

6 Referenzen

1. Rösen P. Endotheliale Dysfunktion: ein Synonym für funktionelle Atherosklerose. J Kardiol 2002; 9: p. 556-62.
2. Pober JS, and R.C. Cotran. Cytokines and endothelial cell biology. Physiol. Rev. 70: 427-451 1990.
3. Gimbrone MJ, Nagel, T, Topper JN. Biomechanical Activation: an Emerging Paradigm in Endothelial Adhesion Biology. J. Clin. Invest. 1997; 99(8): p. 1809-1813.
4. Triggle CR, Hollenberg M, Anderson TJ, et al. The endothelium in health and disease--a target for therapeutic intervention. J Smooth Muscle Res 2003; 39(6): p. 249-67.
5. Lusis AJ. Atherosclerosis. Nature 2000; 407(6801): p. 233-41.
6. Furchtgott RF,Zawadzki JV. The obligatory role of endothelial cells in the relaxation of arterial smooth muscle by acetylcholine. Nature 1980; 288(5789): p. 373-6.
7. Koshland DE, Jr. The molecule of the year. Science 1992; 258(5090): p. 1861.
8. Landmesser U, Hornig B,Drexler H. Endothelial function: a critical determinant in atherosclerosis? Circulation 2004; 109(21 Suppl 1): p. II27-33.
9. Ignarro LJ. Biological actions and properties of endothelium-derived nitric oxide formed and released from artery and vein. Circ Res 1989; 65(1): p. 1-21.
10. Azuma H, Ishikawa M,Sekizaki S. Endothelium-dependent inhibition of platelet aggregation. Br J Pharmacol 1986; 88(2): p. 411-5.
11. Freedman JE, Sauter R, Battinelli EM, et al. Deficient platelet-derived nitric oxide and enhanced hemostasis in mice lacking the NOSIII gene. Circ Res 1999; 84(12): p. 1416-21.
12. Kubes P, Suzuki M,Granger DN. Nitric oxide: an endogenous modulator of leukocyte adhesion. Proc Natl Acad Sci U S A 1991; 88(11): p. 4651-5.
13. Libby P. Inflammation in atherosclerosis. Nature 2002; 420(6917): p. 868-74.
14. Li H,Forstermann U. Nitric oxide in the pathogenesis of vascular disease. J Pathol 2000; 190(3): p. 244-54.
15. Shen YH, Wang XL,Wilcken DE. Nitric oxide induces and inhibits apoptosis through different pathways. FEBS Lett 1998; 433(1-2): p. 125-31.
16. Stamler JS. Redox signaling: nitrosylation and related target interactions of nitric oxide. Cell 1994; 78(6): p. 931-6.
17. Marletta MA. Nitric oxide synthase structure and mechanism. J Biol Chem 1993; 268(17): p. 12231-4.
18. Marletta MA. Nitric oxide synthase: function and mechanism. Adv Exp Med Biol 1993; 338: p. 281-4.
19. Schmidt HH, Lohmann SM,Walter U. The nitric oxide and cGMP signal transduction system: regulation and mechanism of action. Biochim Biophys Acta 1993; 1178(2): p. 153-75.
20. Löffler G, *Basiswissen Biochemie mit Pathobiochemie*. Vol. 4. Auflage. 2001, Berlin, Heidelberg, New York: Springer. 262-264.
21. Candan JC, Souba WW, Copeland EM, 3rd,Lind DS. Cytokines regulate endotoxin stimulation of endothelial cell arginine transport. Surgery 1995; 117(2): p. 213-9.
22. Harrison DG. Cellular and molecular mechanisms of endothelial cell dysfunction. J Clin Invest 1997; 100(9): p. 2153-7.

23. Bogle RG, Baydoun AR, Pearson JD,Mann GE. Regulation of L-arginine transport and nitric oxide release in superfused porcine aortic endothelial cells. *J Physiol* 1996; 490 (Pt 1): p. 229-41.
24. Hecker M, Sessa WC, Harris HJ, Anggard EE,Vane JR. The metabolism of L-arginine and its significance for the biosynthesis of endothelium-derived relaxing factor: cultured endothelial cells recycle L-citrulline to L-arginine. *Proc Natl Acad Sci U S A* 1990; 87(21): p. 8612-6.
25. Moncada S. Nitric oxide in the vasculature: physiology and pathophysiology. *Ann N Y Acad Sci* 1997; 811: p. 60-7; discussion 67-9.
26. Palmer RM, Ashton DS,Moncada S. Vascular endothelial cells synthesize nitric oxide from L-arginine. *Nature* 1988; 333(6174): p. 664-6.
27. Bredt DS,Snyder SH. Nitric oxide: a physiologic messenger molecule. *Annu Rev Biochem* 1994; 63: p. 175-95.
28. Walford G,Loscalzo J. Nitric oxide in vascular biology. *J Thromb Haemost* 2003; 1(10): p. 2112-8.
29. Luzzi SD,Marletta MA. L-arginine analogs as alternate substrates for nitric oxide synthase. *Bioorg Med Chem Lett* 2005; 15(17): p. 3934-41.
30. Vallance P,Moncada S. Hyperdynamic circulation in cirrhosis: a role for nitric oxide? *Lancet* 1991; 337(8744): p. 776-8.
31. Guarner C, Soriano G, Tomas A, et al. Increased serum nitrite and nitrate levels in patients with cirrhosis: relationship to endotoxemia. *Hepatology* 1993; 18(5): p. 1139-43.
32. Fleming I, Bauersachs J, Fisslthaler B,Busse R. Ca²⁺-independent activation of the endothelial nitric oxide synthase in response to tyrosine phosphatase inhibitors and fluid shear stress. *Circ Res* 1998; 82(6): p. 686-95.
