Relative Role of Factors Associated With Cerebral Infarction and Cerebral Hemorrhage

A Matched Pair Case-Control Study


SUMMARY Comprehensive ascertainment of all possible new cases of stroke appearing between January 1, 1970 and June 30, 1971, and admitted to three major hospitals in Winnipeg, Manitoba, has been achieved by reviewing the Manitoba Health Services Commission claim reports. The medical records of these cases were reviewed, pertinent data were abstracted, and rigid criteria for diagnosis were followed. Also, data were obtained from death certificates, autopsy reports and long-term hospital records. A total of 606 ascertained cases (410 infarction, 137 hemorrhage, and 59 undetermined type) were matched for age, sex, residence and year of admission with 606 controls from admissions for other than cardio-vascular and cerebrovascular disorders. The data were analyzed for elucidating the possible risk factors for infarction (INF) and hemorrhage (HGE).

The findings suggested that hypertension was the main risk factor in hemorrhage, whereas in infarction, along with hypertension, other factors such as diabetes, heart enlargement in chest x-ray, ECG abnormalities, and smoking were suggested as risk factors. There was an association also between infarction, on one hand, and the history of receiving anticoagulants, diuretics, and medications for the heart, and the occurrence of myocardial infarction, on the other hand. These features indicate that infarction and ischemic heart disease have similar risk factors.

Hemoglobin and hematocrit were higher in infarction cases than in their controls only when measured at stroke admission. No difference was revealed when they were measured prior to stroke. Their association with infarction therefore may be secondary to other factors and of no significance for its risk.

standing feature of this design is that it deals only with new cases of stroke and it considers each of the two major entities of stroke (INF and HGE) separately, so that the natural history of each entity might be understood and the relative role of the factors associated with one entity versus the other might be clarified.

Methods

Virtually all residents in the province of Manitoba are registered with the Manitoba Health Services Commission (MHSC) — a governmental health care agency which organizes medical and hospital care at no cost for the residents. The patient has the freedom of selecting his own physician.

Since stroke is an acute condition of serious manifestations, and medical care is of no cost to the patient, almost every patient is expected to be brought to the attention of the physician and subsequently will be hospitalized, at least for establishing the diagnosis and for initial care. Thus the MHSC hospital claim reports provide a reasonable source for comprehensive ascertainment of all possible new cases of stroke appearing in the province during a specified period. From these reports, all cases diagnosed as cerebrovascular disease (ISCD rubrics 430-438 Eighth Revision) who were
admitted to the three major hospitals in the greater Winnipeg area (about 500,000 residents) — Winnipeg General Hospital, St. Boniface Hospital, and Victoria General Hospital — during the period January 1, 1970 to June 30, 1971, were reviewed. Further detailed data from hospital medical records were obtained by three field research assistants (trained nurses). The data included personal characteristics, results of the physical examination, history of certain diseases, mode of onset, signs, symptoms, and progress of the case, and laboratory findings. Where available, autopsy reports and data from death certificates and from long-term hospital records also were secured.

The data were thoroughly reviewed by one of us (H.A.H.A.) and the criteria of classification and diagnosis of cerebrovascular diseases, established by the ad hoc committee of the Advisory Council for the National Institute of Neurological Diseases and Stroke, were strictly followed to establish a diagnosis for each case. When sufficient evidence was available, the case was assigned to either the INF group (thrombotic, embolic, or unknown origin) or to the HGE group (subarachnoid hemorrhage, intracerebral hemorrhage, or hemorrhage of unknown origin). Otherwise, if sufficient evidence were not available to identify the type of stroke, the case would be designated as stroke of undetermined type. Only new established cases of acute stroke appearing during the period of the study among Manitoba residents and admitted to the three hospitals mentioned above were included. Thus 606 cases finally satisfied the criteria for inclusion. These were subclassified by age, sex and residence for selection of controls. Each case was then matched with one control for age (within five years), sex, residence (urban and rural), year of admission, and hospital. The sampling frame for the controls included all admissions to the same hospitals for conditions other than diseases of the nervous system (ICD 320-358), ischemic heart disease (410-414), cerebrovascular disease (430-438), and mental disorders (290-315).

