Relationship of Degree of Atherosclerosis of Internal Carotid System in the Brain of Women to Age and Coronary Atherosclerosis

By Malcolm D. Winter, Jr., M.D., George P. Sayre, M.D., Clark H. Millikan, M.D., and Nelson W. Barker, M.D.

Cerebral infarction currently is the third leading cause of death in the United States. Since atherosclerosis of the cerebral arteries is the basis for the majority of strokes, the authors undertook to define more accurately the distribution of such atherosclerosis, its relation to coronary atherosclerosis, and its relation to such other factors as hypertension, obesity, and cerebral infarction. The results of their study are presented here.

Cerebral infarction currently is the third leading cause of death in the United States. The incidence of "cerebral vascular accidents" in various necropsy series has varied between 5 and 24 per cent. Since atherosclerosis of the cerebral arteries is the basis for the majority of strokes, the present study was undertaken in an effort to define more accurately the distribution of such atherosclerosis, its relation to coronary atherosclerosis, and its relation to such other factors as hypertension, obesity, and cerebral infarction.

Histologically, cerebral arteries differ from arteries throughout the rest of the body in several respects. They have a very well-developed internal elastic membrane, but an external elastic membrane is completely lacking. Their medial and adventitial coats are thinner and less well developed than those of other arteries. Very early in life the internal elastic membrane begins to split into 2 laminae at points where vessels bifurcate. The external lamina is thin and smooth, forming the boundary between the intima and media. The internal lamina is irregular and thick, often containing a number of clefts. With aging, the arterial walls thicken in proportion to their increased caliber. The internal elastic membrane splits in other areas at points away from bifurcations, and focal intimal thickening at bifurcations increases. From the age of 20 years on, ruptures may occur in the internal elastic membrane, usually in its outer lamina. Difficulty arises in separating changes due exclusively to age from those due to some pathologic process.

Review of Literature

Wolkoff in 1933 studied specimens from 98 individuals ranging from 2 to 81 years of age; he opened up the arterial system of each brain by longitudinally incising the cerebral arteries in situ out to their smallest ramifications. He found 3 types of atherosclerotic lesions: lipid spots, lipid plaques, and fibrous plaques. Grossly lipid spots first became evident during the middle of the fourth decade of life. Staining the arteries with Sudan III made them visible near the end of the third decade. At first only 1 to 3 small, irregular, round spots ranging in size from that of a pinhead to that of a millet seed could be found per brain. During the fourth decade the number and size increased although some specimens were still completely free of them. When present they tended to stretch out in a longitudinal direction and frequently merged with each other.
lipid content of some of them had increased enough to cause them to stand out from the intimal surface—these Wolkoff classified as lipid plaques. During the fifth decade lipid spots were present in all cases but were of differing number and stage of development. Fibrous plaques were found in 2 cases (ages 46 and 47), and consisted of fine whitish thickenings over the central portions of lipid foci. From the sixth decade on, lipid spots and plaques were found in all cases; fibrous plaques were found more and more frequently and in greater numbers with larger dimensions. Narrow lipid streaks frequently departed from a pronounced lipid or fibrous plaque and extended in a longitudinal direction along the artery. Fibrous plaques reached 1.5 to 2 inches in length, usually being longitudinally placed. Frequently they were fused with one another and occu-
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pied a large part of the entire intimal surface of the artery in question. Their lipid content was large and their fibrous component greatly thickened.

Both Fisher and Wolkoff found the large arteries at the base of the brain to be involved with atherosclerosis earlier and to a more severe degree than were their more distal branches. The carotid and basilar systems were usually approximately equally involved, although exceptions did occur.

Duff and McMillan, and Wolkoff, have expressed the view that atherosclerosis affects the cerebral arteries much later in life than it affects the aorta and coronary arteries. Fisher, on the other hand, has stated that while in most instances cerebral atherosclerosis is somewhat less advanced than atherosclerosis elsewhere, qualitatively its severity roughly parallels that found in other organs. He has said that it is wrong to emphasize differences in cerebral atherosclerosis from atherosclerosis found elsewhere.

