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JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Stroke 1974;5;483-486

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 72514
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1524-4628

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Cigarette Smoking and Strokes

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Abstract:
*Cigarette
Smoking
and
Strokes*

■ Utilizing a defined general population, two investigations were conducted in Washington County, Maryland. In the eight-year mortality study, the relative risk of stroke among cigarette smokers was only 0.85 as compared to nonsmokers. In the two-year morbidity investigation, limited to stroke cases occurring after the age of 50, it appears that the association of cigarette smoking to strokes in the older age groups is at most very small.

In atherosclerotic strokes, there may be an association with cigarette smoking, but only in the younger age groups, as suggested by two other studies. In order to investigate this possibility a retrospective case/control study of young cases is recommended. If there is no age dependency of atherosclerotic strokes, this implies that cigarette smoking may not be associated with the atherosclerotic process in cerebral and coronary arteries.

Additional Key Words
atherosclerosis

cerebral thrombosis
coronary arteries

cerebral hemorrhage

□ Several major prospective studies have yielded discrepant results regarding the relationship between cigarette smoking and strokes. Dorn's study was based on over 290,000 U.S. Government Life Insurance policyholders, virtually all of whom were males.¹ He found that the risk of a stroke death among cigarette smokers was 1.4 times that of nonsmokers. He also noted a progressive increase in stroke death rates with greater daily cigarette consumption, and a decrease in cerebrovascular death rates among ex-cigarette smokers as compared to cigarette smokers. In contrast, Doll and Hill's² investigation of approximately 34,000 British male physicians showed a relative risk for stroke mortality of only 1.12 among cigarette smokers. In addition, they did not find a progressive increase in stroke deaths with greater daily cigarette consumption nor a decrease in rate among ex-smokers. In support of Doll and Hill's findings, Paffenbarger's³ observations of longshoremen revealed a relative risk of only 1.1 for fatal strokes among those who smoked 20 or more cigarettes a day.

In the American Cancer Society study involving

a million participants, Hammond⁴ looked at cerebrovascular death rates by the number of cigarettes smoked daily, degree of inhalation, and the age when the subject started to smoke. He found no clear-cut relationship among men between stroke deaths and any of these three exposure variables. Among women, cigarette smokers had an increased risk of dying from stroke, varying from 2.11 in the 45 to 54 age group to 1.18 in those 75 to 84. There also was a tendency for stroke death rates among women to increase with increased exposure to cigarette smoking, but the small numbers of deaths made the degree of association uncertain.

Two additional investigations separated the stroke cases into different diagnostic categories. A relative risk among cigarette smokers of 1.61 for occlusive stroke mortality and 1.32 for hemorrhagic stroke mortality was noted by Paffenbarger⁵ in his investigation of former male college students. In the Framingham study,⁶ the risk of having an atherothrombotic brain infarction was more than three times greater for a male cigarette smoker than for a nonsmoker. This estimate was based on only 47 cases accumulated over a 16-year period.

Because of these variable findings, it seemed worthwhile to investigate the association of cigarette smoking and strokes under somewhat different circumstances than the studies summarized above.

Methods

Two investigations in Washington County, Maryland, made it possible to examine the relationship of smoking to strokes. Both were based on a private census of the county undertaken in 1963 by the Johns Hopkins School of Hygiene and Public Health, the National Cancer Institute, and the Washington County Health Department.⁷ Information was obtained from more than 98% of the households in the coun-

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*Completed during tenure as an established investigator of the American Heart Association.

Supported in part by research grant PH-86-68-195 from the Public Health Service, U.S. Department of Health, Education, and Welfare; by research grant MH 19844 from the National Institute of Mental Health; by Career Research Award HL 21670 from the National Heart and Lung Institute, Public Health Service, U.S. Department of Health, Education, and Welfare; by general preventive medicine residency traineeship 5-A08-A800059-05 from the Division of Allied Health Manpower, National Institutes of Health; by Program Project Grant No. NS 06229 from the National Institute of Neurological Diseases and Stroke.

ty and included a smoking history in addition to the usual demographic and identification information. County residents were asked if they had ever smoked cigarettes, cigars or pipes; if they were presently smoking cigarettes; and, if so, what was the greatest number of cigarettes they ever smoked regularly. The small proportion of persons who failed to give a complete smoking history have been excluded from the following analyses.

In 1971, the whereabouts of a 5% sample of the 91,909 persons enumerated in the census was determined. From this information, it was possible to estimate the census population still living in the county at the midpoint of each of the two study periods.

MORTALITY INFORMATION

As part of a study of the association of church attendance and health, death certificates of residents of Washington County were matched to the 1963 census listings for an eight-year period from July 15, 1963, to July 15, 1971. The underlying cause of death was assigned by one of the authors (GWC), whose coding was checked for the first three years by an experienced nosologist. Stroke deaths for this part of the study are those allocated to rubrics 331,332, and 334 of the seventh revision of the International Classification of Diseases. Stroke mortality was calculated for persons who did and did not smoke cigarettes in 1963 and were 25 years of age and older at that time. The rates were adjusted for differences in race, sex, age and socioeconomic status by a binary multiple regression technique.⁸

MORBIDITY INFORMATION

As part of the Collaborative Community Stroke Study,⁹ records of Washington County's only general hospital were reviewed every week to record each stroke episode that occurred during the 26-month period from January 1, 1969, through February 28, 1971. The ten smaller hospitals in neighboring counties and 11 nursing homes in adjacent counties were checked every two months for admissions of stroke patients from Washington County.