33. Dimmeler S, Fleming I, Fisslthaler B, Hermann C, Busse R,Zeiher AM. Activation of nitric oxide synthase in endothelial cells by Akt-dependent phosphorylation. *Nature* 1999; 399(6736): p. 601-5.
34. Liu J, Garcia-Cardena G,Sessa WC. Palmitoylation of endothelial nitric oxide synthase is necessary for optimal stimulated release of nitric oxide: implications for caveolae localization. *Biochemistry* 1996; 35(41): p. 13277-81.
35. Fleming I,Busse R. NO: the primary EDRF. *J Mol Cell Cardiol* 1999; 31(1): p. 5-14.
36. Cooke JP, Singer AH, Tsao P, Zera P, Rowan RA,Billingham ME. Antiatherogenic effects of L-arginine in the hypercholesterolemic rabbit. *J Clin Invest* 1992; 90(3): p. 1168-72.
37. Adams MR, Forsyth CJ, Jessup W, Robinson J,Celermajer DS. Oral L-arginine inhibits platelet aggregation but does not enhance endothelium-dependent dilation in healthy young men. *J Am Coll Cardiol* 1995; 26(4): p. 1054-61.
38. Adams MR, Jessup W,Celermajer DS. Cigarette smoking is associated with increased human monocyte adhesion to endothelial cells: reversibility with oral L-arginine but not vitamin C. *J Am Coll Cardiol* 1997; 29(3): p. 491-7.
39. Drexler H, Zeiher AM, Meinzer K,Just H. Correction of endothelial dysfunction in coronary microcirculation of hypercholesterolaemic patients by L-arginine. *Lancet* 1991; 338(8782-8783): p. 1546-50.
40. Quyyumi AA, Dakak N, Diodati JG, Gilligan DM, Panza JA,Cannon RO, 3rd. Effect of L-arginine on human coronary endothelium-dependent and physiologic vasodilation. *J Am Coll Cardiol* 1997; 30(5): p. 1220-7.

41. Chauhan A, More RS, Mullins PA, Taylor G, Petch C, Schofield PM. Aging-associated endothelial dysfunction in humans is reversed by L-arginine. *J Am Coll Cardiol* 1996; 28(7): p. 1796-804.
42. Boger RH, Bode-Boger SM, Thiele W, Creutzig A, Alexander K, Frolich JC. Restoring vascular nitric oxide formation by L-arginine improves the symptoms of intermittent claudication in patients with peripheral arterial occlusive disease. *J Am Coll Cardiol* 1998; 32(5): p. 1336-44.
43. Wolf A, Zalpour C, Theilmeier G, et al. Dietary L-arginine supplementation normalizes platelet aggregation in hypercholesterolemic humans. *J Am Coll Cardiol* 1997; 29(3): p. 479-85.
44. Leiper J, Vallance P. Biological significance of endogenous methylarginines that inhibit nitric oxide synthases. *Cardiovasc Res* 1999; 43(3): p. 542-8.
45. Feron O, Kelly RA. The caveolar paradox: suppressing, inducing, and terminating eNOS signaling. *Circ Res* 2001; 88(2): p. 129-31.
46. Gimbrone A, Topper, JN. Biology of the vessel wall: endothelium. Chien KR (ed.). *Molecular Basis of Cardiovascular Disease* 1999: p. 331-48.
47. Pinkney JH, Stehouwer CD, Coppock SW, Yudkin JS. Endothelial dysfunction: cause of the insulin resistance syndrome. *Diabetes* 1997; 46 Suppl 2: p. S9-13.
48. Ross R, Glomset J, Harker L. Response to injury and atherogenesis. *Am J Pathol* 1977; 86(3): p. 675-84.
49. Cayatte AJ, Palacino JJ, Horten K, Cohen RA. Chronic inhibition of nitric oxide production accelerates neointima formation and impairs endothelial function in hypercholesterolemic rabbits. *Arterioscler Thromb* 1994; 14(5): p. 753-9.
50. Chen J, Kuhlencordt PJ, Astern J, Gyurko R, Huang PL. Hypertension does not account for the accelerated atherosclerosis and development of aneurysms in male apolipoprotein E/endothelial nitric oxide synthase double knockout mice. *Circulation* 2001; 104(20): p. 2391-4.
51. Kuhlencordt PJ, Gyurko R, Han F, et al. Accelerated atherosclerosis, aortic aneurysm formation, and ischemic heart disease in apolipoprotein E/endothelial nitric oxide synthase double-knockout mice. *Circulation* 2001; 104(4): p. 448-54.
52. Pinkney JH, Downs L, Hopton M, Mackness MI, Bolton CH. Endothelial dysfunction in Type 1 diabetes mellitus: relationship with LDL oxidation and the effects of vitamin E. *Diabet Med* 1999; 16(12): p. 993-9.
53. Ross R, Glomset JA. The pathogenesis of atherosclerosis (first of two parts). *N Engl J Med* 1976; 295(7): p. 369-77.
54. Ross R, Glomset JA. The pathogenesis of atherosclerosis (second of two parts). *N Engl J Med* 1976; 295(8): p. 420-5.
55. Ross R. Cell biology of atherosclerosis. *Annu Rev Physiol* 1995; 57: p. 791-804.
56. Simionescu N, Vasile E, Lupu F, Popescu G, Simionescu M. Prelesional events in atherogenesis. Accumulation of extracellular cholesterol-rich liposomes in the arterial intima and cardiac valves of the hyperlipidemic rabbit. *Am J Pathol* 1986; 123(1): p. 109-25.
57. Steinberg D. Antioxidants and atherosclerosis. A current assessment. *Circulation* 1991; 84(3): p. 1420-5.
58. Goldstein JL, Ho YK, Basu SK, Brown MS. Binding site on macrophages that mediates uptake and degradation of acetylated low density lipoprotein, producing massive cholesterol deposition. *Proc Natl Acad Sci U S A* 1979; 76(1): p. 333-7.
