REVIEW ARTICLE:

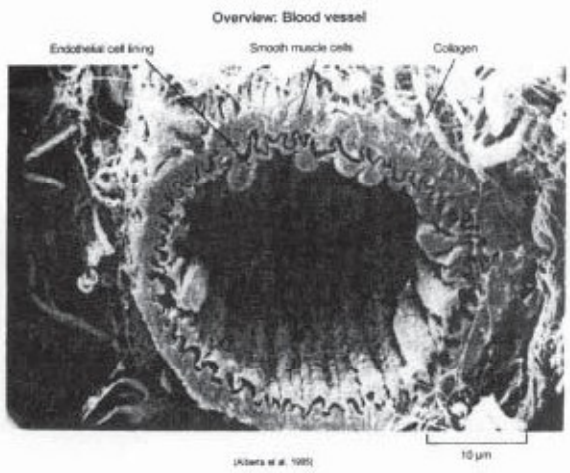
THE ROLE OF ENDOTHELIUM IN REGULATION OF BLOOD VESSEL TONE /BLOOD FLOW

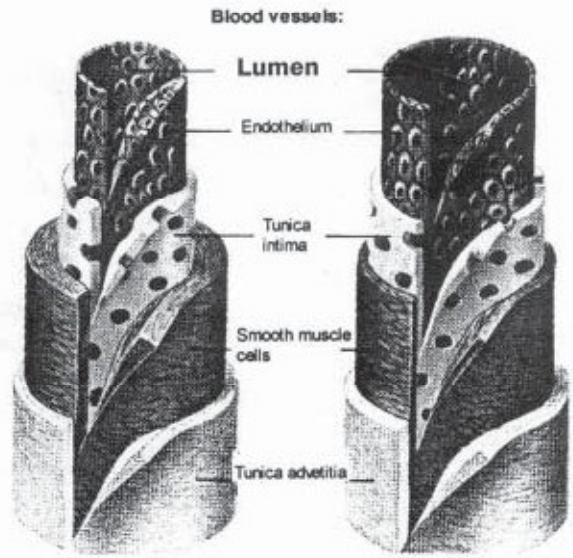
The inner lining of all blood vessels consists of a single layer of endothelial cells. These endothelial cells together form a diffuse tissue; the endothelium is located at the interface between the blood and the vessel wall.[1] The cells are in close contact and form a slick layer that prevents blood cell interaction with vessel wall as blood moves through the vessel lumen. The endothelium is a simple squamous epithelium that lines all blood vessels. It plays a critical role in the mechanics of blood flow, the regulation of coagulation, leukocyte adhesion and vascular smooth muscle cells growth, and also serves as barrier to the transvascular diffusion of liquids and solutes. For years endothelium was thought as inert single layer of cells that passively allows the passage of water and other small molecules across the vessel wall. However this dynamic tissue performs many other active functions, such as the secretion and modification of vasoactive substances and the contraction and relaxation of smooth muscles.[2,3,4]

The blood flow through vascular beds depends on regulating the contractile state of smooth muscle cells in blood vessel wall and controlling the coagulation of blood. Vascular endothelium plays an important role in these and many other important processes. They do so by making, releasing or express on their surface a diverse group of mediators that are directly involved in regulating blood flow, blood clotting, the recruitment of White blood cells (WBCs) at the site of injury /inflammation and growth and repair of blood vessel, as given in the table below.[8]

Table: Factors released from endothelial cells.

Vasoactive Factors:	**Vasoconstrictors** Nitric oxide Endothelium-derived hyperpolarizing factor Prostacyclin (PGI_2) Natriuretic peptide	**Vasoconstrictors** Endothelin-I Angiotensin II Thromboxane A-2 Prostaglandin H_2 Super oxide radicals Peroxynitrite Hydroxyls
Haemostasis & thrombolysis:	**Procoagulant** Prothrombotic factors von Willebrand factor Plasminogen activator inhibitor Platelet activator	**Anticogaulant** Thrombolytic factors Tissue Plasminogen activator Tissue factor pathway inhibitor Nitric oxide PGI_2 Protein S
Endothelial cell growth modulators:	**Promoters** Tumor necrosis factor-a Super oxide radicals	**Inhibitors** Nitric oxide PGI_2 Natriuretic peptide
Inflammatory agents:	**Promoters** Tumor necrosis factor-a Super oxide radicals Peroxynitrite	**Inhibitors** Nitric oxide





Many of the factors given in the table are of great clinical importance including the Nitric oxide (NO) and PGI_2, as these Endothelium derived relaxing factors (EDRFs) protect vasculature from atherogenic insult whereas Endothelium derived constricting factors (EDCFs) i.e. endothelin has opposite effect and participate in the progression of the disease.[9,10]

In almost all of the countries, vascular diseases are the major cause of death and contribute significantly to protracted morbidity.

