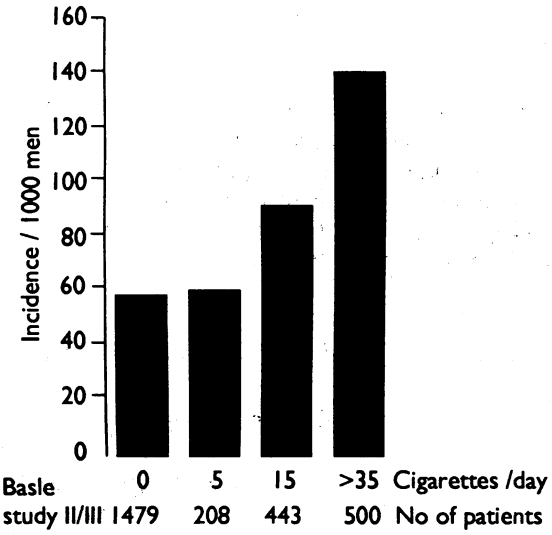
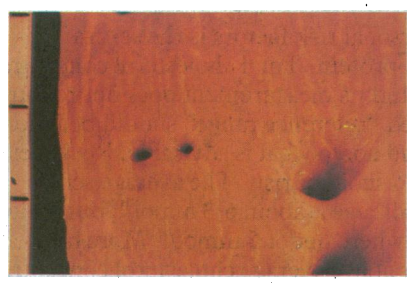
EPIDEMIOLOGY OF ATHEROSCLEROSIS

Geoffrey Rose

The problem: its nature and scale



Five year incidence of peripheral arterial occlusive disease according to how many cigarettes smoked, from the Basle study.



Fatty streaks—the early development of atheroma in areas of low shear stress around ostia.

Most diseases affect only an unfortunate minority, but in Britain few people reach "old age" without a potentially dangerous degree of atherosclerosis. Half of all deaths are caused by circulatory diseases, and over 40% of middle aged men have evidence of ischaemia that is the result of atherosclerosis.

Lipid streaks begin to appear in the aortic intima before the age of 10, but these are not important. Real atherosclerosis starts during the teens and in early life it spreads rapidly. By itself it causes little trouble; increasingly, however, the plaques cause fissures and haemorrhages, which in turn may lead to thrombosis (particularly in the carotid arteries) embolisation and consequent ischaemia.

Often the first clinical event is dramatic—a stroke or sudden death (the first presentation of coronary heart disease in 20% of cases); even in non-fatal presentations there is usually much irreversible disease. The real course of atherosclerotic disease, however, is usually extremely slow, the serious event usually being preceded—years in advance—by small signs of developing ischaemia. For example, only a few people with angina or intermittent claudication actually attend the doctor and are diagnosed. Minor disease usually goes unrecognised but when it is recognised it is the best predictor of future serious disease.

Atherosclerosis is always a more or less generalised—albeit patchy—condition. The patient with intermittent claudication will probably die of a coronary thrombosis, and the surgeon who relieves coronary stenosis needs to remember that the patient still has generalised arterial disease.

The same underlying causes and risk factors are found no matter at what site the problem presents. People with hypertension or hypercholesterolaemia get more of the same sort of atherosclerosis and the pathologist cannot tell one from another. The clinical consequences are, however, extremely varied, and similar clinical syndromes may be caused by non-atherosclerotic disease.

For reasons that we do not understand men are much more prone than women to almost all forms of vascular disease (especially aortic aneurysms). Women's protection wanes gradually with age, and by "old age" the risks are similar for the two sexes. At any age the protection is wiped out by diabetes.

Underlying causes

Mortality from coronary disease in the United States has fallen by 40% in less than 20 years

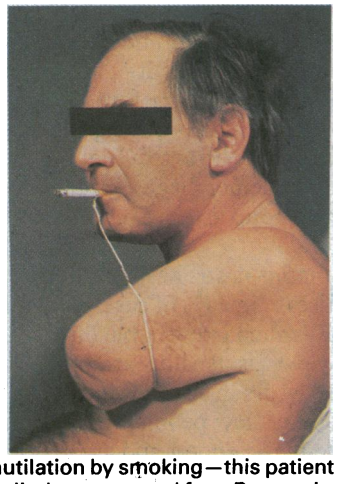
Arterial disease is not—as we used to be taught—degenerative (except for the loss of elasticity in larger arteries and veins that is associated with age). In some remote societies it is uncommon even in old age. Nor is it a necessary accompaniment of twentieth century affluence: mortality from coronary disease is low and falling, and in the United States has fallen by 40% in less than 20 years. In Britain mortality from coronary disease among manual workers continues to rise, but among other groups it is now falling; clearly the incidence of arterial disease is at least potentially reducible.

