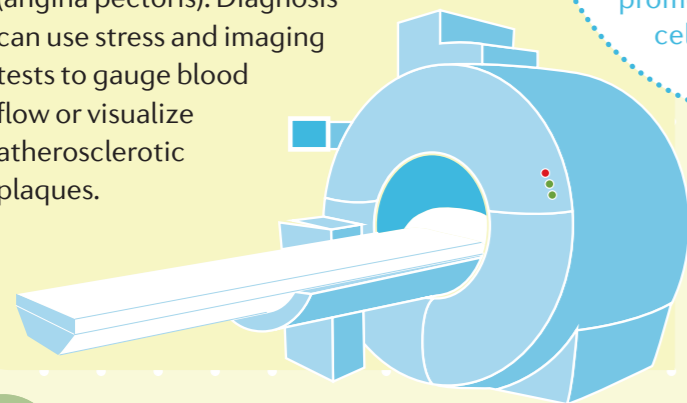


For the Primer, visit doi:10.1038/s41572-019-0106-z

➔ Atherosclerosis refers to the formation of fibrous and fatty lesions in the artery wall. As the atherosclerotic plaque increases in size it can obstruct the arterial lumen, reduce blood flow and lead to ischaemia. Vascular occlusion and ischaemia can also result from rupture or erosion of the plaque, which are triggers for thrombus formation.

DIAGNOSIS

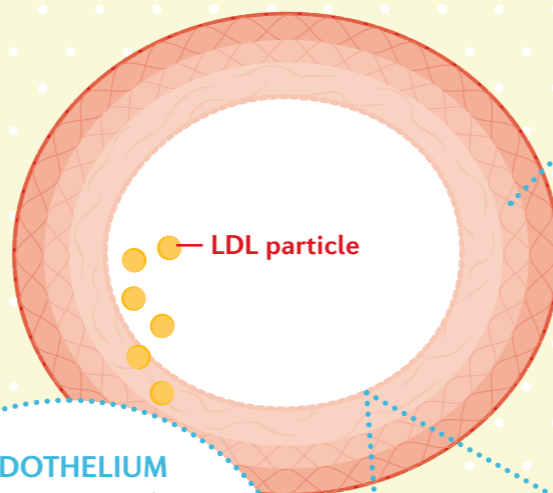
Atherosclerosis usually progresses slowly and, therefore, may not cause symptoms for decades. The clinical presentation varies greatly depending on the arterial vessels involved. In the coronary arteries, which supply blood to the heart, manifestations range from acute coronary syndromes (such as myocardial infarction) to chronic exertional chest discomfort (angina pectoris). Diagnosis can use stress and imaging tests to gauge blood flow or visualize atherosclerotic plaques.



EPIDEMIOLOGY

Atherosclerotic cardiovascular disease (CVD) has spread worldwide. In 2015, >17 million people died from CVD, representing 31% of all global deaths. Although improvements in cardiovascular health may limit CVD mortality, the epidemic of obesity, especially in low-income and middle-income countries, might undermine this progress.

PATHOPHYSIOLOGY



ENDOTHELIUM
Exposure to risk factors impairs the production of endogenous vasodilators by endothelial cells and can activate the expression of adhesion molecules and chemoattractants that promote entry of immune cells into the intima.

PROGRESSION
The continued accumulation of lipids and foam cells results in the formation of a necrotic core. Smooth muscle cells can migrate into the atherosclerotic plaque, proliferate and secrete extracellular matrix macromolecules that entrap LDL particles.

QUALITY OF LIFE

The health-related quality of life of patients with atherosclerosis can be reduced by anxiety and depression due to prognosis and fear of future CVD events, sleep disturbances, adverse drug effects and the presence of comorbidities, among other factors.

OUTLOOK

Improvements in treatment have extended life expectancy in patients with atherosclerosis, but the management of atherosclerotic complications places a major burden on health-care systems. Behavioural changes at the individual and societal levels will be crucial to stem the epidemic of atherosclerosis.

PREVENTION

Subclinical atherosclerosis can start in childhood, and lifetime exposure to risk factors (such as unhealthy diet, tobacco use and sedentary lifestyle) augments CVD risk cumulatively. Thus, long-term prevention strategies include educating and engaging the public about cardiovascular health. Communication of the benefits of early reduction in CVD risk factors can support behavioural changes, particularly when emphasising that the same risk factors associate with cognitive impairment later in life.

INFLAMMATION
Several risk factors for atherosclerosis can provoke inflammation: the release of pro-inflammatory cytokines alters the functions of the cells of the arterial wall, and atherosclerotic plaques contain T cells, indicating activation of adaptive immunity.



MANAGEMENT

All individuals should adopt a lifestyle that limits modifiable risk factors. Lipid-lowering pharmacological therapy aims to reduce primarily LDL cholesterol; statins (which inhibit the rate-limiting enzyme in the synthesis of cholesterol) are the first choice when initiating drug therapy. Antiplatelet therapy increases bleeding risk and, therefore, may only have net benefit in those who have already had an atherosclerotic event. The recognition of the role of inflammation in atherosclerosis has paved the way to several clinical trials testing the effects of anti-inflammatory agents on cardiovascular outcomes.