METHOD AND MATERIAL

In 1949 Ackerman studied the degree of coronary atherosclerosis in women 30 through 89 years of age. He examined 100 hearts in each of 6 decades. They represented a consecutive series running retrogradely from the end of 1946, except that for the age period 80 through 89 years the series was extended forward into 1948 in order to obtain enough specimens. All causes of death were included.

In the current study all available brains from cases used in Ackerman's study were employed for the evaluation of cerebral atherosclerosis. A total of 239 brains were satisfactory for this purpose. The arteries studied were those of the supraclinoid carotid system and included the following: 1. The segments of the supraclinoid portions of the internal carotids which remained attached to the brain at the time of its removal from the skull. 2. The middle cerebrials to the point of their trifurcation or to the point where they had divided into 3 major branches. 3. The anterior cerebrials to the anterior margin of the genu of the corpus callosum.

The internal carotid segments varied greatly in length and were sometimes missing completely because of the difficulty encountered in cutting them at their exact point of emergence from the dura prior to removal of the brain from the skull. Occasionally the middle and anterior cerebral arteries were also either partly or entirely missing. If any portion of an artery was present, it was used in the study. If more than half of the supraclinoid portion of the internal carotid system was absent, that brain was omitted from the study.

The maximal degree of atherosclerosis found in each artery was determined. This was accomplished by sectioning each artery at intervals of 3 to 5 mm. whenever gross atherosclerosis was evident. The 1 or 2 sections from each artery having the greatest degree of atherosclerosis were graded grossly and saved to be made into histologic sections. Later each section was graded microscopically. Gross and microscopic grades of the same section often differed. Frequently the microscopic grade was lower than the gross grade. Often this was due to the microscopic section having been cut a short distance from the area of maximal atherosclerosis. In other instances it was due to contraction of the arterial wall giving a falsely high impression of the degree of atherosclerosis when viewed grossly. In cases in which arteries were contracted, only the microscopic grade was used. In all others, the highest grade, microscopic or gross, was the one used in the study.

The actual grading was on the basis of grade 1 (minimal atherosclerosis) to grade 4 (complete atherosclerotic closure of the lumen). The photomicrographs presented in figure 1 are of representative sections of various grades of atherosclerosis used in this study. The grading is identical to that used by White in male hearts and Ackerman in female hearts. Grades were correlated with percentage of luminal obliteration caused by the atheromatous plaque (table 1). In collapsed or contracted vessels the grade of atherosclerosis was determined from an estimation of what the wall-to-lumen ratio would have been in their expanded form. When a vessel was occluded by a blood clot, only the underlying atherosclerosis was considered. In occasional instances, as

<table>
<thead>
<tr>
<th>Grade</th>
<th>Obliteration of lumen, per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0—12</td>
</tr>
<tr>
<td>1.5</td>
<td>12.5—24</td>
</tr>
<tr>
<td>2</td>
<td>25—37</td>
</tr>
<tr>
<td>2.5</td>
<td>37.5—49</td>
</tr>
<tr>
<td>3</td>
<td>50—74</td>
</tr>
<tr>
<td>3.5</td>
<td>75—99</td>
</tr>
<tr>
<td>4</td>
<td>100</td>
</tr>
</tbody>
</table>
exemplified by the artery shown in figure 1g, the atherosclerotic plaque may represent an
organized thrombus. Because of the difficulty in separating organized thrombi from fibrotic atheroma-
tous plaques, differentiation of the two was not attempted. As with Ackerman’s series of cases, the
ages were rotated during the grading process and were unknown at the time of grading.

The computations to develop the results of the study were as follows: Six numbers representing
the highest grade of atherosclerosis in each of 6 arterial branches were added and the sum divided
by 6 to determine the mean grade of atherosclerosis for each brain. Then all of the latter grades
in each decade were added and the sum divided by the number of cases in that decade to deter-
mine the mean grade of cerebral atherosclerosis for that decade. Next, the highest of the 6 high-
est grades for each brain was recorded and this

was considered to represent the “maximal” grade of atherosclerosis for that brain; all the latter
grades in each decade were added and the sum divided by the number of cases in that decade to
determine the “maximal” grade of atherosclerosis for that decade. Similarly, the highest grades of
atherosclerosis for the internal carotid, anterior cerebral, and middle cerebral arteries respectively
in each decade were averaged to determine the mean grade of cerebral atherosclerosis by major
teripheral brain branch by decade.

