Predisposing Factors in Sudden Cardiac Death in Tecumseh, Michigan
A Prospective Study

By Benjamin N. Chiang, M.D., Lawrence V. Perlman, M.D., Mary Fulton, M.B., M.R.C.P.E., Leon D. Ostrander, Jr., M.D., and Frederick H. Epstein, M.D.

SUMMARY
In an epidemiologic study of the total population of Tecumseh, Michigan, 98 deaths from coronary heart disease were observed between 1959 and 1965. Forty-five of the fatalities occurred within 1 hour of the onset of symptoms and were classified as sudden. The proportion of sudden deaths among men was nearly twice that among women, and the incidence increased progressively with age in both sexes.

Hypertensive heart disease, coronary heart disease, or diabetes mellitus had been detected on prior examination in 62% of those who died suddenly. Physiologic abnormalities associated with a high risk of coronary heart disease were also found more frequently than in the total Tecumseh population.

All but seven of the persons who died suddenly had abnormalities including arrhythmias and conduction defects which were detected in the standard 12-lead electrocardiogram.

Although sudden deaths often seem to occur without warning, the victims are predisposed by conditions which are detectable long before the catastrophic event. The identification of conditions which are precursors of sudden death from coronary heart disease permits a rational consideration of possible preventive measures.

Additional Indexing Words:
Epidemiologic study  Hypertension  Coronary heart disease  Diabetes mellitus
Risk factors  Electrocardiographic abnormalities

RECENT ADVANCES in coronary care have reduced the immediate mortality from myocardial infarction within hospitals, but a large proportion of stricken individuals die so suddenly that they do not reach the hospital. Potential victims must be identified as the first step in the development of a preventive program. Although sudden deaths often occur seemingly without warning, predisposing conditions which were detectable before the catastrophic event are usually found. This is a report of the antemortem findings among 45 persons who died suddenly during a 6-year period in Tecumseh, Michigan.

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Methods

The Tecumseh study is a prospective epidemiologic investigation of nearly the total population of the community. The details of the study have been described previously.\textsuperscript{5-8} During the initial examination of the population in 1959 and 1960, 8,641 participants (88\% of the total population) gave a detailed medical history and had a thorough physical examination, biochemical determinations, anthropometric measurements, chest roentgenograms, and standard 12-lead electrocardiograms.

Initial clinical diagnoses of diseases were made by the examining physicians and then reviewed and classified according to strict criteria by senior staff physicians. Electrocardiograms were recorded on a direct-writing instrument at a paper speed of 50 mm/sec and coded according to the system of Blackburn and associates.\textsuperscript{9} Serum cholesterol was determined by the Abell-Kendall method\textsuperscript{10} and blood glucose by the Somogyi-Nelson method.\textsuperscript{11} Relative weight was computed from the ratio of actual weight to predicted weight, derived from a regression equation involving height, bi-acromial diameter, bicrystal diameter, and sex.\textsuperscript{12} Elevated values for blood pressure, serum cholesterol, and relative weight were defined according to the age and sex-specific upper quintiles of the distributions of the variables in the population. Except for the first 22\% of persons studied in the 1959-1960 series of examinations, blood samples were taken 1 hour after a 100-g oral glucose challenge. Casual specimens were drawn from all unchallenged adults including known diabetics.

Eighty-five adults were classified as diabetics because of earlier blood glucose elevations detected and treated by their personal physicians. Examined persons were grouped according to age, sex, and type of test, either casual or postchallenge, and ranked within their group in order of blood glucose level. Hyperglycemia was arbitrarily defined as any value above the 80th percentile for each group. The known diabetics were added to the upper quintile, so that the hyperglycemic segment included 22\% of men and 24\% of women past 40 years of age.

The data on 3,643 persons 30 years of age or older included information on all the deaths from coronary heart disease which occurred during the first 6 years of surveillance. Sudden coronary death was defined as any fatality which occurred outside of the hospital and within 1 hour of the onset of symptoms. Deaths due to violence or any suspected cause other than coronary heart disease were excluded. This information was carefully collected, documented, and summarized. Death certificates were reviewed for each participant who died, and all obtainable information from physicians’ notes, hospital records, statements from relatives, and coroners’ reports was also examined. Only three of those who died suddenly had autopsies and in each case the postmortem examination revealed extensive coronary artery atherosclerosis and occlusion.