59. Zeiher AM, Fisslthaler B, Schray-Utz B, Busse R. Nitric oxide modulates the expression of monocyte chemoattractant protein 1 in cultured human endothelial cells. *Circ Res* 1995; 76(6): p. 980-6.

60. Tomita H, Egashira K, Kubo-Inoue M, et al. Inhibition of NO synthesis induces inflammatory changes and monocyte chemoattractant protein-1 expression in rat hearts and vessels. *Arterioscler Thromb Vasc Biol* 1998; 18(9): p. 1456-64.
61. Libby P, Friedman GB, Salomon RN. Cytokines as modulators of cell proliferation in fibrotic diseases. *Am Rev Respir Dis* 1989; 140(4): p. 1114-7.
62. Libby P, Ordovas JM, Auger KR, Robbins AH, Birinyi LK, Dinarello CA. Endotoxin and tumor necrosis factor induce interleukin-1 gene expression in adult human vascular endothelial cells. *Am J Pathol* 1986; 124(2): p. 179-85.
63. Ross R. Atherosclerosis--an inflammatory disease. *N Engl J Med* 1999; 340(2): p. 115-26.
64. Tsao PS, Buitrago R, Chan JR, Cooke JP. Fluid flow inhibits endothelial adhesiveness. Nitric oxide and transcriptional regulation of VCAM-1. *Circulation* 1996; 94(7): p. 1682-9.
65. Lefer DJ, Jones SP, Girod WG, et al. Leukocyte-endothelial cell interactions in nitric oxide synthase-deficient mice. *Am J Physiol* 1999; 276(6 Pt 2): p. H1943-50.
66. Butcher EC. Leukocyte-endothelial cell recognition: three (or more) steps to specificity and diversity. *Cell* 1991; 67(6): p. 1033-6.
67. Luscinskas FW, Gimbrone MA, Jr. Endothelial-dependent mechanisms in chronic inflammatory leukocyte recruitment. *Annu Rev Med* 1996; 47: p. 413-21.
68. Dong ZM, Chapman SM, Brown AA, Frenette PS, Hynes RO, Wagner DD. The combined role of P- and E-selectins in atherosclerosis. *J Clin Invest* 1998; 102(1): p. 145-52.
69. Collins RG, Velji R, Guevara NV, Hicks MJ, Chan L, Beaudet AL. P-Selectin or intercellular adhesion molecule (ICAM)-1 deficiency substantially protects against atherosclerosis in apolipoprotein E-deficient mice. *J Exp Med* 2000; 191(1): p. 189-94.
70. Libby P. What have we learned about the biology of atherosclerosis? The role of inflammation. *Am J Cardiol* 2001; 88(7B): p. 3J-6J.
71. Libby P. Current concepts of the pathogenesis of the acute coronary syndromes. *Circulation* 2001; 104(3): p. 365-72.
72. Libby P, Simon DI. Inflammation and thrombosis: the clot thickens. *Circulation* 2001; 103(13): p. 1718-20.
73. Libby P, Geng YJ, Aikawa M, et al. Macrophages and atherosclerotic plaque stability. *Curr Opin Lipidol* 1996; 7(5): p. 330-5.
74. Cai H, Harrison DG. Endothelial dysfunction in cardiovascular diseases: the role of oxidant stress. *Circ Res* 2000; 87(10): p. 840-4.
75. Landmesser U, Harrison DG. Oxidant stress as a marker for cardiovascular events: Ox marks the spot. *Circulation* 2001; 104(22): p. 2638-40.
76. Landmesser U, Merten R, Spiekermann S, Buttner K, Drexler H, Hornig B. Vascular extracellular superoxide dismutase activity in patients with coronary artery disease: relation to endothelium-dependent vasodilation. *Circulation* 2000; 101(19): p. 2264-70.
77. Halliwell B. Antioxidants in human health and disease. *Annu Rev Nutr* 1996; 16: p. 33-50.
78. Rosen P, Nawroth PP, King G, Moller W, Tritschler HJ, Packer L. The role of oxidative stress in the onset and progression of diabetes and its complications: a summary of a Congress Series sponsored by UNESCO-MCBN, the American Diabetes Association and the German Diabetes Society. *Diabetes Metab Res Rev* 2001; 17(3): p. 189-212.

79. Halliwell B. Antioxidant characterization. Methodology and mechanism. *Biochem Pharmacol* 1995; 49(10): p. 1341-8.
80. Fukai T, Siegfried MR, Ushio-Fukai M, Cheng Y, Kojda G, Harrison DG. Regulation of the vascular extracellular superoxide dismutase by nitric oxide and exercise training. *J Clin Invest* 2000; 105(11): p. 1631-9.
81. Southorn PA, Powis G. Free radicals in medicine. II. Involvement in human disease. *Mayo Clin Proc* 1988; 63(4): p. 390-408.
82. Southorn PA, Powis G. Free radicals in medicine. I. Chemical nature and biologic reactions. *Mayo Clin Proc* 1988; 63(4): p. 381-9.
83. Halliwell B, Gutteridge JM, Cross CE. Free radicals, antioxidants, and human disease: where are we now? *J Lab Clin Med* 1992; 119(6): p. 598-620.
84. Beckman KB, Ames BN. Mitochondrial aging: open questions. *Ann N Y Acad Sci* 1998; 854: p. 118-27.
85. Halliwell B, Gutteridge JM. Oxygen toxicity, oxygen radicals, transition metals and disease. *Biochem J* 1984; 219(1): p. 1-14.
86. Kowaltowski AJ, Vercesi AE. Mitochondrial damage induced by conditions of oxidative stress. *Free Radic Biol Med* 1999; 26(3-4): p. 463-71.
