# INTRODUCTION

The use of coronary stents has increased dramatically in the recent years because of the reduction in restenosis risk and other complications following balloon angioplasty, these complications either acute or subacute vessel closure and late restenosis,because of these advantages, Stenting is now performed in majority of percutaneous intervention (PCI). The rate of emergency CABG and the incidence of in-hospital ST segment elevations (STEMI) is 0.4-1.4% percent with stenting ***(De Feyter et al., 1991; Lincoff, Popma et al., 1992)*.**

So the addition of Coronary stents to percutaneous coronary intervention (PCI) make the incidence of restenosis significantly reduced, restenosis rates still range from 16% to 32% ***(Kastrati et al., 2000)*.**

Different intercoronary stent have been used widely since 1990. They were different in Architectural design, length, mode of implantation and composition (stainless steel, versus chromium) ***(Kastrati et al., 2001)*.**

The efforts to reduce restenosis include coating of conventional stents and use of alternative material and design, Drug Eluting Stents (D.E.S) already established in

clinical practices ***(Babapulle et al., 2004)***.

Cobalt chromium stents are being increasingly used in percutaneous coronary intervention (PCI) as cobalt chromium stents represent a more biocom-patible material and due to favourable mechanical properties, the use of chromium allow reduction of stent strut thickness without any compromise in stent radial forces and radiopacity. Such enhancements enable the reduction of endoprothesis profile, increase their flexibility and consequently facilitate stent implantation into tortuous vascular segments or severe obstructive lesions, reducing stent struts thickness may be also of importance in lowering the risk of restenosis ***(Pache et al., 2003)*.**

In comparison with stainless steel stent, cobalt chromium stent has a higher radial strength and radiopacity, this allow the production of thinner struts with a similar radiological visibility ***(Kastrati et al., 2001)***.

# AIM OF THE WORK

This work aims to determine and compare safety and efficacy of cobalt chromium stent versus stainless steel Bare metal stents regarding in hospital, morbidity and mortality, short and intermediate term prognosis in patient undergoing PCI to multivessel disease.

# ATHEROSCLEROSIS

## Introduction

The clinical manifestations of atherosclerosis are well known and include coronary heart disease, stroke, and peripheral vascular disease. Forms of accelerated arteriopathies, such as restenosis following percutaneous coronary intervention with stenting and coronary transplant vasculopathy differ in pathogenesis (***Faxon et al., 2004)***.

## Histology:

The initial lesion in atherosclerosis involves the intima of the artery and begins in childhood with the development of fatty streaks (table 1). In one autopsy study, for example, all 2876 men and women, aged 15 to 34 years, had aortic fatty streaks. The advanced lesions of atherosclerosis occur with increasing frequency with aging. This was illustrated in a second autopsy study of 760 young (age 15 to 34 years) victims of accidents, suicides, or homicides. Advanced coronary atheroma was seen in 2 and 0 percent of men and women aged 15 to 19, and 20 and 8 percent of men and women aged 30 to 34, respectively. The presence of atherosclerotic lesions was associated

with non-HDL cholesterol ≥160mg/dL (4.14mmol/L) and HDL cholesterol less than 35mg/dL (0.91mmol/L) (***McGill et al., 2000 and Tuzcu et al., 2001).***

**Table (1)**: Criteria for American Heart Association Lesion Classification System and Correspondence with Classification of Gross Arterial Specimens

| AHA grade | Criteria | Comments and corresponding gross classification |
|---|---|---|
| 0 | Normal artery with or without adaptive intimal thickening; no hold | Normal tissue |
| 1 | Isolated MFCs containing lipid; no extracellular lipid; variable adaptive intimal thickening grossly with lipid staining | Initial atherosclerotic lesion, sometimes visible grossly with lipid staining |
| 2 | Numerous MFCs, often in layers, with fine particles of extracellular licid; no distinct pools of extracellular lipid: variable adaptive intimal thickening | Fatty streak, visible grossly with III staining |
| 3 | Numerous MFCs with ≥ pools of extracellular lipid; no well-defined core of extracelfular lipid | Fatty plaque, raised fatty streak, intermediate lesion, or transitional lesion |
| 4 | Numerous MFGs plus well-defined core of extracellular lipid, but with luminal surface covered by relatively normal intima | Atheroma, fibrous plaque, or raised lesion |
| 5 | Numerous MFCs, well-defined core or multiple cores of extraceliular lipid, plus reactive fibrotic cap, vascularization, or calcium | Fibroartherema, fibrous plaque, or raised lesion |
| 6 | All of the above plus surface defect, hematoma, hemorrhage, or thrombosis | Complicated lesion |