Results

Incidence of Sudden Death

During the period from 1959 to 1965, 98 persons died of coronary heart disease and 45 of the deaths were sudden. Most of the victims (29 men and 16 women) died at home, but some were at work, traveling, or on the way to the hospital. The incidence of this event increased progressively with age from 2 per 1,000 at ages 30 to 39 to 52 per 1,000 among those past 70 (table 1).

Antecedent Illness

The presence of one of three clinical diseases—diabetes mellitus, hypertensive heart disease, or coronary heart disease—at initial examination of persons past age 30 was associated with an excessive incidence

| Table 1 |

<table>
<thead>
<tr>
<th>Sudden Deaths by Age at Initial Examination in Tecumseh, Michigan (1959-1965)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>30-39</td>
</tr>
<tr>
<td>40-49</td>
</tr>
<tr>
<td>50-59</td>
</tr>
<tr>
<td>60-69</td>
</tr>
<tr>
<td>70+</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

* Sudden death defined as death occurring within 1 hour of onset of symptoms outside of hospital.
Table 2

Incidence of Sudden Death Among Persons 30 Years of Age or Older with Cardiovascular Disease or Diabetes in the Tecumseh Population (1959-1965)

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>No. sudden deaths*</th>
<th>No. observed at initial exam</th>
<th>6-year incidence per 1,000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease (CHD)†</td>
<td>18</td>
<td>108</td>
<td>166.7</td>
</tr>
<tr>
<td>Diabetes mellitus (DM)</td>
<td>8</td>
<td>85</td>
<td>94.1</td>
</tr>
<tr>
<td>Hypertensive heart disease (HHD)‡</td>
<td>6</td>
<td>67</td>
<td>89.5</td>
</tr>
<tr>
<td>None of the above conditions</td>
<td>17</td>
<td>3,387</td>
<td>5.0</td>
</tr>
</tbody>
</table>

*Four persons had multiple conditions: HHD + CHD (1), HHD + DM (1), CHD + DM (2).
†Probable diagnosis of angina pectoris or myocardial infarction.
‡Systolic BP ≥ 160 mm Hg or diastolic BP ≥ 95 mm Hg and left ventricular hypertrophy in ECG (Minnesota Code III_).

Table 3

Expected and Observed Numbers of Five Physiologic Variables in the Highest Quintile (Specific for Age and Sex) Among Persons Who Died Suddenly in Tecumseh, Michigan (1959-1965)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sudden death N = 45 (highest quintile*)</th>
<th>Observed</th>
<th>Expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>19†</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>17†</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Relative weight</td>
<td>15‡</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Serum cholesterol</td>
<td>10</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Blood glucose§</td>
<td>16†</td>
<td>10.4</td>
<td></td>
</tr>
</tbody>
</table>

*Upper quintile, age and sex-specific.
†Difference significant at P < 0.01.
‡Difference significant at P < 0.05.
§Including upper quintile and known diabetes.

The rate of sudden death as compared with persons who had none of these conditions (table 2). Eighteen of 108 persons with coronary heart disease, eight of 85 with diabetes, and six of 67 with hypertensive heart disease died suddenly. Thus, the incidence rate is 15-fold or greater among persons with at least one of the three antecedent illnesses than among unaffected individuals (table 2).

Risk Factors

A higher proportion of the persons with sudden fatalities had systolic or diastolic hypertension, high relative weight, or hyperglycemia than the Tecumseh population as a whole, but there was no excess of hypercholesterolemia (table 3). The smoking habits of those who died suddenly were similar to those of the general Tecumseh population. The proportion of multiple risk factors among the sudden fatalities was significantly higher than among the total adult population (table 4). Fifty-one per cent of the persons who died suddenly had two or more risk factors as compared with 27% in the total population past age 30. Conversely, 41.3% of the total population had none of the five risk factors as

Table 4

Multiple Risk Factors* at Initial Examination in Persons Who Died Suddenly over a 6-Year Period in Tecumseh Population

<table>
<thead>
<tr>
<th></th>
<th>Sudden death (N = 45)</th>
<th>Total population (age ≥ 30) (N = 3,643)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>None</td>
<td>6</td>
<td>13.3</td>
</tr>
<tr>
<td>One factor</td>
<td>16</td>
<td>35.5</td>
</tr>
<tr>
<td>Two factors</td>
<td>16</td>
<td>35.5</td>
</tr>
<tr>
<td>Three or more factors</td>
<td>7</td>
<td>15.7</td>
</tr>
</tbody>
</table>

*Systolic and diastolic pressures, cholesterol, relative weight, and blood glucose in the upper quintile, age and sex specific.

