system was essentially normal; however, the symp-
toms suggest that intracranial collateral flow to the
left cerebral hemisphere was deficient. These cir-
cumstances again favored the preservation of left ICA
perfusion by ECA to ECA collaterals.

The patients in this report demonstrate that CCA
occlusion is not invariably associated with propoga-
tion of the thrombus into the internal carotid artery.
In each patient ultrasonic imaging and pulsed Doppler

techniques identified retrograde filling of the ICA via
the ECA, a situation which may be more common
than previously thought, since it is difficult to
demonstrate angiographically. In one patient this
retrograde flow pattern in the ECA was confirmed
angiographically, although the ICA had probably
thrombosed by the time of the study. Judicious use of
non-invasive ultrasonic techniques in symptomatic
patients with common carotid occlusion can identify
those instances in which patency of the distal vessels is
maintained. After confirmation of these findings by
late subtraction angiograms, carotid-carotid or
subclavian-carotid bypass may then provide relief of
symptoms of cerebral ischemia in selected cases.

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Cardiovascular Mortality in Transient Ischemic Attacks

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ALFRED H. TYROLER, M.D., CURTIS G. HAMES, M.D.,
ULRICH PATZSCHKE, M.D., AND CHRISTIAN MANEGOLD, M.D.

SUMMARY Statistical analyses were made of the mortality of persons diagnosed as having definite TIA in an epidemiologic survey of a biracial Southern community. None of the usual risk factors associated with this illness such as heart disease, hypertension or diabetes appears to account for the excess deaths observed in a 10 year period of follow up.

THE MORTALITY RATE of patients with transient cerebral ischemic attacks (TIA) has been found to be considerably greater than that of the general population of comparable age and sex.1,2 Although the increase in mortality in TIA is usually attributed to the presence of associated factors such as hypertension, diabetes or heart disease, there have been few attempts to quantify the relative significance of these conditions. The purpose of the present paper is to determine by means of statistical analyses which, if any, of these concomitant risk factors contribute to the high death rate from TIA.

Patients and Methods

The study population consists of residents of Evans County, Georgia, a small rural community in the high stroke belt of the Southeastern United States. The initial survey of this community comprising approximately 60% White and 40% Black population

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was carried out in 1960 and included all residents 40 years of age or older and a 50% sample of those 15 to 39 years of age. A follow up survey was made between July, 1967, and July, 1969, to determine the 7 to 9 year incidence of vascular disease in this population. The present report is based on the 2471 stroke-free survivors who were re-examined at that time. Twenty-eight of them gave a history of having had definite focal manifestations of TIA with sudden onset of transient limb paralysis, sensory loss, visual defects or speech disorders lasting for 24 hours or less and clearing without significant deficit.** Seven of these 28 persons were Black, 21 White. An additional 51 persons were diagnosed as having uncertain TIA with a history of non-focal neurologic episodes such as alteration in consciousness, dizziness or drop attacks. The neurologic complaints in these people were often vague and could not be differentiated from anxiety or emotional disturbances. Forty-two of these 51 persons were White, 9 Black. None of the 79 persons with definite or uncertain TIA had evidence of a completed stroke in the period between 1960 and 1967-69.

From the time of the second survey examination to December 31, 1978, a follow up period averaging 10 years, a surveillance was carried out to determine the frequency and cause of death. Death certificates were obtained from all persons dying from any cause. In December 31, 1978, a physical examination and electrocardiogram was made of all survivors who had a diagnosis of definite or uncertain TIA at the second survey examination. Survivorship analyses were carried out employing the Mantel-Haenszel life table method which is free of distributional assumptions and uses the logrank test for hypothesis testing.*

### Results

Table 1 shows the frequency of vascular disease appearing among the survivors of the 79 persons with symptoms of TIA. Eleven of the 28 persons with definite TIA were alive at the end of the follow up period. Three of them developed myocardial infarction during this time, 3 had a completed stroke and 6 had angina, congestive heart failure and other evidence of vascular disease. Of the 51 persons with uncertain TIA, 35 survived. Four of them developed infarction, 4 had a completed stroke and 14 had other manifestations of vascular disease.

Table 2 shows the number and cause of death in the 3 population groups observed in the 9 to 10 year period from the 1967-69 survey to the end of 1978. Seventeen or 61% of the 28 persons with definite TIA died during this interval as compared to only 16 or 31% of the 51 persons with uncertain TIA. Of the 2392 persons remaining, only 52 or 20% died. As would be expected, the deaths in each of these 3 groups were due chiefly to vascular diseases. The mean age of persons with definite and uncertain TIA were approximately the same (59 and 61 years respectively), but was greater than that of the remaining population free of stroke or TIA (52 years).

