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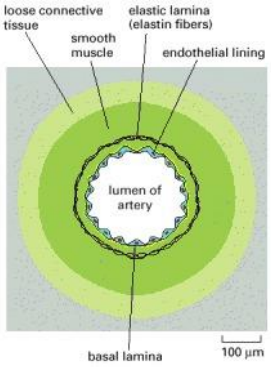
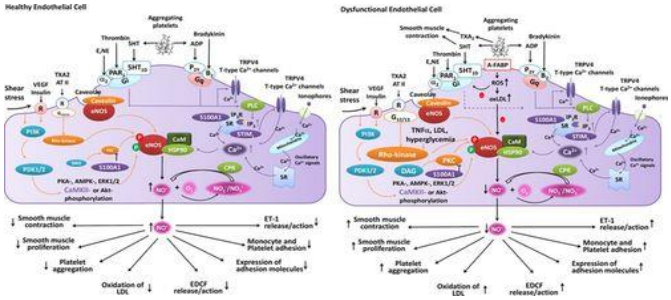
ENDOTHELIAL FUNCTION

What is it?	The vascular endothelium is a monolayer of cells forming the innermost* layer of arteries, veins and capillaries serving a number of key functions. The term 'endothelial dysfunction' relates to the impairment of this cellular monolayer and is a hallmark feature of early cardiovascular disease and vascular aging. The endothelium acts as a physical barrier between the blood and tissues regulating the transport of fluids, ions and macromolecules including blood cells. Secondly, it behaves as an endocrine organ controlling vascular tone and blood flow by interacting with the underlying smooth muscle layer. It achieves this through the release of different vasodilators (e.g., nitric oxide, endothelium derived hyperpolarizing factor) and vasoconstrictors (e.g., angiotensin and endothelin). Thirdly, it maintains the patency of blood vessels through the production of anti-thrombotic and anti-platelet agents carefully balancing the degree of coagulation and fibrinolysis in response to injury, inflammation and angiogenesis. The relative importance of endothelium derived mediators differs dependent on the vessel type and location. *N.B. The endothelium also carries sites for expression of the glycocalyx (formed primarily of glycoproteins and proteoglycans). It forms a luminal meshwork providing endothelial cells with a framework to bind plasma proteins and soluble glycosaminoglycans.
Why do we measure it?	The endothelium is a key regulator of dynamic systemic blood flow and tissue perfusion. It achieves this through the release of vasoactive mediators some of which are stimulated by shear stress. In addition to arterial stiffness, alteration in endothelial function is a key feature of vascular aging. Endothelial function can be measured in humans using flow mediated dilatation which specifically measures changes in the production of the vasodilator nitric oxide in response to shear stress. Diagnostically, these early tests can support clinical decision making regarding pharmacological and non-pharmacological interventions to delay the progression of cardiovascular disease.
How can it be measured	Changes in shear stress are achieved through initial occlusion of a large artery e.g., brachial for a set period of time using an inflatable cuff (suprasystolic cuff occlusion). Once released, a reactive hyperaemia ensues leading to the stimulation of endothelial nitric oxide release. Delta changes in the arterial width before and after cuff occlusion are measured by ultrasound, the lower the delta value indicative of a dysfunctional endothelium (see **Flow-Mediated-Dilation**). Other methods are employed in experimental systems to measure the function of the endothelium such as organ chamber pharmacology to measure contractile and relaxant responses of isolated blood vessels, the use of cultured

	primary endothelial cells and other imaging techniques such as intravital microscopy which is especially useful for measuring trafficking of macromolecules across the endothelium. Microvascular endothelial function may be evaluated by laser Doppler flowmetry (LDF) in the retina or in the cutaneous tissues.
Where is it measured?	Typically, in brachial artery in human studies but other techniques are used to measure endothelial function as described above (see **Flow-Mediated-Dilation**). Endothelium dependent dilation can be measured also by peripheral arterial tone through disposable modified plethysmographic probes on the index fingers measuring the digital pulse waveform pre and post-occlusion of the brachial artery. Endothelial function can be measured also in the skin microvasculature by LDF exploiting the skin and soft tissue penetration of the laser light then partially backscattered by red blood cells, where blood flow velocity can be derived from the frequency of the backscattered light. Whilst the amount of connective tissue, elastin and smooth muscle in the vessel wall varies according to the vessel's diameter and function, the endothelial lining is always present. Endothelial cells perform distinct functions dependent on their location along the vascular network.
Figure	Figure from publications:  *Alberts et al. 2002. Molecular Biology of the Cell. 4th edition. New York: Garland Science. Blood Vessels and Endothelial Cells. Available from: https://www.ncbi.nlm.nih.gov/books/NBK26848/*  *Vanhoutte et al. 2016. Thirty Years of Saying NO: Sources, Fate, Actions, and Misfortunes of the Endothelium-Derived*

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FEEDBACK AND SUGGESTIONS FOR THESE DEFINITIONS* CAN BE SUBMITTED AT

https://vascagenet.eu/feedback-for-current-glossary-of-key-terms

* These definitions have been downloaded from https://vascagenet.eu/official-glossary and were released on 1st April, 2023.