87. Thomson AM, Rogers JT, Leedman PJ. Iron-regulatory proteins, iron-responsive elements and ferritin mRNA translation. *Int J Biochem Cell Biol* 1999; 31(10): p. 1139-52.
88. Cooke JP. Does ADMA cause endothelial dysfunction? *Arterioscler Thromb Vasc Biol* 2000; 20(9): p. 2032-7.
89. Griendling KK, Sorescu D, Ushio-Fukai M. NAD(P)H oxidase: role in cardiovascular biology and disease. *Circ Res* 2000; 86(5): p. 494-501.
90. Spiekermann S, Landmesser U, Dikalov S, et al. Electron spin resonance characterization of vascular xanthine and NAD(P)H oxidase activity in patients with coronary artery disease: relation to endothelium-dependent vasodilation. *Circulation* 2003; 107(10): p. 1383-9.
91. Landmesser U, Dikalov S, Price SR, et al. Oxidation of tetrahydrobiopterin leads to uncoupling of endothelial cell nitric oxide synthase in hypertension. *J Clin Invest* 2003; 111(8): p. 1201-9.
92. Tiefenbacher CP, Blekee T, Vahl C, Amann K, Vogt A, Kubler W. Endothelial dysfunction of coronary resistance arteries is improved by tetrahydrobiopterin in atherosclerosis. *Circulation* 2000; 102(18): p. 2172-9.
93. Vasquez-Vivar J, Duquaine D, Whitsett J, Kalyanaraman B, Rajagopalan S. Altered tetrahydrobiopterin metabolism in atherosclerosis: implications for use of oxidized tetrahydrobiopterin analogues and thiol antioxidants. *Arterioscler Thromb Vasc Biol* 2002; 22(10): p. 1655-61.
94. d'Uscio LV, Milstien S, Richardson D, Smith L, Katusic ZS. Long-term vitamin C treatment increases vascular tetrahydrobiopterin levels and nitric oxide synthase activity. *Circ Res* 2003; 92(1): p. 88-95.
95. Fuster V, Badimon L, Badimon JJ, Chesebro JH. The pathogenesis of coronary artery disease and the acute coronary syndromes (1). *N Engl J Med* 1992; 326(4): p. 242-50.
96. Fuster V, Badimon L, Badimon JJ, Chesebro JH. The pathogenesis of coronary artery disease and the acute coronary syndromes (2). *N Engl J Med* 1992; 326(5): p. 310-8.
97. Davies MJ, Thomas A. Thrombosis and acute coronary-artery lesions in sudden cardiac ischemic death. *N Engl J Med* 1984; 310(18): p. 1137-40.
98. MLP DR, *Innere Medizin -Sonderausgabe*. 2001: Springer Verlag. 932-959.

99. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. *Nature* 2001; 414(6865): p. 782-7.
100. Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001; 24(4): p. 683-9.
101. Herold G, *Innere Medizin, eine vorlesungsorientierte Darstellung*. 2004. p. 595-619.
102. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care* 1997; 20(4): p. 537-44.
103. Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001; 344(18): p. 1343-50.
104. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care* 1998; 21(9): p. 1414-31.
105. Hauner H, Koster I, von Ferber L. [Prevalence of diabetes mellitus in Germany 1998-2001. Secondary data analysis of a health insurance sample of the AOK in Hesse/KV in Hesse]. *Dtsch Med Wochenschr* 2003; 128(50): p. 2632-7.
106. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. *Jama* 1979; 241(19): p. 2035-8.
107. Kannel WB, McGee DL. Diabetes and glucose tolerance as risk factors for cardiovascular disease: the Framingham study. *Diabetes Care* 1979; 2(2): p. 120-6.
108. Hayat SA, Patel B, Khattar RS, Malik RA. Diabetic cardiomyopathy: mechanisms, diagnosis and treatment. *Clin Sci (Lond)* 2004; 107(6): p. 539-57.
109. Cosentino F, Luscher TF. Endothelial dysfunction in diabetes mellitus. *J Cardiovasc Pharmacol* 1998; 32 Suppl 3: p. S54-61.
110. Giugliano D, Marfella R, Coppola L, et al. Vascular effects of acute hyperglycemia in humans are reversed by L-arginine. Evidence for reduced availability of nitric oxide during hyperglycemia. *Circulation* 1997; 95(7): p. 1783-90.
111. Angulo J, Rodriguez-Manas L, Peiro C, Neira M, Marin J, Sanchez-Ferrer CF. Impairment of nitric oxide-mediated relaxations in anaesthetized autoperfused streptozotocin-induced diabetic rats. *Naunyn Schmiedebergs Arch Pharmacol* 1998; 358(5): p. 529-37.
112. Pieper GM, Adams MB, Roza AM. Pancreatic transplantation reverses endothelial dysfunction in experimental diabetes mellitus. *Surgery* 1998; 123(1): p. 89-95.
113. Koltai MZ, Hadhazy P, Posa I, et al. Characteristics of coronary endothelial dysfunction in experimental diabetes. *Cardiovasc Res* 1997; 34(1): p. 157-63.
114. Palmer AM, Gopaul N, Dhir S, Thomas CR, Poston L, Tribe RM. Endothelial dysfunction in streptozotocin-diabetic rats is not reversed by dietary probucol or simvastatin supplementation. *Diabetologia* 1998; 41(2): p. 157-64.
115. Pieper GM, Langenstroer P, Siebeneich W. Diabetic-induced endothelial dysfunction in rat aorta: role of hydroxyl radicals. *Cardiovasc Res* 1997; 34(1): p. 145-56.
116. Rosen P, Du X, Tschope D. Role of oxygen derived radicals for vascular dysfunction in the diabetic heart: prevention by alpha-tocopherol? *Mol Cell Biochem* 1998; 188(1-2): p. 103-11.

