CLINICAL PROGRESS

Management of Spontaneous Intracranial Subarachnoid Hemorrhage

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UNTIL recently many clinicians considered subarachnoid hemorrhage a diagnostic entity. Since no specific form of treatment was available regardless of the underlying pathology, a painstaking inquiry into etiology appeared to have more academic than practical value. This fact and the high mortality of patients treated only by bed rest and supportive therapy (table 1) often led to a relative lack of interest in the problem.

It is becoming increasingly apparent, however, that a more vigorous therapeutic approach can be beneficial if the specific cause of the bleeding can be discovered. As with all relatively new concepts, differences of opinion concerning details of diagnosis and treatment have produced a massive and predominantly confusing body of literature. From a critical review of the written evidence and our own experiences, we have attempted to fashion a rational approach to this problem for the physician who must currently choose a therapeutic regimen for his patient.

ETIOLOGY AND INCIDENCE

Bleeding into the intracranial subarachnoid space is a finding common to a variety of pathologic states, both local and systemic. Among the more common local causes are trauma, intracranial aneurysm of the "congenital," "arteriosclerotic," and "myotic" varieties, angiomatos malformation, "hypertensive" and "spontaneous" intracerebral hemorrhage, and tumor. Systemic diseases that must be considered in the differential diagnosis include sources of septic embolization, such as bacterial endocarditis, and the causes of generalized bleeding tendencies, such as the blood dyscrasias and scurvy.

By use of the term "spontaneous" we are restricting this discussion to those instances of subarachnoid hemorrhage due to an intrinsic fault in the cerebrovascular tree. Thereby we exclude bleeding secondary to trauma, neoplasm, and the systemic diseases. The literature is often confusing in reference to this definition, particularly in regard to the inclusion of hypertensive-arteriosclerotic cerebral hemorrhage with subarachnoid extension. Since the latter entity is common and carries a high natural mortality, its inclusion, whether deliberate or unwitting, will markedly affect any statistical conclusions. Most authors have attempted to eliminate this large group, but in many cases presenting with subarachnoid hemorrhage differential diagnosis is difficult. Individuals with hypertension can bleed from anomalies of the intracranial circulation. Furthermore, intracranial bleeding may of itself raise blood pressure. For these reasons and since specific therapy is occasionally available for this condition, we consider that hypertensive subarachnoid hemorrhage should be included in the group under discussion. For clearer presentation of the other etiologic groups, and for consistency with existing reports, however, we must attempt to separate hypertensive hemorrhage in statistical analysis.

In surveying the literature Walton1 concluded that nontraumatic subarachnoid hemorrhage accounts for about 8 per cent of

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cerebrovascular disease seen clinically. If neoplastic and systemic causes are eliminated, 4 basic etiologic groups are found to be responsible for nearly all spontaneous bleeding into the subarachnoid space: hypertensive arteriosclerotic cerebral hemorrhage, "spontaneous" intracerebral hematoma, angiomatous malformation, and intracranial aneurysm.

It is difficult to assess from published reports the number of cases comprising the first group. Excluding this group, it is generally agreed that the other diagnostic categories are responsible in the following order of frequency: "spontaneous" intracerebral hematoma 9 per cent, angiomatous malformation 11 per cent, and intracranial aneurysm 80 per cent. These ratios are only approximate, since autopsy figures are influenced by differing mortality rates for the 3 conditions, and in the living patients angiography does not reveal each type of lesion with equal facility. Furthermore, the age of the patient population will influence the frequency with which each lesion is seen. Hypertensive hemorrhage will predominate in a home for aged couples, arteriovenous malformation in a children's hospital. The importance of considering the patient's age when attempting to arrive at an exact diagnosis has been graphically presented by Tönnis (fig. 1).