Rudolf Virchow, whose triad of the causes of thrombosis remains valid today: disease of the wall, consistency of the blood, and abnormality of the flow.

The one essential underlying cause of serious atherosclerosis seems to be a high concentration of low density lipoprotein in the blood, which reflects a high intake of dietary saturated fat. The Japanese do not have this and so—despite a high incidence of smoking and hypertension—they have fewer atherosclerotic problems. When the concentration of low density lipoprotein is high, however, other factors may aggravate the process. In particular, the enormous variation in incidence seems to depend on the number of smokers and patients with diabetes or high blood pressure in the particular community (the last two reflecting overweight).

Large pieces of this jigsaw remain to be discovered. Probably some key pieces concern the regulators of thrombosis. Thus men in Edinburgh have twice the incidence of coronary disease as their Stockholm contemporaries despite similar "classic" risk factors. The explanation may be that they have a much lower intake of linoleic acid, an amino acid essential for prostaglandin synthesis and possibly an important determinant of platelet and endothelial stickiness. Atherosclerosis may be the precursor of ischaemia but thrombosis is commonly the precipitator.

Who is at risk?

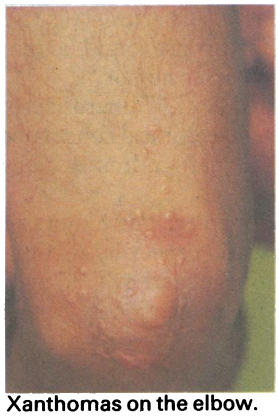


Self mutilation by smoking—this patient had all four limbs amputated for a Buerger's type of arteritis. His cigarette holder was made out of a coat hanger by one of his friends on the ward.

The simple answer is that everyone is at risk, but some much more than others. Even those in the lowest risk category are more likely to die of cardiovascular disease than of any other single cause, but they will get the disease later in life. The same risk factors apply to all the main forms of arterial disease but the balance is different. Stroke is dominated by blood pressure, whereas diabetes and smoking are most strongly linked with ischaemia of the legs.

Clues from the patient's background come from:

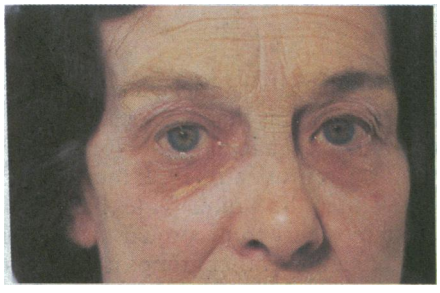
- Residence—south west Scotland and northern Ireland have the highest incidences
- Occupation—the rates are highest, and still rising, among manual and unskilled workers, and
- Family history—but only if the relatives developed the disease before the age of 60.



Xanthomas on the elbow.

Serum low density lipoprotein concentration

The first of the three main personal risk factors is the serum concentration of low density lipoprotein. Total cholesterol concentration is, however, an adequate guide and its measurement does not require fasting. The laboratory's so called "reference range" should be ignored; it refers only to what is common and not to what is advisable. Recent evidence makes it clear that there is no threshold of risk. The average serum cholesterol concentration in middle age is about 6·3 mmol/l, but biologically this is high and the ideal is somewhere under 5 mmol/l. More heart attacks occur in patients with average or above average cholesterol concentrations (because they are so numerous) than among the small minority with conspicuous hypercholesterolaemia. This minority, however, do need special help. Blood cholesterol screening should be selective and measurement of high density lipoproteins and triglycerides does not add much to the basic assessment of risk if other risk factors are already known.



Xanthelasma.

Blood pressure

As a guide to risk systolic blood pressure is as valid as the diastolic measurement, and the initial measurement can be regarded as predictive. As a guide to treatment, however, multiple checks at several visits are needed. Risk is graded, as for cholesterol measurement, and most vascular disease is associated with mild hypertension because it is so common. The risk of stroke reflects current blood pressure, and it is swiftly reversed by treatment. For reasons that we do not understand the same is not true of the risk of coronary thrombosis; this is less affected by antihypertensive drugs and we must control other risk factors to reduce it.

