

# Distribution of Cerebral Atherosclerosis by Geographic Location, Race, and Sex

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Mortality rates from vascular lesions of the central nervous system differ among populations,<sup>177, 415, 477</sup> and increasing mortality rates for these diseases have accompanied rising death rates for coronary heart disease.<sup>284, 479</sup> Little is known, however, about the severity of the arterial lesions of cerebral atherosclerosis among populations or about its association with the reported differences in mortality rates.

Most investigators concerned with atherosclerosis of the cerebral arteries have studied stenosis and thrombosis in cases with central nervous system disease.<sup>216, 217, 442, 480</sup> In this study, severity of cerebral atherosclerotic lesions has been determined quantitatively in persons from different geographic and ethnic groups. This study was conducted as a part of the International Atherosclerosis Project, an international cooperative survey of atherosclerosis in autopsied persons from different geographic and ethnic groups. The results indicate that there are differences in cerebral atherosclerosis among groups of persons from different countries and races. The differences appear at ages much younger than the ages in which clinically manifest cerebral vascular disease occurs.

## MATERIALS AND METHODS

### COLLECTION OF ARTERIES

Cooperating pathologists in five countries collected 1547 sets of cerebral arteries from autopsied persons 10 to 69 years of age between August 1961 and September 1965.<sup>215, 312, 400</sup> These cerebral arteries were collected from persons whose coronary arteries and aortae were included in a larger study of the geographic pathology of atherosclerosis. A technician in each laboratory opened the arteries longitudinally, fixed them in formalin with the adventitial surfaces adhered to cardboard, and packaged them in plastic bags.<sup>198</sup> The pathologist submitted the arteries to a central laboratory with identifying and accessory clinical and pathologic data. The central laboratory staff screened the arteries for quality of dissection and completeness of data, stained them with Sudan IV, and repackaged them in plastic bags.<sup>198</sup>

### DEFINITION OF TERMS

As used in this study, the term "cerebral arteries" refers to both the extracranial and intracranial cerebral arteries supplying the brain. The following segments of the extracranial cerebral arteries are considered separately: the left common carotid artery from its origin to its bifurcation into the internal and external carotid

artery; the right common carotid artery from its origin to the bifurcation; internal carotid arteries, including the petrous and cavernous portions, from their origin to their points of entrance into the cranial cavity; and the vertebral arteries from their origin to their points of entrance into the cranial cavity. The intracranial portions of the internal carotid arteries and vertebral arteries removed with the other intracranial arteries are not considered in this study. The intracranial arterial segments considered separately include main trunks of the middle cerebral arteries from their origin to their first major bifurcations into Sylvian branches, and the entire basilar artery.

### GRADING ATHEROSCLEROSIS

The supervising statistician assigned each set of coronary arteries and each aorta to one member of a team of five pathologists for grading.<sup>198</sup> A different team of two pathologists working together graded each set of cerebral arteries. The graders estimated the percentage of intimal surface involved by each of four different types<sup>198, 400</sup> of atherosclerotic lesions (fatty streaks, fibrous plaques, complicated lesions, and calcified lesions) in each common carotid artery, internal carotid artery, vertebral artery, and middle cerebral artery, and also in the basilar artery.

### DATA PROCESSING AND ANALYSIS

The statistical laboratory transferred coded information and estimates of atherosclerosis to punched cards and performed tabulations and computations with electronic data-processing equipment. The laboratory computed mean values for extent of atherosclerosis by geographic origin, race, age, sex, type of lesion, artery, and cause of death.

An over-all mean for raised atherosclerotic lesions (the sum of percentage of intimal surface involved with fibrous plaques, complicated lesions, and calcified lesions) was computed for the aorta and coronary arteries for each location-race group; then the groups were ranked from highest to lowest according to that mean.<sup>436</sup>

### SELECTION OF MEASURES OF LESIONS

The percentage of intimal surface involved with raised atherosclerotic lesions was used as the most meaningful measure of atherosclerosis. Complicated lesions and calcified lesions are rare in the cerebral arteries from many location-race groups; thus mean values for percentage intimal surface involvement have little mean-

ing. Therefore, we compared the percentage of cases positive (prevalence) for each type of lesion, as well as extent of lesions.

In order to make comparisons of prevalence and mean extent of lesions among subgroups, arterial segments were combined into the following major groups:

*Carotid Arteries.* Left and right common and extracranial internal carotid arteries, including the petrous and cavernous portions.

*Vertebral Arteries.* Extracranial portions of the two vertebral arteries.

*Intracranial Arteries.* The two middle cerebral arteries and the basilar artery.

#### SELECTION OF CASES FOR GEOGRAPHIC COMPARISONS

Persons with coronary heart disease, hypertension, peripheral arterial disease, diabetes mellitus, cerebral infarction, and cerebral hemorrhage are reported to have more atherosclerosis in the cerebral arteries than those who do not have these diseases.<sup>25, 169, 170, 192, 234, 313</sup> These cases were divided into those with and those without clinical or morphologic evidence of coronary heart disease, cerebrovascular disease, hypertension, diabetes mellitus, syphilitic or other types of aortitis, chronic renal disease, and other atherosclerotic complications such as peripheral vascular disease, aortoiliac occlusion, and mesenteric thrombosis. For convenience, this group is referred to as associated diseases. The two groups of cases were analyzed separately. The persons who had no clinical or morphologic evidence of the diseases listed above formed a basal group for location-race comparisons.<sup>436</sup>

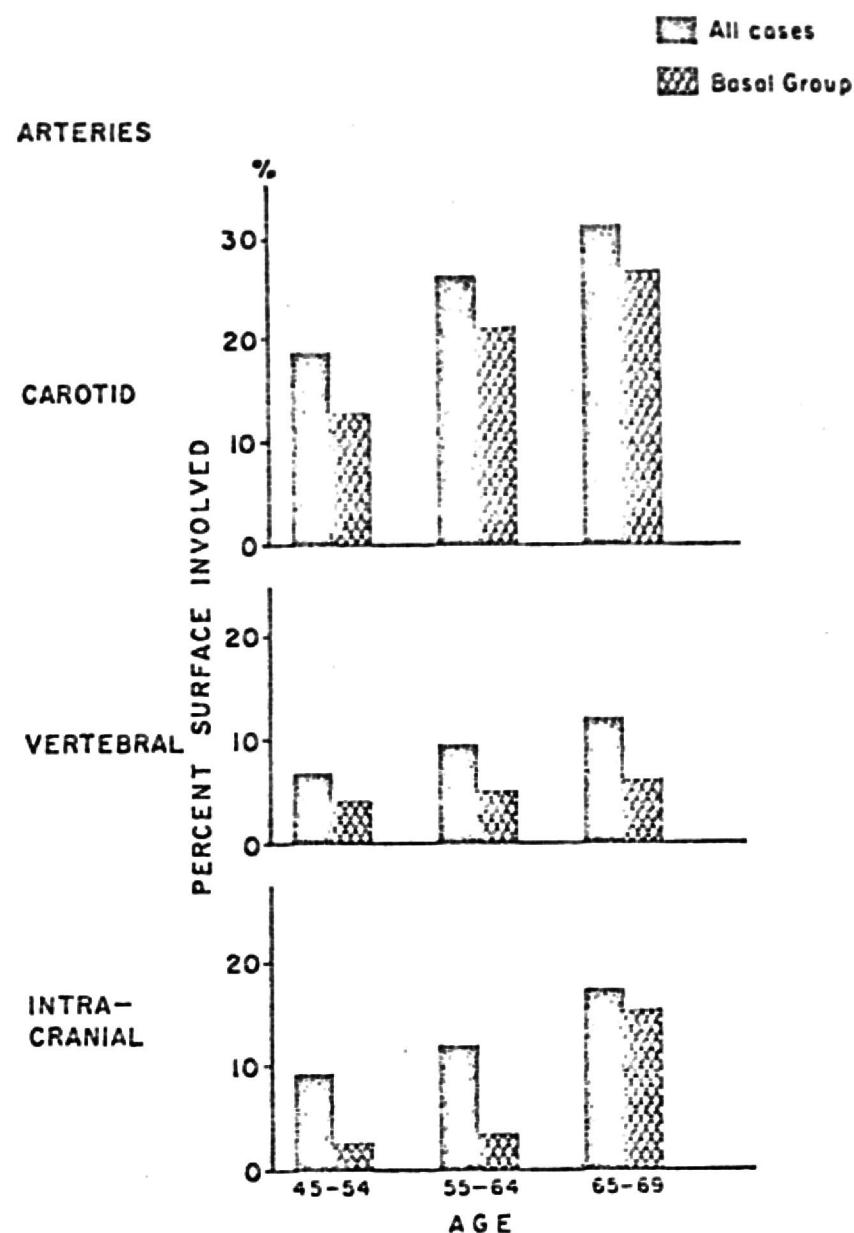
After the basal groups of cases were further divided by age and sex, small numbers of cases were present in many subgroups. Only the Oslo (Norway) and Guatemala collections contained five or more cases in each subgroup and were used to make the principal comparisons. These two locations differ greatly in prevalence of cerebrovascular diseases<sup>222, 477</sup> and also in prevalence and extent of aortic and coronary artery raised atherosclerotic lesions.<sup>436</sup> Cases from New Orleans (Louisiana), Santiago (Chile), and Jamaica were used in selected comparisons.