The minimum criteria for classification as a stroke were a hospital discharge diagnosis of a stroke and at least one of the following clinical or laboratory findings: (1) a specific diagnosis of a stroke based on craniotomy or carotid surgery; (2) a specific diagnosis of a stroke as a cause of death based on autopsy findings; (3) positive physical examination or laboratory findings of: (a) aphasia or slurred speech; (b) weakness or paralysis of at least one extremity; (c) stiff neck, nuchal rigidity, Kernig's or Brudzinski's sign; (d) lumbar puncture with opening pressure greater than 150 mm H₂O or with xanthochromia or gross blood or with more than 999 red blood cells per cubic millimeter; (e) angiography showing occluded or stenosed intracranial or extracranial vessels or intracranial aneurysm with or without clot.

Although any stroke occurring during the 26-month period was recorded regardless of whether it was an initial or recurrent attack, a patient was counted only once. The type of stroke stated in the hospital discharge summary or in the autopsy report was accepted for this study, following the categories given in rubrics 430 to 435 of the eighth revision of the International Classification of Diseases, with an undifferentiated category added to include diagnostic causes in rubrics 436 to 438.

Records of these stroke cases were matched against alphabetical listings from the 1963 private census of

Washington County. The study population was limited to whites over the age of 45 years in 1963 because of the very small number of persons from other ethnic groups in the county and the small number of stroke cases below the age of 45. As a result of this age limitation, all of the stroke episodes which caused a person to be identified as a case for this part of the study had to have occurred after the age of 50, because the youngest person in the population was 45 years old in July 1963 and case collection did not begin until 1969. A total of 313 persons met the clinical and demographical criteria for inclusion in the morbidity study.

Stroke rates were calculated for cigarette smokers, ex-cigarette smokers, and nonsmokers, according to their status in 1963. To remove the effects of differences in age distributions, the rates were adjusted by the direct method.

Results

MORTALITY

In the eight-year period after the 1963 census, a total of 659 stroke deaths occurred among the 47,423 Washington County residents identified as being 25 years of age or older at that time. The stroke death rates for smokers and nonsmokers are shown in table 1. The unadjusted death rates among smokers was much lower than among nonsmokers but adjustments for the effects of demographical and socioeconomic factors, especially age, brought the rate among smokers up much closer to that among nonsmokers. The relative risk of stroke mortality among smokers was only 0.85.

MORBIDITY

Of the 313 cases of stroke in the morbidity study population, there were 15 persons with subarachnoid hemorrhage, 13 with cerebral embolism, 12 with occlusion of the precerebral arteries, and six with transient cerebral ischemia. Because of the small numbers in each of these categories, they have been excluded from the analysis. Among the 267 cases remaining, and hereafter classified as total strokes, there were 157 persons with cerebral thrombosis, 54 with cerebral hemorrhage, and 56 in the undifferentiated category.

The average annual age-adjusted stroke rates by cigarette smoking history and diagnostic groups are

TABLE 1

Stroke Death Rates Among Washington County Residents 25 Years of Age and Older, for the Period 1963 to 1971, by Cigarette Smoking Status in 1963

Cigarette smoking status	Midpoint population	Number	Stroke deaths	
			Unadjusted	Rates* Adjusted†
Total	42,017	659	196	—
Smoker	17,547	121	86	178
Nonsmoker	24,470	538	275	209

*Average annual deaths per 100,000.

†Adjusted for effects of race, sex, age, marital status, housing, education and church attendance.

CIGARETTE SMOKING AND STROKES

TABLE 2

Average Annual Age-Adjusted Case Rate/1,000 by Sex and by Diagnosis and Cigarette Smoking Status in 1963

Cigarette smoking status	Cerebral thrombosis		Cerebral hemorrhage		Undifferentiated		Total
	Males						
Present	2.7	(25)	1.2	(12)	1.3	(13)	5.2 (50)
Past only	3.5	(17)	1.1	(5)	1.0	(5)	5.6 (27)
Never	3.4	(24)	1.4	(10)	1.0	(7)	5.8 (41)
	Females						
Present	4.2	(14)	1.0	(3)	0.5	(1)	5.7 (18)
Past only	4.0	(4)	2.2	(2)	1.6	(2)	7.8 (8)
Never	3.7	(73)	1.1	(22)	1.4	(28)	6.2 (123)

Numbers of cases in parentheses.

given for men and women in table 2. In general, persons who smoked cigarettes in 1963 had lower rates than nonsmokers. The relative risk associated with cigarette smoking for men was 0.90 for all strokes (5.2/5.8) and 0.79 for cerebral thrombosis (2.7/3.4). For women it was 0.92 for all strokes and 1.14 for cerebral thrombosis.