117. Clarkson P, Celermajer DS, Donald AE, et al. Impaired vascular reactivity in insulin-dependent diabetes mellitus is related to disease duration and low density lipoprotein cholesterol levels. *J Am Coll Cardiol* 1996; 28(3): p. 573-9.
118. Gazis A, White DJ, Page SR,Cockcroft JR. Effect of oral vitamin E (alpha-tocopherol) supplementation on vascular endothelial function in Type 2 diabetes mellitus. *Diabet Med* 1999; 16(4): p. 304-11.
119. Nitenberg A, Valensi P, Sachs R, Dali M, Aptecar E,Attali JR. Impairment of coronary vascular reserve and ACh-induced coronary vasodilation in diabetic patients with angiographically normal coronary arteries and normal left ventricular systolic function. *Diabetes* 1993; 42(7): p. 1017-25.
120. Yu HI, Sheu WH, Lai CJ, Lee WJ, Chen YT. Endothelial dysfunction in type 2 diabetes mellitus subjects with peripheral artery disease. *Int J Cardiol* 2001; 78(1): p. 19-25.
121. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. *Nature* 2001; 414(6865): p. 813-20.
122. Du XL, Edelstein D, Dimmeler S, Ju Q, Sui C, Brownlee M. Hyperglycemia inhibits endothelial nitric oxide synthase activity by posttranslational modification at the Akt site. *J Clin Invest* 2001; 108(9): p. 1341-8.
123. Bierhaus A, Hofmann MA, Ziegler R, Nawroth PP. AGEs and their interaction with AGE-receptors in vascular disease and diabetes mellitus. I. The AGE concept. *Cardiovasc Res* 1998; 37(3): p. 586-600.
124. Schmidt AM, Hori O, Brett J, Yan SD, Wautier JL, Stern D. Cellular receptors for advanced glycation end products. Implications for induction of oxidant stress and cellular dysfunction in the pathogenesis of vascular lesions. *Arterioscler Thromb* 1994; 14(10): p. 1521-8.
125. Nishikawa T, Edelstein D, Du XL, et al. Normalizing mitochondrial superoxide production blocks three pathways of hyperglycaemic damage. *Nature* 2000; 404(6779): p. 787-90.
126. Hink U, Li H, Mollnau H, et al. Mechanisms underlying endothelial dysfunction in diabetes mellitus. *Circ Res* 2001; 88(2): p. E14-22.
127. Milstien S, Katusic Z. Oxidation of tetrahydrobiopterin by peroxynitrite: implications for vascular endothelial function. *Biochem Biophys Res Commun* 1999; 263(3): p. 681-4.
128. Forstermann U, Munzel T. Endothelial nitric oxide synthase in vascular disease: from marvel to menace. *Circulation* 2006; 113(13): p. 1708-14.
129. Komers R, Schutzer WE, Reed JF, et al. Altered endothelial nitric oxide synthase targeting and conformation and caveolin-1 expression in the diabetic kidney. *Diabetes* 2006; 55(6): p. 1651-9.
130. Srinivasan S, Hatley ME, Bolick DT, et al. Hyperglycaemia-induced superoxide production decreases eNOS expression via AP-1 activation in aortic endothelial cells. *Diabetologia* 2004; 47(10): p. 1727-34.
131. Ho FM, Liu SH, Liau CS, Huang PJ, Shiah SG, Lin-Shiau SY. Nitric oxide prevents apoptosis of human endothelial cells from high glucose exposure during early stage. *J Cell Biochem* 1999; 75(2): p. 258-63.
132. Salt IP, Morrow VA, Brandie FM, Connell JM, Petrie JR. High glucose inhibits insulin-stimulated nitric oxide production without reducing endothelial nitric-oxide synthase Ser1177 phosphorylation in human aortic endothelial cells. *J Biol Chem* 2003; 278(21): p. 18791-7.

133. Cosentino F, Hishikawa K, Katusic ZS,Luscher TF. High glucose increases nitric oxide synthase expression and superoxide anion generation in human aortic endothelial cells. *Circulation* 1997; 96(1): p. 25-8.
134. Celermajer DS. Endothelial dysfunction: does it matter? Is it reversible? *J Am Coll Cardiol* 1997; 30(2): p. 325-33.
135. Sasaki K, Heeschen C, Aicher A, et al. Ex vivo pretreatment of bone marrow mononuclear cells with endothelial NO synthase enhancer AVE9488 enhances their functional activity for cell therapy. *Proc Natl Acad Sci U S A* 2006; 103(39): p. 14537-41.
136. Herr RR,Reusser F. New antibacterial agent (U-24,544) isolated from *Streptomyces griseus*. *Appl Microbiol* 1967; 15(5): p. 1142-4.
137. Junod A, Lambert AE, Orci L, Pictet R, Gonet AE, Renold AE. Studies of the diabetogenic action of streptozotocin. *Proc Soc Exp Biol Med* 1967; 126(1): p. 201-5.
138. Konrad RJ, Mikolaenko I, Tolar JF, Liu K,Kudlow JE. The potential mechanism of the diabetogenic action of streptozotocin: inhibition of pancreatic beta-cell O-GlcNAc-selective N-acetyl-beta-D-glucosaminidase. *Biochem J* 2001; 356(Pt 1): p. 31-41.
139. Arison RN,Feudale EL. Induction of renal tumour by streptozotocin in rats. *Nature* 1967; 214(94): p. 1254-5.
140. Giorgino F, Chen JH,Smith RJ. Changes in tyrosine phosphorylation of insulin receptors and a 170,000 molecular weight nonreceptor protein in vivo in skeletal muscle of streptozotocin-induced diabetic rats: effects of insulin and glucose. *Endocrinology* 1992; 130(3): p. 1433-44.