#### RESULTS

##### DIFFERENCES IN ATHEROSCLEROTIC LESIONS BETWEEN THE TOTAL SAMPLE AND THE BASAL GROUP

Fatty streaks in the basal group differ only slightly from fatty streaks in the total sample (data not shown). The mean extent of raised atherosclerotic lesions in the total sample of Oslo cases and that of the basal group of Oslo cases are compared in Figure 1. Raised lesions are more extensive, on the average, in all cases than in the basal cases. The difference between all cases and basal cases is approximately equal in both sexes. These trends are similar in Guatemalans. The greater extent of lesions in all cases as compared with the extent in basal cases was also found in a larger sample of aortae and coronary arteries.<sup>436</sup>

The differing proportions of persons with diseases associated with atherosclerosis among location-race sub-



Note: All illustrations were derived from the International Atherosclerosis Project, 1960 to 1965.

FIG. 1. Extent of raised atherosclerotic lesions in the cerebral arteries of Oslo men by age and arterial segments, using the total sample of cases (all cases) and a subsample of cases (basal group of cases) which were formed by excluding persons having coronary heart disease, peripheral arterial disease, cerebral hemorrhage and infarction, other atherosclerotic complications, chronic renal disease, hypertension, and diabetes mellitus.

groups would introduce serious bias in the samples. Therefore in comparing the various subgroups in this study, only the basal group was used.

#### VARIABILITY IN LESIONS

The extent of fatty streaks and raised atherosclerotic lesions (Figs. 2 and 3) in the cerebral arteries varies from one person to another, even in the most homogeneous subgroups. This variability demonstrates the need for large samples when comparisons among location-race groups are based on mean extent of lesions.

#### PREVALENCE OF ATHEROSCLEROTIC LESIONS BY AGE

All four types of atherosclerotic lesions are more prevalent in the carotid arteries than in the vertebral arteries or intracranial arteries. Fatty streaks are present in the carotid arteries of all persons in the age groups studied. Complicated lesions and calcified lesions are rare in all arteries except the carotid arteries in which calcified lesions are moderately common. The prevalence of fatty streaks in the vertebral and intracranial arteries increases in succeeding age groups (Table 1). The prevalence of fibrous plaques increases in each succeeding age group in all arteries (Table 2), and so does the prevalence

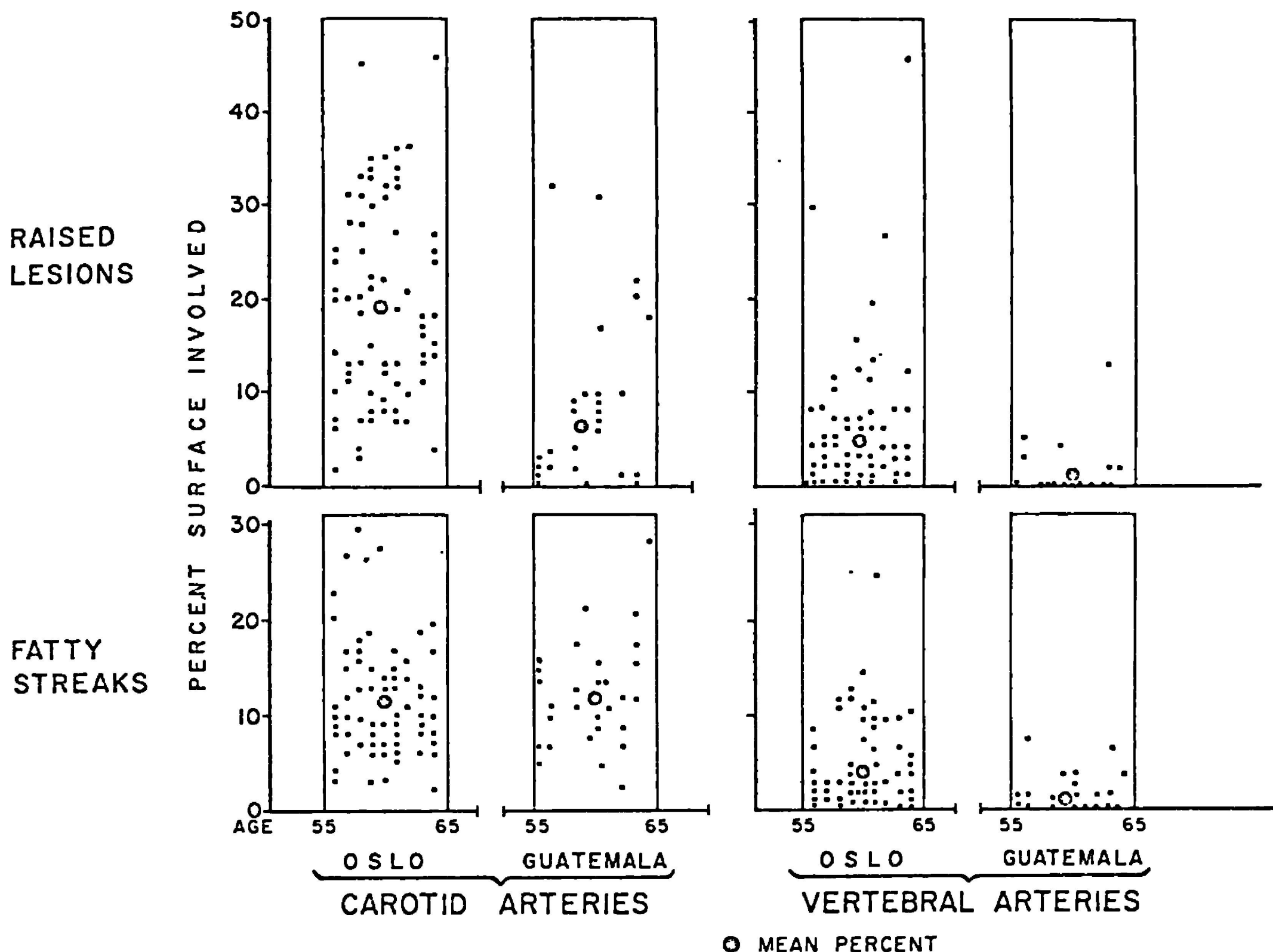


FIG. 2. Variability in estimates of fatty streaks and raised atherosclerotic lesions in the extracranial arteries of men from Oslo and

Guatemala, 55 to 64 years of age, in the basal group, by two arterial segments.

of calcified lesions in the carotid arteries (Table 3). The trends are similar in both sexes.