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Table 5

*Antecedent ECG Findings in 45 Persons Who Died Suddenly over Six-Year Period (1959-1965) in Tecumseh Population*

<table>
<thead>
<tr>
<th>ECG Findings</th>
<th>Minnesota Code</th>
<th>No. of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q pattern</td>
<td>I</td>
<td>5</td>
</tr>
<tr>
<td>Left axis deviation</td>
<td>II</td>
<td>8</td>
</tr>
<tr>
<td>High R amplitude</td>
<td>III</td>
<td>6</td>
</tr>
<tr>
<td>S-T segment depression</td>
<td>IV</td>
<td>6</td>
</tr>
<tr>
<td>T-wave changes</td>
<td>V</td>
<td>5</td>
</tr>
<tr>
<td>First degree A-V block</td>
<td>VI</td>
<td>2</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete left BBB</td>
<td>VII</td>
<td>5</td>
</tr>
<tr>
<td>Complete right BBB</td>
<td>VII</td>
<td>3</td>
</tr>
<tr>
<td>Incomplete right BBB</td>
<td>VII</td>
<td>1</td>
</tr>
<tr>
<td>Electrocardiographic abnormalities</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Three of four persons with "bilateral bundle-branch block" (complete right and partial left bundle-branch block manifest by left axis deviation beyond −30° in the frontal plane), five...
Sudden Cardiac Death

of the 26 persons with old myocardial infarct, five of 18 with left bundle-branch block, 10 of 165 with ventricular premature beats, six of 124 with left ventricular hypertrophy, and three of 100 with first degree A-V block, died suddenly in the 6-year period. Conversely, only seven of 2,454 persons in the population who had normal ECGs died suddenly in the same period.

Multiple Conditions

Most of the 45 victims had more than one antecedent abnormality. Only one person had no evidence of coronary or hypertensive heart disease, diabetes, coronary risk factors, or electrocardiographic abnormalities (as defined in table 5) at the time of the initial examination.

Discussion

The reported frequency of sudden death as the initial manifestation of coronary heart disease varies from 20% to 25%.5, 13, 14 Careful investigation of such cases reveals that few individuals were free of significant predisposing abnormalities prior to death. In a series of 1,098 sudden deaths reported by Kuller,13 only 8% of the persons had no history of diabetes, heart disease, hypertension, or stroke, had not seen a physician within a month prior to death, or had not been hospitalized during the year before death. The reports of several large series support the impression that most sudden deaths among white Americans are due to coronary heart disease. In a study of 1,348 sudden deaths, Myerburg and Davis15 found that 25.8% had a definite history of coronary heart disease, and another 33.4% had suggestive symptoms. In a large autopsy study from Westchester County, New York, Spain et al.16 reported that 90% of sudden fatalities resulted from coronary artery disease.

All 45 sudden deaths in Tecumseh occurred outside the hospital and within 1 hour of the onset of symptoms. All obtainable information from physicians’ notes, prior hospital records, witnesses to the event, coroners' reports, and autopsy data were reviewed in addition to the death certificates. Because postmortem examinations of sudden fatalities are infrequent in Tecumseh, coronary heart disease is strongly suspect but usually unproven as the cause of such deaths among the study population. Deaths known or suspected to have occurred from conditions other than coronary heart disease were excluded from the analysis.

