vestigation. Our present experimental study indicated the possibility that the examination of platelet survival or turn- 
over might be useful as one of the measures to detect minute alterations of hypertensive vascular damages in the sub-
clinical state and to predict the development of severe vascular lesions such as stroke. Such detection of minutevascular damages or prediction of stroke is obviously in-
dispensable for the prevention of stroke, one of the three commonest causes of death in most civilized societies.

Acknowledgment

The authors wish to express their cordial thanks to Dr. Kozo Okamoto, Emeritus Professor of Pathology, Kyoto University, for his great contribution to the development of stroke-prone SHR, without which the present studies could not have been performed. This study was partly carried out at the Radioisotope Research Center, Kyoto University.

References

4. Wintrobe MM, Lee GR, Buggs DR, et al: Thrombosis and anti-

Temporal Profile (Clinical Course) of Acute Carotid System Cerebral Infarction

H. ROYDEN JONES, M.D.,* AND CLARK H. MILLIKAN, M.D.+T

SUMMARY The records of 179 consecutive patients with acute carotid system cerebral infarction were studied to describe the temporal profile of the clinical events during the first week of the illness. Only those patients admitted to the cerebrovascular hospital service within 36 hours of the onset of the first symptom were included.

The neurological status of 39% was stable (unchanged) at the end of seven days; 35% of the patients gradually improved. Nineteen percent had a progressing neurological deficit from the onset which stabilized within 48 hours of onset. Six patients (3%) had a remitting-relapsing course during the first 36 hours. Eight patients (4%) had a significant late worsening, after 48 hours of stable or improving course.

Mortality was 11% for the entire group. However, a high risk of death group was identified — the mortality was 41% for those patients who had any degree of decreased level of consciousness and hemiplegia at the time of admission.

WHAT is the temporal profile of acute progressing carotid system cerebral infarction? How often does the progressing course halt (apparently becoming a completed stroke) only to have serious additional progression take place a few hours later? Another way of saying this: if 100 consecutive patients are observed within the first few hours of beginning carotid system cerebral infarction, what is the expected natural history — progression, stasis, regression, etc? An obvious secondary question is: does any particular type of treatment make any difference in this natural history or expected condition of the patient at the conclusion of a relatively short period of time (one or two weeks)?

Lack of clarity of definition or use of the term “progressing stroke” (stroke-in-evolution) may partially explain the lack of definite answers in the literature to these important questions. Care in defining the categories making up the temporal profile of stroke is primary to the issue of studying the natural history of each category.

Definitions

It is now customary to divide the temporal profile of stroke into three principal categories:1,2 transient ischemic...
attacks (TIA), progressing stroke, and completed stroke. By common usage, this temporal categorization is practically limited to the temporal profile of focal cerebrovascular events secondary to occlusive disease; less commonly is this categorization used to define the temporal profile of intracranial bleeding. Transient focal cerebral ischemic attacks (TIA) are episodes of temporary focal cerebral dysfunction of vascular origin. The onset of each episode is rapid. The duration of attacks is variable, although commonly they last two to 30 minutes and only rarely continue as long as 24 hours, with resolution or disappearance of each episode being swift. A progressing stroke (stroke-in-evolution) is that temporal category in which there has been progression (increased severity of the neurological signs) within recent minutes. This value judgment may be made from analysis of the history or from repeated examination of the patient. It may be difficult to be certain from minute to minute or even from hour to hour whether progression will occur. However, if there has been definite worsening of the neurological deficit during the few minutes immediately prior to making a judgment about a particular patient’s status, the situation is classified as a progressing cerebral infarction (stroke-in-evolution). Completed stroke refers to a category in which the focal neurological deficit is stable. The word “completed” does not imply that a particular neurological sign has become maximum in quantity, i.e., hemiplegia as distinguished from hemiparesis, but refers only to the temporal aspect of the event. Thus, a cerebral infarct may be judged to be completed when the neurological deficit is either minor or severe.

The natural history of TIA’s has been reasonably well explored by a number of investigators during the last 20 years.1-3 Although there are different limits to the figures cited for the natural history of TIA’s, there is general agreement that the TIA constitutes a warning event and that individuals who have one or more TIA’s are at risk of having significant cerebral infarction, the risk being somewhat variably described in the literature. The limits of the estimates range from about 20% of TIA patients having a stroke in five years after a TIA to some 35% or 40% having a stroke in the same length of time (except for the report of Marshall14).