MFC indicates macrophage foam cell; AHA, American Heart Association

Early arterial accumulation of cholesterol causes a reduction in arterial distensibility, which occurs before other vessel wall changes become apparent; the loss of distensibility, which increases with age, is related to the development of atherosclerosis. A loss of vessel

distensibility also occurs with accumulation of cholesterol in the vessel wall, even in young subjects (***Lesson et al., 2000)***.

## Fatty streaks:

The first phase in atherosclerosis histologically presents as focal thickening of the intima with an increase in smooth muscle cells and extracellular matrix (Fig. 1 and 2) ***(Davies et al., 1988)***.

These smooth muscle cells, which are possibly derived from hematopoietic stem cells, migrate and proliferate within the intima. This is followed by accumulation of intracellular lipid deposits or extracellular lipids or both, which produce the fatty streak. Biglycan, a small dermatan sulfate proteo-glycan, can be detected in the intima of atherosclerotic coronary artery segments; it can bind and trap lipoproteins, including apolipoprotein E, VLDL remnants, LDL, and HDL. The fatty streak also consists of macrophages with a variable number of T-lymphocytes.

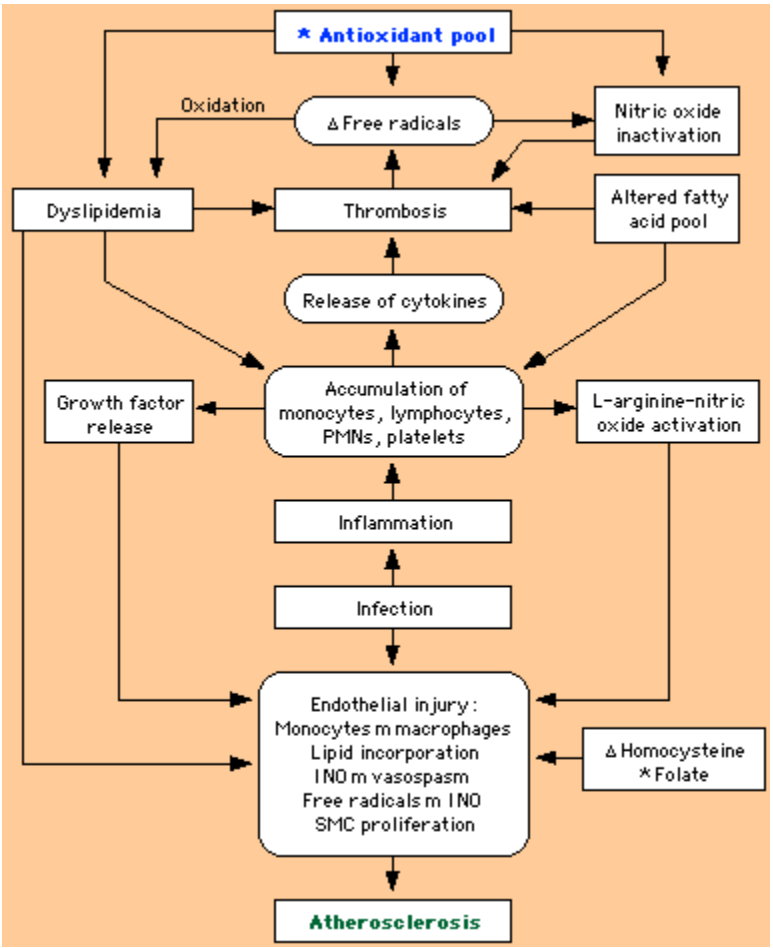
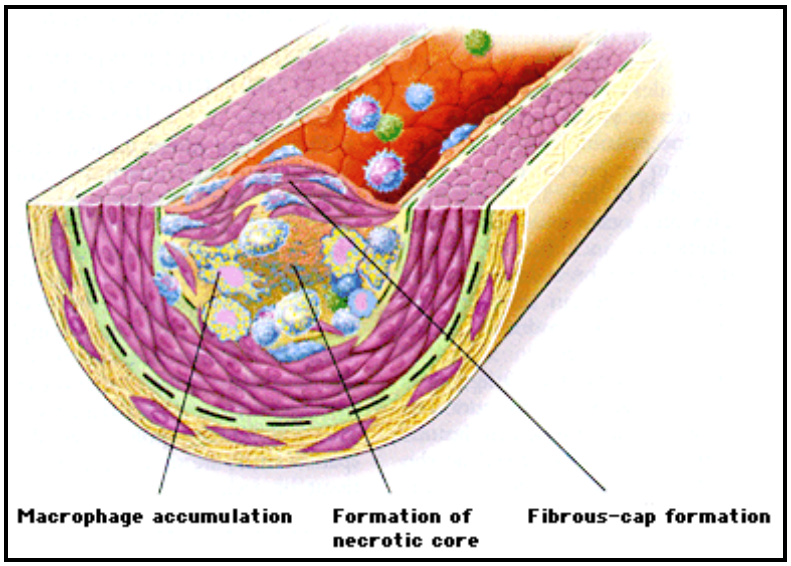