141. Van Voorhis K, Said HM, Abumrad N,Ghishan FK. Effect of chemically induced diabetes mellitus on glutamine transport in rat intestine. *Gastroenterology* 1990; 98(4): p. 862-6.
142. Rakieten N, Rakieten ML,Nadkarni MV. Studies on the diabetogenic action of streptozotocin (NSC-37917). *Cancer Chemother Rep* 1963; 29: p. 91-8.
143. Riva E, Andreoni G, Bianchi R, et al. Changes in diastolic function and collagen content in normotensive and hypertensive rats with long-term streptozotocin-induced diabetes. *Pharmacol Res* 1998; 37(3): p. 233-40.
144. Tomlinson KC, Gardiner SM,Bennett T. Diabetes mellitus in Brattleboro rats: cardiovascular, fluid, and electrolyte status. *Am J Physiol* 1989; 256(6 Pt 2): p. R1279-85.
145. Jensen T, Bjerre-Knudsen J, Feldt-Rasmussen B,Deckert T. Features of endothelial dysfunction in early diabetic nephropathy. *Lancet* 1989; 1(8636): p. 461-3.
146. Stehouwer CD, Nauta JJ, Zeldenrust GC, Hackeng WH, Donker AJ,den Ottolander GJ. Urinary albumin excretion, cardiovascular disease, and endothelial dysfunction in non-insulin-dependent diabetes mellitus. *Lancet* 1992; 340(8815): p. 319-23.
147. Dorenkamp M, Riad A, Stiehl S, et al. Protection against oxidative stress in diabetic rats: role of angiotensin AT(1) receptor and beta 1-adrenoceptor antagonism. *Eur J Pharmacol* 2005; 520(1-3): p. 179-87.
148. DePaola N, Gimbrone MA, Jr., Davies PF,Dewey CF, Jr. Vascular endothelium responds to fluid shear stress gradients. *Arterioscler Thromb* 1992; 12(11): p. 1254-7.
149. Lerman-Garber I,Rull Rodrigo JA. Epidemiology of diabetes in Mexico and associated coronary risk factors. *Isr Med Assoc J* 2001; 3(5): p. 369-73.

150. Alexander CM, Landsman PB, Teutsch SM. Diabetes mellitus, impaired fasting glucose, atherosclerotic risk factors, and prevalence of coronary heart disease. *Am J Cardiol* 2000; 86(9): p. 897-902.
151. Marks JB, Raskin P. Cardiovascular risk in diabetes: a brief review. *J Diabetes Complications* 2000; 14(2): p. 108-15.
152. Sowers JR, Lester MA. Diabetes and cardiovascular disease. *Diabetes Care* 1999; 22 Suppl 3: p. C14-20.
153. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care* 1993; 16(2): p. 434-44.
154. Butler WJ, Ostrander LD, Jr., Carman WJ, Lamphier DE. Mortality from coronary heart disease in the Tecumseh study. Long-term effect of diabetes mellitus, glucose tolerance and other risk factors. *Am J Epidemiol* 1985; 121(4): p. 541-7.
155. Pan WH, Cedres LB, Liu K, et al. Relationship of clinical diabetes and asymptomatic hyperglycemia to risk of coronary heart disease mortality in men and women. *Am J Epidemiol* 1986; 123(3): p. 504-16.
156. Kleinman JC, Donahue RP, Harris MI, Finucane FF, Madans JH, Brock DB. Mortality among diabetics in a national sample. *Am J Epidemiol* 1988; 128(2): p. 389-401.
157. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* 1998; 339(4): p. 229-34.
158. De Vriese AS, Verbeuren TJ, Van de Voorde J, Lameire NH, Vanhoutte PM. Endothelial dysfunction in diabetes. *Br J Pharmacol* 2000; 130(5): p. 963-74.
159. Ding Y, Vaziri ND, Coulson R, Kamanna VS, Roh DD. Effects of simulated hyperglycemia, insulin, and glucagon on endothelial nitric oxide synthase expression. *Am J Physiol Endocrinol Metab* 2000; 279(1): p. E11-7.
160. Guo X, Chen LW, Liu WL, Guo ZG. High glucose inhibits expression of inducible and constitutive nitric oxide synthase in bovine aortic endothelial cells. *Acta Pharmacol Sin* 2000; 21(4): p. 325-8.
161. Steinberg HO, Chaker H, Leaming R, Johnson A, Brechtel G, Baron AD. Obesity/insulin resistance is associated with endothelial dysfunction. Implications for the syndrome of insulin resistance. *J Clin Invest* 1996; 97(11): p. 2601-10.
162. Makimattila S, Virkamaki A, Groop PH, et al. Chronic hyperglycemia impairs endothelial function and insulin sensitivity via different mechanisms in insulin-dependent diabetes mellitus. *Circulation* 1996; 94(6): p. 1276-82.
163. Pflueger AC, Osswald H, Knox FG. Adenosine-induced renal vasoconstriction in diabetes mellitus rats: role of nitric oxide. *Am J Physiol* 1999; 276(3 Pt 2): p. F340-6.
164. Dai FX, Diederich A, Skopec J, Diederich D. Diabetes-induced endothelial dysfunction in streptozotocin-treated rats: role of prostaglandin endoperoxides and free radicals. *J Am Soc Nephrol* 1993; 4(6): p. 1327-36.
165. Hennersdorf MG, Kelm M, Schannwell CM, Rosen P, Strauer BE. [Cardiac complications in diabetes mellitus]. *Med Klin (Munich)* 2000; 95(9): p. 487-95.
166. Hornig B, Kohler C, Drexler H. Role of bradykinin in mediating vascular effects of angiotensin-converting enzyme inhibitors in humans. *Circulation* 1997; 95(5): p. 1115-8.