For the 606 controls, data similar to those collected for the cases (except for data related specifically to the condition of stroke such as signs, symptoms and others) were also obtained from the medical records in hospitals. The analysis was carried out using the matched-pair Z-test for testing the difference between cases and controls in case of categorical or discrete variables, and the t-test for testing the difference between the means of the matched pairs in case of continuous or numerical variables.

Results

Of the 606 cases, 410 (67.7%) were INF, 137 (22.6%) HGE, and 59 (9.7%) strokes of undetermined type. A total of 338 cases (55.8%) were from Winnipeg General Hospital, 227 cases (37.5%) from St. Boniface Hospital and 41 (6.8%) from Victoria General Hospital. Three hundred forty-six (57.1%) were men and 260 (42.9%) women.

Of the 606 controls, 189 (31.2%) were admitted for diseases of the digestive and genitourinary systems; 88 (14.5%) for endocrinal, nutritional, metabolic, musculoskeletal and skin diseases; 83 (13.7%) for neoplasms; 77 (12.7%) for diseases of the sense organs; 66 (10.9%) for diseases of blood and circulatory system other than cerebrovascular and cardiovascular diseases, and 103 (17%) for miscellaneous conditions including accidents, poisoning, violence, complications of pregnancy and puerperium, and diseases of the respiratory system.

The mean age of cases was 66.99 ± 14.1 years and for the controls was 66.84 ± 14.1 years, indicating a successful match. The results to follow deal with INF and HGE separately.

Table 1 shows the comparison between cases and controls with respect to marital status, religion, birthplace and occupation for INF and HGE. Pairs in which subjects were of unknown status regarding any of these variables were excluded from the analysis. However, among the excluded pairs, the pattern of differences in these variables was examined between the cases for whom the controls' status was unknown and the controls for whom the cases' status was unknown and found to be similar to that of the pairs included in the analysis. As shown in the table there were more of married, separated, divorced, or widowed and less of singles among the cases than among the controls for the INF group (p = 0.04); no difference was revealed for the HGE

### Table 1 Differences Between Paired Cases and Controls in Some Personal Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relationship</th>
<th>Infarction Case+</th>
<th>Infarction Control+</th>
<th>Relative risk</th>
<th>P</th>
<th>Hemorrhage Case+</th>
<th>Hemorrhage Control+</th>
<th>Relative risk</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital status</td>
<td>Married, separated, widowed or divorced versus single</td>
<td>44</td>
<td>27</td>
<td>1.6</td>
<td>0.04</td>
<td>12</td>
<td>11</td>
<td>1.1</td>
<td>NS</td>
</tr>
<tr>
<td>Religion</td>
<td>Jews versus others</td>
<td>18</td>
<td>25</td>
<td>0.7</td>
<td>NS</td>
<td>7</td>
<td>4</td>
<td>1.8</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Mennonite and Hutterite versus others</td>
<td>8</td>
<td>4</td>
<td>2.0</td>
<td>NS</td>
<td>(3)</td>
<td>(1)</td>
<td>(3)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Catholic versus others</td>
<td>71</td>
<td>68</td>
<td>1.0</td>
<td>NS</td>
<td>13</td>
<td>29</td>
<td>0.5</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td></td>
<td>Protestant versus others</td>
<td>82</td>
<td>79</td>
<td>1.0</td>
<td>NS</td>
<td>29</td>
<td>18</td>
<td>1.6</td>
<td>NS</td>
</tr>
<tr>
<td>Birthplace</td>
<td>Northern Europe versus others</td>
<td>23</td>
<td>16</td>
<td>1.4</td>
<td>NS</td>
<td>(4)</td>
<td>(5)</td>
<td>(0.8)</td>
<td>(NS)</td>
</tr>
<tr>
<td></td>
<td>Eastern Europe versus others</td>
<td>25</td>
<td>23</td>
<td>1.1</td>
<td>NS</td>
<td>5</td>
<td>8</td>
<td>0.6</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Other Foreign versus others</td>
<td>9</td>
<td>8</td>
<td>1.1</td>
<td>NS</td>
<td>(2)</td>
<td>(0)</td>
<td>(—)</td>
<td>(—)</td>
</tr>
<tr>
<td></td>
<td>Canada versus others</td>
<td>35</td>
<td>41</td>
<td>0.9</td>
<td>NS</td>
<td>12</td>
<td>8</td>
<td>1.5</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>United States versus others</td>
<td>5</td>
<td>5</td>
<td>1.0</td>
<td>NS</td>
<td>(1)</td>
<td>(2)</td>
<td>(0.5)</td>
<td>(NS)</td>
</tr>
<tr>
<td>Occupation</td>
<td>Managerial, professional, or clerk versus sales service, transportation, primary or craftsman</td>
<td>29</td>
<td>22</td>
<td>1.3</td>
<td>NS</td>
<td>5</td>
<td>6</td>
<td>0.8</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Figures between parentheses indicate results based on an expected frequency <5.
*NS = not significant at α = 0.05.
*+ = those who have the characteristic before the word versus, and — = those who do not have such characteristic.
group. Aside from the fewer Catholics among HGE cases than among controls (p < 0.02) there were no other observed significant differences in other variables.