**DIAGNOSTIC FEATURES**

The onset of subarachnoid hemorrhage is sudden, usually with headache, stiff neck, and altered consciousness, the latter varying from a minimal reduction in awareness to profound coma. Bloody cerebrospinal fluid, usually under increased pressure, is obtained by spinal puncture. In cases of cerebral thrombosis and embolism, however, the clinical picture may be similar: sudden neurologic defects are usual, the patient occasionally complains of headache, and coma can occur. Therefore, the first procedure for an exact diagnosis in a case of "stroke" is a careful lumbar puncture. If a needle of a small caliber is employed, if little or no cerebrospinal fluid is lost, if manometric determinations are carried out without jugular compression, and if only 1 to 2 ml. of cerebrospinal fluid are slowly withdrawn, lumbar puncture is safe even if intracranial pressure is increased.

**TABLE 1.—Mortality Following Spontaneous Subarachnoid Hemorrhage in Patients Treated by Bed Rest and Supportive Therapy**

<table>
<thead>
<tr>
<th>Per cent of total</th>
<th>Patients</th>
<th>Source of information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total mortality during acute illness (8 wk.) 45</td>
<td>1637</td>
<td>References: 1 (summary), 36</td>
</tr>
<tr>
<td>Total mortality after an average of 5 years . 57</td>
<td>919</td>
<td>References: 1, 5-8</td>
</tr>
<tr>
<td>Late mortality (recurrent hemorrhage) .......... 12</td>
<td>From above percentages</td>
<td></td>
</tr>
<tr>
<td>Late mortality in survivors of acute illness . 22</td>
<td>From above percentages</td>
<td></td>
</tr>
<tr>
<td>Recurrent bleeding first 8 weeks ............ 22.5</td>
<td>592</td>
<td>References: 1, 6</td>
</tr>
<tr>
<td>Mortality recurrent bleeding first 8 weeks ... 67</td>
<td>164</td>
<td>References: 1, 6, 8, 36</td>
</tr>
<tr>
<td>Gross mortality contributed by early recurrent bleeding .. 15</td>
<td>From above percentages</td>
<td></td>
</tr>
<tr>
<td>Gross mortality contributed by original hemorrhage .......... 30</td>
<td>From above percentages</td>
<td></td>
</tr>
</tbody>
</table>

*Patients with hypertensive hemorrhage are excluded; the mortality in these patients is over 90 per cent.
SPONTANEOUS INTRACRANIAL SUBARACHNOID HEMORRHAGE

Fig. 2. Cumulative mortality from primary or recurrent subarachnoid hemorrhage charted as a function of time from first bleeding. Data were obtained from Walton's series of 312 patients with subarachnoid hemorrhage from all causes exclusive of hypertensive-arteriosclerotic brain hemorrhage. Survivors were observed for periods varying from 1 to 12 years (average 5 to 6 years) after the original hemorrhage. However, only those deaths which occurred within 5 years of the first hemorrhage are included in this tabulation.

FIG. 3. The cumulative mortality from recurrent subarachnoid bleeding within 5 years of the initial hemorrhage, as reported by Walton for 312 patients with subarachnoid hemorrhage from all causes exclusive of hypertensive-arteriosclerotic brain hemorrhage. Patients in this series were observed for periods varying from 1 to 12 years (average 5 to 6 years) after the original hemorrhage. However, only those deaths due to recurrence of bleeding within 5 years of the first hemorrhage are included in this tabulation. Note the sharp rise in the death rate from the first through the third week after ictus.

Course of Subarachnoid Hemorrhage Treated by Bed Rest and Supportive Therapy

More than 9 of 10 individuals with arteriosclerosis and hypertension die within a few hours or days after rupture of a cerebral artery, if hemorrhage has been extensive enough to penetrate into the subarachnoid space. The fate of those patients whose subarachnoid hemorrhage results from the other 3 causes previously listed has been extensively reported by many authors (table 1). The data compiled by Walton are representative and include much other helpful information. Figure 2 has been derived from his reports concerning 312 patients treated by bed rest and appropriate supportive therapy. Approximately 15 per cent of these patients were dead within 24 hours of the ictus, 26 per cent died within 1 week, 45 per cent within 8 weeks.

Figure 3 illustrates the mortality resulting from recurrent hemorrhage and emphasizes the "danger period" 1 to 3 weeks after the initial episode. It is at this time that the physician, gratified at the continuing recovery of his patient, may be shocked by a sudden unexpected fatal outcome.