**Fig. (1)**: Postulated steps in the Pathogenesis of Atherosclerosis.

As these lesions expand, more smooth muscle cells migrate into the intima. The smooth muscle cells within the deep layer of the fatty streak are susceptible to apoptosis which is associated with further macrophage infiltration and cytoplasmic remnants that can calcify, perhaps contributing to the transition of fatty streaks into atherosclerotic plaques (***Kockx et al., 1998).***

## Fibrous plaque:

The fibrous plaque evolves from the fatty streak via accumulation of connective tissue with an increased number of smooth muscle cells ladened with lipids and often a deeper extracellular lipid pool.



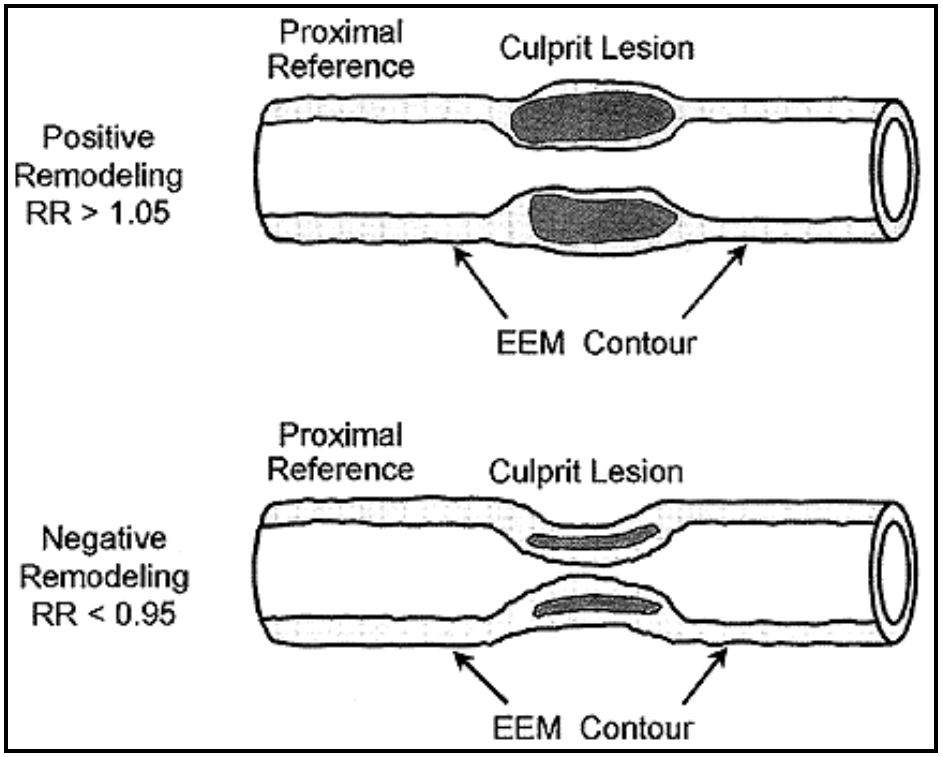

Formation of an advanced, complicated lesion of atherosclerosis as fatty streaks progress to intermediate and advances lesion, they tend to form a fibrous plaque that wall off the lesion from the lumen. This represents a type of healing or fibrous response to the injury. The fibrous plaque covers a mixture of leukocytes, lipid, and debris, which may form a necrotic core. These lesions expand at their shoulders by means of continued leukocyte adhesion and entry, principally due to macrophage colony-stimulating factor, monocyte chemotactic protein 1, and oxidized low density lipoprotein. The necrotic core