167. Haynes WG, Webb DJ. Contribution of endogenous generation of endothelin-1 to basal vascular tone. *Lancet* 1994; 344(8926): p. 852-4.

168. Taylor SG, Weston AH. Endothelium-derived hyperpolarizing factor: a new endogenous inhibitor from the vascular endothelium. *Trends Pharmacol Sci* 1988; 9(8): p. 272-4.
169. Kessler P, Popp R, Busse R, Schini-Kerth VB. Proinflammatory mediators chronically downregulate the formation of the endothelium-derived hyperpolarizing factor in arteries via a nitric oxide/cyclic GMP-dependent mechanism. *Circulation* 1999; 99(14): p. 1878-84.
170. Goode GK, Miller JP, Heagerty AM. Hyperlipidaemia, hypertension, and coronary heart disease. *Lancet* 1995; 345(8946): p. 362-4.
171. Egashira K, Inou T, Hirooka Y, et al. Impaired coronary blood flow response to acetylcholine in patients with coronary risk factors and proximal atherosclerotic lesions. *J Clin Invest* 1993; 91(1): p. 29-37.
172. Vita JA, Treasure CB, Nabel EG, et al. Coronary vasomotor response to acetylcholine relates to risk factors for coronary artery disease. *Circulation* 1990; 81(2): p. 491-7.
173. Reddy KG, Nair RN, Sheehan HM, Hodgson JM. Evidence that selective endothelial dysfunction may occur in the absence of angiographic or ultrasound atherosclerosis in patients with risk factors for atherosclerosis. *J Am Coll Cardiol* 1994; 23(4): p. 833-43.
174. Treasure CB, Klein JL, Vita JA, et al. Hypertension and left ventricular hypertrophy are associated with impaired endothelium-mediated relaxation in human coronary resistance vessels. *Circulation* 1993; 87(1): p. 86-93.
175. Zeiher AM, Drexler H, Wollschlager H, Just H. Modulation of coronary vasomotor tone in humans. Progressive endothelial dysfunction with different early stages of coronary atherosclerosis. *Circulation* 1991; 83(2): p. 391-401.
176. Hasdai D, Gibbons RJ, Holmes DR, Jr., Higano ST, Lerman A. Coronary endothelial dysfunction in humans is associated with myocardial perfusion defects. *Circulation* 1997; 96(10): p. 3390-5.
177. Britten MB, Zeiher AM, Schachinger V. Clinical importance of coronary endothelial vasodilator dysfunction and therapeutic options. *J Intern Med* 1999; 245(4): p. 315-27.
178. Suwaidi JA, Hamasaki S, Higano ST, Nishimura RA, Holmes DR, Jr., Lerman A. Long-term follow-up of patients with mild coronary artery disease and endothelial dysfunction. *Circulation* 2000; 101(9): p. 948-54.
179. Heitzer T, Schlinzig T, Krohn K, Meinertz T, Munzel T. Endothelial dysfunction, oxidative stress, and risk of cardiovascular events in patients with coronary artery disease. *Circulation* 2001; 104(22): p. 2673-8.
180. Ozaki Y, Keane D, Serruys PW. Progression and regression of coronary stenosis in the long-term follow-up of vasospastic angina. *Circulation* 1995; 92(9): p. 2446-56.
181. Zeiher AM, Krause T, Schachinger V, Minners J, Moser E. Impaired endothelium-dependent vasodilation of coronary resistance vessels is associated with exercise-induced myocardial ischemia. *Circulation* 1995; 91(9): p. 2345-52.
182. Widlansky ME, Gokce N, Keaney JF, Jr., Vita JA. The clinical implications of endothelial dysfunction. *J Am Coll Cardiol* 2003; 42(7): p. 1149-60.
183. Vita JA, Keaney JF, Jr. Endothelial function: a barometer for cardiovascular risk? *Circulation* 2002; 106(6): p. 640-2.
184. Vlassara H. Advanced glycation end-products and atherosclerosis. *Ann Med* 1996; 28(5): p. 419-26.

185. Feener EP, King GL. Vascular dysfunction in diabetes mellitus. *Lancet* 1997; 350 Suppl 1: p. SI9-13.
186. Golovchenko I, Goalstone ML, Watson P, Brownlee M, Draznin B. Hyperinsulinemia enhances transcriptional activity of nuclear factor-kappaB induced by angiotensin II, hyperglycemia, and advanced glycosylation end products in vascular smooth muscle cells. *Circ Res* 2000; 87(9): p. 746-52.
187. Schmidt AM, Stern DM. Hyperinsulinemia and vascular dysfunction: the role of nuclear factor-kappaB, yet again. *Circ Res* 2000; 87(9): p. 722-4.
188. Thurberg BL, Collins T. The nuclear factor-kappa B/inhibitor of kappa B autoregulatory system and atherosclerosis. *Curr Opin Lipidol* 1998; 9(5): p. 387-96.
189. Karin M, Delhase M. The I kappa B kinase (IKK) and NF-kappa B: key elements of proinflammatory signalling. *Semin Immunol* 2000; 12(1): p. 85-98.
190. Bierhaus A, Schiekofer S, Schwaninger M, et al. Diabetes-associated sustained activation of the transcription factor nuclear factor-kappaB. *Diabetes* 2001; 50(12): p. 2792-808.
191. Baeuerle PA. Pro-inflammatory signaling: last pieces in the NF-kappaB puzzle? *Curr Biol* 1998; 8(1): p. R19-22.
192. Baeuerle PA. IkappaB-NF-kappaB structures: at the interface of inflammation control. *Cell* 1998; 95(6): p. 729-31.
193. Castell JV, Gomez-Lechon MJ, David M, et al. Interleukin-6 is the major regulator of acute phase protein synthesis in adult human hepatocytes. *FEBS Lett* 1989; 242(2): p. 237-9.
