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لم ترد بالأصل

STUDY OF THE CORRELATION BETWEEN CHLAMYDIA PNEUMONIAE INFECTION AND CORONARY HEART DISEASE

Thesis

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By

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CORONARY ARTERY DISEASE

Chronic coronary artery disease (CAD) is most commonly due to obstruction of the coronary arteries by atheromatous plaques. [1] In addition, almost all myocardial infarctions result from coronary atherosclerosis, generally with superimposed coronary thrombosis. [2]

THE PATHOGENESIS OF ATHEROSCLEROSIS: [3]

Atherosclerosis is a term derived from the Greek "athero" (gruel or porridge) and "sclerosis" (hardening). It is now recognized as a multifactorial process and is manifested principally in the medium-sized muscular arteries, including the coronary, carotid, basilar, and vertebral arteries. Several other arteries are also affected particularly the iliac, the superficial femoral, and larger arteries, such as the aorta. Advanced lesions demonstrate three fundamental biological processes:

1) Accumulation of intimal smooth muscle cells with variable numbers of macrophages and T-lymphocytes.

2) Formation of large amounts of connective tissue matrix, including collagen, elastic fibres, and proteoglycans.

3) Accumulation of lipid, principally in the form of cholesteryl esters, and free cholesterol within the cells as well as the surrounding tissues. [4, 5]

Cells potentially involved in atherogenesis

Many cells are believed to be involved in atherogenesis, these include: Endothelium, smooth muscle, macrophage, platelets, and T-Lymphocytes. [3]

1. Endothelium:

In the arterial system the endothelium forms smooth uninterrupted surface. It forms a highly selective permeability barrier, it is a highly active metabolic tissue, and is usually thought to be a non-thrombogenic surface. Endothelial cells have low turnover rate in adulthood, and a particular characteristic is that endothelial cells grow in an obligate monolayer, this fact is important in that cells cannot crawl over one another at sites of injury to cover the de-endothelialized areas. Thus if a particular site is repeatedly injured and cells loose their capacity to replicate, cells distal to the site may not be able to participate in regeneration process. [6, 7]

The endothelium provides a non-thrombogenic surface by forming prostacyclin, [8] which is a potent vasodilator and platelet aggregation inhibitor, also by a surface coat of heparan sulfate. Also the endothelium forms the most potent vasodilator, the endothelial-derived relaxing factor [EDRF] which is a thiolated form of nitric oxide. [9]

Endothelial cells have receptors for different molecules on their surface, including receptors for low-density lipoprotein [LDL], for growth factors, and other pharmacological agents. [10]

Of special importance in atherogenesis is the ability of lipoprotein modification. LDLs appear to be modified by a low-level oxidation process into oxidized LDLs [oxLDL] which play an important role in atherogenesis; by injuring endothelial and smooth muscle cells, inducing increased adherence and migration of monocytes and T-lymphocytes into the arterial wall, and inducing the formation of the vascular cell adhesion molecule-1 [VCAM-1] and intercellular adhesion molecule-1 [ICAM-1], which can participate in increased adhesion of monocytes and T-cells to the endothelium through receptor-ligand type interactions. [11]

2. Smooth muscle

Smooth muscle cells are originally derived from the media, [12] and is now widely accepted that their accumulation in the intima is essential for the definition of the lesions of advanced atherosclerosis. Smooth muscle cells are derived locally from individual organ parenchyma during embryogenesis in contrast with endothelium; that is derived from embryonic vasculature that invades the organ. As a consequence, smooth muscle cells respond differently to agonists presented to them. This fact may explain why different arterial beds respond differently to local stimuli associated with the process of atherogenesis. [13]

Smooth muscle cells appear to have two different phenotypes when cultured:

a) The contractile phenotype cells contain extensive myofibrils of actin and myosin filaments. These cells respond to various stimuli e.g. epinephrine, angiotensin II [AII], and endothelin [ET] by contraction

and to prostacyclin, prostaglandin E, neuropeptides, leukotrienes, and nitric oxide [NO] by relaxation, and thus maintain the tone of the arterial wall. It is appropriate to note that these cells are not capable to respond to mitogens such as the platelet derived growth factor [PDGF]. [14]

b) The synthetic phenotype smooth muscle cells have decreased content of myofilaments and contain an extensively developed rough endoplasmic reticulum and Golgi complex. They are formed by appropriate stimulation of the contrctile phenotype. The synthetic phenotype responds to mitogens such as PDGF. Cells can express genes for a number of growth regulatory molecules and cytokines, and can release growth factors such as fibroblast growth factor [FGF]. Also they are involved in the formation of numerous secretory proteins, and connective tissue matrix macromolecules. [15]

For the lesions of atherosclerosis to form, the smooth muscle cells must migrate from the media into the intima, where they can respond mitogenically, where they become the principal contributor to the reparative, fibroproliferative process. One characteristic feature of the smooth muscle cells found in the lesions of atherosclerosis is the accumulation of lipid that results in formation of vacuolated cells, the foam cells. [11, 14]

3. Macrophages

Macrophages are cells derived from the circulating monocytes. [16] When the monocytes enter the tissue during inflammation, they take on characteristics peculiar to the host tissue. They act as scavenger cells, removing foreign substances by phagocytosis and intracellular hydrolysis, and as a second line of defense after the neutrophil against