Dr A Markus, Thame; Dr D Leggatt, Oxford; Dr M Agass, Berinsfield; Dr D Otterburn, Abingdon; Dr S Street, Kidlington; Dr V Drury, Wantage; Dr R Pinches, Abingdon; Dr N Crossley, Abingdon; and Dr H O'Donnell, Deddington.

Addendum
Since this report was first prepared a further 175 cases of clinically definite first stroke have been registered. None of the patients had non-stroke lesions detected by CT or found at necropsy. The frequency of non-stroke lesions in patients with a clinically definite first stroke is therefore five out of 498 (1.0%).

Appendix

POSSIBLE INDICATIONS FOR PERFORMING CT SCAN ON PATIENT WITH STROKE

To establish diagnosis:
Differentiate "stroke" from "non-stroke" in patients with a poor history (dysphasia, confusion, coma) or a progressive deficit
Identify the pathological type of stroke (intracranial haemorrhage or cerebral infarction)

To identify surgically treatable type of stroke:
Supratentorial haematomas suitable for evacuation
Cerebellar haematomas or infarcts, with or without obstructive hydrocephalus
Arteriovenous malformations or aneurysms

To exclude intracranial haemorrhage:
Already receiving or before anticoagulant treatment
Already receiving or before antiplatelet treatment
Before angiography (for presumed ischaemic minor stroke, etc)

REFERENCES

(Accepted 19 October 1984)

Smoking and coronary artery disease assessed by routine coronary arteriography

DAVID R RAMSDALE, ERIC B FARAGHER, COLIN L BRAY, DAVID H BENNETT, CHRISTOPHER WARD, DAVID C BETON

Abstract
The association between extent and duration of smoking habit and severity of coronary atheroma was examined in 387 patients undergoing routine coronary arteriography before valve replacement surgery. Total number of cigarettes smoked in life correlated significantly with severity of coronary artery disease (p < 0.001) and number of coronary arteries with stenoses of 50% or more (p < 0.001). Severity of coronary artery disease in current smokers was similar to that in former smokers. Multiple regression analysis showed diastolic blood pressure, cigarette consumption, age, ratio of total cholesterol to high density lipoprotein cholesterol, and history of angina to be the important predictors of severity of coronary artery disease.

An estimate of the number of cigarettes smoked in life can be useful in identifying patients with coronary artery disease if used in conjunction with data on other important risk factors.

Introduction
Since White first described an association between smoking and myocardial infarction, numerous studies have shown the same association. 2 Most prospective epidemiological studies with severity of coronary artery disease (p < 0.001) and number of coronary arteries with stenoses of 50% or more (p < 0.001). Severity of coronary artery disease in current smokers was similar to that in former smokers. Multiple regression analysis showed diastolic blood pressure, cigarette consumption, age, ratio of total cholesterol to high density lipoprotein cholesterol, and history of angina to be the important predictors of severity of coronary artery disease.

An estimate of the number of cigarettes smoked in life can be useful in identifying patients with coronary artery disease if used in conjunction with data on other important risk factors.

Since White first described an association between smoking and myocardial infarction, numerous studies have shown the same association. 2 Most prospective epidemiological studies with

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sufficient data have shown that the incidence of developing coronary heart disease is directly related to the number of cigarettes smoked.4,25 Myocardial infarction4,13-15 and sudden death,14,15 occur two and four times, respectively, more often in heavy smokers than in non-smokers. Overall the risk for smokers dying from coronary heart disease is twice that for non-smokers,17-18 but among those smoking more than 20 cigarettes a day17 29 and those starting to smoke before the age of 2021 the risks are between three and five times those for non-smokers.

Although necropsy studies have reported that coronary atheroma is increased in cigarette smokers,29,31 only one small study has correlated cigarette consumption with the severity of coronary artery disease found at necropsy.4 In a large prospective study we examined the association between the quantity of cigarettes smoked and duration of the habit and the severity of coronary atheroma in patients undergoing routine coronary arteriography before valve replacement surgery, as such patients are probably more representative of the general population than those with clinical evidence of ischaemic heart disease. The value of a detailed history of cigarette smoking for predicting the presence and severity of coronary artery disease was also assessed as was the interrelation between smoking and the other coronary risk factors.