For comparing the family history or the history of certain diseases between cases and controls, the number of pairs of which the case but not the control had such history mentioned in the medical records was compared with the number of pairs in which the control but not the case had that history. Table 2 shows these differences in family history of stroke, cardiovascular diseases, hypertension and in the history of hypertension in the patient. In INF but not in HGE the cases had more family history of hypertension than the controls (p = 0.01). In both INF and HGE, however, there was definite history of hypertension in the patients more than in the controls (p < 0.00002), but no significant difference in the family history of cardiovascular disease or stroke.

The medical records were searched for a history or a diagnosis of cardiovascular diseases as well as for a variety of other diseases occurring prior to the stroke for the cases and prior to the condition for which the control was admitted last. Tables 3 and 4 show the frequency of these diseases among the paired cases and controls. It clearly appears that more INF cases than controls had diabetes mellitus (p < 0.0002), myocardial infarction (p < 0.00002), hypertensive heart disease (p = 0.004), rheumatic heart disease (p = 0.001) and embolism (p < 0.05). These differences were not revealed for HGE. On the other hand, in HGE there was a significantly lower frequency of peripheral vascular diseases (p = 0.04), and higher frequency of kidney disease (p = 0.02) and alcoholism (p < 0.03) in the cases than in the controls. In both INF and HGE there was a greater frequency of prior arteriosclerotic heart disease and atrial fibrillation in the cases than in the controls, but no significant difference in the frequency of congestive heart failure and angina pectoris. For other diseases and conditions listed in table 4 no apparent significant differences were revealed except for the higher frequency of orthopedic disease and other unlisted conditions in the controls than in the cases.

The history of receiving specific medications such as antihypertensives, anticoagulants, diuretics, sedatives, and medication for the heart, during admissions prior to stroke and prior to control admission, was compared in both INF and HGE with their controls. Table 5 shows that the antihypertensives and sedatives were more frequently prescribed for the cases than for the controls in both INF and HGE. Whereas only in INF was the previous administration of anticoagulants, medications for the heart and diuretics clearly in excess for the cases than for the controls (p < 0.0002, 0.007, < 0.001, respectively).

Abnormalities in chest x-ray and in the ECG tracings during the first hospital admission prior to the occurrence of stroke or control condition were also checked. These findings are presented in tables 6 and 7 respectively. The mean difference in the period between the first hospital admission prior to stroke (or control) and stroke (or control) admission was compared in cases and in controls and no significant difference was revealed. From table 6 it is evident once more that in INF but not in HGE the frequency of detection of heart enlargement in x-ray, ECG abnormalities (particularly ST and T changes) prior to stroke was significantly more in cases than in controls. No difference between cases and controls was detected in the ECG for conduction or rhythm prior to stroke in either INF or HGE. During stroke or control admission, however, both INF and HGE showed a significantly higher frequency of enlarged heart in x-ray, T and ST changes, abnormalities in heart rhythm and generally more ECG abnormalities in the cases than in the controls; the statistical significance was higher in INF than in HGE.

