blood pressure) and vasoactive substances (eg, histamine in inflammation).
- They maintain a non-thrombogenic interface between blood and tissue, regulate thrombosis, thrombolysis and platelet adhesion.
- They modulate vascular tone and blood flow.
- They metabolize hormones.
- They regulate immune and inflammatory reactions by acting on the interaction between the vessel wall and leukocytes.
- They modify lipoproteins in the artery wall.
- They regulate the proliferation of other cells, especially vascular smooth muscle.

Properties and functions of the endothelium

<i>Maintaining Barrier Permeability</i>	<i>Blood flow modulation of vessel reactivity</i> - vasoconstrictors: endothelin, angiotensin-converting enzyme - vasodilators: NO \cdot , prostacyclin
<i>Synthesis of anticoagulant and antithrombotic molecules</i> - prostacyclin - thrombomodulin - plasminogen activator - heparin-like molecules	<i>Regulation of inflammatory and immune processes</i> - IL-1, IL-6, IL-8 - adhesive molecules - histocompatibility antigens
<i>Synthesis of prothrombotic molecules</i> - von Willebrand factor - tissue factor - plasminogen activator inhibitor	<i>Cell growth regulation</i> - growth stimulators: PDGF, FGF, CSF - growth inhibitors: heparin, TGF- β
<i>Extracellular matrix formation (collagen, proteoglycans)</i>	<i>LDL oxidation</i>

The vascular endothelium is a dynamic endocrine organ that regulates the contractile, secretory and mitogenic activities of the vessel wall and hemostatic processes in the vessel lumen. In addition to participating in the formation of a blood clot (thrombus), damage to the endothelium is a key moment in the development of atherosclerosis, indirectly also hypertension, and participates in the diseases of a number of other organs.

The endothelium **produces vasoactive substances** in response to changes in blood flow, oxygen tension, and various other stimuli via receptors. Endothelium-dependent dilation of blood vessels is mainly realized by the nitric oxide radical NO \cdot (previously referred to as EDRF = endothelium-derived relaxing factor), to a lesser extent by prostacyclin and hyperpolarizing factor, which is an activator of ATP- and Ca A²⁺-dependent K⁺-ion channel. Vasoconstrictor substances produced by the endothelium include endothelin-1 (ET-1) and thromboxane A₂. The balance between the two opposing substances in both physiological and pathological situations determines the

contractile and probably also the mitogenic state of the smooth muscle of the respective vessel. NO[•] is synthesized in various cell types by converting L-arginine to L-citrulline catalyzed by NO-synthase (NOS). 3 NOS isoforms have been identified.

 For more information see NO-synthase.

Endothelial Dysfunction

Dysfunction of the endothelium leads to impaired vascular relaxation, promotes platelet aggregation, increases the proliferation of vascular smooth muscle and the adhesion of leukocytes to the surface of endothelial cells. Surface adhesive molecules are expressed, facilitating the capture of circulating leukocytes. Adhesion of leukocytes together with proliferation of smooth muscle are key moments in the development of atherosclerotic plaques. The state of mechanical integrity of the plaque determines the clinical manifestation of atherosclerosis. Rupture of the plaque cover with subsequent thrombus formation is the cause of most sudden coronary events. A stable atheromatous plaque usually has a firm fibrous envelope, a smaller lipid core, and fewer leukocyte infiltrates than a ruptured plaque. Mediators of inflammation such as cytokines, oxidized LDL, and infectious agents (cytomegalovirus, Chlamydia pneumoniae) can weaken the integrity of the fibrous envelope. Endothelial dysfunction is therefore not only an early marker of atherosclerosis, but also significantly contributes to the development of atherogenesis.

Neuronal and endothelial NOS consistently produce small amounts of NO[•], while consistently large amounts of NO[•] are produced by macrophage NOS or NOS from smooth muscle cells upon induction by certain cytokines. Vessels affected atherosclerosis suffers from endothelial dysfunction, which is documented by the impairment of vasomotor function due to the loss of the action of NO[•], which has an antiatherogenic and anti-inflammatory effect. The inactivation of endothelial NO[•] also leads to the formation of superoxide anion, which causes vasoconstriction and hypertension. Endothelial dysfunction is also attributed to abnormal or excessive release of vasoconstrictor substances such as endothelin-1 (its plasma concentration is increased in patients with advanced atherosclerosis and acute coronary syndrome). Oxidative stress leads to the oxidation of LDL particles, which then inhibit NOS. Macrophages and smooth muscle cells are the main source of reactive oxygen species in atherosclerotic vessels. The final effect depends on the balance of the interaction of antioxidants and oxidants. Oxidative stress is involved in the atherogenic process by the induction of pro-inflammatory mediators:

Activation of the pro-inflammatory transcription factor (nuclear factor kappa B (NF-κB) or activator protein-1 (AP-1) and early growth response factor - egr-1) is caused by the effect of hydrogen peroxide, created during the oxidation cascade. Adhesion molecules such as VCAM-1, ICAM-1 and E-selectin, numerous cytokines, growth factors such as M-CSF contain functional DNA-binding sequences for NF-κB, AP-1 and egr-1, whose expression is induced by these transcription factors. NF-κB activation is inhibited by antioxidants and anti-inflammatory drugs such as salicylates or corticoids. Atherosclerosis is considered a chronic inflammatory process initiated and enhanced by oxidative stress. Thus, antioxidants prevent the development of atherosclerosis by inhibiting the activation of pro-inflammatory transcription factors that are required for the expression of cellular adhesion molecules, cytokines and growth factors in the vessel wall.

The nitric oxide radical formed in the endothelial cell inhibits the expression of cellular adhesive molecules on the surface of the endothelium and thereby prevents the attachment of leukocytes to the vessel wall. This is done by inhibiting the pro-inflammatory transcription factor NF-κB (the expression of pro-inflammatory cytokines, adhesive molecules and growth factors depends on their transcriptional induction by NF-κB).

The reduction of vasodilatation induced by the reduction of endothelial NO[•] contributes to the disorder of myocardial blood flow; oxidative stress inhibits NO-synthase by peroxynitrite formed from superoxide anion oxidizing its key cofactor - tetrahydropterin. It has been shown that the formation of reactive forms of oxygen and nitrogen in the endothelium is influenced by the activity of xanthine oxidase; the administration of its inhibitor - allopurinol - can therefore contribute to the prevention of myocardial damage in chronic heart failure.

Links

Related Articles

- Atherosclerosis

Source

- MASOPUST, Jaroslav, et al. *Patobiochemie buňky*. 1. edition. Praha : Univerzita Karlova, 2. lékařská fakulta, 2003. 344 pp. pp. 88-92. ISBN 80-239-1011-6.