Patients and methods

In 1980, 387 patients underwent routine coronary arteriography before valve surgery at this hospital. The arteriograms were scored independently by a radiologist using coronary artery maps to indicate the site and severity of the lesions.25 A severe stenosis of the left main stem or left anterior descending coronary artery carried a high score, whereas a distal irregularity in a non-dominant right coronary artery carried a low score. The total score reflected the overall severity of the coronary artery disease, and the number of vessels affected indicated the extent of the disease.

All patients gave details of their past and present smoking habits including age at starting and stopping and the average number of cigarettes smoked each week. These data allowed us to estimate the number of cigarettes that each patient had smoked in his or her lifetime. In addition to the clinical history and physical examination, blood samples for estimating fasting serum lipid and blood glucose concentrations were collected in 90% of patients. The specimens were analysed using standard techniques.24 27

STATISTICAL ANALYSIS

Categorical data were analysed using χ² tests for association. Age, blood pressure, and serum lipid concentration were examined using a one way analysis of variance and the Tukey multiple comparison tests. The numbers of cigarettes smoked in patients' lifetimes and coronary scores were not normally distributed and were therefore analysed using either non-parametric tests (Kruskal-Wallis test and Spearman correlation coefficient) or a logarithmic transformation (multiple regression analysis).

Results

We studied 180 men and 207 women with mean (SD) ages 54.0 (10.7) and 54.8 (8.8) years respectively. One hundred and forty nine had aortic, 122 mitral, and 115 both aortic and mitral valve disease. One patient had pulmonary stenosis. Two hundred and twenty nine patients had been or were currently cigarette smokers, and 151 were non-smokers. There were three cigar and four pipe smokers.

Age, sex, cigarette smoking, and coronary artery disease—Age was significantly correlated with overall severity of coronary artery disease (coronary score) (r = 0.260; p < 0.001), although there was no correlation between age and total number of cigarettes smoked (r = 0.046; p = 0.364). The median (range) coronary scores for men and women were 4.0 (0.45) and 3.0 (0.50) (p < 0.001). Men smoked significantly more cigarettes than women (p < 0.001).

Angina, cigarette smoking, and coronary artery disease—One hundred and four patients (36.7%) had angina. Sixty five (45.7%) of these patients had appreciable coronary artery disease in contrast with 47 (19.2%) of 245 patients without angina (p < 0.001). Of those with angina, 93 (65.5%) were either current or ex-smokers in contrast with 51 (55.4%) of those without angina (p = 0.035). The number of patients with ischemic heart disease was twice in contrast with only 100 (48.5%) of 206 patients with normal coronary arteries (p < 0.001). One hundred and six (70.2%) of the 151 non-smokers had normal coronary arteries in contrast with only 100 (43.7%) of the smokers (p < 0.001). Of the 112 patients with appreciable coronary artery disease (one or more stenoses of 50%, or more), 90 (80.4%) were current or former cigarette smokers in comparison with 137 (50.3%) of 275 patients without out appreciable disease (p < 0.001). The median (range) number of cigarettes smoked in life were 2.0 × 10⁵ (0.8-8.7 × 10⁵) for patients with appreciable coronary artery disease and 0.05 × 10⁵ (0.8-7.4 × 10⁵) for those without (p < 0.001).

Cigarette smoking and the severity of coronary artery disease—The figure shows the range of coronary scores in patients with various cigarette smoking habits. The median (range) coronary score for smokers (current and former) was 4.6 (0-45) compared with 0.2 (0-50) for non-smokers (p < 0.001). There was a significant correlation between coronary score and the total number of cigarettes smoked in life (r = 0.373; p < 0.001). The number of coronary arteries affected by one or more appreciable stenoses was significantly greater in smokers than non-smokers (r² = 0.32; p < 0.001) (table I). Moreover, there was a significant correlation between the total number of cigarettes smoked and the number of coronary arteries with appreciable disease (r = 0.350; p < 0.001). The severity of coronary artery disease in current smokers was similar to that in former smokers irrespective of whether they had given up smoking five or 10 years previously (table II). The median (range) number of cigarettes smoked by current (1.89 × 10⁵ (0.02-7.4 × 10⁵)) and former (1.45 × 10⁵ (0.18-8.74 × 10⁵)) smokers were not, however, significantly different (p = 0.242). Based on the number of packs smoked a day (one pack = 20 cigarettes), the severity of coronary artery disease was greater in those smoking two or more packs a day than in those smoking less than that (p < 0.001) (table III).