results from apoptosis and necrosis, increased proteolytic activity, and lipid accumulation. The fibrous cap forms as a result of increased activity of platelet derived growth factor, transforming growth factor β, interlukin-1, tumor necrosis factor alpha, and osteoprotein and decreased connective tissue degradation (Reproduced with permission from: Ross RN Engl J Med 1999; 340: 115. Copyright®1999 Massachusetts Medical Society).

**Fig. (2)**: Formation of an advanced, complicated lesion of atherosclerosis.

## Advanced lesions:

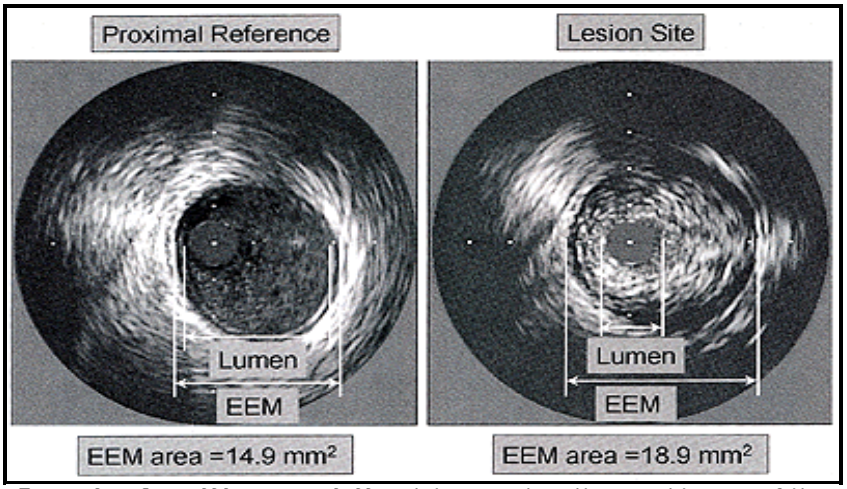
More advanced lesions become revascularized from both the luminal and medial aspects, and often contain a necrotic lipid rich core, which can eventually become calcified (Table 1 and Fig. 3) (***Stary et al., 1995)***.

Advanced lesions are associated with coronary artery remodeling (Fig. 3). Positive remodeling is defined as a positive correlation between plaque and external elastic membrane area due to a compensatory increase in local vessel size in response to increasing plaque burden (dilated coronary atherosclerosis), while negative remodeling refers to a smaller external elastic membrane area at the lesion site due to the local shrinkage of vessel size (obstructive coronary atherosclerosis) (Fig. 4A-4B) (***Schoenhagen et al., 2001)***.