#### MEAN EXTENT OF ATHEROSCLEROTIC LESIONS BY AGE

In the carotid arteries the mean extent of fatty streaks is about the same in all age groups over 35 years. In vertebral and intracranial arteries (Fig. 4) the mean extent of fatty streaks increases in each succeeding age group throughout the age-span examined. Raised lesions in all arterial segments also increase in each succeeding age group.

#### COMPARISONS OF LESIONS AMONG CEREBRAL ARTERIES

Fatty streaks and raised lesions are more extensive in the carotid arteries than in the vertebral and intracranial arteries of both Oslo and Guatemala men (Fig. 4). A similar trend is present in women.

#### COMPARISONS OF LESIONS AMONG CEREBRAL ARTERIES, CORONARY ARTERIES, AND AORTA

Comparisons of lesions in the cerebral arteries with lesions in coronary arteries and aortae are shown in Tables 4 and 5. The mean extent of atherosclerosis in

the vertebral and intracranial arteries is less than in the coronary arteries and aorta. Carotid arteries are involved to about the same degree as the coronary arteries. Similar trends are present in both sexes.

Cerebral arteries were graded by a different team of pathologists than that which graded the coronary arteries and aorta. Both teams were members of the same research group, both used identical definitions and criteria, both were supervised by the same statistician, and both graded coded specimens blindly.<sup>198, 400</sup> However, the possibility that the lesions were estimated differently in the two systems limits the value of these comparisons.

#### DIFFERENCES BETWEEN MEN AND WOMEN

In the vertebral and carotid arteries there are no consistent differences in the prevalence of fatty streaks and fibrous plaques between men and women. In the intracranial arteries the prevalence of fibrous plaques is higher in men, but the differences are not statistically significant.

Sex differences in mean extent of fatty streaks are small (Fig. 5) and are generally not statistically significant. Raised atherosclerotic lesions, however, are more ex-



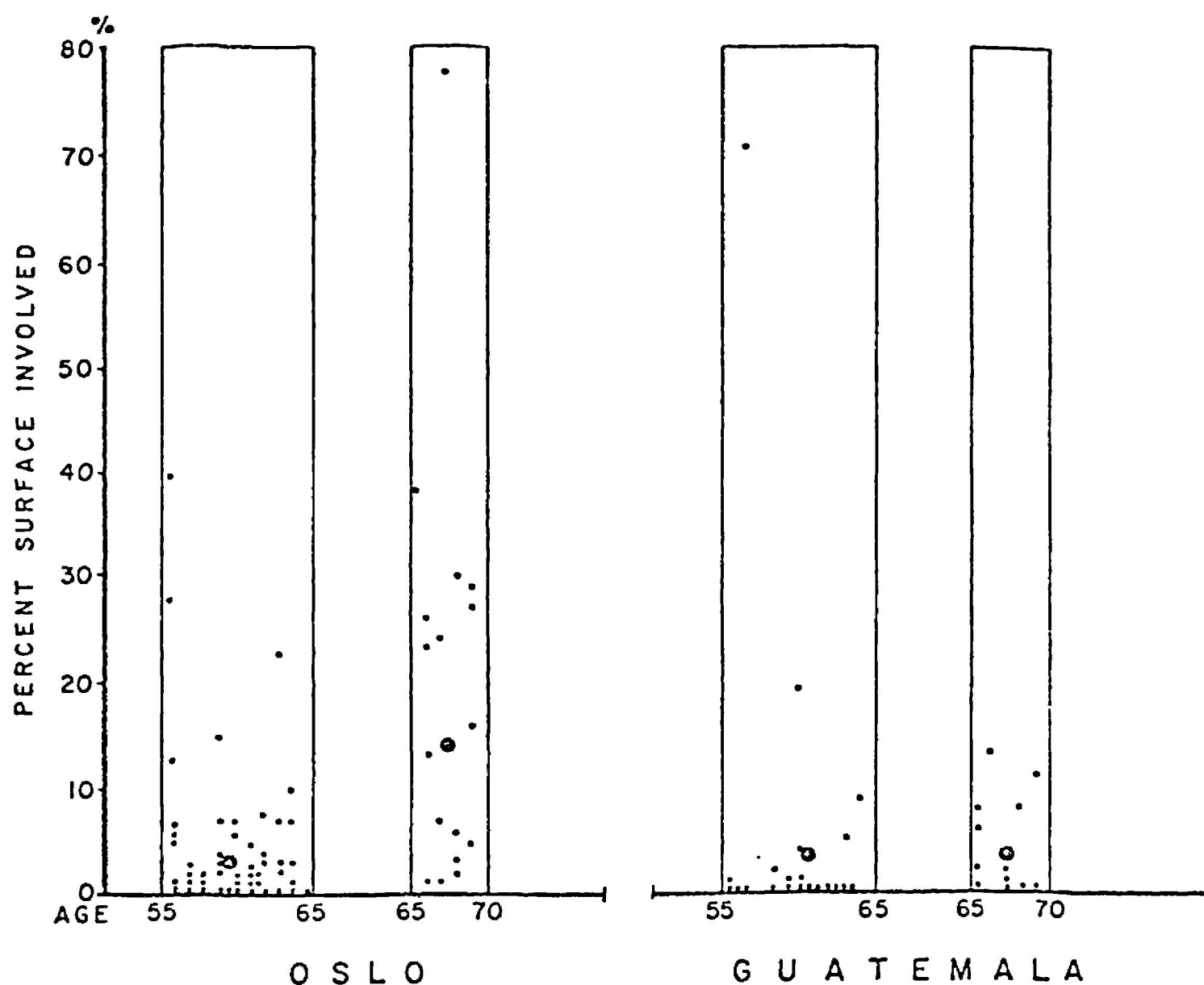


FIG. 3. Variability in estimates of raised atherosclerotic lesions in the intracranial arteries of men from Oslo and Guatemala in the basal group, from two age groups.

tensive in men than women in all of the cerebral arteries and in almost all age groups. The sex difference is significant ( $p < 0.05$ ) in the carotid arteries for groups over 55 years and in the intracranial arteries for those 65 to 69 years of age.

#### DIFFERENCES BETWEEN LOCATIONS IN PREVALENCE OF LESIONS

Prevalence rates of fatty streaks and fibrous plaques (Tables 6 and 7) are consistently higher in Oslo cases than in Guatemalans in all age groups, but the prevalence of carotid artery fatty streaks is 100 per cent in all groups. Differences in prevalence of fatty streaks and fibrous plaques between geographic locations appear to be greater for the vertebral and intracranial arteries than for the carotid arteries.

No complicated lesions were detected in the carotid arteries in persons younger than 45 years of age (Table 8). In persons 45 years of age and older, complicated lesions were more frequent in Oslo than in Guatemalan cases. There is no consistent trend of differences in prevalence of calcified lesions between the two location groups (Table 8).