The history of smoking and alcohol drinking was not

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**Table 2 Differences Between Paired Cases and Controls in Family History of Cardiovascular Disease and History of Hypertension**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Infarction Case+/control -</th>
<th>Control+/case +</th>
<th>Relative Risk</th>
<th>P</th>
<th>Hemorrhage Case+/control -</th>
<th>Control+/case +</th>
<th>Relative Risk</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of stroke</td>
<td>41</td>
<td>26</td>
<td>1.6</td>
<td>NS</td>
<td>8</td>
<td>11</td>
<td>0.7</td>
<td>NS</td>
</tr>
<tr>
<td>Family history of cardiovascular disease</td>
<td>66</td>
<td>47</td>
<td>1.4</td>
<td>NS</td>
<td>18</td>
<td>17</td>
<td>1.1</td>
<td>NS</td>
</tr>
<tr>
<td>Family history of hypertension</td>
<td>19</td>
<td>6</td>
<td>3.2</td>
<td>&lt;0.01</td>
<td>10</td>
<td>8</td>
<td>1.3</td>
<td>NS</td>
</tr>
<tr>
<td>History of hypertension in patient</td>
<td>127</td>
<td>58</td>
<td>2.2</td>
<td>&lt;0.0002</td>
<td>47</td>
<td>10</td>
<td>4.7</td>
<td>&lt;0.0002</td>
</tr>
</tbody>
</table>

See footnote of table 1 for explanation.

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**Table 3 Differences Between Paired Cases and Controls in Occurrence of Certain Cardiovascular Diseases Prior to Stroke or Control Condition**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Infarction Case+/control -</th>
<th>Control+/case +</th>
<th>Relative Risk</th>
<th>P</th>
<th>Hemorrhage Case+/control -</th>
<th>Control+/case +</th>
<th>Relative Risk</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>72</td>
<td>27</td>
<td>2.7</td>
<td>&lt;0.0002</td>
<td>6</td>
<td>3</td>
<td>2 (NS)</td>
<td></td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>19</td>
<td>16</td>
<td>1.2</td>
<td>NS</td>
<td>4</td>
<td>6</td>
<td>0.7</td>
<td>NS</td>
</tr>
<tr>
<td>Arteriosclerotic heart disease</td>
<td>44</td>
<td>25</td>
<td>1.8</td>
<td>&lt;0.02</td>
<td>10</td>
<td>2</td>
<td>5.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>72</td>
<td>53</td>
<td>1.4</td>
<td>NS</td>
<td>18</td>
<td>9</td>
<td>2.0</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertensive heart disease, prior to stroke</td>
<td>18</td>
<td>4</td>
<td>4.5</td>
<td>0.004</td>
<td>(4)</td>
<td>(1)</td>
<td>(4) (NS)</td>
<td></td>
</tr>
<tr>
<td>Rheumatic heart disease, prior</td>
<td>20</td>
<td>3</td>
<td>6.7</td>
<td>&lt;0.001</td>
<td>(6)</td>
<td>(3)</td>
<td>(2.0) (NS)</td>
<td></td>
</tr>
<tr>
<td>Peri-vascular disease, prior</td>
<td>41</td>
<td>37</td>
<td>1.1</td>
<td>NS</td>
<td>10</td>
<td>20</td>
<td>0.5</td>
<td>0.04</td>
</tr>
<tr>
<td>Atrial fibrillation, prior</td>
<td>40</td>
<td>11</td>
<td>3.6</td>
<td>&lt;0.0002</td>
<td>(7)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
</tr>
<tr>
<td>Embolism</td>
<td>(4)</td>
<td>(0)</td>
<td>(-)</td>
<td>(&lt;0.05)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
</tr>
</tbody>
</table>

MI = myocardial infarction.