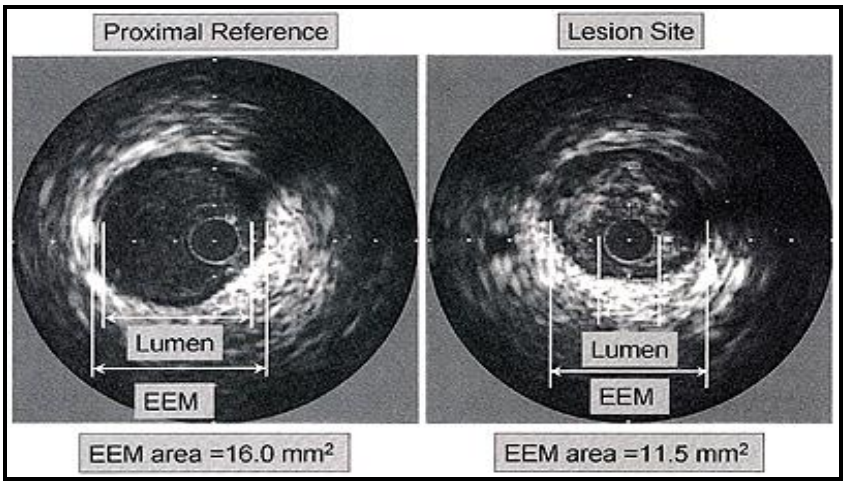

**Positive and negative arterial remodeling extremes of the remodeling response** Longitudinal sections through vessel segments show positively and negatively remodeled lesions. The lumen diameter is maintained with positive remodeling, while there is significant luminal narrowing with negative remodeling. EEM, external elastic membrane; RR, remodeling ratio (EEM area lesion/EEM area proximal reference). (Reprinted with permission from Schoenhagen, P, Ziada, KM, Vince, DC, et al. J Am Coll Cardiol 2001; 38:297. Copyright © 2001 American College of Cardiology.)

**Fig. (3)**: Positive and negative arterial remodeling extremes of the remodeling response.




**Example of positive remodeling** Intravascular ultrasound images of the proximal reference and lesion site are shown. The remodeling ratio (EEM area lesion/EEM area proximal reference) is 1.32. EEM, external elastic membrane. (Reprinted with permission from: Schoenhagen, P, Ziada, KM, Vince, DC, et al. J Am Coll Cardiol 2001; 38:297. Copyright © 2001 American College of Cardiology.

**Fig. 4(A)**: Example of Positive remodeling.

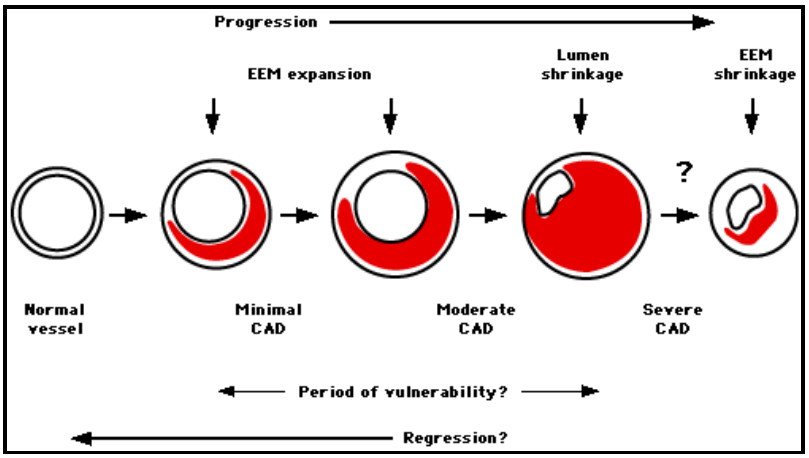



**Example of negative remodeling** Intravascular ultrasound images of the proximal reference and lesion site are shown. The remodeling ratio (EEM area lesion/EEM area proximal reference) is 0.71. EEM, external elastic membrane. (Reprinted with permission from: Schoenhagen, P, Ziada, KM, Vince, DG, et al. J Am Coll Cardiol 2001; 38:297. Copyright © 2001 American College of Cardiology.)