In addition to the grading of cerebral athero-
sclerosis in each case, the heart weight, the nutri-
tional state, the principal and contributing causes
of death, and the nature of the cerebral lesions
found were recorded after a survey of each proto-
col. All instances of atrial or ventricular mural
thrombi, rheumatic heart disease, hypertensive
heart disease, or myocardial infarction were tabu-
lated.

RESULTS*

1. Relationship of Degree of Cerebral
Atherosclerosis to Age. Mean Grade of Cere-
bral Atherosclerosis. The results of determina-
tion of the mean grade of cerebral atheroscle-
sis are plotted in figure 2 and are listed
with their standard deviation, standard error,
and sample size in table 2. These values are
lower than those usually reported in describ-
ing degrees of cerebral or coronary atheroscle-
sis. This is because the value derived for
any individual case is an average of 6 highest
values and not the single highest value for all
cerebral arteries, as is usually recorded.

*In order to simplify terminology, atherosclerosis
in the supraclinoid portion of the carotid circulation
will hereinafter be referred to simply as cerebral
atherosclerosis. The ordinate of all the following
graphs represents the mean grade of atherosclerosis
present.
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For comparison, averages were also calculated from the latter values and are listed in table 2 under the heading "maximal" cerebral atherosclerosis.

Mean grade of cerebral atherosclerosis by decade of life steadily increases from 1.03 in the fourth decade to 1.96 in the ninth. Progression of the atherosclerotic process appears to become more rapid after the fourth decade.

The percentage of brains in each decade with minimal (grade 1.00) atherosclerosis decreases from 74 per cent in the fourth decade to only 5 per cent in the eighth and 3 per cent in the ninth (table 3). On the other hand, the percentage of brains with severe atherosclerosis, that is, having a mean of grade 2.00 or more, is zero in the fourth decade and increases from 2 per cent in the fifth decade to 39 per cent in the ninth.

Mean Grade of Cerebral Atherosclerosis by Major Arterial Branch by Decade. Since the grades of atherosclerosis on the right and left sides were about the same, they were averaged together and the values obtained for the intracranial portion of the internal carotid, the middle cerebral, and the anterior cerebral arteries by decade were plotted (fig. 3). There is some increase in atherosclerosis from decade to decade in each of the 3 pairs of arteries. After the fourth decade, the middle cerebral arteries tend to show the highest grades of atherosclerosis, and the internal carotid arteries the lowest. Both the internal carotid and anterior cerebral arteries show a somewhat uneven progression of their atherosclerosis.

2. Comparison of Cerebral Atherosclerosis and Coronary Atherosclerosis. Since similar methods were used to grade the atherosclerosis present in the hearts and brains of this series of necropsies, the mean grades of cerebral and coronary atherosclerosis were determined. In each series of cases the final mean was derived by averaging the highest grades of atherosclerosis found in each of 6 vessels. The thicknesses of coronary and cerebral arterial walls differ, but grading was performed in such a manner that it was not affected by this factor. The length and caliber of the 2 sets of vessels were not the same and therefore some differences between the relative values of the final figures for the 2 sets are to be expected.

Comparison of Severity and Rates of Progression of Cerebral and Coronary Atherosclerosis with Age. According to the methods used, coronary atherosclerosis in each decade is more severe than cerebral atherosclerosis in the same decade (fig. 4). It progresses steadily until the ninth decade, when its rate of progression markedly decreases. The curve for cerebral atherosclerosis, except for the fourth and ninth decades, tends to follow the same rate of climb as the curve for coronary atherosclerosis in the same series.