See footnote of table 1 for explanation.
however, for cholesterol and triglycerides there were very
among controls (p < 0.05), whereas the diastolic BP was
condition, was significantly higher among INF cases than
provided information for the above-mentioned variables;
any pair in which one or both members lacked the data was
out only on the pairs with available data from the records;
in table 9. It should be noted that this analysis was carried
by applying the t-test for the pairs and the results are shown
The differences between cases and controls in continuous
variables such as blood pressure (BP), blood sugar,
reduction, body weight and height were tested by
applying the t-test for the pairs and the results are shown
in table 9. It should be noted that this analysis was carried
out only on the pairs with available data from the records;
any pair in which one or both members lacked the data was
not included. In general, a reasonably large number of pairs
provided information for the above-mentioned variables;
however, for cholesterol and triglycerides there were very
few data in the records. The analysis of such data was con-
sidered unreliable for meaningful results and, therefore, will
not be presented here.
From table 9 it is evident that systolic BP, measured during
the first hospital admission prior to stroke or control
condition, was significantly higher among INF cases than
among controls (p < 0.05), whereas the diastolic BP was
higher in the case of HGE (p < 0.01). During stroke ad-
mission, however, both systolic and diastolic BPs were higher
in the cases than in the controls for INF and for HGE
(p < 0.001). The fasting blood sugar level at stroke or con-
trol admission was also higher in cases than in controls for
INF (p < 0.001) and for HGE (p < 0.05). The data on fast-
ing blood sugar level prior to stroke admission were not
available on sufficient cases and controls for analysis. With
respect to hemoglobin and hematocrit, there was no signifi-
cant difference between cases and controls in INF or in
HGE when the measurement was made during admission
prior to stroke or condition of control. At stroke or control
admission, however, hemoglobin and hematocrit levels were
significantly higher in cases than in controls for the INF
group only. No difference in body weight and height was
observed between cases and controls in both INF and HGE.

Discussion
It has been shown previously that the incidence of INF
and HGE varied markedly according to age, sex, residence,
occupation, religion and birthplace. 1-2 In this report a fe-
findings dealing with religion, occupation and birthplace
have not attained statistical significance as that revealed
from the incidence data. 2 However, one should keep in mind
that the previous report was based on incidence data relat-
ing new cases to the total population, whereas in this report
two groups of cases and controls were compared, and the
controls were hospitalized cases other than stroke or cardio-
vascular diseases. For certain religions and ethnic groups
there is a possible bias toward admissions to hospitals,
particularly for the control group in which there is a good
chance that the disease might not have serious
manifestations. For this reason we believe that our previous
incidence data dealing with these specific variables (religion
and birthplace) are more reliable than the case control data.
The findings in this study strongly support the hypothesis
that the epidemiological features of INF resemble those of
ischemic heart disease. It was shown even that the frequency
of occurrence prior to stroke of conditions such as myo-
cardial infarction, hypertensive heart disease, and the fre-
cency of receiving, prior to stroke, antihypertensive drugs,
This study also confirms the very important role of high blood pressure in the genesis of both INF and HGE. The observed significantly high systolic BP in INF and high diastolic BP in HGE prior to stroke may suggest a specific role of each in the genesis of these conditions. However, the differences in diastolic BP for INF and in systolic BP for HGE were of borderline significance (0.05 < p < 0.10); also, both systolic and diastolic BPs were equally significantly higher in the cases than in the controls in either INF or HGE when measured at stroke admission. Hypertension has been labeled universally as the most common and potent precursor of INF. Hypertension may also lead to heart enlargement and to heart abnormalities. The fact that such abnormalities appeared sometime before the occurrence of HGE in this study may indicate that the level of blood pressure might have been elevated for a long period in INF, whereas the elevation was for a shorter period in HGE.

The clear excess of diabetes mellitus in INF but not in HGE supports its role in the development of INF. Such a role also has been shown from the Framingham data in which an increased risk of INF was observed in persons with anticoagulants, medications for the heart, and diuretics were significantly higher in the INF cases than in the controls. Likewise, during the first hospital admission prior to stroke, the chest x-ray showed a greater frequency of heart enlargement and the ECG showed more occurrences of general abnormalities and of ST and T changes as well as abnormalities in conduction in the INF group than in the controls. On the other hand, in HGE, except for the significantly higher frequency of receiving antihypertensives prior to stroke by the cases than by the controls, none of the above-mentioned abnormalities in chest x-ray and ECG, or of the frequency of occurrence of diseases or receiving medications, were significant. This indicates that hypertension is a common factor in INF and in HGE; but other features of ischemic heart disease are commonly shared with INF only. The occurrence of rheumatic heart disease, atrial fibrillation, and embolism more in INF cases than in controls explains the factors related to the embolic component of the INF group.

