Passive smoking and early arterial damage

Active cigarette smoking has long been known to predispose to atherosclerotic vascular disease, but recently passive smoking has been identified as an important risk factor for cardiovascular morbidity and mortality, accounting for up to 20,000 deaths per year in non-smokers in the United States alone\(^1\).

Cigarette smoking has deleterious effects on haemodynamics, myocardial perfusion and response to anti-anginal drugs in patients with coronary artery disease and we have previously reported evidence of damage to the vascular endothelium, a key early event in the atherogenic process, in the systemic arteries of young smokers before clinical evidence of arterial disease\(^2\). In a recent study, we have now been able to demonstrate that endothelial dysfunction may also occur in teenagers and young adults as the result of environmental tobacco smoke exposure\(^3\). Furthermore, the endothelial dysfunction that results is dose-related and may be equivalent to the degree of vascular abnormality in age-matched active smokers. Seventy-eight healthy men and women (age 15–30 years) were studied using a non-invasive high resolution ultrasound technique to compare brachial artery vascular responses to increased flow (an endothelium-dependent dilator stimulus) and to nitroglycerin (an endothelium-independent dilator). Twenty-six of the subjects had never smoked nor had had regular exposure to environmental tobacco smoke, 26 were non-smokers but had had environmental tobacco smoke exposure for at least 1 h per day for 3 or more years and 26 were active cigarette smokers. The three groups were matched for other important baseline characteristics, including blood pressure, lipid profiles and vessel size. Flow mediated dilatation was markedly impaired in the passive smokers to an equivalent degree to that seen in young active smokers. When the average intensity of exposure to environmental tobacco smoke was assessed by questionnaire, there was a significant inverse relationship between the environmental tobacco smoke intensity and endothelial-dependent arterial function. In contrast, arterial responses to nitroglycerin, whose action is independent of endothelial function, were normal in all three groups.

Clearly, no quantitative comparison between the deleterious effects of active and passive smoking is possible from this study, but the findings suggest that the toxic substance or substances responsible for vascular injury at this early stage appear to be present in both environmental and inhaled cigarette smoke. Environmental tobacco smoke consists of approximately 85% sidestream smoke (from the burning ends of cigarettes) and 15% exhaled mainstream smoke. It is noteworthy that many toxic components such as carbon monoxide or benzopyrene are present in higher concentrations in side stream than in inhaled smoke, since cigarettes burn at higher temperatures at inhalation and combustion is thus more complete\(^4\). The human data on the effects of passive smoking extend experimental observations from laboratory animals which have shown accelerated aortic atherosclerosis, even at levels of environmental tobacco smoke routinely encountered by people in smoke-filled rooms\(^5\).

The precise mechanism(s) by which passive smoking induces arterial damage remain unclear. Short-term exposure to passive smoking results in an increase in circulating damaged endothelial cells, enhanced platelet aggregation and adverse effects on lipid profiles\(^5,6\). Our recent observations demonstrate significant impairment in arterial endothelial function, measuring flow mediated dilatation of the brachial artery which is largely dependent on release of nitric oxide (endothelium derived relaxant factor). It is likely, therefore, that bioavailability of endothelium derived nitric oxide is impaired in passive smokers. This may be important as nitric oxide acts as an anti-atherogenic influence, inhibiting platelet aggregation, monocyte adhesion to the vessel wall and proliferation of smooth muscle cells\(^7\). In vitro work and our own previous studies of young active cigarette smokers have also implicated decreased nitric oxide bioavailability in smoking-related endothelial damage\(^8\). Dietary supplementation with L-arginine, the substrate for nitric oxide production by endothelial cells, has been shown to protect cholesterol-fed rabbits from environmental tobacco smoke-related arterial damage, suggesting that nitric oxide deficiency may be pathogenetically important for atherogenesis in this animal model\(^9\). The effects of L-arginine on endothelial function in human active and passive smokers are not yet known.
Endothelial dysfunction has now been demonstrated in young adults with a variety of risk factors which are recognised to predispose to morbidity and mortality from atherosclerotic vascular disease in later life, including hypercholesterolaemia, insulin-dependent diabetes and subjects with an adverse family history of coronary disease. These risk factors have been shown to interact at the preclinical stage of the disease to increase the likelihood of endothelial damage as they do to increased risk in population studies of older patients\(^1\). The observation of objective evidence of arterial damage in healthy teenagers and young adults exposed to environmental tobacco smoke supports the epidemiological link between passive smoking and increased cardiovascular morbidity and mortality and suggests that this potentially avoidable factor needs to be considered in risk stratification. The public health implications are enormous and the new evidence of early arterial damage will further fuel the social and medical debate about the acceptability of cigarette smoking in the community.

J. DEANFIELD
Cardiothoracic Unit,
Great Ormond Street Hospital,
London, U.K.

References