Table 3.—Comparison of Minimal and Severe Cerebral Atherosclerosis with Coronary Atherosclerosis Found by Decade of Age*

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Total Cases</th>
<th>Mean Grade 1 Cerebral</th>
<th>Mean Grade 1 Coronary</th>
<th>Mean Grade 2 or Over Cerebral</th>
<th>Mean Grade 2 or Over Coronary</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td>50</td>
<td>37 74</td>
<td>23 46</td>
<td>0 0</td>
<td>1 2</td>
</tr>
<tr>
<td>40-49</td>
<td>45</td>
<td>24 53</td>
<td>13 29</td>
<td>1 2</td>
<td>4 9</td>
</tr>
<tr>
<td>50-59</td>
<td>48</td>
<td>22 46</td>
<td>8 17</td>
<td>5 10</td>
<td>3 6</td>
</tr>
<tr>
<td>60-69</td>
<td>26</td>
<td>8 31</td>
<td>3 12</td>
<td>3 12</td>
<td>5 19</td>
</tr>
<tr>
<td>70-79</td>
<td>37</td>
<td>2 5</td>
<td>0 0</td>
<td>13 35</td>
<td>14 38</td>
</tr>
<tr>
<td>80-89</td>
<td>33</td>
<td>1 3</td>
<td>0 0</td>
<td>13 39</td>
<td>15 45</td>
</tr>
</tbody>
</table>

* Patients with mean atherosclerosis between grade 1.0 and grade 2.0 are not included.
Atherosclerosis tends steadily through the fifth decade, but then increases only slightly from the fourth to the fifth decade, but then increases steadily up through the ninth decade when it becomes almost as severe as coronary atherosclerosis.

Comparison of Grades of Cerebral and Coronary Atherosclerosis in Individual Cases. Figures 5 and 6 are scattergrams that compare coronary and cerebral atherosclerosis in each case. Although there are objections to the validity of quantitatively comparing the mean values derived in each case with each other, the variation in values found in different cases in each system is accurate, since grading of each system is consistent within itself. Also, one can assume with a fair degree of certainty that the finding of grade 1 atherosclerosis is comparable between the 2 arterial systems in each case. The scattergrams vividly demonstrate that the degree of atherosclerosis in the cerebral arteries may vary widely from that in the coronary arteries in any one case. Extreme examples are found in one patient having grade 2.9 coronary atherosclerosis and only grade 1.02 cerebral atherosclerosis, and in another patient having grade 1 coronary atherosclerosis and grade 2.3 cerebral atherosclerosis. Thus in individual cases there is very little correlation between degrees of atherosclerosis in the 2 systems. In the earlier decades a fairly large proportion of the patients have no atherosclerosis in either system or have but one system involved (table 4). As an example, in the fourth decade 38 per cent of the patients have no evidence of either coronary or cerebral atherosclerosis, while 36 per cent have evidence of coronary atherosclerosis.
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Table 4.—Patients in Each Decade without Atherosclerosis in Either System, with Only Coronary Atherosclerosis, with Only Cerebral Atherosclerosis, and with Both

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Total cases</th>
<th>Atherosclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
<td>Coronary only</td>
</tr>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>30-39</td>
<td>50</td>
<td>19</td>
</tr>
<tr>
<td>40-49</td>
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<td>9</td>
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<tr>
<td>50-59</td>
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<td>7</td>
</tr>
<tr>
<td>60-69</td>
<td>26</td>
<td>2</td>
</tr>
<tr>
<td>70-79</td>
<td>37</td>
<td>0</td>
</tr>
<tr>
<td>80-89</td>
<td>33</td>
<td>0</td>
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</table>

without any cerebral atherosclerosis as compared to only 8 per cent in which the reverse is found. The percentage of patients without atherosclerosis in either system steadily declines until the eighth decade, when all patients have some degree of atherosclerosis in their coronary systems. Some patients without cerebral atherosclerosis are present in all decades.

Comparison of Ages at Onset of Coronary and Cerebral Atherosclerosis. By listing the percentage of the sample in each decade involved with minimal (grade 1) or severe (grade 2 or more) cerebral and coronary atherosclerosis, a comparison can be made between the onsets and to a lesser extent the severity of atherosclerosis in the 2 systems. Table 3 shows that only a quarter of the patients in the fourth decade are affected with more than minimal cerebral atherosclerosis while about half of them have more than minimal coronary atherosclerosis. Severe grades of cerebral atherosclerosis start occurring a decade later than do severe grades of coronary atherosclerosis. By the ninth decade 45 per cent of patients have severe coronary atherosclerosis compared to 39 per cent with severe cerebral atherosclerosis.