It has become apparent that dysfunction of endothelium contributes to clinical manifestation in thrombosis, vascular spasm as well as in arteriosclerosis and its consequences i.e. Acute myocardial infarction, angina, stroke, claudication and pathological manifestation of acute and chronic inflammatory diseases including rheumatoid arthritis.[2,9,11,12]

The lifetime of endothelial cells is not infinite and these cells continuously multiply. However with advancing age, some of these specialized functions of endothelial cells i.e. barrier function, prevention of thrombosis and angiogenesis become blunted. The self-renewal process weakens. The endothelial barrier becomes leaky. Signals to vascular smooth muscle to regulate their function become altered. Vascular smooth muscle cells as if perceiving endothelial injury migrates to intima, multiply there, produce collagen and matrix protein. The addition of these cells and matrix within sub endothelial space results in intimal thickening and so the intima becomes a battle ground where multiple reactions occur like a chronic injury and hence a fertile land is provided in which the seeds of arteriosclerosis flourish.

We can reverse /stop the battle occurring within the blood vessel by:

1. Becoming aware of the risk factors.
2. Taking steps to reduce these risk factors.

So far the known risk factors are: high blood cholesterol, cigarette smoking, diabetes mellitus, obesity, lack of exercise and high blood pressure. New risk factors continue to be identified. Unfortunately age itself has been identified as major risk factor for atherosclerosis.

CONCLUSION

Alteration in the release and action of endothelium derived vasoactive factors is responsible for change in vascular reactivity early in the course of vascular disease. Because endothelial dysfunction occurs at early stages of lesion, it may reflect physiological changes that if allowed to become chronic are responsible for changes in vascular structure, growth and adhesivity to platelets and leukocytes, ultimately leading to atherosclerosis and thromobosis.[2,9,11,12]

Each of the major risk factors predisposing to vascular disease is associated with endothelial cell dysfunction, suggesting direct etiological links between effects of risk factors on endothelial cells and their propensity to accelerate vascular disease. Restoration and replacement of endothelial derived factors i.e. NO and PGI_2 which prevent the progression of vascular disease or prevent the action of such mediators, which accelerate progression of vascular disease, has become a useful paradigm in treatment and prevention of vascular disease.[2]

The understanding of endothelium derived vasoactive factors is a necessary part of every physician's education, which needs further discussion.

REFERENCES

1. Fajurdo L.F. The complexity of endothelial cells. Am J Clin Path 1989 (92): 241-250.

2. Cohen RA. The role of nitric oxide and other endothelium derived vasoactive substances in vascular disease. Prog cardiovasc Dis 1995 Sep-Oct; 38 (2): 105-28. Review.

3. Henrich WL . The endothelium –a key rgulator of vascular tone. Am J Med Sci. 1991 Nov; 302 (5): 319-28. Review.

4. Luscher TF. Edothelium-derived vasoactive factors and regulation of vascular tone in human blood vessels. Lung. 1990; 168 Suppl: 27-34. Review.

5. Tanner FC, Boulanger CM, Luscher TF. Endothelium-derived nitric oxide, endothelin, and platelet vessel wall interaction: alteration in hypercholestrolemia and atherosclerosis. Semin Thromb Hemost. 1993; 19(2): 167-75. Review.

6. Luscher TF. Platelet-vessel wall interaction: role of nitric oxide, prostglandins and endothelins. Baillieres Clin Haematol. 1993 Sep; 6 (3): 609-27. Review.

7. Loscalzo J, Endothelial injury, vasoconstriction, and its prevention. Text Heart Inst J. 1995; 22 (2): 180-4. Review.

8. Bernd Nilius and Guy Droomans. Ion channels and their functional role in vascular endothelium. Physiol.Rev.2001: 81(4); 1415-1459

9. Raij L. Hypertension, endothelium, and cardiovascular risk factors. Am J Med 1991 Feb 21; 90 (2A): 13S-18S.

10. Matsuoka H, Imaizumi T. Recent trends in studies of the etiology of hypertension: Endothelium-derived factors. Nippon Rinsho 2001 May; 59 (5): 878-85. Review. Japanese.

11. De Vriese AS, Veberuren TJ, Van de Voorde J, Lameire NH, Venhoutte PM. Endothelium dysfunction in diabetes. Br J Pharmacol. 2001 Jul; 130 (5): 963-74. Review.

12. Vane JR,Botting RM. Regulatory mechanisms of the vascular endothelium: an update. Pol J Pharmacol. 1994 Nov-Dec; 46 (6): 499-21. Review.