#### DIFFERENCES BETWEEN LOCATIONS IN MEAN EXTENT OF LESIONS

Fatty streaks in the carotid arteries differ only slightly in mean extent between Oslo and Guatemala, and the differences are not consistent in direction (Fig. 4 and Table 9). Vertebral and intracranial artery fatty streaks differ in mean extent, and involvement is consistently greater in all age groups in Oslo cases. The mean extent of raised atherosclerotic lesions is consistently higher

TABLE 1. NUMBER AND PERCENTAGE OF CASES WITH FATTY STREAK (FS) IN TWO ARTERIAL SEGMENTS IN WOMEN OF THE BASAL GROUP BY AGE AND LOCATION-RACE GROUP<sup>a</sup>

Age group	Oslo cases			Guatemala cases		
	No.	Arteries with FS		No.	Arteries with FS	
		Vertebral	Intracranial		Vertebral	Intracranial
yr.		%			%	
10-34	15	47	40	44	36	18
35-44	14	57	86	25	44	68
45-54	26	96	96	35	57	86
55-64	40	93	100	29	72	90
65-69	18	94	100	7	86	71

<sup>a</sup> In this and all subsequent tables, unless otherwise specified the data were derived from the International Atherosclerosis Project, 1960 to 1965.

TABLE 2. NUMBER AND PERCENTAGE OF CASES WITH FIBROUS PLAQUES (FP) IN THREE ARTERIAL SEGMENTS IN WOMEN OF THE BASAL GROUP BY AGE AND LOCATION-RACE GROUP

Age group	Oslo cases				Guatemala cases			
	No.	Arteries with FP			No.	Arteries with FP		
		Carotid	Vertebral	Intracranial		Carotid	Vertebral	Intracranial
yr.		%				%		
10-34	15	60	27	2	44	36	0	0
35-44	14	86	50	7	25	84	12	4
45-54	26	100	58	50	35	94	29	20
55-64	40	100	75	63	29	97	38	24
65-69	18	100	94	78	7	100	57	43



TABLE 3. NUMBER AND PERCENTAGE OF CASES WITH COMPLICATED LESIONS AND CALCIFIED LESIONS IN CAROTID ARTERIES IN WOMEN OF THE BASAL GROUP BY AGE AND LOCATION-RACE GROUP

Age group	Oslo cases			Guatemala cases		
	No.	Complicated lesions	Calcified lesions	No.	Complicated lesions	Calcified lesions
yr.		%	%		%	%
10-34	15	0	13	44	0	2
35-44	14	0	7	25	0	24
45-54	26	0	8	35	0	31
55-64	40	3	45	29	7	31
65-69	18	11	56	7	0	0

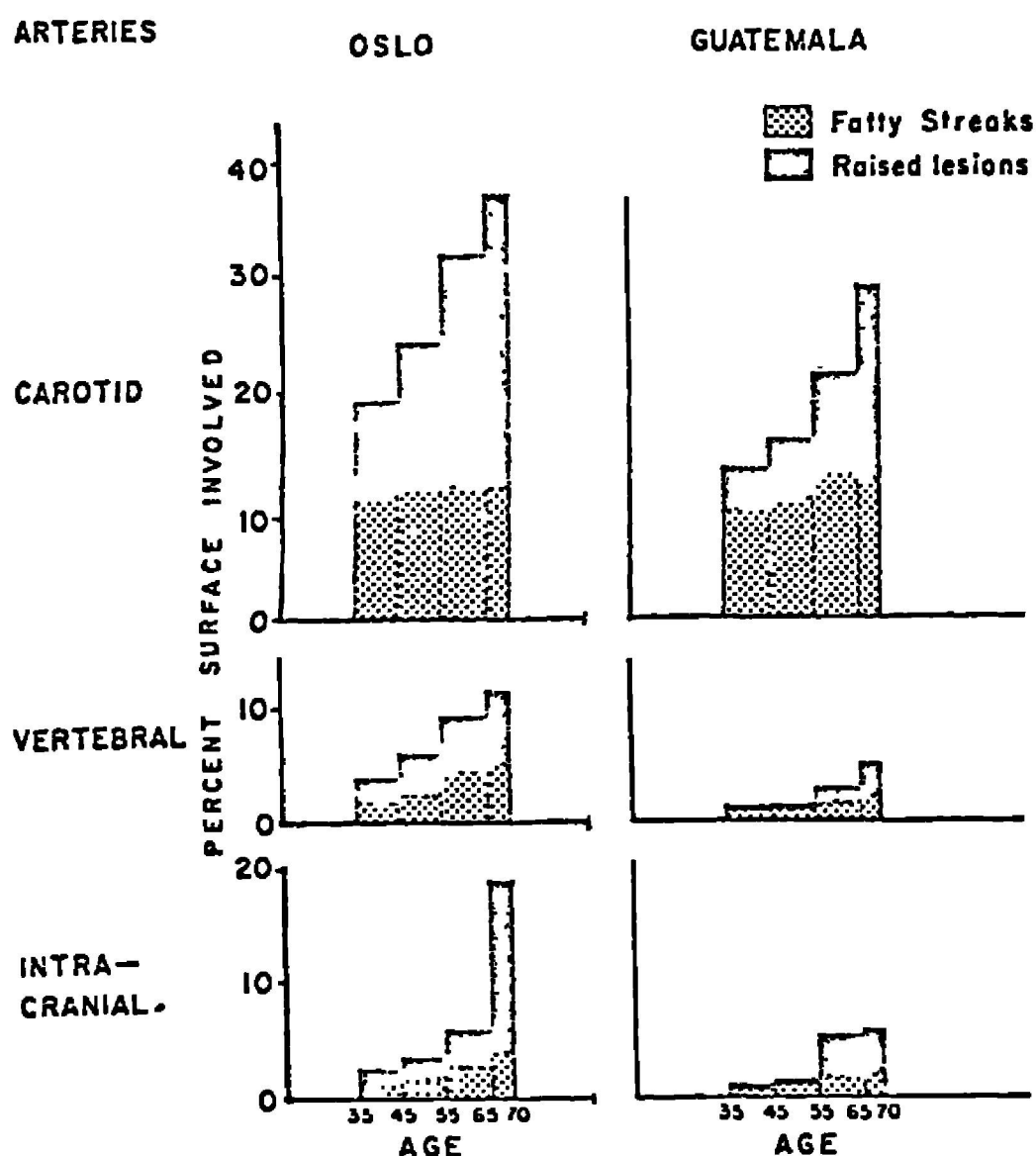


FIG. 4. Mean extent of atherosclerotic lesions in men from Oslo and Guatemala in the basal group, by age and arterial segments.

in all cerebral arteries from Oslo, and the differences between geographic locations generally are more striking in the older age groups (Fig. 6 and Table 9). There is one exception to this generalization. Raised lesions in the intracranial arteries in 55- to 64-year-old Guatemala men exceed raised lesions in comparable Oslo men. Examination of individual cases (Fig. 3) shows that a single heavily involved case contributes to the high mean for Guatemalan men. Another peculiarity is the large amount of raised lesions in 65- to 69-year-old Oslo men. Examination of individual cases (Fig. 3) shows that the mean is not the result of a few severely involved cases but is actually representative of the total group.

The consistency of the differences in prevalence and extent of lesions between Oslo and Guatemalan men suggests that the differences are real even though some

of the differences are not statistically significant (Table 9). Statistical tests for location-race differences among groups of women were not performed, but the location differences among women parallel those among men.

#### DIFFERENCES BETWEEN LOCATIONS IN PROGRESSION OF CEREBRAL ATHEROSCLEROSIS

In both location-race groups the prevalence and mean extent of all types of lesions increase in each succeeding age group. However, the mean extent of raised lesions in the carotid and vertebral arteries of Guatemalan men in each age group is about the same as that of Oslo men 20 years younger (Fig. 7). Raised lesions in the intracranial arteries follow a similar pattern of age and geographic differences except for the peculiar high level in 55- to 64-year-old Guatemalans.