3. Relationship of Cerebral Atherosclerosis in Various Age Groups to Cerebral Infarction. Sixty cerebral infarcts were found in the 239 necropsies. Cerebral infarcts of all kinds were included: recent, healed, small, large, miliary, and focal. These cases were separated from the remainder and both the mean and "maximal" grades of cerebral and coronary atherosclerosis were calculated and compared with corresponding data from patients without infarcts (fig. 7 and table 5). One half of the 60 patients with cerebral infarcts had less than grade 2 cerebral atherosclerosis. A high proportion of these patients with low grades of atherosclerosis had only miliary infarcts.

Cerebral and Coronary Atherosclerosis and Cerebral Infarction. As might be expected,
Brains having evidence of cerebral infarcts as a group have a higher degree of atherosclerosis than those without infarcts (fig. 7). The difference between patients with and without cerebral infarcts is most pronounced when only the highest of the 6 maximal values determined in each case is used in deriving each group's average. Coronary atherosclerosis is also higher in patients with cerebral infarcts. The differences become less marked in the ninth decade.

4. Role of Thromboembolic Phenomena in Cerebral Infarction. Of the 239 patients studied, 15 had left-sided mural thrombi in their hearts. Nine of the 15 had cerebral infarcts. Of these 9, 3 had complete absence of cerebral atherosclerosis. The others all had high grades of cerebral atherosclerosis (mean 2.28).

5. Relationship of Heart Weight and Hypertensive Heart Disease to Cerebral Atherosclerosis. Cerebral Atherosclerosis and Heart Weight. Ackerman⁶,⁷ compared heart weight with coronary atherosclerosis. Since the weight beyond which a heart is to be considered enlarged is not definite, he used 3 different dividing points, namely 300 Gm., 350 Gm., and 400 Gm., and computed data on coronary atherosclerosis in hearts whose weights were over or under each of these dividing points. No matter which one was used, coronary atherosclerosis was found to be more severe in the heavier hearts.

Table 6 demonstrates the relationship between heart weight and cerebral atherosclerosis on the basis of the same 3 heart-weight dividing points used by Ackerman. These data fairly consistently show that individuals with heavy hearts have more cerebral atherosclerosis than those with lighter hearts. This is true in the younger decades as well.

### Table 5.—Cerebral Atherosclerosis in Patients with and without Cerebral Infarcts*

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Infarcts absent</th>
<th>Infarcts present</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Grade</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
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<td>40-49</td>
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<td>1.02</td>
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<tr>
<td>70-79</td>
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<td>1.34</td>
</tr>
<tr>
<td>80-89</td>
<td>14</td>
<td>1.94</td>
</tr>
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</table>

* See text for definitions of mean and "maximal."

### Table 6.—Relationship of Heart Weight to Cerebral Atherosclerosis

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Normal</th>
<th>Hypertension</th>
<th>Difference, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hearts of given weight</td>
<td>Cerebral sclerosis, mean grade</td>
<td>Hearts of given weight</td>
</tr>
<tr>
<td></td>
<td>100-299 Gm.</td>
<td>300 Gm. or more</td>
<td>100-349 Gm.</td>
</tr>
<tr>
<td>30-39</td>
<td>29</td>
<td>1.02</td>
<td>21</td>
</tr>
<tr>
<td>40-49</td>
<td>21</td>
<td>1.01</td>
<td>24</td>
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<td>50-59</td>
<td>15</td>
<td>1.08</td>
<td>33</td>
</tr>
<tr>
<td>60-69</td>
<td>6</td>
<td>1.35</td>
<td>20</td>
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<tr>
<td>70-79</td>
<td>11</td>
<td>1.43</td>
<td>26</td>
</tr>
<tr>
<td>80-89</td>
<td>8</td>
<td>1.70</td>
<td>25</td>
</tr>
<tr>
<td>100-399 Gm.</td>
<td>300 Gm. or more</td>
<td></td>
<td>100-349 Gm.</td>
</tr>
<tr>
<td>30-39</td>
<td>39</td>
<td>1.01</td>
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<td>1.87</td>
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<td>400 Gm. or more</td>
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</tr>
<tr>
<td>80-89</td>
<td>23</td>
<td>1.89</td>
<td>10</td>
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as the older ones, and is true whether the dividing line between normal and hypertrophied hearts is taken at 300, 350, or 400 Gm. The small change noted in patients with hearts weighing more than or less than 300 and 400 Gm. in the seventh decade may be attributable to the small number of cases (26) in the age group.