However, the natural history of acute progressing stroke remains essentially undefined. In studies of anticoagulant medication, there have been several observations made concerning small groups of patients and the natural history of progression or lack of progression during the first few hours following hospital admission. If the site of focal ischemia is in the carotid system, there has been a general impression that 18 to 24 hours without progression is ordinarily sufficient time to mean that further progression is unlikely and that the status of the temporal profile should no longer be categorized as “progressing stroke.” If the lesion is in brain supplied by the vertebrobasilar system, a longer period of time (up to 72 hours) should probably elapse before the patient is removed from the progressing stroke category and is designated as a “completed stroke,” since there seems to be a tendency for a period of progression to be separated by many hours when the impaired circulation is in the vertebrobasilar system. These matters are somewhat uncertain; in our experience there have been some instances of late worsening (e.g., worsening occurring after 36 or even 48 hours in carotid system cerebral infarction patients) which were both surprising and catastrophic — leaving the patient dead or permanently disabled.

Literature

Mills and Moersch dealt with the temporal profile in acute carotid system cerebral infarction and noted that the prognosis was affected by the speed of onset of the symptoms and abnormal physical signs. The temporal profile was recorded in 93 instances. Of 37 patients in whom hemiplegia developed within three hours of onset, 33 (89%) were hemiplegic or dead two weeks later. In contrast, of 39 patients in whom hemiplegia developed after six hours of onset, 20 (51%) were hemiplegic or dead 14 days later. This observation is of considerable value in assessing the ultimate outcome in an individual patient early in the course of the disease.

Fisher found occlusion of one or both carotid arteries in 28 of 432 routine autopsy cases. In this paper the orientation was toward the arterial pathology. There was no description of the temporal profile in those patients who had a progressing cerebral infarction. As one would anticipate, there were instances of unilateral occlusion without symptoms and instances of unilateral occlusion with very severe neurological deficits.

SastrasDeal wrote a lengthy description concerning 65 consecutive patients with carotid thrombosis. Unfortunately, no data are given about the acute temporal profile of the disorder other than the statement: “Twenty-four patients were found to have a sudden apoplectic attack with or without loss of consciousness. Forty-one had a progressive onset with intermittent attacks.” This statement does not clarify the nature of the acute temporal profile since an accompanying table reveals that “progression with intermittent attacks” took place from three months to more than five years.

Webster et al. summarized the findings in 70 patients with angiographical evidence of carotid artery occlusion; these were selected from 803 angiograms performed. Unfortunately, it is impossible to determine how many of these patients had progressing stroke. The authors reported that the most common finding was hemiparesis or hemiplegia, present in 57 of the 70 patients. Twenty-five patients had aphasia or other speech defects. Thirty-eight of the 57 hemiplegic patients had the hemiplegia or hemiparesis as the first manifestation of the disease. The onset was abrupt in 50 of the 57 instances; however, the definition of abrupt was not given. There was no description of the period of time elapsing between the onset of the symptoms and the hospitalization of the patient. Five of the 70 patients died in the hospital at the time of the first admission; again, the interval between onset of symptoms and death was not given. Four others died in the hospital upon re-admission, and the time interval was not listed. The natural history of acute progressing stroke in the carotid system cannot be determined from these data.

In 1957, Rankin reviewed his experience in 248 patients (over the age of 40) in whom a “cerebrovascular accident” had occurred within the seven days prior to hospital admission. One hundred forty-nine patients were admitted within
24 hours of the onset of the first neurological phenomena. The author does not make any distinction between patients having cerebral infarction, intracerebral hemorrhage or subarachnoid hemorrhage. These categories of pathology were combined. Therefore, although much data concerning physical signs are provided, the reader cannot learn which basic type of pathology was most frequently associated with which abnormal sign or constellation of signs. No information was provided concerning the temporal profile of acute carotid system cerebral infarction.

In Fisher’s 1958 paper concerning anticoagulants in cerebral thrombosis, there were 14 patients recorded as having progressing stroke with or without TIA treated with anticoagulant and another 23 patients said to have “stepwise development of a stroke with or without TIAs.” However, no quantitative description was given of the neurological deficits, so it is impossible to make any presumptions about the practical natural history of acute progressing stroke. One can only make a comparison between two values: the number of untreated patients having progression and the number of treated patients having progression. Apparently, of the 14 control patients, 64% showed progression, while of 14 treated patients, 21% showed progression. The duration of time between the initial observation and the judgment about progression was not clear.