#### FINDINGS IN OTHER LOCATION-RACE GROUPS

In Tables 10 and 11 differences are indicated in New Orleans white and Negro, Jamaica Negro, Santiago,

TABLE 4. NUMBER OF CASES AND MEAN PERCENTAGE OF INTIMAL SURFACE INVOLVED WITH FATTY STREAKS IN SIX ARTERIAL SEGMENTS IN WOMEN OF THE BASAL GROUP BY AGE AND LOCATION-RACE GROUP

Age group	Location-race group	No. of cases	Surface involved with fatty streaks					
			Abdominal aorta	Thoracic aorta	Coronary arteries	Carotid arteries	Vertebral arteries	Intracranial arteries
yr.			mean %					
10-34	Oslo	15	31.9	21.2	5.4	5.8	1.1	0.1
	Guatemala	44	25.0	17.6	2.5	6.0	0.2	0.0
35-44	Oslo	14	25.4	19.7	17.8	10.3	1.4	1.4
	Guatemala	25	34.3	25.5	6.6	9.5	0.3	0.5
45-54	Oslo	26	24.9	21.8	12.6	11.5	2.5	1.8
	Guatemala	35	28.4	22.9	8.2	12.2	0.5	1.0
55-64	Oslo	40	22.6	24.7	14.7	10.8	2.7	3.1
	Guatemala	29	29.9	24.4	14.3	11.9	1.1	1.2
65-69	Oslo	18	18.7	20.8	15.3	12.3	3.7	2.7
	Guatemala	7	22.6	22.3	14.0	9.3	1.9	1.4

TABLE 5. NUMBER OF CASES AND MEAN PERCENTAGE OF INTIMAL SURFACE INVOLVED WITH RAISED ATHEROSCLEROTIC LESIONS IN SIX ARTERIAL SEGMENTS IN WOMEN OF THE BASAL GROUP BY AGE AND LOCATION-RACE GROUP

Age group	Location-race group	No. of cases	Surface involved with raised lesions					
			Abdominal aorta	Thoracic aorta	Coronary arteries	Carotid arteries	Vertebral arteries	Intracranial arteries
yr.			mean %					
10-34	Oslo	15	0.5	0.0	6.1	2.4	0.7	0.0
	Guatemala	44	0.2	0.0	0.0	0.4	0.0	0.0
35-44	Oslo	14	22.2	4.9	10.9	7.4	1.4	1.3
	Guatemala	25	6.7	1.0	0.9	2.0	0.0	0.3
45-54	Oslo	26	33.9	13.9	12.2	10.9	1.7	0.6
	Guatemala	35	12.3	7.3	4.4	4.5	0.3	0.6
55-64	Oslo	40	41.2	25.7	23.3	14.4	3.0	3.8
	Guatemala	29	29.0	18.2	8.6	7.5	1.2	2.7
65-69	Oslo	18	51.7	40.3	20.6	16.9	4.3	5.3
	Guatemala	7	49.9	34.6	17.0	11.1	1.7	3.0

Oslo, and Guatemala cases for the two age groups containing five or more persons in all subgroups. The location-race groups are arranged for convenience in reference rank order based on raised lesions in the aorta and the coronary arteries.<sup>436</sup> Rankings of the six location-race groups by prevalence of fibrous plaques and mean extent of raised lesions in each cerebral artery are similar to the reference rank order; the ranking by mean extent of raised lesions in all cerebral arteries combined is even more similar to the reference rank order. One exception is the higher extent of raised lesions in New Orleans Negroes than in New Orleans whites. Jamaican

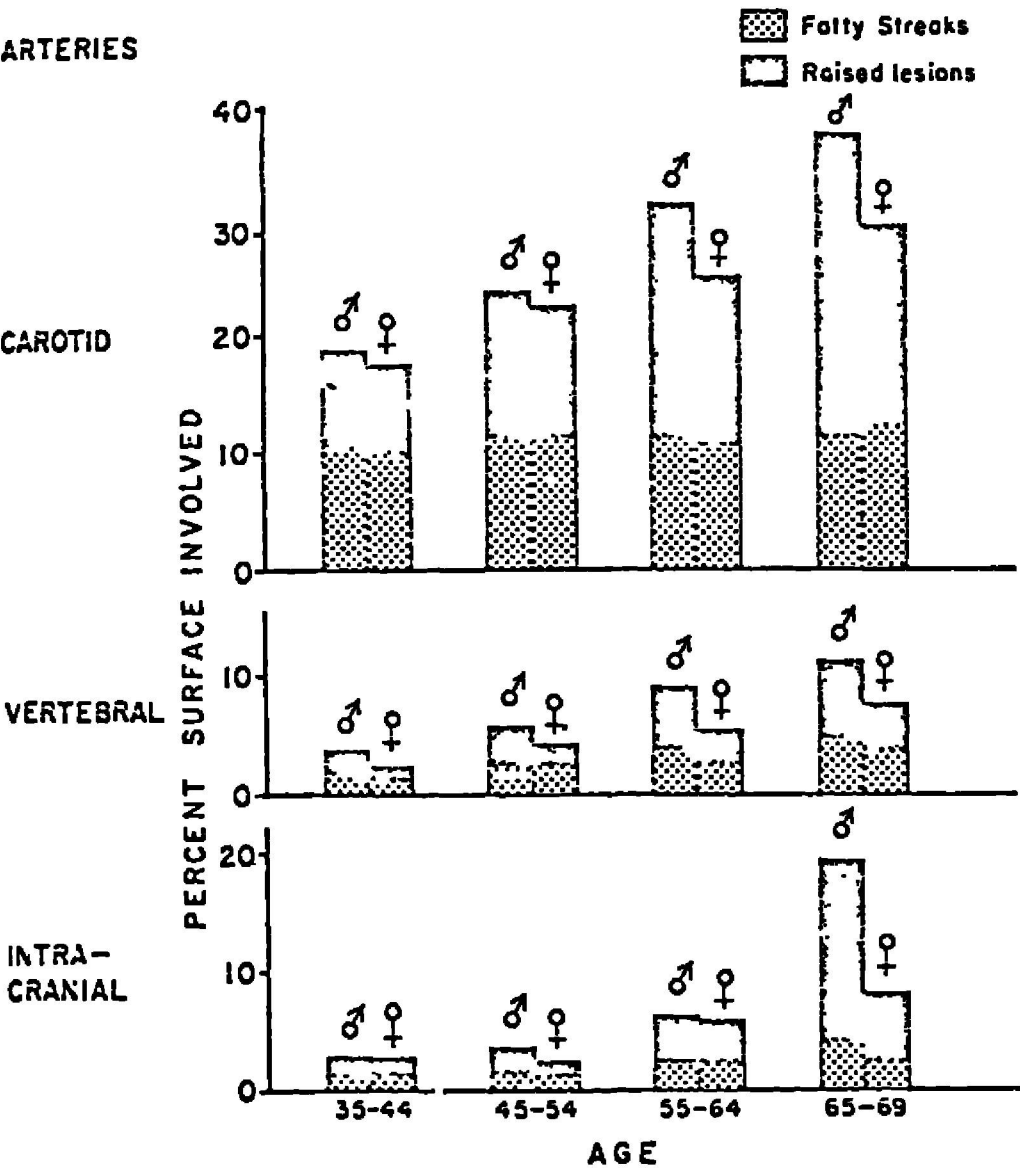


FIG. 5. Sex differences in mean extent of atherosclerotic lesions of Oslo men and women in the basal group, by age and arterial segments.