Cerebral Atherosclerosis and Hypertensive Heart Disease. A diagnosis of hypertensive heart disease was made when hearts without congenital or valvular disease weighed more than normal in relation to body weight as determined by the method of Smith.\(^{10}\) Table 7 compares cerebral atherosclerosis in cases in which hypertensive heart disease was encountered at necropsy with cerebral atherosclerosis in the remaining cases studied in each decade. The mean grade of cerebral atherosclerosis in normotensive subjects remains the same during the fourth and fifth decades. It then climbs from 1.02 in the fifth decade to 1.79 in the ninth decade. Hypertensive patients have nearly the same grade of cerebral atherosclerosis in the fourth decade as normotensive subjects. By the fifth decade their mean grade of atherosclerosis has climbed sharply to 1.43, and by the ninth decade it has risen to 2.12. After the fourth decade, patients having hypertensive heart disease develop cerebral atherosclerosis earlier and to a more severe degree than do those whose hearts show no evidence of long-standing hypertension. In the seventh decade only 7 patients with hypertensive hearts were available for study, and their mean cerebral atherosclerosis is only 1.31. Since this value is so out of line with the others, it is thought to be due to sampling error.

6. State of Nutrition and Cerebral Atherosclerosis. Patients were subdivided into obese, average, and underweight groups according to the subjective impressions recorded at necropsy. Grades of cerebral atherosclerosis by decade of age were derived for each group; no differences were readily apparent.

**DISCUSSION**

The concept that atherosclerosis steadily progresses with age was modified by White\(^{8,9}\) in 1948, when he demonstrated that in necropsy cases coronary atherosclerosis in males progressed through the sixth decade and then tended to level off. The next year Ackerman\(^{6,7}\) in a similar study demonstrated that coronary atherosclerosis in females progressed through the eighth decade before leveling off. Findings in the present study indicate that cerebral atherosclerosis of the supraclinoid carotid system in females continues to progress through the ninth decade.

In several instances, graphs in this series of patients have shown atherosclerosis to progress to a certain level and then remain at about the same level throughout the remaining decades. This may mean that death is more likely to occur when atherosclerosis reaches this level. It does not mean that the atherosclerotic process continues to increase to a certain age and then slows down. Rather, it is an indication of the type of data derived from a series of necropsy cases. If it were possible to do the same type of study in living individuals and follow them from decade to decade, an entirely different set of curves would likely result.

Cerebral atherosclerosis severe enough to narrow the lumen of a vessel occurred in 26 per cent of the cases in the fourth decade (table 3). Wolkoff\(^{3}\) noted that lipid plaques first began to occur in the fourth decade. Comparison of his classification with the present one is not possible. However, lipid plaques probably represent the first stage of arterial narrowing. Lipid spots as described
would not narrow an arterial lumen. Wol-koff found that lipid plaques were present in all cases by the sixth decade. By the sixth decade in the current series, arterial narrow-
ing was found in only 54 per cent of cases.

