

Case 2

A 26 year old waitress with chronic alcohol abuse was admitted because of increasing, predominantly left sided abdominal pain for three weeks, formation of ascites, and yellow vaginal discharge. Laboratory findings were normal except for a sedimentation rate of 44 mm in the first hour and platelet count of $511 \times 10^9/l$. Laparoscopy showed severe diffuse fibrinous peritonitis, most pronounced in the right upper quadrant, and a moderate amount of ascites. *C trachomatis* was cultured from the ascites and vaginal discharge. The patient was treated successfully with doxycycline 200 mg daily for 10 days.

Comment

Shabot and colleagues found *C trachomatis* in ascitic fluid of patients with chronic liver disease but were unable to say whether the organism was pathogenic in those cases.³ Diffuse peritonitis and ascites formation in our patients without chronic liver disease were definitely due to an infectious agent, as shown by the rapid response to antibiotic treatment. Preceding genital infection and manipulation of the uterus are classic features of the Fitz-Hugh-Curtis syndrome.⁴ *C trachomatis* was the most likely aetiological agent in both patients.

In case 2 the organism was cultured from the cervical secretion and ascitic fluid and in case 1 the patient showed a fourfold decline of immunofluorescent IgM antibodies after treatment.⁵

These two patients show that *C trachomatis* may cause severe chronic peritoneal infections with chronic ascites formation. Timely diagnosis and correct treatment lead to rapid cure.

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Cigarette smoking and risk of premature stroke in men and women

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Abstract

A case-control study was carried out of the relation between cigarette smoking and hypertension and stroke. A total of 132 cases of stroke (79 in men, 53 in women) identified as a part of a population based register were compared with 1586 controls (1017 men, 569 women) from a survey of cardiovascular risk factors conducted in the same population. Cigarette smokers had a threefold increase in the risk of stroke compared with current non-smokers. This association remained significant after adjusting for hypertension. Those who both smoked and had hypertension had an increased risk of stroke of almost 20-fold compared with those who neither smoked nor had hypertension.

Overall, in this population roughly 37% of stroke events may be attributed to cigarette smoking and 36% to hypertension.

Introduction

High blood pressure is consistently reported as the most important known risk factor for stroke.¹⁻⁴ Other risk factors such as cigarette smoking or serum lipid, blood glucose, and plasma fibrinogen concentrations have shown varying associations.^{3,4} In particular,

many studies have failed to identify cigarette smoking as a significant risk factor for stroke. When a positive association has been found this has usually been confined to young men.^{5,6}

We present a population based case-control analysis of the association of cigarette smoking and hypertension with stroke in both men and women. The proportions of stroke events that could be attributed to smoking and hypertension are also estimated as this does not appear to have been done before. In addition, the study investigates the possible synergism between smoking and hypertension.

Subjects and methods

Cases of stroke were identified from a population based cardiovascular disease register, in which a 50% random sample of all new episodes of stroke in Auckland was studied in the year ending 1 March 1982. The study area (population 829 545) encompassed one quarter of the total population of New Zealand. Full details of the case finding methods have been published.⁷ The diagnostic criteria and methods were based on the World Health Organisation guidelines.⁸ Stroke was defined as the rapid onset of focal neurological deficit, presumably of vascular origin, lasting 24 hours or longer or leading to death. Patients with subarachnoid haemorrhage were excluded.

Information was obtained from patients using a standard questionnaire as soon after the event as possible. If the patient had died the same questionnaire was administered to a close relative after six weeks. Details about treatment for high blood pressure and cigarette smoking were collected. Current pharmacological treatment for high blood pressure was used as a surrogate measure of hypertension. A current smoker was defined as a person smoking at least one cigarette a day.

Controls for the analysis came from a population based survey in Auckland, the sampling methods and results of which have been reported.⁹ Briefly, 1017 men and 569 women aged 35-64 were interviewed between January and July 1982 after being randomly selected from the 1981 Auckland general electoral rolls (response rate 82%). The questionnaire included the same questions about blood pressure history and cigarette smoking as were asked of the patients with stroke.

Analyses were restricted to events that occurred in men and women aged

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35-64. Odds ratios (OR), used as estimates of relative risks, were calculated using the Mantel-Haenszel method, controlling for age.¹⁰ Confidence limits (CL) of the relative risks were calculated by the test based method of Miettinen.¹⁰ As a measure of the importance of smoking and hypertension to public health population attributable risks were calculated using the maximum likelihood method of Whittemore.¹¹ Multiplicative and additive models were compared using the method of Breslow and Storer.¹²

Results

Table I gives the age and sex distribution of the patients with stroke (cases) and the community controls. A total of 132 cases (79 men, 53 women) were available for comparison with 1586 controls (1017 men, 569 women). The cases included 105 patients with a first episode of stroke and 27 with recurrent strokes. Results are presented for the total group since these were the same whether or not analyses were restricted to the incident cases.