### Table I—Relation between cigarette smoking and number of coronary arteries with appreciable stenoses. (Three pipe and four cigar smokers excluded)

<table>
<thead>
<tr>
<th>No. of coronary arteries affected</th>
<th>Non-smokers (n = 66)</th>
<th>Former smokers (n = 86)</th>
<th>Current smokers (n = 163)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>131 (95.7)</td>
<td>42 (53.6)</td>
<td>97 (59.5)</td>
</tr>
<tr>
<td>1</td>
<td>11 (7.3)</td>
<td>10 (12.2)</td>
<td>22 (13.9)</td>
</tr>
<tr>
<td>2</td>
<td>5 (3.3)</td>
<td>7 (10.6)</td>
<td>24 (14.7)</td>
</tr>
<tr>
<td>3</td>
<td>5 (2.0)</td>
<td>2 (3.0)</td>
<td>10 (6.1)</td>
</tr>
<tr>
<td>4</td>
<td>1 (0.6)</td>
<td>5 (7.6)</td>
<td>10 (6.1)</td>
</tr>
</tbody>
</table>

### Table II—Severity of coronary artery disease in current and former cigarette smokers.* (Three pipe smokers and four cigar smokers excluded)

<table>
<thead>
<tr>
<th>n</th>
<th>Median (range) coronary score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-smokers</td>
<td>0.2 (0-50)</td>
</tr>
<tr>
<td>Current smokers</td>
<td>0.8 (0-44)</td>
</tr>
<tr>
<td>Ex-smokers 5-9 years</td>
<td>5.0 (0-44)</td>
</tr>
<tr>
<td>Ex-smokers 9-19 years</td>
<td>5.0 (0-44)</td>
</tr>
<tr>
<td>Ex-smokers 10-14 years</td>
<td>7.5 (0-30)</td>
</tr>
</tbody>
</table>

*Ex-smokers = current smokers: p = 0.659.

### Table III—Relation between smoking habit and severity of coronary artery disease according to current cigarette consumption

<table>
<thead>
<tr>
<th>Smoking habit</th>
<th>n</th>
<th>Median (range) coronary score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-smokers</td>
<td>151</td>
<td>0.2 (0-50)</td>
</tr>
<tr>
<td>Current smokers by No of packs smoked a day:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1</td>
<td>67</td>
<td>1.8 (0-44)</td>
</tr>
<tr>
<td>&gt; 1</td>
<td>78</td>
<td>1.8 (0-44)</td>
</tr>
<tr>
<td>&gt; 2</td>
<td>18</td>
<td>8.5 (0-39)</td>
</tr>
</tbody>
</table>

*p < 0.001.

One pack = 20 cigarettes.
Cigarette smoking and other coronary risk factors—Table IV provides clinical and risk factor data for smokers and non-smokers and table V shows the relation between cigarette consumption and the presence of such risk factors. Significant direct correlations exist between cigarette consumption and systolic and diastolic blood pressure, serum triglyceride concentrations, and the ratio of total cholesterol to high density lipoprotein cholesterol. A significant inverse correlation exists with the serum high density lipoprotein cholesterol concentration.

The box shows the clinical and risk factor variables studied by

**TABLE IV**—Association between smoking habit and other coronary risk factors. (Three pipe and four cigar smokers excluded.)