In the present study atherosclerosis de-
veloped less rapidly in the intracranial portions of the internal carotid arteries than in either of their 2 branches. This is best explained by their very short length. If the segments of the middle cerebral arteries had been short-
ened so as to have been equal in length to the supraclinoid portions of the internal carotid arteries, their mean atherosclerosis would have been much lower than that recorded. That this is not the entire answer, however, is shown by the fact that the middle cere-
bral arteries have more atherosclerosis than the anterior cerebral. The segments of the anterior cerebral artery were 2 to 3 times as long as those of the middle cerebral arteries. Probably of more importance than the actual grade of atherosclerosis for each pair of branches are the characteristics of their curves when plotted against age. In every instance the grade of atherosclerosis is low in the fourth decade and then increases rap-
idly. In the anterior and middle cerebral arteries the increase continues through the ninth decade. Internal carotid atherosclero-
sis also continues to increase but at a slower rate.

The wide variation in degree of ather-
sclerosis between the cerebral and the coro-nary blood vessels in any one case may be stri-k ing. Since atherosclerosis is a spotty disease, these findings may be explained simply by the hit-or-miss pattern of severe degrees of atherosclerotic narrowing found throughout the body. However, the degrees of atherosclerosis in different arterial sys-
tems, at least in some instances, may be de-
termined by different factors. In chickens atherosclerosis in the coronary vessels is in-
hibited by estrogen administration, while atherosclerosis in the aorta is unaffected. Whether or not similar influences affect human cerebral and coronary arterial systems has not been determined.

The exact mechanisms by which cerebral in-
farcts are produced have not been fully eluci-dated. Cerebral blood flow is determined by blood pressure and vascular resistance. The latter may change uniformly throughout the cerebral vascular bed so that relative blood flow to all parts of the brain remains the same. Athero-
sclerosis is one process that may interfere with this change, resulting in diminished blood flow to certain parts. If impairment is severe enough, infarction re-
sults. This view is supported by the finding of more severe degrees of cerebral athero-
sclerosis in the group of patients with cerebral in-
farcts and also by the finding of a greater difference between "maximal" values for the 2 groups than between mean values.

Interesting changes in the mean values for cerebral and coronary atherosclerosis are evi-
dent when patients are divided according to whether or not they have had cerebral in-
farcts. The curve for cerebral atheroscle-
rosis in females with cerebral infarcts becomes similar to that for coronary atherosclerosis in Ackerman's series of female hearts in that it rises steadily from the fourth through the eighth decade and then levels off. The curve for coronary atherosclerosis in females with cerebral infarcts becomes similar to that for coronary atherosclerosis in White's series of male hearts, in that it rises through the sixth decade and then levels off. Cerebral ather-
sclerosis in females without cerebral infarcts occurs only occasionally before the sixth decade. From the sixth through the eighth decade it increases at a moderate rate, becom-
ing severe in the ninth decade, so that it differs little from that in patients with cere-
bral infarcts.

Of the 60 patients who had cerebral in-
farcts, only 9 had evidence of mural thrombi in the heart. The finding of only 3 out of the 60 patients with strokes who had no cerebral atherosclerosis and who had a possible source for cerebral emboli is quite striking. In 1 of these patients infarcts were small and mul-
tiple. In the other 2 they were large. If the assumption that these 3 patients had cerebral em-
bolization in 60 patients with strokes is 5 per cent or greater. This is similar to the incidence of 4.6 per cent in Towbin's series of 325 state hospital patients with organic disease of the brain.

Since hypertension is known to affect the severity of atherosclerosis, and since it is extremely common in patients with strokes, a higher degree of cerebral atherosclerosis in patients with hypertension is to be expected. In this series a total of 67 patients died with hypertensive heart disease and 60 with cerebral infarcts; 34 had both.

Correlating state of nutrition with severity of atherosclerosis is difficult because of the variety of factors that enter into the evaluation. A patient's terminal state of nutrition is often different from that during health. Determination of state of nutrition itself is open to wide margins of error. No correlation could be found in this series.

Summary and Conclusions

The supraclinoid portions of the carotid arterial systems from 239 women whose ages ranged from 30 to 89 years were examined to determine the degrees of narrowing caused by cerebral atherosclerosis. Cases chosen for study were from a series previously reported in which the degree of coronary atherosclerosis was determined. The following observations were made:

1. The mean of the maximal grades of atherosclerosis present in 6 cerebral arterial branches of the carotid system steadily increased with age. Progression of atherosclerosis became more rapid after the fourth decade of life and then continued to increase at about the same rate through the ninth decade.