Life table analyses were used to contrast the mortality during the 10 year follow up period. The comparison of the mortality experience of each of the 3 population groups takes into consideration the person-years of follow up contributed by each person until death or termination of the study. As shown in the figure, deaths occurred almost uniformly during this 10 year period. The logrank test of the survival probabilities showed the 3 groups to be significantly different from each other ($\chi^2 = 22.9; p < 0.00001$). The age standardized mortality rate ratio was 2.15 for definite TIA compared to uncertain TIA; and 2.90 and 1.30 respectively for definite TIA and uncertain TIA compared to the stroke and TIA-free population.

Discriminant function analyses were performed to assess the risk factor attribute of TIA, adjusting simultaneously for the other risk factors of mortality. Using a stepwise procedure, the following variables (as determined in 1967-69) were entered into the

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*This represents a heterogeneous group of patients with respect to time of occurrence of neurologic manifestations, between the first and the second examination, i.e., 1960 through 1967/69.

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### Table 1. Vascular Illness Occurring Among Survivors of 28 Persons with Definite and 51 with Uncertain TIA

<table>
<thead>
<tr>
<th>Types of vascular disease*</th>
<th>11 survivors with definite TIA</th>
<th>35 survivors with uncertain TIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Completed stroke</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Other cardiac conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(angina, congestive failure, etc.)</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Hypertension (BP ≥ 160/90)</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>No evidence of heart disease</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

*Categories not mutually exclusive.
model: age, smoking status, diabetes, diastolic blood pressure, electrocardiographic abnormalities, serum cholesterol and diagnosis of TIA. With the exception of serum cholesterol, each of these variables was a significant independent predictor of total mortality ($p < 0.00001$). Thus, with all other risk factors present in the discriminant function, the diagnosis of TIA per se was a significant predictor of mortality.

This information is summarized in table 3 as relative risks, i.e., mortality rate ratios, both unadjusted and adjusted for all other risk factors in the model. The risk factors are ranked by the magnitude of their adjusted rate ratios. The strongest predictor of mortality in this population was age, followed by major electrocardiographic abnormalities (normal vs any major abnormality) at the time of the 1967-69 survey. A diagnosis of definite TIA ranked third as a prognostic factor of death in this multivariable analysis. The diagnosis of uncertain TIA, however, was no longer a significant risk factor for death once adjusted for the other risk factors. Cigarette smoking (current smoker vs non-smoker), diastolic blood pressure ($< 90$ mm Hg vs $\geq 90$ mm Hg) and diabetes (definite or probable vs non-diabetic) each carried significant additional risk of mortality ($p = 0.05$). The level of serum cholesterol ($< 240$ mg/dl vs $\geq 240$ mg/dl) by contrast, was not predictive of death after adjustment for the other variables.

**Discussion**

This study of mortality of persons with TIA is based on an epidemiologic investigation of cerebrovascular disease in a biracial community in which survivorship following the diagnosis of TIA was monitored for approximately 10 years. Our analyses were primarily concerned with mortality of persons diagnosed as having either definite or uncertain TIA as compared with that of the general population free of TIA or stroke. The mortality ($61\%$) found in persons with definite TIA was significantly higher than that ($31\%$) found in persons with uncertain TIA or than that ($20\%$) of the stroke and TIA-free population. The number of persons in this study with definite TIA was small and one must, therefore, be cautious in making generalizations. Nevertheless, these observations are of interest in the prediction of TIA outcome.

One of the major purposes of the study was to demonstrate whether the higher mortality noted in persons with definite TIA could be attributed to their age or to any of the usual concomitant cardiovascular risk factors. On the basis of the analyses described above, neither age nor hypertension, diabetes, major electrocardiographic abnormalities, smoking or hypercholesterolemia could account solely for the excess number of deaths in this group of individuals. Thus, it would appear that the diagnosis of definite TIA carried with it a mortality risk by mechanisms which are not yet clear.

The excess mortality associated with TIA has been reported in other studies. As shown in table 4, the annual mortality found in 4 studies of TIA are remarkably similar to rates of approximately 6% per year. These studies on the relationship of risk factors and the outcome of TIA usually compare various
groups of patients with this illness and do not contrast the prognosis of TIA with a similar cohort who are free of cerebrovascular disease. The results of this epidemiologic study of a biracial community, however, indicate that persons with definite TIA have an excess mortality for reasons outlined above.

References


TABLE 4  Mortality in Persons with TIA During 5 to 16 Year Period of Observation

<table>
<thead>
<tr>
<th>Study location</th>
<th>Years of followup</th>
<th>Total no. TIA cases</th>
<th>No. deaths at end of followup</th>
<th>Percent deaths per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winston-Salem (6)</td>
<td>5.5</td>
<td>225</td>
<td>82</td>
<td>6.5</td>
</tr>
<tr>
<td>Framingham (2)</td>
<td>8</td>
<td>85</td>
<td>31</td>
<td>4.1</td>
</tr>
<tr>
<td>Evans County</td>
<td>10</td>
<td>28</td>
<td>17</td>
<td>6.1</td>
</tr>
<tr>
<td>Rochester (1)</td>
<td>15</td>
<td>199</td>
<td>187</td>
<td>6.1</td>
</tr>
</tbody>
</table>
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