<table>
<thead>
<tr>
<th></th>
<th>Non-smokers (n = 151)</th>
<th>Former smokers (n = 66)</th>
<th>Current smokers (n = 163)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of men</td>
<td>36</td>
<td>50**</td>
<td>94†</td>
</tr>
<tr>
<td>Sex</td>
<td>54 (9.5)</td>
<td>56? (9.5)</td>
<td>53 (9.2)</td>
</tr>
<tr>
<td>Mean (SD) (years)</td>
<td>142 (20.0)</td>
<td>189 (20.0)‡</td>
<td>197 (26.6)†</td>
</tr>
<tr>
<td>Mean (SD) systolic blood pressure (mm Hg)</td>
<td>82 (9.8)</td>
<td>87.2 (10.6)‡†</td>
<td>94.2 (11.7)</td>
</tr>
<tr>
<td>No with family history of ischaemic heart disease</td>
<td>32</td>
<td>22</td>
<td>49</td>
</tr>
<tr>
<td>No overweight</td>
<td>13</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>No with diabetes mellitus</td>
<td>5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mean (SD) blood glucose (mmol/l)</td>
<td>5.19 (1.71) n = 140</td>
<td>5.61 (1.12) n = 63</td>
<td>4.90 (1.71) n = 157</td>
</tr>
<tr>
<td>Mean (SD) total cholesterol (mmol/l)</td>
<td>5.96 (1.33) n = 134</td>
<td>6.16 (1.30) n = 61</td>
<td>5.90 (1.41) n = 149</td>
</tr>
<tr>
<td>Mean (SD) high density lipoprotein cholesterol (mmol/l)</td>
<td>1.20 (0.59) n = 133</td>
<td>1.09 (0.44) n = 61</td>
<td>1.12 (0.47) n = 148</td>
</tr>
<tr>
<td>Mean (SD) cholesterol ratio</td>
<td>5.40 (0.91) n = 133</td>
<td>6.06 (1.72)* n = 61</td>
<td>5.90 (2.18†) n = 148</td>
</tr>
<tr>
<td>Mean (SD) serum triglycerides (mmol/l)</td>
<td>1.59 (0.73) n = 133</td>
<td>1.98 (0.75) n = 61</td>
<td>1.74 (0.76) n = 149</td>
</tr>
</tbody>
</table>

Significance of difference between non-smokers and former smokers: *p < 0.05; **p < 0.01; ***p < 0.001. Significance of difference between non-smokers and current smokers: *p < 0.05, **p < 0.001. All other differences non-significant.

Fifteen per cent or more above mean weight for height. Total cholesterol: high density lipoprotein cholesterol.

Conversion: 1 mmol/l = 18 mg/100 ml. Cholesterol: 1 mmol/l = 38 mg/100 ml. Triglyceride: 1 mmol/l = 88.5 mg/100 ml.

**TABLE V**—Relation between total number of cigarettes smoked in life and other coronary risk factors

<table>
<thead>
<tr>
<th>Coronary risk factor</th>
<th>Median (range) No of cigarettes smoked</th>
<th>r</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.46 x 10¹⁰ (0.8-7.4 x 10¹⁰)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>0.002 x 10¹⁰ (0.8-8.0 x 10¹⁰)</td>
<td>0.040</td>
<td>0.364</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td></td>
<td>0.164</td>
<td>0.002</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td></td>
<td>0.175</td>
<td>0.001</td>
</tr>
<tr>
<td>Family history of ischaemic heart disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.09 x 10¹⁰ (0.8-6.8 x 10¹⁰)</td>
<td>0.028</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.40 x 10¹⁰ (0.8-5.4 x 10¹⁰)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.06 x 10¹⁰ (0.8-6.8 x 10¹⁰)</td>
<td>0.355</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.73 x 10¹⁰ (0.8-6.8 x 10¹⁰)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.06 x 10¹⁰ (0.5-5.4 x 10¹⁰)</td>
<td>0.239</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.73 x 10¹⁰ (0.8-6.8 x 1⁰¹⁰)</td>
<td>0.014</td>
<td>0.788</td>
</tr>
<tr>
<td>Blood glucose (n = 365)</td>
<td></td>
<td>0.023</td>
<td>0.667</td>
</tr>
<tr>
<td>Total cholesterol (n = 350)</td>
<td></td>
<td>0.014</td>
<td>0.788</td>
</tr>
<tr>
<td>High density lipoprotein cholesterol (n = 348)</td>
<td></td>
<td>0.023</td>
<td>0.667</td>
</tr>
<tr>
<td>Total: high density lipoprotein cholesterol ratio (n = 366)</td>
<td></td>
<td>0.162</td>
<td>0.003</td>
</tr>
<tr>
<td>Serum triglycerides (n = 349)</td>
<td></td>
<td>0.153</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Fifteen per cent or more above mean weight for height.