TABLE I—Patients with stroke and community controls distributed by age, sex, hypertension, and smoking state

	Patients with stroke		Community controls	
	Men	Women	Men	Women
Total	79	53	1017	569
Age (years):				
35-44	10	3	226	201
45-54	21	16	430	194
55-64	48	34	361	174
Hypertensive	35	22	111	74
Smoker	43	23	284	140
Both hypertensive and smoker	16	8	22	11

HYPERTENSION

Those being treated for hypertension at the time of the stroke were compared with those not currently having treatment. This second group included subjects who had been treated for hypertension in the past. Altogether 111 men (11%) and 74 women (13%) in the control group were receiving treatment for hypertension compared with 35 (44%) of the men and 22 (42%) of the women with stroke. Table II shows the relation between hypertension and the risk of stroke, controlling for age. For men and women combined hypertension was associated with a fourfold increase in the risk of stroke (OR 4.1; 95% CL 2.8, 5.7). The association was stronger in men than in women but not significantly so ($p > 0.05$).

TABLE II—Risk of stroke associated with hypertension and smoking, controlling for age. Results expressed as odds ratios

Risk factor	Men	Women	Both sexes*
Hypertension	5.0 (3.2, 7.8)†	3.0 (1.7, 5.3)	4.1 (2.8, 5.7)
Smoking	3.1 (2.0, 4.9)	2.6 (1.4, 4.6)	2.9 (2.0, 4.1)

*Also controlling for sex.

†95% Confidence limits in parentheses; all categories significant ($p < 0.001$).

CIGARETTE SMOKING

Current cigarette smokers were compared with subjects not smoking at the time of the stroke. This second group included ex-smokers. Among the controls 284 (28%) of the men and 140 (25%) of the women were current smokers compared with 43 (54%) and 23 (43%) of the men and women with stroke. Smoking was significantly associated with an increased risk of stroke (OR 2.9; 95% CL 2.0, 4.1) (table II). As with hypertension the relation between cigarette smoking and stroke was significant in both men and women; the difference in risk between the sexes, however, was not significant.

Figure 1 shows evidence of a dose response relation between the number of cigarettes smoked and the risk of stroke. The risk for those smoking 1-20 cigarettes a day was 3.3 compared with non-smokers (95% CL 2.0, 5.5), while the risk for heavier smokers (more than 20 cigarettes a day) was 5.6 (95% CL 3.2, 9.9) compared with non-smokers. The pattern was similar when men and women were analysed separately. No significant difference in

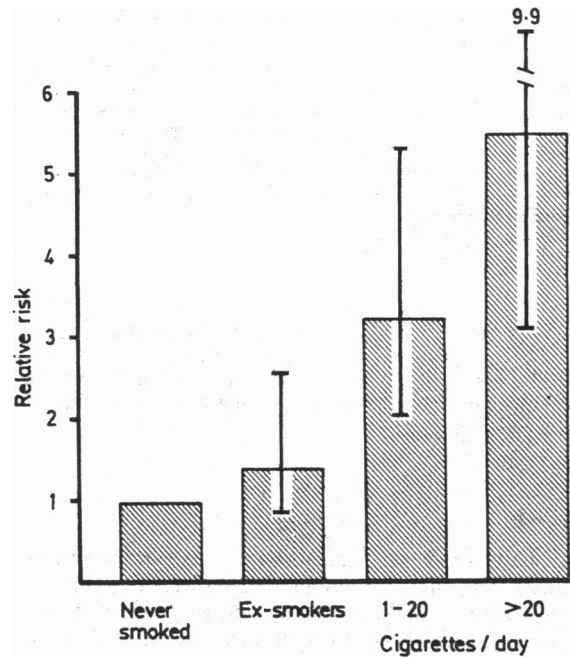


FIG 1—Cigarette smoking and risk of stroke, adjusted for age and sex. Bars are 95% confidence limits.

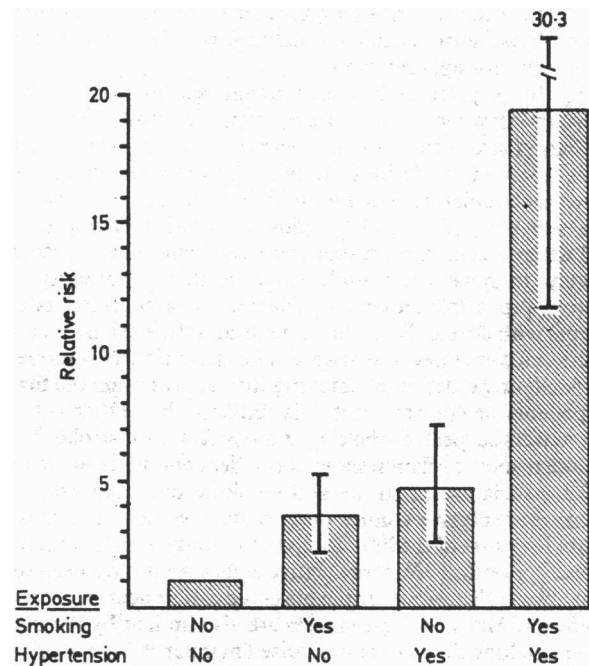


FIG 2—Smoking, hypertension, and risk of stroke, adjusted for age and sex. Bars are 95% confidence limits.

risk was found between ex-smokers and non-smokers (OR 1.4; 95% CL 0.8, 2.6).