It is interesting to note that during stroke admission manifestations of heart disease such as heart enlargement in x-ray, ECG abnormalities in rhythm, T, ST, and general ECG abnormalities were also significantly more evident in HGE cases than in controls. Such abnormalities did not exist during hospitalization prior to stroke. This indicates that in HGE, heart abnormalities occur very closely or concomitant with the occurrence of stroke, whereas in INF, such abnormalities appeared prior to the stroke indicating the probability of their being risk factors in INF or that both share common factors.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Infarction</th>
<th>Hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case+ -</td>
<td>Control+ -</td>
</tr>
<tr>
<td>Heart enlarged in x-ray</td>
<td>50</td>
<td>28</td>
</tr>
<tr>
<td>ECG, rhythm</td>
<td>45</td>
<td>31</td>
</tr>
<tr>
<td>ECG, conduction</td>
<td>23</td>
<td>21</td>
</tr>
<tr>
<td>ECG, T and ST changes</td>
<td>48</td>
<td>25</td>
</tr>
<tr>
<td>ECG, diagnosis</td>
<td>77</td>
<td>43</td>
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</table>

See footnote of table 1 for explanation.

<table>
<thead>
<tr>
<th>Variable</th>
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<th>Hemorrhage</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Case+ -</td>
<td>Control+ -</td>
</tr>
<tr>
<td>Heart enlarged in x-ray</td>
<td>118</td>
<td>43</td>
</tr>
<tr>
<td>ECG, rhythm</td>
<td>121</td>
<td>55</td>
</tr>
<tr>
<td>ECG, conduction</td>
<td>58</td>
<td>48</td>
</tr>
<tr>
<td>ECG, T and ST changes</td>
<td>123</td>
<td>53</td>
</tr>
<tr>
<td>ECG, diagnosis</td>
<td>142</td>
<td>56</td>
</tr>
</tbody>
</table>

See footnote of table 1 for explanation.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Infarction</th>
<th>Hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case+ -</td>
<td>Control+ -</td>
</tr>
<tr>
<td>Smoking</td>
<td>43</td>
<td>18</td>
</tr>
<tr>
<td>Alcohol drinking</td>
<td>19</td>
<td>13</td>
</tr>
</tbody>
</table>

See footnote of table 1 for explanation.
even modest evidence of impaired glucose tolerance.13 The observed unusually high level of fasting blood sugar for INF in this study and the impaired glucose tolerance among stroke candidates reported in other studies6,18,19 provide further support for the same thesis. That diabetes or impaired glucose tolerance increases the risk for INF may result from its probable contribution to cerebral atherosclerosis, for autopsy studies have shown that diabetes is associated with an increased frequency of cerebral atherosclerosis.16,17

It has been shown in our data also that the fasting blood sugar level in HGE was high. This, however, may be a transient hyperglycemia which may result from disturbed sugar metabolism due to cerebral injury.4 Further support for this is provided from the observation that diabetes as such was not associated with HGE as it was with INF.

From this study it seems also that the smoking habit is associated with INF but not with HGE. Along with the observed high level of blood pressure and more occurrence of diabetes in the INF group, smoking may initiate or enhance the atherogenic process in cerebral vessels. No evidence has been found in this series to indicate any association between body weight and stroke. Results similar to ours in this regard were reported from prospective data.6,18

The high level of hemoglobin and hematocrit observed in INF but not in HGE is of interest and warrants further consideration. The pathophysiologic mechanism of these factors in the genesis of INF may involve high blood viscosity and trauma to the intimal lining of blood vessels, possibly due to larger, heavier, or increased number of red blood cells than usual. These factors also may lead to thrombosis. The Framingham study has initially shown that the risk of developing INF among those at the high scale of the normal range of hemoglobin was significantly higher than among those at the lower end of the scale.19 However, when the data were adjusted for hypertension — a factor related to both hemoglobin and stroke — the residual risk was small and not significant. Thus, the association between INF and hemoglobin or hematocrit may be a secondary one and of no causal significance. The same relationship was also revealed from cross-sectional data between hemoglobin and ischemic heart disease risk factors;20 also, this association was later shown from prospective data to be of no significance in the genesis of this disease.21

