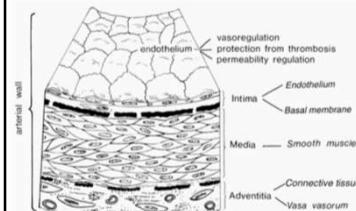


Endothelium, smooth muscle, vessels

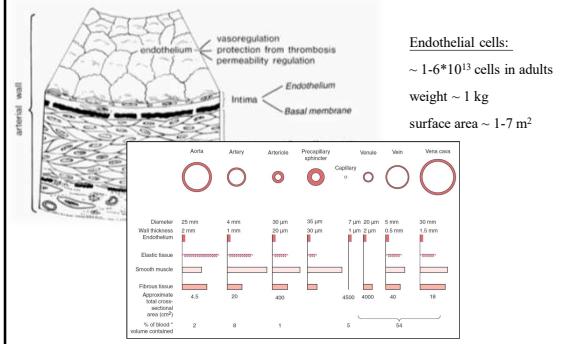
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UD Faculty of Medicine
Division of Clinical Physiology

Vessels



Vessels - endothelium as an organ



Functions of vascular endothelium

Release of vasodilator agents

Nitric oxide (EDRF)
Prostacyclin (PGI₂)
Bradiakinin
EDHF (endothelium derived hyperpolarizing factor)

Release of vasoconstrictor agents

Endothelins

Protection of vascular smooth muscle

vasoconstrictory → to vasodilatory stimuli
(acetylcholine and serotonin)

Antiaggregatory effect

Acts via NO (nitric oxide) and PGI₂ (thrombocyte activation ↓)

Functions of vascular endothelium

Prevention of coagulation

Thromboresistant surface (heparan sulfate – antithrombin cofactor)

Immune and barrier function

Supply of antigens to immunocompetent cells
Secretion of interleukin I, E-selectin (rolling)

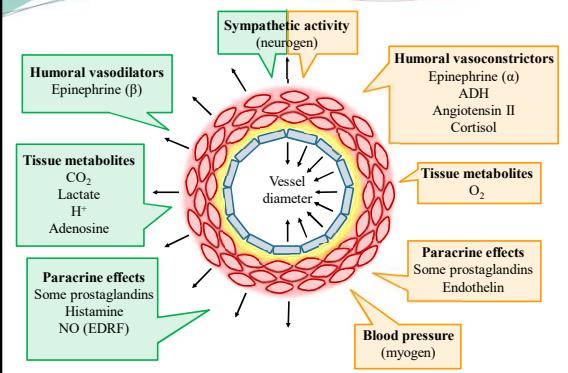
Enzymatic activity

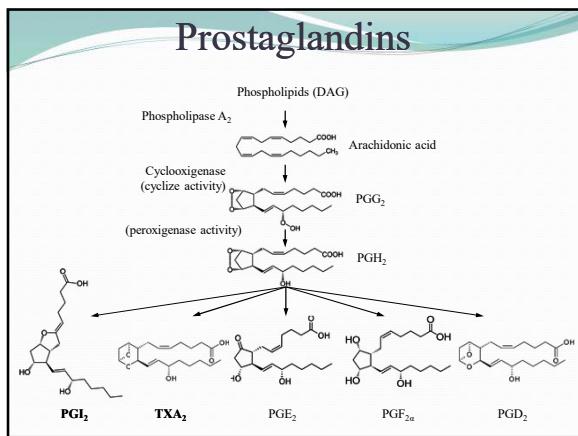
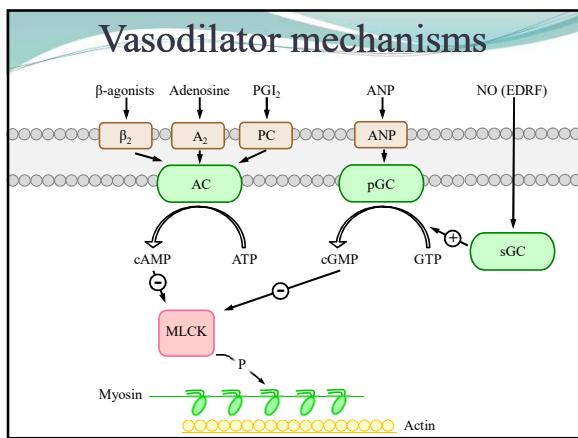
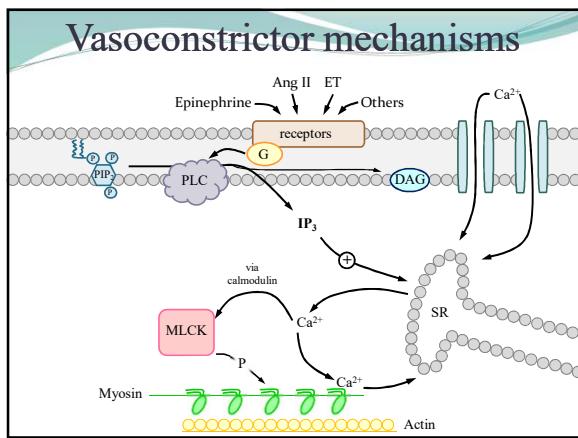
Angiotensin-converting enzyme
Carbonic anhydrase (large amounts in lung endothelium)