Calculations by the Mantel-Haenszel method showed that cigarette smoking and hypertension did not confound each other's association with an increased risk of stroke. By contrast, figure 2 shows that the risk associated with both variables combined (OR 18.6; 95% CL 11.6, 30.3) was similar to the product of the risk of smoking (OR 3.4; 95% CL 2.1, 5.3) and hypertension (OR 4.4; 95% CL 2.7, 7.1). The use of Breslow and Storer's methods confirmed that the relation was multiplicative rather than additive, suggesting a synergistic effect between smoking and hypertension on the risk of stroke.

Estimates were made of the proportion of stroke events that could be attributed to smoking or hypertension, or both. Table III shows that in this population cigarette smoking and hypertension were equally important in both men and women. Overall, 37% and 36% of the stroke events could be attributed to cigarette smoking and hypertension, respectively. Roughly two

TABLE III—Percentage of cases of stroke attributable to smoking or hypertension or both, controlling for age

Risk factor	Men	Women	Both sexes
Smoking*	40 (25, 54)‡	29 (12, 46)	37 (26, 48)
Hypertension†	37 (24, 49)	30 (14, 46)	36 (26, 46)
Smoking or hypertension or both	64 (49, 79)	50 (29, 71)	58 (46, 70)

*Controlling for hypertension.

†Controlling for smoking.

‡95% Confidence limits in parentheses.

thirds of the stroke events in men and half of the stroke events in women were attributable to these two risk factors. Sixteen of the men (20%) and eight of the women (15%) with stroke were exposed to both risk factors compared with only 22 of the men (2%) and 11 of the women (2%) in the control group (table I).

Discussion

This analysis based on patients with stroke and controls sampled at random from the same population showed a strong association between cigarette smoking and an increased risk of stroke in men and women aged 35-64. Furthermore, the risk associated with cigarette smoking was similar to that associated with hypertension in men and women. A dose response relation was found between the number of cigarettes smoked and the risk of stroke. The relative risks presented are likely to be conservative because for both cases and controls the non-smoking category included ex-smokers and the non-hypertension category included people with a past history of treatment for hypertension.

High blood pressure has been recognised for years as the most important risk factor for stroke, while in most reviews of the aetiology of stroke the evidence regarding cigarette smoking has not been consistent.^{3,4} We have confidence in our results because the study was population based with high response rates (over 95% of cases and 82% of controls), reducing the risk of selection bias. Well defined standard criteria were used and stroke events were unlikely to have been undetected in this community among controls. A possible uncertainty concerns the risk factor state of the patients with stroke. Both the patients and their relatives as well as the interviewers knew the disease state at the time of interview. No independent validation of smoking history was available for either the patients or controls, but it is unlikely that either patients or interviewers suspected smoking as a risk factor for stroke. Further, the dose response relation shown provides confidence in the results.

The association of stroke and smoking has been examined in several retrospective studies but results have not been consistent, possibly because of the limitations of the study design or methods of analysis, or both.¹³⁻¹⁷ Where positive associations have been found it is not always clear whether the observed differences are statistically significant. Many of these studies are also limited by the failure to gather smoking data in a standardised manner.¹³⁻¹⁷

Prospective studies of the relation between smoking and mortality from stroke, usually confined to men,¹⁸⁻²⁶ have also yielded conflicting results. While some studies have shown an overall association between smoking and subsequent stroke¹⁸⁻²² and others have shown this in restricted age groups,²³ a similar number have failed to detect a positive association.²⁴⁻²⁸ An unequivocal association has not been found in women.^{5, 29, 30} No explanation is apparent for these discordant results, though the lack of significant findings may possibly be due to the small numbers of patients in several of these studies.

Estimates of the proportions of cases of stroke in the community attributable to high blood pressure (36%) and cigarette smoking (37%) in this study suggest that these risk factors are of comparable importance for public health. Evidence of a synergistic effect of smoking and hypertension on the risk of stroke had been suggested in a study of Harvard alumni, although in that study the presence of synergism was not evaluated statistically and the risk factor data were not collected in a standardised manner.³¹

Though our study was confined to subjects aged less than 65, a

quarter of all strokes occur in this age group.³² Extrapolation from our results to the population of New Zealand aged 35-64 suggests that roughly 600 (95% CL 470, 740) new episodes of stroke each year may be explained by smoking or hypertension, or both, among people in this age group.

Given the large decline in mortality from stroke in New Zealand in recent years,³³ relatively little of which can be explained by improvements in the treatment of hypertension,³⁴ the contribution of the decline in cigarette smoking which has also occurred over this period³⁵ warrants further attention. Further reduction in the prevalence of smoking in the population, especially in those already being treated for hypertension, may contribute more to the prevention of stroke than has previously been acknowledged.

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