It was reported previously that the incidence of INF was significantly higher in men than in women of urban areas, and, among men, those of urban areas had a higher incidence than those of rural areas.1,2 For HGE, the incidence was higher in women than in men of urban areas, and, among women, the incidence was higher in those of urban than of rural areas. Based on this pattern it was suggested that the prevalence of possible risk factors such as hypertension, high serum lipids and smoking may vary according to sex and residence, and may explain this pattern of incidence for INF and for HGE. The analysis of the available data for the control group used in this study partly supports this hypothesis. The mean systolic BP was significantly higher in women than in men (148.9 mm Hg versus 143.2, p < 0.025); this was particularly evident among residents of urban areas (149.5 mm Hg for women versus 143.3 for men, p < 0.01). The diastolic BP was also higher in women of urban areas than in those of rural areas (84.2 mm Hg versus 71.1, p < 0.001). These patterns in blood pressure concur with the incidence patterns of HGE by sex and residence. The data from medical records on serum lipids and smoking were very few for the control group and, therefore, were not presented. However, the results from this case-control study along with our previous descriptive incidence results indicate that high blood pressure is so far the main risk factor in HGE, whereas in INF high blood pressure and other factors associated with the genesis of ischemic heart disease all appear to be important.

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References

cerebrovascular diseases. Neurology 8: 397-437, 1958

Reserpin and Cerebral Vasospasm

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SUMMARY Cerebral vasospasm was produced in the dog basilar artery by topically applied five-day-old clotted autologous blood, but not by freshly drawn blood. The spasm was reversed by methysergide, an antiserotonin agent. However, vasospasm was not produced by five-day-old clotted autologous blood from dogs pretreated with reserpine. This suggests platelet serotonin or a similar, unidentified substance as the vasospastic element in dog blood responsible for experimental vasospasm from topically applied whole blood. Other experimental data support these findings.

Introduction

CEREBRAL VASOSPASM often complicates the management of patients with intracranial aneurysms and is usually associated with blood in the subarachnoid space. It has been concluded that the predominant vasoconstrictor elements of blood are contained in the platelet fraction. The storage in platelets of certain vasoactive amines liberated during normal clotting is influenced by reserpine, a phosphodiesterase inhibitor. The present study was undertaken to ascertain the vasoactive effect upon the basilar artery of autologous blood from dogs pretreated with reserpine.

Methods

The basilar artery was exposed in 13 mongrel dogs using a transclival approach under intravenous pentobarbital anesthesia with endotracheal intubation and spontaneous, unassisted respiration. A Zeiss operating microscope was used to open the dura and remove the arachnoid membrane. Observations of the ventral brain stem and the basilar artery and its branches were made continuously through the operating microscope. The changing diameter of the basilar artery was measured through the microscope by a micrometer calibrated to the nearest 0.1 mm.

There were three experimental groups. Group A contained three dogs. The basilar artery of each dog was bathed in fresh autologous blood for 30 minutes and then washed briefly with normal saline at 37.5°C. The diameter of the artery was measured immediately before and after treatment.

Group B contained six dogs. They were treated as were the dogs in Group A. The blood used, however, had been drawn from the specific animal tested five days prior to the experiment, allowed to clot, and then stored at 37.5°C until used in the experiment. After the blood was irrigated from around the vessel and the posttreatment diameter was measured, the vessels of three dogs were bathed in a solution of methysergide (1 mg/cc) for 15 minutes. The diameter was again measured.

There were four dogs in Group C. Each dog received reserpine, 0.1 mg per kilogram intramuscularly, daily for four days. Then blood was drawn from each animal, allowed to clot, and stored at 37.5°C for five days. At the end of that period, the basilar artery of each dog was exposed as noted above and then treated with autologous blood, as in Group A.

Results

The results are summarized in table 1. In Group A, no vasospasm was produced in any animal by the treatment of the basilar artery with fresh autologous blood. Vasospasm was seen in the basilar artery of each animal in Group B. These vessels were treated with five-day-old
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H A Abu-Zeid, N W Choi, K K Maini, P H Hsu and N A Nelson

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