Hurwitz et al. described the clinical picture in 57 patients with occlusion of a carotid artery in the neck. The cases were selected because arteriography showed the carotid artery occlusion. The data do not describe the natural history of acute progressing stroke in the carotid artery. Thirty-three of the patients had a sudden onset, but sudden was not further defined. Of those individuals (17) having a mild hemiparesis, recovery was excellent in all 17. Of the 32 individuals having moderate or severe hemiparesis, recovery was excellent in only five. The authors report that 13 of the patients were initially comatose; six of these died during the first few days of their hospitalization while the remaining seven patients were comatose for one hour or less. The theme of this paper concerns the clinical findings in patients having an occluded carotid artery, which is quite different from a description of the clinical course of acute cerebral infarction in the carotid system.

Hass and Goldensohn reported a consecutive series of 35 patients with verified (by arteriography) carotid occlusive disease. Although the title of the article implies that clinical phenomena are going to be reviewed, there are no facts about the temporal profile of the course of the illness. A table is included in which the 35 patients are described. However, of the 35 individuals, only two were seen less than one week after the onset of the clinical phenomena and two others were seen one week after the onset, while the remainder were first observed more than a week after the onset.

Wells wrote “The present study is an effort to delineate the clinical features and course of cerebral embolic phenomena.” Fifty-three patients with 63 episodes were available for detailed clinical evaluation. The diagnosis was made only when there was a sudden onset of the focal cerebral symptomatology. “Sudden onset” was not defined, and the reader does not know whether this means a minute, an hour, or a day. The arterial system was not mentioned. It was noted that the onset occurred most commonly in the morning hours. Among items suggesting a bad prognosis were: onset accompanied by seizures, persisting loss of consciousness (the duration was not stated), speech impairment as part of the abnormal neurological status, and Cheyne-Stokes respirations. When the neurological abnormality worsened in the first few minutes after onset, the worsening suggested a bad prognosis and that patient was unlikely to have a good recovery. When improvement from focal weakness began within 48 hours after the onset, the prognosis appeared to be fairly good, and when improvement began later, the degree of recovery was often unsatisfactory. It was not stated how often worsening after the initial onslaught occurred, and the temporal profile of the acute phenomenon was not discussed. Sixteen of the 53 patients (30%) died within two and one-half hours to two months after the onset, and five (9%) died within 24 hours while 12 (23%) were dead within one week. It should be emphasized that these data concern patients who had cerebral emboli (the emboli coming from a cardiac source); thus, the data do not represent a cross section of the events relating to cerebral infarction in general.

Carter reported the results of anticoagulant treatment in 38 patients and contrasted the findings with the results of 38 patients not receiving anticoagulant treatment. These patients were classified as having “progressing stroke.” The period of observation in which the judgments were made was six months. No data are provided concerning the nature of onset of the neurological abnormality or the temporal profile of the first hours, days or even weeks of the illness.

Baker et al. reported a cooperative study of anticoagulant therapy in which the patients were divided into control and treated groups. In the stroke-in-evolution category (not defined as to whether it is carotid or vertebro-basilar system), there were 128 patients, 67 in the control group and 61 in the treated group. Death was due primarily to cerebral infarction in ten control patients and five treated patients. There was severe progression of infarction in 14 patients in the control group and in only three treated patients; there was moderate progression of infarction in seven control patients and in three treated patients, and mild progression of infarction in five control patients and three treated patients. Only a mortality figure on the natural history of acute progressing stroke was provided and this did not include the time between onset and death. At the conclusion of the paper, there was a summary of “neurological events” but there was no way of knowing how soon after the onset of the progressing stroke these events began.

Hardy et al. presented a study of 153 patients with carotid artery occlusion proved by angiography. There were 80 patients whose onset of symptoms was sudden. However, the time interval between onset of symptoms and hospitalization ranged from one day to 16 years. Thirty-four patients were seen during the first week following the onset of symptoms; seven were admitted during the second week, 22 during the third week. Twenty-one patients were hospitalized one year or longer after the sudden onset of their symptoms. Another category comprised 52 individuals whose onset of symptoms was episodic. The time from onset
of their symptoms to hospitalization ranged from five days to seven years. The course of events in those individuals whose onset was closely related to the hospital admission was not described. There were no data regarding the length of time or neurological characteristics of the progressing stroke in those individuals who had a severe or even lethal neurological picture. Twenty patients (28%) died from their original stroke. The time interval between the onset of the original stroke and the immediate death was not stated.