TABLE 6. NUMBER AND PERCENTAGE OF CASES WITH FATTY STREAKS IN TWO ARTERIAL SEGMENTS IN MEN OF THE BASAL GROUP BY AGE AND LOCATION-RACE GROUP

Age group	Location-race group	No. of cases	Cases with fatty streaks	
			Vertebral arteries	Intracranial arteries
yr.			%	
10-34	Oslo	17	77	41
	Guatemala	30	47	37
35-44	Oslo	31	77	81
	Guatemala	19	37	58
45-54	Oslo	37	89	89
	Guatemala	39	62	77
55-64	Oslo	85	98	95
	Guatemala	30	70	77
65-69	Oslo	29	100	97
	Guatemala	14	93	100

TABLE 7. NUMBER AND PERCENTAGE OF CASES WITH FIBROUS PLAQUES IN THREE ARTERIAL SEGMENTS IN MEN OF THE BASAL GROUP BY AGE AND LOCATION-RACE GROUP

Age group	Location-race group	No. of cases	Cases with fibrous plaques		
			Carotid arteries	Vertebral arteries	Intracranial arteries
yr.			%		
10-34	Oslo	17	59	12	0
	Guatemala	30	46	10	3
35-44	Oslo	31	100	55	29
	Guatemala	19	79	5	11
45-54	Oslo	37	100	76	43
	Guatemala	39	92	21	21
55-64	Oslo	85	100	91	75
	Guatemala	30	97	23	43
65-69	Oslo	29	100	90	83
	Guatemala	14	100	71	57

TABLE 8. NUMBER AND PERCENTAGE OF CASES WITH COMPLICATED LESIONS AND CALCIFIED LESIONS IN CAROTID ARTERIES IN MEN OF THE BASAL GROUP BY AGE AND LOCATION-RACE GROUP

Age group	Location-race group	No. of cases	Cases with complicated lesions	Cases with calcified lesions
			%	
yr.				
10-34	Oslo	17	0	0
	Guatemala	30	0	7
35-44	Oslo	31	0	3
	Guatemala	19	0	11
45-54	Oslo	37	3	16
	Guatemala	39	0	18
55-64	Oslo	85	11	42
	Guatemala	30	3	53
65-69	Oslo	29	24	69
	Guatemala	14	0	57

Negroes also have more raised lesions in the vertebral and intracranial arteries.

DISCUSSION

NATURAL HISTORY OF CEREBRAL ATHEROSCLEROSIS

These data suggest that atherosclerosis increases with age in all cerebral arteries, as others have reported for the intracranial arteries alone<sup>274, 312, 350</sup> and the neck arteries alone.<sup>303, 313</sup> The lesions appear later in life and involve a lesser percentage of intimal surface of the vertebral and intracranial arteries than of the coronary arteries and aorta, also in accordance with other reports.<sup>106, 274, 307</sup> Atherosclerosis begins earlier in the carotid arteries than in other cerebral arteries, and carotid artery lesions tend to follow the pattern of change with age followed by aortic atherosclerosis. The high prevalence of calcified lesions at younger ages may be due to a process other than atherosclerosis. The relationship of calcified lesions in the petrous and cavernous portions of carotid arteries to atherosclerosis is not clear.<sup>139, 356</sup>

It is not known why atherosclerosis develops more

TABLE 9. NUMBER OF CASES AND MEAN PERCENTAGE OF INTIMAL SURFACE INVOLVED WITH FATTY STREAKS (FS) AND RAISED ATHEROSCLEROTIC LESIONS (RL) IN THREE ARTERIAL SEGMENTS IN MEN OF THE BASAL GROUP BY AGE AND LOCATION-RACE GROUP

Age group	Location-race group	No. of cases	Surface involved with FS			Surface involved with RL		
			Carotid arteries	Vertebral arteries	Intracranial arteries	Carotid arteries	Vertebral arteries	Intracranial arteries
yr.			mean %			mean %		
10-34	Oslo	17	3.2	1.1	0.2	1.6	0.0	0.0
	Guatemala	30	8.0	0.9	0.4	1.4	0.7	0.0
35-44	Oslo	31	10.5	1.9	1.2	8.5 <sup>a</sup>	2.2	1.2
	Guatemala	19	9.4	0.7	0.5	2.4 <sup>a</sup>	0.1	0.1
45-54	Oslo	37	11.5	2.2 <sup>a</sup>	1.8 <sup>a</sup>	12.1 <sup>a</sup>	3.6 <sup>a</sup>	1.9
	Guatemala	39	10.4	0.7 <sup>a</sup>	0.6 <sup>a</sup>	4.5 <sup>a</sup>	0.3 <sup>a</sup>	0.3
55-64	Oslo	85	11.4	4.1 <sup>a</sup>	2.8 <sup>b</sup>	20.2 <sup>a</sup>	4.9 <sup>a</sup>	3.2
	Guatemala	30	12.9	1.5 <sup>a</sup>	1.6 <sup>b</sup>	8.2 <sup>a</sup>	1.0 <sup>a</sup>	3.8
65-69	Oslo	29	11.4	5.0 <sup>b</sup>	4.2 <sup>b</sup>	25.8 <sup>b</sup>	6.4	15.0 <sup>b</sup>
	Guatemala	14	11.8	2.3 <sup>b</sup>	2.0 <sup>b</sup>	16.4 <sup>b</sup>	2.6	3.6 <sup>b</sup>

<sup>a</sup> Statistically significant difference (*t*-test:  $p < 0.05$ ) between Oslo and Guatemalan men.

<sup>b</sup> Statistically significant difference (*t*-test:  $p < 0.01$ ) between Oslo and Guatemalan men.