**Fig. 4(B)**: Example of Negative remodeling.

Positive remodeling has been felt to be a compensatory mechanism in early coronary artery disease, preventing luminal loss despite plaque accumulation (Fig. 5).

However, arterial remodeling is associated with plaque physiology and the clinical presentation. Positive remodeling is seen with complex, unstable plaques in patients presenting with unstable angina; in contrast negative remodeling is associated with a smoother, stable plaques in patients with stable angina ***(Schoenhagen et al., 2000).***

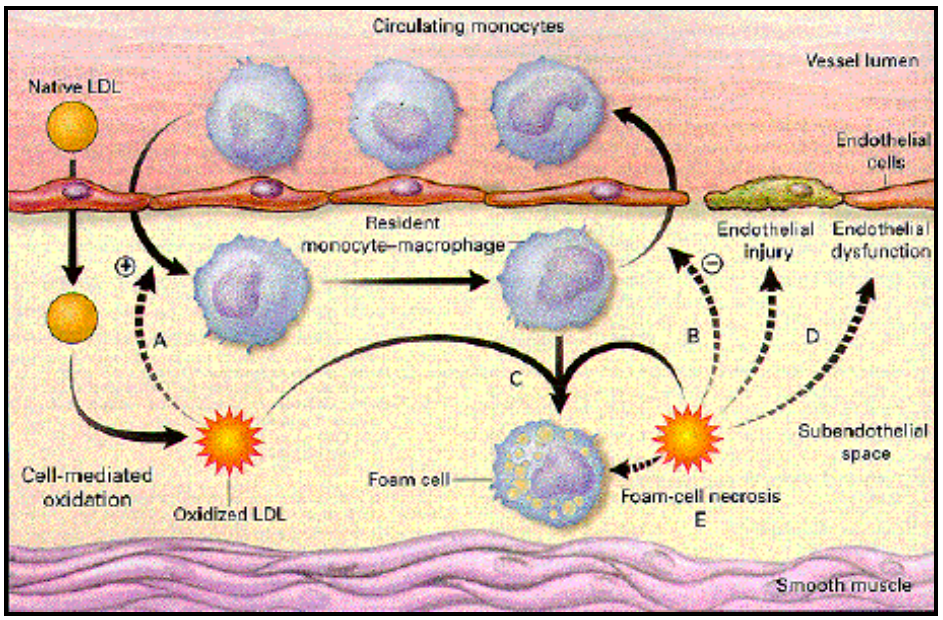



**Early plaque accumulation in human coronary arteries is associated with compensatory enlargement of vessel size (positive remodeling)** In the early phases of atherosclerosis development, when coronary artery disease (CAD) is minimal, luminal size is not affected by plaque growth because of expansion of the external elastic membrane (EEM) and enlargement of vessel size; this represents "postive remodeling". As CAD becomes moderate, there is no further increase in vessel size, but rather the plaque encroaches on the lumen, which shrinks. These complex changes of lumen, plaque and EEM may also affect plaque regression. (With permission from Glagov, S, Weisenberg, E, Zarins, CK, N Engl J Med 1987; 316:1371).

**Fig. (5)**: Early accumulation in human coronary arteries is associated with compensatory enlargement of vessel size (positive remodeling).

## Pathogenesis:

Multiple factors contribute to the pathogenesis of atherosclerosis including endothelial dysfunction, dyslipidemia, inflammatory and immunologic factors, plaque rupture, and smoking.