Cooper et al. reported that 47 of 74 patients with cerebral infarction died, a mortality rate of 63.5%. The length of time between the onset of symptoms and admission to the hospital or the onset of symptoms and the time to death of the fatally afflicted patients was not stated. Of those patients who were unconscious (deep coma) at the time of admission, 92.3% died, while only 16.7% of the patients who were alert at the time of admission died. There was increased mortality as the focal weakness increased—from 28.6% in seven patients with grade 0 to 1 weakness to 86.6% in 15 patients with grade 3 weakness. No information about the temporal profile was provided.

Carter reported that 26% of 612 patients (1952 to 1961) with “atherosclerotic thrombotic infarction” died within the first four weeks. He showed a definite relationship of coma to mortality. The percentage of mortality for 430 patients not comatose on admission was 12% at four weeks; with coma less than 24 hours (95 patients) the mortality was 44% at four weeks, with coma less than 48 hours (41 patients) the mortality was 86% at four weeks, and with coma more than 48 hours (36 patients) the mortality was 95% at four weeks. The patients’ state of consciousness refers to the condition on admission to the hospital, usually a few hours after they were found or after the stroke developed. The history of unconsciousness before admission was found to be frequently unreliable except, of course, in the case of patients admitted in coma. Simultaneous myocardial infarction was usually disastrous. There were 14 patients in this category; 12 of these died within a week. Carter noted that “if a patient is going to walk again, there should be some movement of the leg within a few days of the stroke, and if the hand is ever going to be useful, movement of the fingers and thumb must appear within the first two weeks. Most patients after hemispheric infarction are eventually able to stand and walk with mechanical aids and most can move the shoulder on the affected side.” In 1952 and 1953, 34 patients with cerebral embolism from a cardiac source were observed. Eighteen died but ten died “from a large cerebral infarction immediately.” This was mortality of approximately 30% for immediate hospitalization; however, immediate hospitalization was not fully defined in terms of days or weeks.

Marshall reported 72 patients (it was not stated whether these were consecutive admissions) with carotid occlusion or stenosis proved angiographically and followed in an attempt to determine the natural history of these lesions. With the selection made on this basis (angiographical evidence) one would expect to find complete variation in the natural history, from patients who were asymptomatic to patients who were dead. This is essentially what was found. No data were presented about the natural history of acute progressing stroke in the carotid system. There was one “immediate” death among 19 patients with carotid occlusion and four “immediate” deaths among 31 patients with carotid stenosis. No definition was given for the word “immediate.”

Lougheed et al. reported 109 patients with carotid artery occlusion or stenosis who had carotid surgical reconstructive procedures. Twelve of these patients had progressing stroke. No description of the duration of symptoms and signs, rate of progression, or subsequent state of the patient’s nervous system was given.

Torvik and Jørgensen studied the relationship of the clinical course and the autopsy findings of 52 patients with “carotid occlusive disease.” The study included the entire carotid system. Clinical symptoms related to the carotid occlusion were found in 41 of the 52 patients. In 33 of the 41 symptomatic cases, the carotid occlusion was considered to be the underlying cause of death (63%). Intracranial occlusion was lethal more often than extracranial occlusion. For instance, deaths caused by carotid occlusion extracranially numbered 10 and intracranially numbered 21. The length of survival after the onset of the first symptoms of carotid disease varied from eight hours to nine years. Fifty percent of the symptomatic patients had died within 20 days. One-half of the patients with intracranial occlusion died before five days, while half of the patients with extracranial occlusion were dead within six months. All patients with recent emboli (questionable source) died within five days. Twenty-seven patients or 66% of the 41 symptomatic cases had a sudden onset characterized by development of the symptoms within minutes or a few hours. (“A few hours” was not defined.) However, no temporal profile of acute carotid system cerebral infarction was provided.