2. In the fourth decade, three fourths of the patients were free of more than minimal cerebral atherosclerosis. In the ninth decade only 3 per cent remained free of cerebral atherosclerosis. Severe cerebral atherosclerosis was nonexistent in the fourth decade and occurred in less than a tenth of the cases in the fifth, sixth, and seventh decades. In the eighth and ninth decades it occurred in one third of the cases.

3. The middle cerebral arteries had a slightly greater degree of atherosclerosis than did the anterior cerebral arteries.

4. Coronary arteries tended to develop atherosclerosis earlier than did cerebral arteries. A wide degree of variability often existed between the severity of atherosclerosis in the coronary arteries and the cerebral arteries in any one case. When the figures from a number of cases were considered, the mean atherosclerosis steadily progressed in severity with age in both vascular systems through the eighth decade. Mean cerebral atherosclerosis also increased through the ninth decade in contrast to mean coronary atherosclerosis, which tended to level off after the eighth decade.

5. Brains in this study having recent or healed cerebral infarcts had a greater degree of atherosclerosis than did brains without infarcts. This difference still existed but was less marked in the ninth decade.

6. Cerebral atherosclerosis was more severe in patients with hypertrophied hearts than in those with nonhypertrophied hearts. After the fourth decade this difference averaged between 10 and 50 per cent.

7. The state of nutrition at the time of death seemed to have little relation to the severity of cerebral atherosclerosis.

Summario in Interlingua

Le portiones supraclinoide del systemas de arterias carotic de 239 feminas de etates de inter 30 e 89 annos esseva examinate pro determinar le grados de restriction causate per atherosclerosis cerebral. Le casos seligite pro le presente studio pertineva a un serie pro le qual le grados de atherosclerosis coronari havbe essite determinate in le curso de un previemente reportate investigation. Le se-

quente observationes esseva facite.

1. Le valores medie del grados maximal de atherosclerosis trovate in 6 brancas cerebro-
arterial del sistema carotic cresceva uniformemente con le etate del subjectos. Le progression del atherosclerosis se accelerava
Post le quarte decennio del vita e continuava subsequentemente accelerar se de modo constante usque al fin del none decennio.

2. In le quarte decennio, tres quartos del patientes eseva libere de plus que minimal grados de atherosclerosis cerebral. In le none decennio, solmente 3 pro cento eseva libere de atherosclerosis cerebral. Sever grados de atherosclerosis cerebral non existeva in le quarte decennio e occurreva in minus que un decimo del casos in le quinte, le sexte, e le septime decennio. In le octave e le none decennio illo occurreva in un tertio del casos.

3. Le arterias medio-cerebral eseva un levemente plus alte grado de atherosclerosis que le arterias antero-cerebral.

4. Le arterias coronari tendeva a devenir atherosclerotic plus tosto que le arterias cerebral. Le casos individual monstrava extense variationes in le relation inter le severitate de atherosclerosis in le arterias coronari e le severitate de atherosclerosis in le arterias cerebral. Quando le valores trovate in un numero de casos eseva combine, le severitate medie de atherosclerosis accresceva continuamente con le etate del individuos, tanto in le arterias cerebral como etiam in le arterias coronari. Le valor medie pro atherosclerosis cerebral tendeva a crescer a transverso le none decennio, per contrasto con le valor medie pro atherosclerosis coronari le qual tendeva a formar un plateau post le octave decennio.

5. In isto studio, cerebros con recente o curate infarcimentos cerebral exhibiva plus alte grados de atherosclerosis que cerebros sin infarcimento. Iste differentia persisteva sed eseva minus marcate in le none decennio.

6. Atherosclerosis cerebral eseva plus sever in patientes con hypertrophia cardiac que in patientes con cordes non hypertrophiate.

Post le quarte decennio iste differentia habezva un valor medie de inter 10 e 50 pro cento.

7. Le stato de nutrition al tempore del morte pareva monstrar paue correlation con le severitate del atherosclerosis cerebral.

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