**Age**

Sex

Percentage above weight for height

History of angina

Family history of ischaemic heart disease

History of diabetes mellitus

History of hypertension

More than two blood pressure readings > 150/90 mm Hg

Systolic blood pressure at presentation

Diastolic blood pressure at presentation

Total number of cigarettes smoked

Total serum cholesterol concentration

High density lipoprotein cholesterol concentration

Total: high density lipoprotein cholesterol ratio

Fasting blood glucose concentration

Serum triglyceride concentration

*Order of entry to multiple regression equation for predicting coronary score (all p < 0.001).
multiple regression analysis, which showed diastolic blood pressure, cigarette consumption, age, ratio of total to high density lipoprotein cholesterol, and history of angina to be the important predictors of coronary score. No other variables were significant at 0.1% level.

Discussion

Our findings support the current epidemiological evidence in favour of an association between cigarette smoking and coronary artery disease. Such an association has not been reported previously in patients undergoing routine coronary arteriography, although a similar relation has been found in 113 patients with angina undergoing investigation before coronary bypass surgery. As there is no evidence to suggest that patients with valvular heart disease have more coronary atheroma than members of the general population we suggest that this relation between cigarette smoking and coronary artery disease may exist in the general population as well as in patients with clinical evidence of ischaemic heart disease.

An estimate of the total number of cigarettes smoked in life correlated with the overall severity of coronary artery disease as well as with the number of coronary arteries with appreciable stenoses. When assessing the importance of cigarette smoking as a risk factor for coronary artery disease we found that such an estimate of previous as well as current smoking habits (quantity and duration of risk exposure) was more valuable than the number of packs currently being smoked. Pack years (packs or fractions of packs per day time years) may be similarly useful. Former cigarette smokers—that is, people who, having smoked for at least 10 years, had stopped for at least one year—had less appreciable coronary artery disease than current smokers irrespective of whether they had stopped smoking five or 10 years before. The numbers of cigarettes smoked for current and former smokers did not, however, differ significantly. To our knowledge no current evidence is available to suggest that coronary atheroma per se regresses on stopping smoking, although the major epidemiological prospective studies have shown that subsequent death rates are lower in people who stop smoking than in those who continue smoking. The incidence in the occurrence of myocardial infarction and death after stopping smoking is likely to be due to some other beneficial effects of stopping such as lower catecholamine concentrations, lower serum cholesterol, reduced blood viscosity, reduced endothelial hypoxia, reduced platelet adhesiveness, or reduced tendency to ventricular arrhythmias.

Necropsy studies support the epidemiological and current arteriographic findings in showing an increased prevalence of coronary atherosclerosis in cigarette smokers. Auerbach et al initially reported advanced coronary atheroma three times more often in men smoking two packs (40 cigarettes) a day than in those not smoking regularly and subsequently reported that microscopic fibrous intimal thickening of coronary arteries was related to cigarette consumption. This relation was particularly pronounced in the myocardial arteries. Here the strongest association with cigarette smoking was found with hyaline thickening of the myocardial arteries, which was observed in 98% of those smoking two or more packs a day and never in non-smokers. Although in our study we could not assess this last correlation, these findings are important when relating the histopathological and clinical effects of cigarette smoking on the myocardium.

The complex interrelation between cigarette smoking and other cardiovascular risk factors makes assessing the importance of smoking habit as an independent risk factor for coronary artery disease difficult. We have shown the limited value of a history of cigarette smoking as a sole indicator of the presence and severity of coronary artery disease and presume that this is due to the multifactorial aetiology of the disease process. Nevertheless, here, and in a previous study, we have established using multiple regression analysis that an estimate of the number of cigarettes smoked in life can be useful for identifying patients with coronary artery disease when taken in conjunction with data on arterial blood pressure, age, family history of ischaemic heart disease, severity of angina, and the ratio of total to high density lipoprotein cholesterol.

We thank Mrs C A McLaughlin for typing the manuscript.

References

5. Kahan HA. The relationship of cigarette smoking to coronary heart disease; the second report of the combined group (of the Albany, NY and Framingham, Massachusetts) studies. JAMA 1964; 190: 866-90.

(Accepted 18 October 1984)

Correction

Perforation of intestinal duplication by enteroliths after trauma

We regret that an error occurred in this article by Mr P V Marks and Mr A E Stuart (22-29 December, p 1744). Mr A E Stuart’s name was wrongly spelt as A E Stunt.