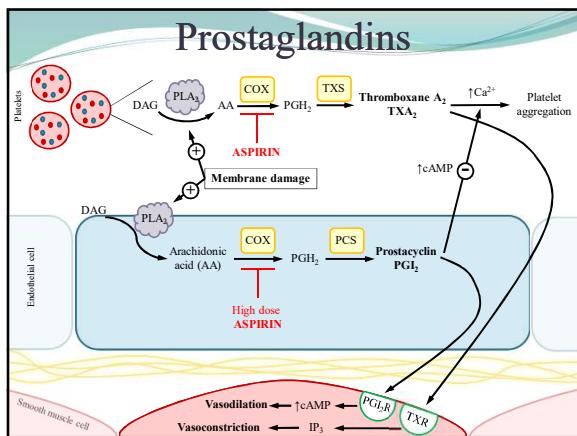
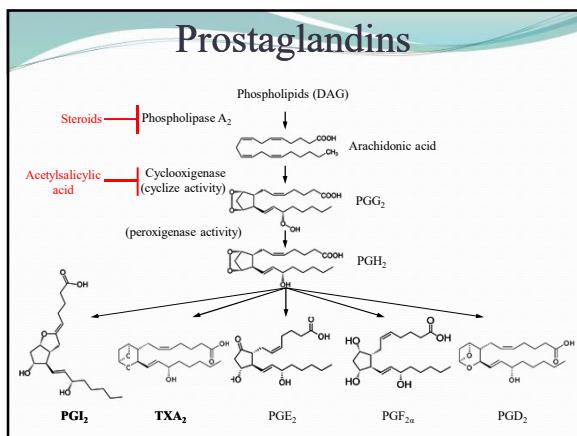
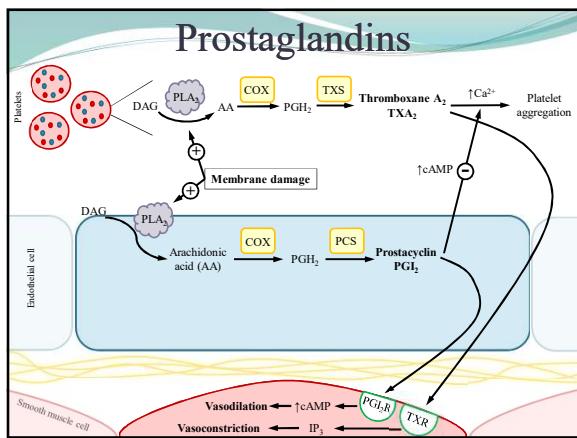
Growth signal to vascular smooth muscle

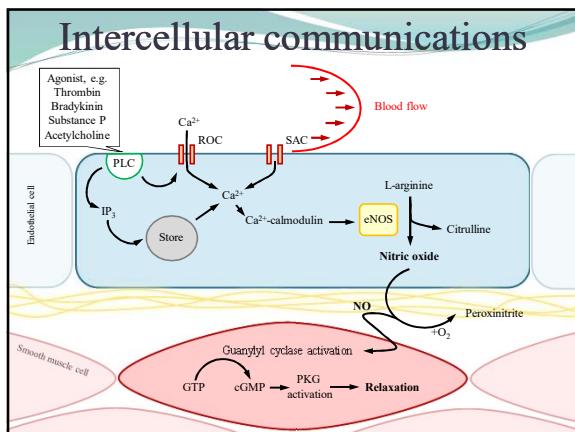
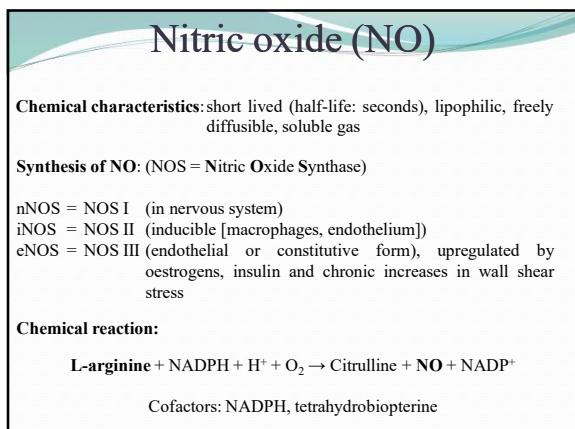
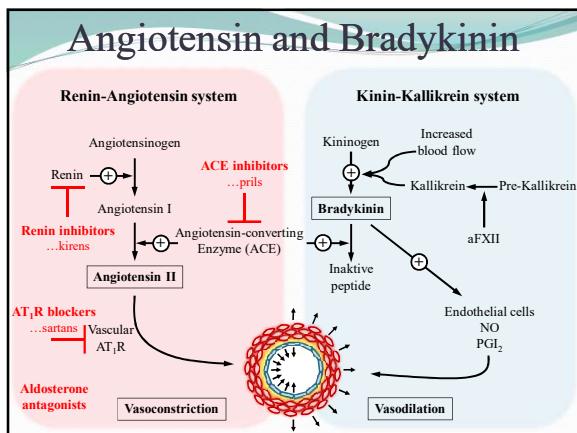
VEGF (vascular endothelial growth factor), angiopoietin
Heparin-like inhibitors of growth