194. Cha-Molstad H, Agrawal A, Zhang D, Samols D, Kushner I. The Rel family member P50 mediates cytokine-induced C-reactive protein expression by a novel mechanism. *J Immunol* 2000; 165(8): p. 4592-7.
195. Bermudez EA, Rifai N, Buring J, Manson JE, Ridker PM. Interrelationships among circulating interleukin-6, C-reactive protein, and traditional cardiovascular risk factors in women. *Arterioscler Thromb Vasc Biol* 2002; 22(10): p. 1668-73.
196. Thorand B, Lowel H, Schneider A, et al. C-reactive protein as a predictor for incident diabetes mellitus among middle-aged men: results from the MONICA Augsburg cohort study, 1984-1998. *Arch Intern Med* 2003; 163(1): p. 93-9.
197. Mojiminiyi OA, Abdella N, Moussa MA, Akanji AO, Al Mohammedi H, Zaki M. Association of C-reactive protein with coronary heart disease risk factors in patients with type 2 diabetes mellitus. *Diabetes Res Clin Pract* 2002; 58(1): p. 37-44.
198. Grimble RF. Inflammatory status and insulin resistance. *Curr Opin Clin Nutr Metab Care* 2002; 5(5): p. 551-9.
199. Esposito K, Nappo F, Marfella R, et al. Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans: role of oxidative stress. *Circulation* 2002; 106(16): p. 2067-72.
200. Schiekofer S, Andrassy M, Chen J, et al. Acute hyperglycemia causes intracellular formation of CML and activation of ras, p42/44 MAPK, and nuclear factor kappaB in PBMCs. *Diabetes* 2003; 52(3): p. 621-33.
201. Collins T, Cybulsky MI. NF-kappaB: pivotal mediator or innocent bystander in atherogenesis? *J Clin Invest* 2001; 107(3): p. 255-64.
202. Collins T, Read MA, Neish AS, Whitley MZ, Thanos D, Maniatis T. Transcriptional regulation of endothelial cell adhesion molecules: NF-kappa B and cytokine-inducible enhancers. *Faseb J* 1995; 9(10): p. 899-909.

203. Libby P,Aikawa M. New insights into plaque stabilisation by lipid lowering. *Drugs* 1998; 56 Suppl 1: p. 9-13; discussion 33.
204. Baeuerle PA,Baltimore D. NF-kappa B: ten years after. *Cell* 1996; 87(1): p. 13-20.
205. Bierhaus A, Chen J, Liliensiek B,Nawroth PP. LPS and cytokine-activated endothelium. *Semin Thromb Hemost* 2000; 26(5): p. 571-87.
206. Cavallo-Perin P, Lupia E, Gruden G, et al. Increased blood levels of platelet-activating factor in insulin-dependent diabetic patients with microalbuminuria. *Nephrol Dial Transplant* 2000; 15(7): p. 994-9.
207. Gimbrone MA, Jr., Bevilacqua MP,Cybulsky MI. Endothelial-dependent mechanisms of leukocyte adhesion in inflammation and atherosclerosis. *Ann N Y Acad Sci* 1990; 598: p. 77-85.
208. Morigi M, Angioletti S, Imberti B, et al. Leukocyte-endothelial interaction is augmented by high glucose concentrations and hyperglycemia in a NF- κ B-dependent fashion. *J Clin Invest* 1998; 101(9): p. 1905-15.
209. Elhadd TA, Kennedy G, Hill A, et al. Abnormal markers of endothelial cell activation and oxidative stress in children, adolescents and young adults with type 1 diabetes with no clinical vascular disease. *Diabetes Metab Res Rev* 1999; 15(6): p. 405-11.
210. Dosquet C, Weill D,Wautier JL. Molecular mechanism of blood monocyte adhesion to vascular endothelial cells. *Nouv Rev Fr Hematol* 1992; 34 Suppl: p. S55-9.
211. Kado S, Wakatsuki T, Yamamoto M,Nagata N. Expression of intercellular adhesion molecule-1 induced by high glucose concentrations in human aortic endothelial cells. *Life Sci* 2001; 68(7): p. 727-37.
212. Fasching P, Waldhausl W,Wagner OF. Elevated circulating adhesion molecules in NIDDM--potential mediators in diabetic macroangiopathy. *Diabetologia* 1996; 39(10): p. 1242-4.
213. Fasching P, Veitl M, Rohac M, et al. Elevated concentrations of circulating adhesion molecules and their association with microvascular complications in insulin-dependent diabetes mellitus. *J Clin Endocrinol Metab* 1996; 81(12): p. 4313-7.
214. Steiner M, Reinhardt KM, Krammer B, Ernst B,Blann AD. Increased levels of soluble adhesion molecules in type 2 (non-insulin dependent) diabetes mellitus are independent of glycaemic control. *Thromb Haemost* 1994; 72(6): p. 979-84.
215. Taddei S, Virdis A, Ghiadoni L, Sudano I,Salvetti A. Effects of antihypertensive drugs on endothelial dysfunction: clinical implications. *Drugs* 2002; 62(2): p. 265-84.
216. Matsuda Y, Akita H, Terashima M, Shiga N, Kanazawa K,Yokoyama M. Carvedilol improves endothelium-dependent dilatation in patients with coronary artery disease. *Am Heart J* 2000; 140(5): p. 753-9.
217. Goto K, Fujii K, Onaka U, Abe I,Fujishima M. Renin-angiotensin system blockade improves endothelial dysfunction in hypertension. *Hypertension* 2000; 36(4): p. 575-80.
218. O'Driscoll G, Green D,Taylor RR. Simvastatin, an HMG-coenzyme A reductase inhibitor, improves endothelial function within 1 month. *Circulation* 1997; 95(5): p. 1126-31.