Toole and Patel divided patients with carotid artery syndrome into three clinical groups: (1) those with recurring attacks of neurological deficit which subsided completely within minutes or hours (they probably meant TIA), (2) those with an apoplectic onset characterized by hemiplegia without previous episodes of insufficiency, and (3) those with slowly progressive neurological deficit compatible with a variety of expanding intracranial lesions, particularly brain tumor. However, they gave no data and made no comment about the natural history of any of these three groups; i.e., if one sees a patient in the first 12 hours or first 36 hours of the “apoplectic onset characterized by hemiplegia,” what is likely to be the state of that patient, statistically, at the end of 7 or 14 days? Is the patient likely to be much improved, about the same, or dead?

Gilroy et al. studied the “treatment of acute stroke with Dextran 40.” Although “each patient had the acute onset of moderate to severe neurological deficit without improvement of 24 to 72 hours’ duration when accepted into this study and hence each patient would be classified as a victim of progressive stroke or stroke-in-evolution, rather than a completed stroke,” details or any description of the acute course of events in 100 patients with “acute stroke” were not available. From the description mentioned above, most of the patients probably were not in the progressing stroke category. Ordinarily, patients should be placed in the “progressing stroke” category when there is a history of progressing symptoms and signs during the few minutes...
prior to hospitalization or when there has been an increase in severity or distribution of the neurological deficit after admission to the hospital. If patients are included whose neurological deficit reached its maximum degree 24 hours prior to admission or certainly as long as 48 to 72 hours prior to admission, one will find the "progressing stroke" category contaminated with many instances in which the dynamic pathophysiological process has stopped its progression. Gilroy et al. excluded patients whose systolic blood pressure was more than 180 mm Hg and patients who had any cardiac or renal disease. Such exclusions changed the nature of the case material since hypertension and some renal pathology or cardiac pathology are common in patients with stroke. Of 54 "control patients" (not receiving Dextran 40) evaluated ten days after admission, 57% were improved, 15% unchanged, 13% worse, and 15% dead.

Jörgensen and Torvik found that of 320 patients with ischemic cerebrovascular disease discovered among 994 consecutive autopsies, a sudden onset (seconds to a few hours) was by far the most common, occurring in 139 of 171 instances in which the clinical development was known (actually in 126 patients). The authors gave no temporal profile for the first hours or days of the ischemic event; i.e., there were no data concerning the impact of the immediate severity of the neurological deficit upon either the short-range or long-range prognosis.

Shafer et al. analyzed the quality of survival in 527 consecutive stroke patients. The authors wrote that "on the first day after stroke, the changes for survival can be reckoned quite reliably." However, the authors never explained how to do this. The data presented concern the distribution of outcomes at hospital discharge in stroke survivors by (1) type of lesion clinically diagnosed, (2) age group, (3) level of consciousness on admission, and (4) blood pressure history. No information was provided concerning the type of onset of the clinical events or the acute temporal profile of carotid system infarction.

Viala et al. studied the short-term prognosis of cerebral infarction by reviewing the first eight days of 150 patients. About one-third of the individuals died, one-third being fed intravenously at eight days, and one-third of the patients could be fed by mouth. The most important factor in prognosis was the state of consciousness. The mortality was 19% if consciousness was normal, 29% if some impairment of consciousness existed, and 61% if the patients were unconscious at the time of admission. The mortality rate was 42% in patients with hemiplegia and 25% in patients with hemiparesis. These figures were also "clearly related to the level of consciousness" but the meaning of this statement was not evident. It was not clear whether all of the infarctions were in the carotid system or not.

It is apparent that the literature contains no account of the natural history of acute progressing carotid system cerebral infarction. Because of the extraordinary need for this information in developing a prognosis about individual patients and in making judgments concerning the potential effectiveness of any regimen of treatment, it was decided to study this matter further.

Methods

The record of every patient admitted to the Neurology Cerebrovascular Hospital Service during the period January 1, 1967, through December 31, 1969, with a diagnosis of acute cerebral infarction (due to occlusive arterial disease) was reviewed.

Acute was defined as meaning that the patient was first seen on the Neurology Cerebrovascular Service within 36 hours or less following the onset of the first symptom of the illness.

Patients were not included who had: (1) intracerebral and/or subarachnoid hemorrhage, (2) a focal neurological deficit which disappeared within 24 hours of onset (by definition such patients were in the TIA category rather than the progressing stroke category), and (3) bacterial endocarditis, systemic lupus erythematosus, polyarteritis nodosa, giant cell arteritis or syphilis.