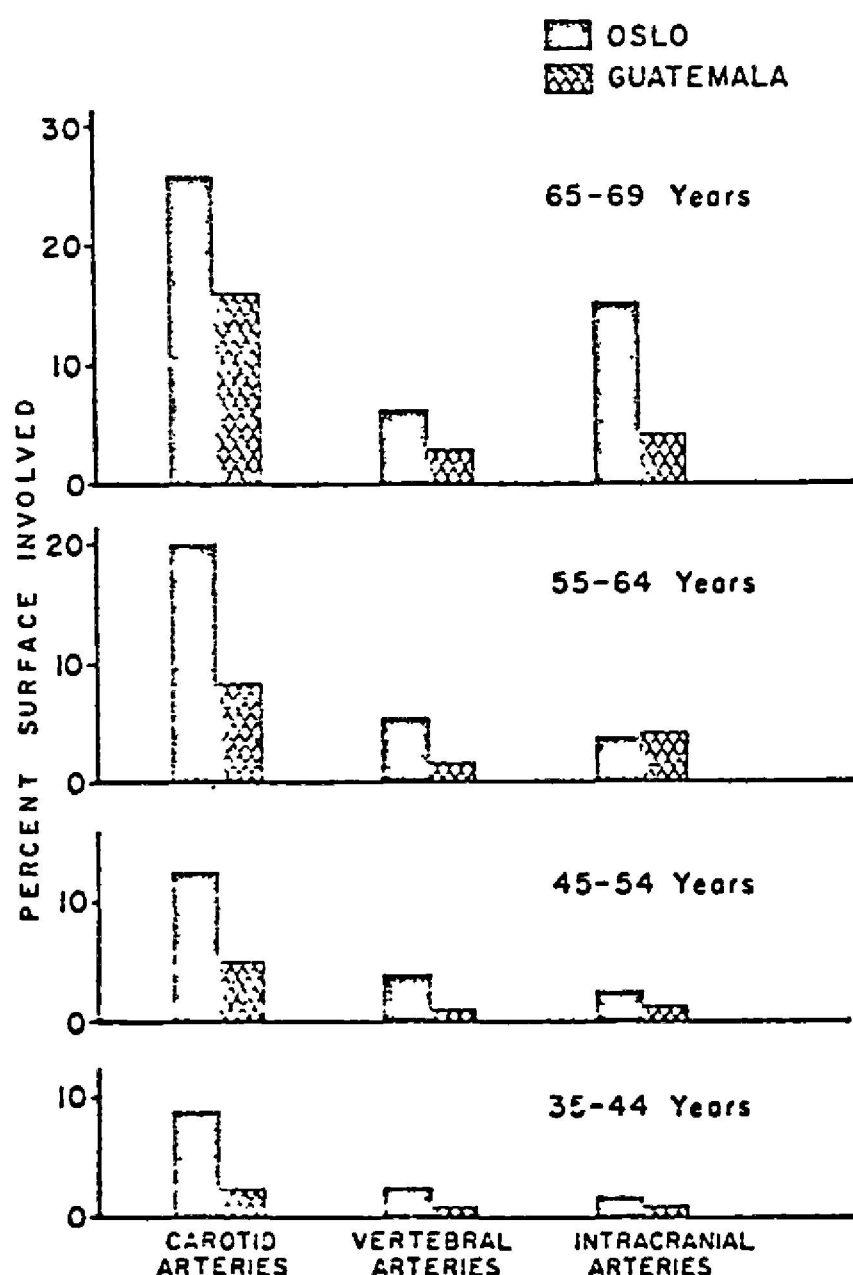


FIG. 6. Location-race differences in mean extent of raised atherosclerotic lesions in men from Oslo and Guatemala in the basal group, by age and arterial segments.

slowly with age in the vertebral and intracranial arteries than in other arteries. The slower rate of the process may be due to differences in structure, hemo-

dynamic conditions, other physical stresses, or arterial wall metabolism.<sup>325, 391, 423, 438, 461</sup>

#### SEX DIFFERENCES IN CEREBRAL ATHEROSCLEROSIS

These data show that men have consistently more severe cerebral atherosclerosis than women. Some previous studies have found sex differences;<sup>274, 303, 359</sup> others have not.<sup>299, 322</sup> The differences are small in location-race and age groups which have little cerebral atherosclerosis, but they are more pronounced in older persons and in location-race groups with more severe atherosclerosis. Larger samples will be required to make conclusive statements about the degree of difference in cerebral atherosclerosis between men and women.

#### LOCATION-RACE DIFFERENCES IN CEREBRAL ATHEROSCLEROSIS

These data establish location-race differences in prevalence and mean extent of atherosclerotic lesions in the cerebral arteries. These differences parallel differences in the coronary arteries and the aorta.<sup>436</sup> The few reported geographic comparisons of cerebral atherosclerosis have not shown differences,<sup>22, 322</sup> probably because the cases were from populations with similar environmental backgrounds. Populations in this study differ greatly in environmental conditions.

#### ASSOCIATION OF CEREBRAL, AORTIC, AND CORONARY ATHEROSCLEROSIS

Several studies have shown an association between coronary, aortic, and cerebral atherosclerosis.<sup>23, 166, 273, 390, 482, 483</sup> The results of this study also indicate that the extent of atherosclerosis in one arterial segment reflects the extent of atherosclerosis in another arterial segment on a group basis. When individual persons are considered, the severity of atherosclerosis in one cerebral artery cannot be predicted from the severity of lesions in other cerebral arteries.<sup>407</sup>

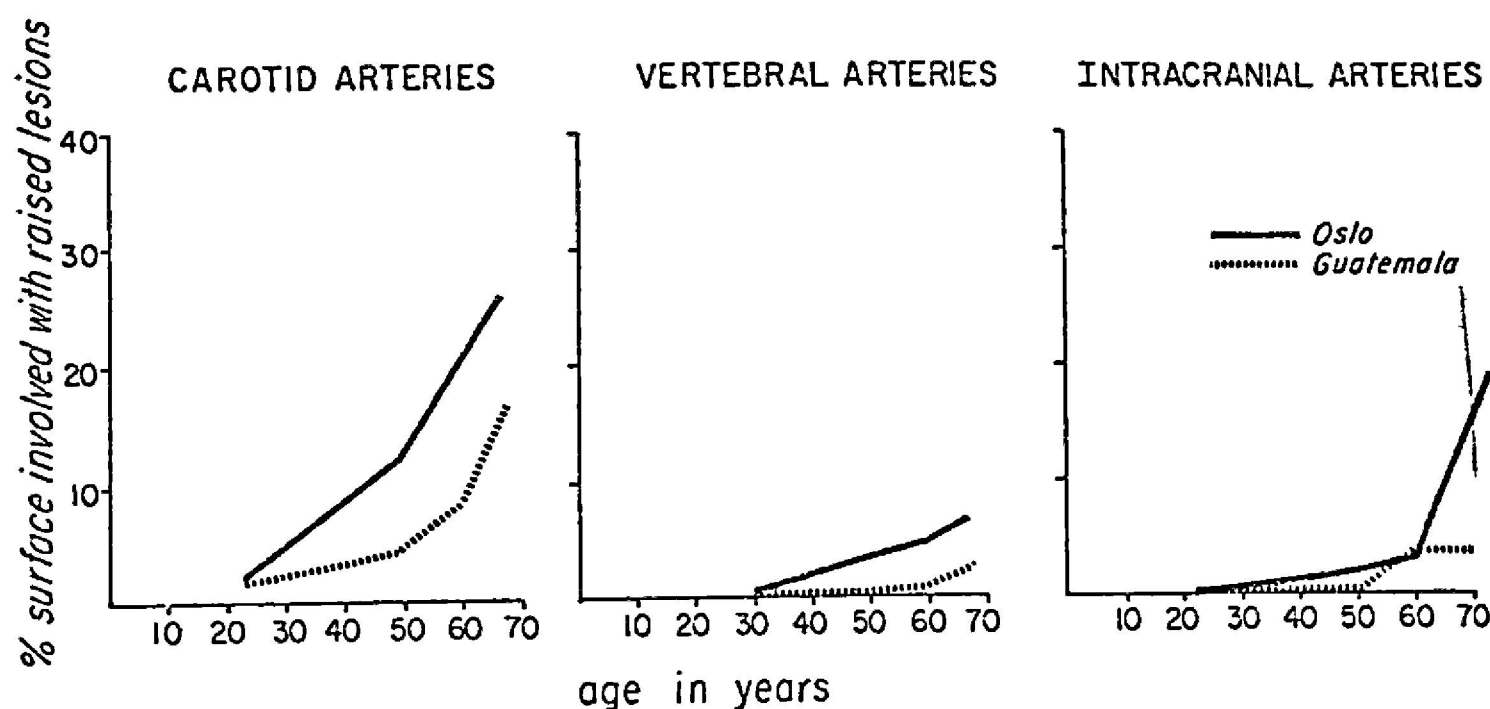
#### CEREBRAL ATHEROSCLEROSIS, CEREBRAL VASCULAR DISEASE, AND HYPERTENSION

Most investigators believe that cerebral infarction is principally related to cerebral atherosclerosis and that cerebral hemorrhage is principally related to hypertension. However, cerebral infarction also frequently occurs in hypertensive persons.<sup>21, 138, 214, 220</sup> This association may be due to increased severity of atherosclerosis in persons with hypertension. The aggravation of cerebral atherosclerosis in persons with hypertension and other diseases thought to be associated with increased atherosclerosis is examined in detail in another analysis of this material.<sup>408a</sup>