Only a few prospective studies of predisposing factors among sudden fatalities have been reported. In general, the same risk factors (hypertension, hypercholesterolemia, overweight, diabetes, cigarette smoking, and physical inactivity) which predispose to other manifestations of coronary disease have been associated with sudden death.5, 13 The reported incidence increases with age and shows a marked male predominance.5, 4, 13 In the Framingham study, high serum cholesterol concentrations and electrocardiographic evidence of left ventricular hypertrophy were associated with sudden deaths.5, 17 Pell and D’Alonzo,4 in a study of employees of a large company, found that immediate mortality from acute myocardial infarction was associated with increasing age, antecedent hypertension, and prior electrocardiographic abnormalities such as conduction defects and ventricular premature beats. Morris and coworkers18 reported that physical inactivity was related to sudden death. Cigarette smoking has also been implicated in sudden demise from coronary heart disease.19

In Tecumseh, 45.9% of coronary heart disease fatalities were sudden. Although intensive coronary care may reduce early mortality in the hospital, a large proportion of coronary fatalities occur beyond such assistance. Most of those who died suddenly in Tecumseh had hypertension, diabetes, coronary heart disease, or electrocardiographic abnormalities which were recognized long before death (tables 2 and 5). Only one of the 45 victims was free of recognizable antecedent disease, predisposing risk factors, or abnormalities detected in the electrocardiogram at the time of the initial examination.

Risk factors which predispose to other manifestations of coronary heart disease were also closely associated with sudden deaths in Tecumseh (table 3). Those who died sudden-
ly had the greatest number of risk factors, with hypertension, hyperglycemia, and overweight predominant. Multiple risk factors were detected more frequently among the sudden fatalities than in the total Tecumseh population (table 4). Hypercholesterolemia was no more prevalent among those who died suddenly than in the total population.

The risk factor analyses in Tecumseh, which are based on age and sex-specific levels rather than fixed cutting points, may minimize the biologic importance of conditions whose median and upper quintile values tend to be in a high range among certain groups. The serum cholesterol is an example. The mean cholesterol concentration for the persons who died suddenly was 235 mg%, and 35% had values of 250 mg% or higher, which are far in excess of "ideal" concentrations. On the other hand, values for the total Tecumseh population of like age and sex are similarly high, so that discrimination is not improved by the use of fixed cutting points unless one ignores age and sex differences. Such a maneuver would, therefore, not be helpful. Also, the association between serum cholesterol level and coronary heart disease incidence diminishes with age, so that the present findings among persons, many of whom are older, should not be taken to apply to sudden deaths in general.

There was no excess of cigarette smokers among participants who died suddenly. Analysis of the 1959-1960 examination results in Tecumseh revealed that cigarette smoking was no more prevalent among persons with coronary disease than in the general Tecumseh population, but smoking was significantly associated with the incidence of new disease during the succeeding years, particularly among persons less than 65 years of age. It is not surprising, then, that the smoking habits of the sudden death group, who were generally elderly and had a high prevalence of known heart disease, were similar to those of unaffected members of the Tecumseh population of like age and sex.

The immediate cause of sudden death in coronary heart disease is almost always either ventricular fibrillation or asystole. In the Tecumseh population various abnormal findings in the electrocardiogram including rhythm disturbances and conduction defects were more commonly detected among individuals destined to die suddenly than among other persons. An analysis of the relationship of ventricular premature beats to coronary heart disease morbidity and mortality in Tecumseh has been published earlier. Three of the four participants with "bilateral bundle-branch block syndrome" died suddenly. This condition has been implicated in the development of complete atioventricular heart block. Abnormalities detected in the electrocardiogram, particularly arrhythmias and conduction defects, may increase the risk of sudden death but they were so frequently associated with other predisposing factors among the 45 Tecumseh victims that their relative contribution to the fatal outcome remains conjectural.

Since myocardial ischemia lowers the threshold for ventricular arrhythmias and delays conduction velocities, electrocardiographic evidence of ischemic heart disease may favor electrical failure, especially when associated with pre-existent rhythm disturbances or conduction defects. While other risk factors, such as hypertension, hypercholesterolemia, overweight, and hyperglycemia, are probably atherogenic, abnormal findings detected in electrocardiograms, particularly arrhythmias and conduction defects, may precipitate sudden death.

Although sudden death often seems to occur without warning, the victims are almost always predisposed to their fate by conditions which are detectable long before the fatal event. Recognition of these specific abnormalities is a necessary prerequisite to preventive efforts. Presumably, any regimen which corrects the conditions predisposing to coronary heart disease in general might also be beneficial in the prevention of sudden death. However, the factors which cause electrical instability and mechanistic myocardial failure would probably require more specific prophylactic measures.

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References


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