The 95% confidence limits of these relative risks were determined by Woolf's method.¹⁰ The results, together with the relative risks, are shown in table 3.

Table 4 shows the average annual age-adjusted stroke rates according to the greatest number of cigarettes smoked regularly. Ex-smokers have been excluded from this table. There was no indication that stroke rates were associated with the number of cigarettes smoked daily. When each diagnostic group was analyzed separately, there was still no evidence of a dose-response effect.

Discussion

When smoking histories are taken at the start of observation in a prospective study, ex-smokers may be weighted with persons who have recently given up the habit because of ill health. As Hammond and Garfinkel¹¹ have pointed out, this can cause abnormally high rates among ex-smokers. Under these circumstances, if ex-smokers are classed as nonsmokers, a relative risk associated with smoking can thereby be obscured. In the present morbidity study, this

possibility was minimized by identifying cases five to seven years after the smoking history was obtained. The possibility of misclassification resulting from persons starting to smoke at this age seems remote.

In considering the validity of the clinical diagnosis of a stroke, Kuller and colleagues¹² analyzed the charts of hospitals in the counties of eastern and western Maryland. The review diagnosis of a stroke agreed with that in 124 (82.1%) of 151 charts listing a stroke diagnosis; in only 13 (3%) of 432 hospital records without a cerebrovascular disease diagnosis did the reviewer make a stroke diagnosis. In the present report, the validity of the diagnosis of a stroke is probably better than the preceding figures suggest because the record review occurred before a case was accepted for the study.

A measure of the accuracy of the diagnosis of each type of stroke was not available in this investigation. However, the predominance of cases of cerebral thrombosis in this population-based study was similar to the findings from other population surveys.^{6, 13}

Between this and other prospective studies of cigarette smoking and strokes, there are a number of procedural differences, which on balance seem advantageous, in that the association can be examined under somewhat different circumstances. Five of the previous studies were essentially limited to males,^{1-3, 5, 6} and three of them were heavily weighted with persons of

TABLE 3

Relative Risks of Stroke and Cerebral Thrombosis Associated With Cigarette Smoking, by Sex

	Relative risk	95% confidence limits of the relative risk
Total strokes		
Men	0.90	0.56 - 1.45
Women	0.92	0.55 - 1.56
Cerebral thrombosis		
Men	0.79	0.45 - 1.55
Women	1.14	0.61 - 2.09

TABLE 4

Average Annual Age-Adjusted Case Rate/1,000 by Sex and Amount of Cigarettes Smoked Daily in 1963

Cigarettes smoked daily	Men	Women
None	6.1 (41)	6.0 (123)
Less than 10	3.2 (5)	6.0 (8)
10 - 20	6.6 (31)	6.2 (9)
21 - 40	3.9 (12)	1.0 (1)
41+	2.3 (1)	0 (0)
Not stated	4.2 (1)	0 (0)

Numbers of cases in parentheses.

middle to upper socioeconomic status.^{1, 2, 5} The present study was conducted in a defined general population which included both sexes and a broad range of socioeconomic circumstances. Unfortunately, the population of Washington County is deficient in ethnic groups other than whites.

The five larger studies were limited to fatal cases of stroke and were not able to refine the death certificate diagnosis by record reviews.¹⁻⁵ This was also the situation with respect to the mortality study in the present report. With respect to diagnostic validity, the present morbidity study probably ranks between the large prospective studies using death certificate diagnoses and the Framingham study. It shares with Framingham the advantage of including a range of fatal and nonfatal cases and has the advantage over Framingham in having an appreciably larger case group.

In this study and the four studies which combined all cases of stroke in one category, the vast majority of strokes occurred after the age of 55.¹⁻⁴ Although differences in relative risks found in these studies have been emphasized, calculation of confidence limits indicates that it is probable that most, if not all, of the observed differences could have occurred by chance. If that be so, the average of the relative risks might be closer to the truth than the result of any single study. It appears likely, therefore, that the association of cigarette smoking with all strokes in the older age groups is at most very small.

In atherosclerotic strokes, the Framingham study and Paffenbarger's investigation of former college students included a greater percentage of young stroke cases under the age of 55. Because these two studies found an association between cigarette smoking and atherosclerotic strokes and the present study did not, it may be that the association is age dependent. In order to further investigate this possibility of age dependency, a very large population base would be required because of the very low incidence of this type of stroke in younger age groups. Therefore, only a retrospective case/control study is likely to clarify the association in young adults.

If the relationship between cigarette smoking and atherosclerotic strokes is not age dependent, it follows that cigarette smoking may not be associated with the atherosclerotic process per se. This in turn suggests that the commonly observed association of cigarette smoking with arteriosclerotic heart disease operates

through some mechanism other than an effect on atherosclerosis of coronary vessels, or that cigarette smoking has a differential effect on the coronary as compared to the cerebral arteries.

Finally, it is possible but unlikely that, compared to nonsmokers, more cigarette smokers in whom a stroke would have developed at an older age succumbed at an earlier age from arteriosclerotic heart disease.

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