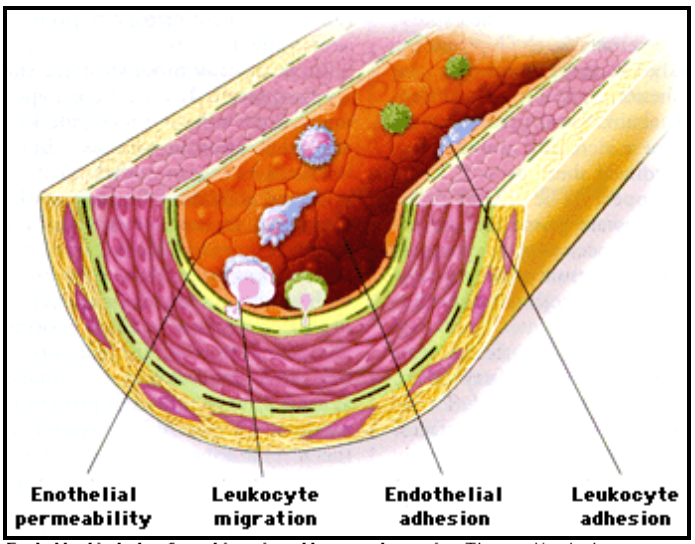



**Early events in pathogenesis of atherosclerosis** Schematic representation of the initial events of atherogenesis. Native low density lipoprotein (LDL) becomes trapped in the subendocardial space and can undergo oxidation by macrophages as well as smooth muscle cells and endothelial cells. Oxidized LDL can stimulate monocyte chemotaxis (A,+) as well as inhibit the monocyte from exiting through the vascular wall (B,–). Monocytes transform into macrophages that take up oxidized LDL, becoming foam cells (C). Oxidized LDL can also lead to foam cell necrosis (E) with the release of lysosomal enzymes, and endothelial injury and dysfunction (D). (Reproduced with permission from Diaz, MN, Frei, B, Vita, JA, et al. N Engl J Med 1997; 337:408.)

**Fig. (6)**: Early events in pathogenesis of atherosclerosis.

## Endothelial dysfunction:

Among patients with normal or minimally diseased coronary vessels, a positive family history of coronary artery disease is an important predictor of impaired coronary artery blood flow regulation, which represents coronary endothelial dysfunction in the microcirculation. The association with family history is independent of other well established risk factors; however, a positive family history aggravates the endo-thelial dysfunction associated with hypercholesterol-emia and age, suggesting additive effects of genetic and environmental risk factors (***Schachinger et al., 1999)***.




**Endothelial dysfunction in atherosclerosis** The earliest changes that precede the formation of lesions of atherosclerosis take place in the endothelium. These changes include increased endothelial permeability to lipoproteins and other plasma constituents, which is mediated by nitric oxide, prostacyclin, platelet-derived frowth factor, angiotensin II, and enothelin; up-regulation of leukocyte adhesion molecules, including L-selectin, integrins, and platelet-endothelial-cell adhesion molecule-1, and vascular-cell adhesion molecule 1; and migration of leukocytes into the artery wall, which is mediated by oxidized low-density lipoprotein, monocyte chemotactic protein 1, interleukin-8, platelet-derived growth factor, macrophage colony-stimulating factor, and osteopontin.


**Fig. (7)**: Endothelial dysfunction in atherosclerosis.

Endothelial dysfunction and impaired vascular reactivity, perhaps representing early large vessel disease, have also been documented in asymptomatic young adults with a family history of premature coronary disease but no other risk factors, in normal first degree relatives of patients with type 2 diabetes, and in patients who have insulin-dependent diabetes. Autonomic dysfunction and altered neurotransmission may be an important determinant of vascular reactivity (***Balletshofer et al., 2000)***

**Table (2)**: Factors that cause and Interventions that improve endothelial dysfunction

| Factors associated with endothelial dysfunction | Interventions that improve endothelial function |
|---|---|
| Increased age | L-arginine |
| Male sex | Estrogen |
| Family history of CHD | Antioxidants |
| Smoking | Smoking cessation |
| Increased serum cholesterol | Cholesterol lowering |
| Low serum HDL-cholesterol | ACE inhibitors |
| Hypertension | Exercise |
| Increased serum homocysteine | Homocysteine lowering |
| Diabetes mellitus | |
| Obesity | |
| High-fat meal | |

Endothelial dysfunction is induced by oxidized LDL, can be worsened by cigarette smoking, and can be reversed with correction of hyperlipidemia by diet or by therapy with a statin (HMG-coenzyme A reductase inhibitor), which increases the bioavailability of nitric oxide, with ACE