Data collected included the following items: patient's age and sex; date, hour and circumstances of patient's or other observers' first awareness of first symptom; date and hour of admission to Mayo Clinic; physical examination findings on admission; blood pressure, pulse, respiration, etc.; state of consciousness (normal, stupor, coma); speech (dysphasia-aphasia); cranial nerve function; motor function (hemiparesis-hemiplegia); stretch reflexes, pathological reflexes; cerebrospinal fluid examination; the "usual" laboratory data; results of roentgenograms of head and chest; electrocardiogram; results of special tests (electroencephalogram, brain scan, arteriogram, etc.); previous treatment (antiocoagulant, antihypertensive, etc.); hospital course with physical examination findings (as listed above) daily or more often for the first seven days, then at appropriate intervals; treatment in the hospital (antiocoagulant, antihypertensive, cardiac failure, steroid, etc.); physical examination findings at time of dismissal; autopsy findings, if available.

(Notation was made as to whether the patient received any form of antiocoagulant therapy either prior to or as a method of treatment in the first week of illness. Most patients were not maintained on long-term antiocoagulant treatment; those included in the antiocoagulant group were
patients who had received even one dose of the medication.)

From the daily (or more often) listing of neurological findings in the record, a graph was drawn representing the clinical course of events for each patient, i.e., depicting whether consciousness (and/or speech and/or motor function) improved, remained the same, worsened, or consisted of several variable patterns. The abscissa of the graph represents time and the ordinate represents the severity of the neurological deficit (figs. 1 and 2). Inspection of each graph quickly gives the viewer knowledge about the course of clinical events for that patient.

The severity of the neurological deficit is noted in some of the tables and is defined according to previously described criteria,* i.e., $-4$ = paralysis, $-3$ = severe paresis, $-2$ = moderate paresis, and $-1$ = minimal paresis.

Results

Of the 220 consecutive patients, 179 (81%) had the locus of cerebral ischemia in the carotid system and 38 (17%) in the verteobasilar system. In addition, there were three patients whose only symptom and neurological abnormality were homonymous hemianopia. This locus of ischemia may be produced by a defect in primary flow in either the carotid or verteobasilar system.

Table 1 shows the age, sex distribution and tabulation of the cardiovascular abnormalities present in addition to previous cerebrovascular events.

The 179 patients with carotid system acute focal ischemia were placed in categories according to the evolution of the neurological deficit during the first week of the illness. Five distinct temporal profiles emerged: (1) essentially unchanged deficit, (2) improved deficit, (3) progressive worsening of the deficit, (4) improvement and relapse, and (5) late exacerbation.

Tables 2 and 3 show the distribution of patients in these five temporal categories as well as the arrangement of the severity of the initial neurological deficit by temporal category.

Thirty-nine percent (69 of 179 patients) had essentially no change in the neurological deficit during the first seven days of the illness. Sixty-one of these 69 patients (88%) had loss of focal neurological function (e.g., hemiplegia in contrast to hemiparesis).

Thirty-five percent of the total group (62 of 179) showed improvement, without any neurological exacerbation, during the first week of the illness. Only 26 of the 62 (42%) in this category initially had loss of a focal neurological function.

The patients in the progressing deficit subcategory, of course, included those individuals whose neurological status was characterized by progressive deterioration of a focal neurological function, lowering of the level of consciousness, or both, starting within the first 48 hours of the onset of the initial symptoms (patients admitted to the hospital within 36 hours of onset). Thirty-four of the 179 patients (19%) were classified in this category. Of these 34 patients who had a progressive increase in the focal neurological deficit, 21 (62%) had the progression during the initial stages of the illness. In the first few minutes or hours of the temporal course, these patients had a mild or very moderate focal neurological deficit; within a matter of a few hours the degree of worsening could be categorized as producing a severe or complete focal deficit (17 of the 21 patients). The remaining 13 of 34 patients (38%) in this temporal category showed a progressive deterioration in the level of consciousness, beginning almost at the onset in 11 of 13 and within the first 48 hours in the remaining two of 13.

Only six of 179 patients (3%) had a course characterized by at least one definite remission in the focal deficit followed almost as rapidly by a further exacerbation in the neurological abnormality. In five of the six, the initial deficit ultimately became a loss of focal neurological function.