To relate the data presented here on cerebral atherosclerosis in the basal group to death rates from cerebral infarction would require an estimate of cerebral infarction mortality rates in the same populations. Such figures are not easily available. Vital statistics usually do not distinguish between different types of cerebral vascular diseases because it is sometimes difficult to differentiate cerebral infarction from cerebral hemorrhage on clinical grounds. There are indications, how-



FIG. 7. Location-race difference in progression of raised atherosclerotic lesions from Oslo and Guatemala men in the basal group, by age and arterial segments.



ever, that the incidence of cerebral infarction parallels the incidence of coronary heart disease in a population.<sup>235, 479</sup> Coronary heart disease and cerebral infarction coincide with higher frequency than expected;<sup>35, 231</sup> part of this coincidence may be due to embolism from the heart to the brain causing cerebral infarction.<sup>226</sup>

The prevalence of coronary heart disease is much lower in Guatemala, Chile, and Jamaica than in New Orleans and Oslo.<sup>222, 320, 477</sup> If the suspected association between coronary heart disease and cerebral infarction is real, the incidence of cerebral infarction should be lower in Guatemala, Chile, and Jamaica than in New Orleans and Oslo. In the groups of autopsied persons for this study, cerebral infarction was recorded in 11 per cent of the Oslo cases 35 to 69 years of age; the figure for New Orleans white was 11 per cent; New Orleans Negro, 11 per cent; Jamaica, 8 per cent; Guatemala, 3 per cent; and Santiago, 2 per cent. As has been demonstrated previously, the severity of cerebral atherosclerosis is also lower in Guatemala, Chile, and Jamaica than in New Orleans and Oslo. Thus, it is suggested that the incidence of cerebral infarction parallels the severity of cerebral atherosclerosis in a population.

#### RACIAL DIFFERENCES IN CEREBRAL ATHEROSCLEROSIS

New Orleans Negro men seem to have more extensive cerebral atherosclerosis than New Orleans white

TABLE 10. NUMBER AND PERCENTAGE OF CASES WITH FIBROUS PLAQUES IN THREE ARTERIAL SEGMENTS IN MEN BY AGE AND LOCATION-RACE GROUPS

Location-race group	45-54 age group				55-64 age group			
	No. of cases	Arteries with fibrous plaques			No. of cases	Arteries with fibrous plaques		
		Ca- rotid	Verte- bral	Intra- cranial		Ca- rotid	Verte- bral	Intra- cranial
		%				%		
New Orleans white	10	100	80	70	13	100	77	77
Oslo	37	100	76	43	85	100	91	75
New Orleans Negro	11	100	73	55	18	100	94	94
Jamaica Negro	5	100	80	40	7	100	71	71
Santiago	5	100	20	20	7	86	57	71
Guatemala	39	93	21	21	30	97	23	43

men, although white men have more severe coronary atherosclerosis.<sup>436</sup> This discrepancy is an exception to the generalization that the severity of cerebral atherosclerosis parallels the severity of atherosclerosis in the coronary arteries on a group basis. The tentative findings in the cerebral arteries are supported by vital statistics which show that cerebrovascular diseases<sup>45</sup> are more frequent among Negroes than whites. However, either cerebral infarction or cerebral hemorrhage in Negroes may be responsible for the racial differential in cere-

TABLE 11. NUMBER OF CASES AND MEAN PERCENTAGE OF INTIMAL SURFACE INVOLVED WITH FATTY STREAKS (FS) AND RAISED ATHEROSCLEROTIC LESIONS (RL) IN THREE ARTERIAL SEGMENTS IN MEN BY AGE AND LOCATION-RACE GROUP

Location-race group	45-54 age group									55-64 age group <sup>a</sup>								
	No. of cases	Surface involved								No. of cases	Surface involved							
		Carotid arteries		Vertebral arteries		Intracranial arteries		All three arteries			Carotid arteries		Vertebral arteries		Intracranial arteries		All three arteries	
		FS	RL	FS	RL	FS	RL	FS	RL		FS	RL	FS	RL	FS	RL	FS	RL
		mean %									mean %							
New Orleans white	10	7.2	22.3	1.5	2.6	1.6	7.2	3.4	10.7	13	7.3	18.2	3.0	6.5	1.5	2.9	3.9	9.2
Oslo	37	11.5	12.1	2.2	3.6	1.8	1.9	5.2	5.9	85	11.4	20.2	4.1	4.9	2.8	3.2	6.1	9.4
New Orleans Negro	11	12.6	14.8	2.0	4.6	1.9	3.5	5.5	7.6	18	11.6	21.6	3.3	9.2	3.2	7.9	6.0	12.9
Jamaica Negro	5	13.8	8.8	3.2	2.2	0.4	0.0	5.8	3.7	7	12.3	12.3	3.3	3.6	1.4	3.9	5.7	6.6
Santiago	5	8.0	6.6	0.2	0.4	0.4	0.2	2.9	2.4	7	8.0	8.0	1.9	1.0	1.4	1.3	3.7	3.4
Guatemala	39	10.4	4.5	0.7	0.3	0.6	0.3	3.9	1.7	30	12.9	8.2	1.5	1.0	1.6	3.8	5.3	4.3

brovascular disease. The higher incidence of cerebral hemorrhage in Negroes may be due to their high prevalence of hypertension. This survey will be continued in New Orleans to see whether the observed differences in atherosclerotic lesions between white and Negro are confirmed in larger numbers of cases.

#### IMPLICATIONS OF THESE FINDINGS REGARDING ETIOLOGY

Differences in cerebral atherosclerosis among location-race-sex-age subgroups generally parallel differences in coronary and aortic atherosclerosis with only slight discrepancies. The carotid artery lesions develop much in the same way and to approximately the same degree as aortic lesions. The other cerebral arteries are similar to the coronary arteries, except that cerebral artery lesions develop later in life.

These data indicate that cerebral atherosclerosis is associated with the same environmental conditions as coronary atherosclerosis and aortic atherosclerosis. Change in any environmental condition which would prevent or retard coronary atherosclerosis may also prevent or retard cerebral atherosclerosis and would, therefore, reduce the risk of the major sequelae of cerebral atherosclerosis—cerebral ischemia and infarction.

#### SUMMARY

The cerebral arteries (common carotid, internal carotid, vertebral, middle cerebral, and basilar arteries) were examined from 1517 autopsied persons in five countries (Norway, Guatemala, United States, Jamaica, and Chile).

Subgroup comparisons were made using a basal group of cases from which were excluded all persons with coronary heart disease, peripheral arterial disease, other atherosclerotic complication, hypertension, and diabetes.

The prevalence and mean extent of atherosclerotic lesions increase in each succeeding age group. Lesions appear to develop later in life in the cerebral arteries than in the aorta and the coronary arteries. Men have more raised atherosclerotic lesions than women.

The mean extent of fatty streaks in the carotid arteries does not differ among age groups from 35 to 69 years of age, nor does it differ among location-race groups. The mean extent of raised atherosclerotic lesions in the carotid arteries increases in each succeeding age group after 35 years of age, and differs among location-race groups. The pattern of development of atherosclerosis in the carotid arteries follows that of the aorta.

Fatty streaks appear in the intracranial and vertebral arteries much later in life than they do in the carotid arteries. The mean extent of both fatty streaks and raised lesions increases in each succeeding age group after 35 years of age, and the average involvement of both types of lesions differs among location-race groups. The pattern of development of atherosclerosis in the vertebral and intracranial arteries follows that of the coronary arteries.

When location-race groups are ranked by extent of cerebral atherosclerosis, they rank in approximately the same order as when they are ranked by aortic and coronary atherosclerosis.