Mediators of vascular control









Agonists of NO production

1. **Humoral agonists of eNOS increase $[Ca^{2+}]$:**
acetylcholine (M_3 -receptor), bradykinin, thrombin, substance P, vasoactive intestinal polypeptide (VIP), insulin, histamine
2. **Mechanical agonists (wall shear stress):**
- flow induced vasodilation
- mechanosensitive ion channels
3. **Inflammation and endotoxin shock (iNOS):**
in inflammation: - in reaction to interleukins (e.g. IL-1) and TNF
- contributes to reddening (rubor) and local heat (calor) in inflammation
in shock: - lipopolysaccharide induced shock
- direct reaction to TNF α from macrophages
- results **too much NO** → general vasodilation
4. **Organic nitrates:** - glyceryl trinitrate
- isosorbide mononitrate
- sodium nitroprusside

EDHF (endothelium derived hyperpolarizing factor)

Soluble secretion of EDHF during Ach/bradykinin evoked SM hyperpolarization/relaxation when NO and PGI₂ productions blocked.

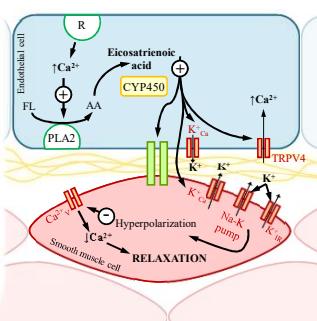
Chemical structure is uncertain: CYP450 product, K⁺, H₂O₂ ...

Half-life of action ~70 sec

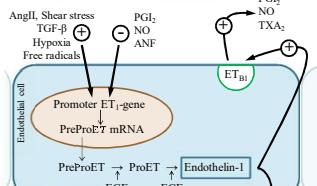
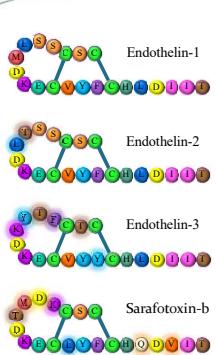
EDHF: in vessels with smaller diameter (resistance vessels)
NO: in vessels with higher diameter

EDHF independent SM hyperpolarization may occur because of myoendothelial gap junctions.

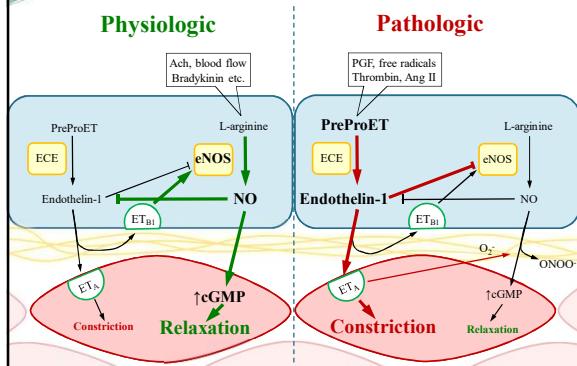
(If junctions are blocked, Ach induced hyperpolarization develops only in endothelial cells.
Ach → Ca²⁺↑ → I_{K,Ca} open → hyperpol.)



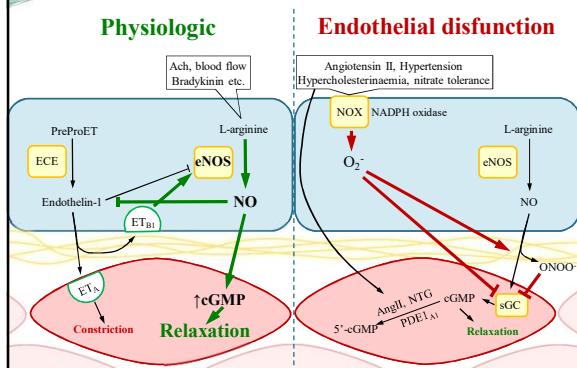
Endothelin



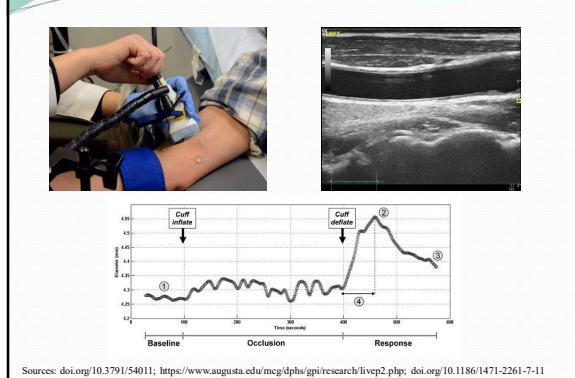
Interactions during health and disease



Interactions during disease



Flow-mediated vasodilatation

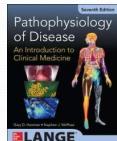


Literature



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