The temporal category named "late exacerbation" included eight of 179 patients (4%). In each instance, the patient appeared to have achieved a clinically stable profile at the end of 48 hours, only to have a later worsening in neurological status, between days three and seven. If it had not been for this late worsening, these eight individuals would have been placed in one of the three major categories already described. For the first 48 hours, these patients could have been classified as four with unimproved deficits, three

\[ \begin{array}{c|c|c}
\text{Age} & \text{No.} & \% \\
<60 & 36 & 20 \\
\geq 60 & 143 & 80 \\
\end{array} \]

Table 1 Acute Carotid System Infarction in 179 Consecutive Patients

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>36</td>
</tr>
<tr>
<td>≥60</td>
<td>143</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cardiovascular abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Valvular heart disease</td>
</tr>
<tr>
<td>Recent MI</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prior cerebrovascular event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed infarction</td>
</tr>
<tr>
<td>TIA</td>
</tr>
</tbody>
</table>

MI = myocardial infarction, TIA = transient ischemic attack.
with improved deficits, and one with a slightly progressive deficit. The exacerbation was of focal nature in five of the eight patients. The late exacerbation consisted of a deterioration in general responsiveness in three other patients. In each of these, the change in consciousness appeared on a background of initial focal paralysis and very mild impairment of the level of consciousness. The latter (mild impairment of the level of consciousness) had initially improved during the first 48 hours only to worsen markedly on the third and fourth days. This alteration in consciousness implied a poor prognosis, with two patients dying on days six and ten and the third requiring nursing home care.

Table 3 shows the neurological status of the patients seven days after admission by category of severity of initial neurological abnormality. Only 4% of patients with a maximum neurological deficit at admission were normal seven days later; 17% had died. Thirty-three percent of the patients with the least grade of neurological deficit at admission were normal seven days later.

Table 4 lists the deaths in three groups of patients classified by the quality of the neurological deficit: (1) an incomplete neurological sign (paresis as contrasted to paralysis), (2) a complete neurological sign, and (3) a complete neurological sign and altered consciousness. There were no deaths among patients who had a partial neurological sign, while 18 of 44 (41%) patients died who had hemiplegia and decreased consciousness when admitted.

The various clinical subgroups were subdivided into those receiving heparin and/or Coumadin at any time during the acute illness. Table 5 shows that 53 patients (30%) received anticoagulant and 126 (70%) did not, and gives the number of patients in each result category at the end of seven days. The results were similar in the “no improvement” and “incomplete improvement” categories of the treated and untreated groups; 14% of the untreated group were dead by the seventh day, and one treated patient died.

Autopsies were performed in 11 of the 19 fatal cases. Every patient had cerebral infarction. In seven of eight cases from the progressing deficit category, there were cerebral infarction with edema, convolutional flattening, midline shift, uncal notching and secondary brain stem hemorrhages. Two patients (autopsy group) had cerebral infarction with unchanged neurological deficit and died of myocardial infarction, and one patient was comatose when admitted and remained comatose for three days before death. At autopsy, there were two acute cerebral infarcts, one in each hemisphere.

Discussion

From the experience recorded more than 20 years ago and this current study, certain important facts appear concerning the natural history of acute progressing stroke in the carotid arterial system.

1. If hemiplegia develops within three hours of the onset of symptoms and persists for 36 hours, there is a 90+% chance that the patient will have a permanent incapacitating motor deficit. Carter's approach to this subject in his book published in 1964 but does not make a definitive statement concerning the matter. Hutchinson and Acheson wrote: "It is clear from the literature that there is no consistent pattern of evolution where observations have been made on the mode of onset of stroke." These authors apparently are not aware that within a consecutive series of admissions with cerebral infarction there will be categories of patients in which the prognosis is reasonably clear because of certain signs or group of characteristics. Thus, the group with hemiplegia developing within three hours of onset of symptoms (hemiplegia which persists for 36 hours) has an entirely different prognosis than the group which has a grade 2 hemiparesis developing within 6 to 12 hours of onset.