Risk factors for atherosclerosis

- Smoking
- Blood pressure
- Diet
- Diabetes
- Blood cholesterol concentration

The risk of heart attack is trebled if the patient smokes, has a serum cholesterol concentration of 6 mmol/l, *and* has a diastolic blood pressure of 85 mm Hg

Treatment of arterial disease

- Operation
- Control of hypertension, blood sugar, and lipids
- Thrombolytic drugs
- **STOP SMOKING**

Smoking

The third important risk factor is smoking—especially cigarettes but probably also pipes and cigars if the smoke is inhaled. Smoking roughly doubles the risk of heart attack and (in hypertensive patients) of stroke, and it massively aggravates the progression of ischaemic complications of peripheral arterial disease. The number of cigarettes smoked seems less important than the mere fact of smoking, and the type of cigarette is largely irrelevant (for the vascular system there is no "safer cigarette"). Unfortunately we still do not know the guilty component(s) of tobacco smoke or their mode of action, but this probably includes thrombogenesis, and stopping smoking brings swift benefit.

Combinations of risk factors

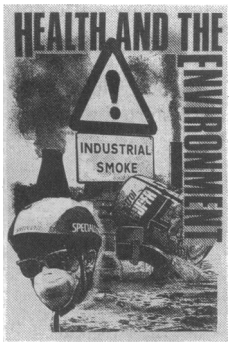
Combinations of risk factors are the main trouble makers. The risk of coronary disease is roughly trebled by a serum cholesterol concentration of 9 mmol/l or by a diastolic blood pressure of 115 mm Hg, and when seen these will not be overlooked because they are most unusual. The risk is also trebled (compared with a low risk subject) by cigarette smoking, plus a cholesterol concentration of 6 mmol/l, plus a diastolic pressure of 85 mm Hg—a combination so common that the doctor may say "My patient has no risk factors." Most vascular disease is caused by such combinations because the arteries stand up reasonably well to one single factor in isolation. The therapeutic corollary of this is that management must also take account of all aspects. Surgery, acute care of patients with myocardial infarction, control of blood sugar concentrations in diabetes, or control of blood pressure in hypertension—each is just one component in the management of a chronic disease with many causes.

The data from the Basle study were presented by Schering. The pictures of self mutilation by smoking and the fatty streaks are reproduced by kind permission of Professor Sir Geoffrey Slaney, KBE, FRCS, and Professor Neville Woolf, PHD, FRCPATH, respectively. We acknowledge with thanks the assistance of the audiovisual department, St Mary's Hospital, London, in the preparation of the illustrations.

Professor Geoffrey Rose was formerly consultant in medicine and epidemiology, St Mary's Hospital, London.

The ABC of Vascular Diseases has been edited by Mr John H N Wolfe, FRCS.

Health and the Environment



Air pollution: II—road traffic and modern industry

Fiona Godlee

Summer smog is a cocktail of volatile hydrocarbons, oxides of nitrogen, sulphur dioxide, and carbon monoxide emitted from road vehicles, industry, and power stations. When acted on by sunlight it produces ozone, which is a potent respiratory irritant. At best photochemical smog is unpleasant, at worst it is harmful to health (table).

Ozone

Ozone at ground level builds up on sunny, still days when temperature inversion—a cold layer of air at ground level covered by a zone of warmer air—prevents the air from circulating. Concentrations reach a peak in the early afternoon and are often highest in rural areas. This is because anticyclones spread photochemical smog from cities, and rural areas lack nitric oxide, a constituent of urban pollution that scavenges ozone to form nitrogen dioxide and oxygen.

At low concentrations ozone causes coughing; nausea; irritation of the eyes, nose, and throat; and headaches. At higher concentrations, 150-200 parts per billion, it damages lung function. Laboratory studies have shown reversible reduction in forced vital capacity, forced expiratory volume, and peak expiratory flow rate in people with asthma and in healthy volunteers.[1] The effects of ozone are worsened by exercise and prolonged exposure, although tolerance seems to occur after a few days. Ozone may also increase the susceptibility of people with asthma to common allergens.[2]

The link between ambient ozone concentrations and impaired lung function has been shown by studies on children in summer camps in the United States. Children had reduced forced vital capacity, forced expiratory volume, and peak expiratory flow rate when ozone concentrations rose during hazy weather. Lung function in children is affected to the same extent as in adults but children develop fewer symptoms and so are less aware of respiratory irritation.[3]

Chronic exposure to ozone may cause structural damage to the lungs. A pathologist in Los Angeles found that 29 out of 107 healthy teenagers who died in road accidents or of other non-respiratory causes had severe respiratory bronchiolitis of the type found in young smokers and in monkeys chronically exposed

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