2. Only 4% of the patients had a "late exacerbation" during the acute illness. This category was of particular interest to us; a patient with carotid system cerebral infarction is doing well for 48 hours (often has definite improvement of neurological function) and then suddenly has a severe worsening of the defect (a change which is a catastrophe). This problem category has not been dealt with in the

**Table 2** Severity of Initial Deficit

<table>
<thead>
<tr>
<th>Neurological status</th>
<th>Severity of initial deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-4</td>
</tr>
<tr>
<td>Unchanged deficit</td>
<td>61</td>
</tr>
<tr>
<td>Improved deficit</td>
<td>26</td>
</tr>
<tr>
<td>Progressive deficit</td>
<td>13</td>
</tr>
<tr>
<td>Remission and relapse</td>
<td>5</td>
</tr>
<tr>
<td>Late exacerbation</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>111</td>
</tr>
</tbody>
</table>

**Table 3** Neurological Status on Day 7

<table>
<thead>
<tr>
<th>Severity*</th>
<th>Total No.</th>
<th>Normal</th>
<th>Improved</th>
<th>Same or worse</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>-4</td>
<td>4(4%)</td>
<td>2(22%)</td>
<td>11(99%)</td>
<td>3(31%)</td>
<td>179 (100%)</td>
</tr>
<tr>
<td>-3</td>
<td>3(3%)</td>
<td>2(22%)</td>
<td>11(99%)</td>
<td>3(31%)</td>
<td>179 (100%)</td>
</tr>
<tr>
<td>-2</td>
<td>0(0%)</td>
<td>2(22%)</td>
<td>11(99%)</td>
<td>3(31%)</td>
<td>179 (100%)</td>
</tr>
<tr>
<td>-1</td>
<td>0(0%)</td>
<td>2(22%)</td>
<td>11(99%)</td>
<td>3(31%)</td>
<td>179 (100%)</td>
</tr>
</tbody>
</table>

*Initial neurological abnormality.

**Table 4** Effect of Neurological Findings at Admission on Mortality

<table>
<thead>
<tr>
<th>Initial examination</th>
<th>No.</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete neurological sign (paresis)</td>
<td>68</td>
<td>0</td>
</tr>
<tr>
<td>Complete neurological sign (paralysis)</td>
<td>67</td>
<td>1</td>
</tr>
<tr>
<td>Complete neurological sign (hemiplegia) and altered consciousness</td>
<td>44</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>179</td>
<td>19</td>
</tr>
</tbody>
</table>
literature. There was no clue to identify these patients; fortunately, the percent with this course is small.

3. Highly significant in mortality prognosis was the combination of hemiplegia and any decrease in consciousness on admission (within 36 hours of onset). There were 44 such patients; 18 (41%) died, while of 67 patients having a complete neurological deficit (hemiplegia, aphasia, etc.) with normal consciousness only one died, a mortality of less than 2%. Hurwitz et al.10 noted a mortality of 46% among patients already comatose when admitted; the duration of coma was not mentioned. Cooper et al.24 reported a 92% mortality among patients admitted in coma from cerebral infarction. However, the time from onset to admission was not stated. The mortality was only 16.7% when the patients were alert at the time of admission. Carter26 reported the relationship of coma to prognosis: for one group of patients with coma of less than 24 hours' duration, the mortality was 44% at four weeks. Viala et al.33 also noted the adverse effect of coma on prognosis: for one group of patients with coma from cerebral infarction. However, the length of time between the onset of symptoms and admission to the hospital was not given. This interval is vital to the description of the temporal profile of acute carotid system cerebral infarction.

The high mortality (41%) for patients admitted with the combination of hemiplegia and decrease in consciousness is now a standard baseline statistic for judging the effect of any new method of treatment for acute carotid system cerebral infarction. The mortality (10.6%) in the 179 patients is only slightly below the 13% of 144 patients reported14 more than 20 years ago.

<table>
<thead>
<tr>
<th>Neurological status</th>
<th>No improvement</th>
<th>Incomplete improvement</th>
<th>Normal</th>
<th>Dead</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unchanged deficit</td>
<td>47</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>62</td>
</tr>
<tr>
<td>Improved deficit</td>
<td>34</td>
<td>10</td>
<td>6</td>
<td>11</td>
<td>51</td>
</tr>
<tr>
<td>Progressive deficit</td>
<td>1</td>
<td>10</td>
<td>8</td>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>Remission and relapse</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Late exacerbation</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>45</td>
<td>21</td>
<td>18</td>
<td>126</td>
</tr>
</tbody>
</table>

A/C = anticoagulant.

References

21. Wells CE: Cerebral embolism. The natural history, prognostic signs, and effects of anticoagulation. AAMA Arch Neurol 81: 667-677 (June) 1959
Temporal profile (clinical course) of acute carotid system cerebral infarction.
H J Jones and C H Millikan

Stroke. 1976;7:64-71
doi: 10.1161/01.STR.7.1.64

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/7/1/64