It has been postulated that reflex vasoconstriction induced by the first hemorrhage disappears over the early period and that the removal of its protective effect is responsible for secondary hemorrhage. This early recurrence is most frequent in the second and third weeks of convalescence. Several bouts of recurrent bleeding may be seen in the same patient. A second bleeding during the first period of hospitalization (usually 6 to 8 weeks following the original ictus) is responsible for one third of the mortality of this period: 15 per cent of Walton's entire patient population. As to late prognosis, of the 55 per cent surviving the 8 weeks, 19 per cent (10.5 per cent of the entire population) died from "late" recurrent bleeding within 5 years, the majority of these within 1 year. It should be noted that a third of Walton's survivors were not observed for a full 5 years after the original hemorrhage. Had this observation period been fulfilled in every case, there might have been a greater mortality reported. Deaths from recurrent hemorrhage
have been reported after as long as 30 years.5

Thus at least 55 per cent of these unfortunate patients are dead after 5 years, 30 per cent with the initial bleeding and 25 per cent from early or late recurrence. Primary concern with such an appalling mortality overshadows any detailed consideration of the survivors' condition, but it should be noted that of 348 patients reported in the literature1,5-8 to have survived an average of 5 years, 43 per cent were seriously impaired. These figures for the natural course of the syndrome are in agreement with the conclusion of Ask-Upmark and Ingvar: of those suffering subarachnoid hemorrhage, only 1 patient in 5 will ultimately make a good recovery.5

PATHOPHYSIOLOGY IN RELATION TO MORTALITY

Although important differences in prognosis and therapy are found when the major causes for spontaneous subarachnoid hemorrhage are considered separately, they have certain important features in common. All subarachnoid hemorrhage is consequent to rupture of a vascular channel, blood being released either directly into the subarachnoid space or rupturing into it secondarily after parenchymal hemorrhage. Subarachnoid bleeding per se is responsible for no significant part of the mortality. Two factors, alone or in combination, account for the majority of the neurologic defects or deaths that occur: primary destruction of brain tissue by the hydrostatic pressure of the escaping blood, and the secondary effects of an intracranial hematoma, which acts as a space-taking lesion. The physician is usually powerless to alter the first of these phenomena; he can often deal effectively with the second.

Any clinically significant intracranial hematoma will shift the brain from its normal position in the skull and alter its relation to the tentorium, the rigid membrane that separates the posterior and middle fossae. If there is a marked lateral displacement of the brain, the medial portions of the temporal lobes may herniate through the tentorium, causing pressure upon and necrosis of the midbrain. Similarly, a downward shift may cause the cerebellar tonsils to herniate through the foramen magnum, producing pressure necrosis of the medulla. These complications are manifested by rapidly deepening coma, pupillary inequality (if there is unilateral temporal lobe herniation), bilateral Babinski responses, episodes of hyperextension rigidity, and death. Evacuation of the hematoma early, when the effects of midbrain or medullary compression are reversible, is often a life-saving procedure. It should be borne in mind that this is equally true for the treatment of intracerebral hematoma without subarachnoid extension.9

Reflex spasm of vessels adjacent to a bleeding point is observed in many parts of the body, and the brain is no exception. In one view, this reflex may be regarded as protective against further hemorrhage. On the other hand, local constriction may be so severe, especially if superimposed upon the already narrowed vasculature of a hypertensive and arteriosclerotic patient, that areas of cerebral ischemia or infarction may be produced. On angiography, vasospasm adjacent to a bleeding point may cause nonfilling in this portion of the vascular tree, thwarting diagnosis. Observations at surgery and by carotid angiography have shown that this spasm diminishes gradually after the bleeding episode and is minimal or absent after the third week.10

In addition to the 2 prime causes of immediate mortality, overwhelming brain damage and the effects of intracerebral hematoma, a third factor, recurrent bleeding, may be responsible for most of the late mortality from subarachnoid hemorrhage. This phenomenon is seldom seen with hypertensive hemorrhage, owing to the high initial death rate. It is quite common in cases of aneurysm and angiomatous malformation. At least 50 per cent of the total mortality from ruptured aneurysms is thought to be due to recurrent episodes of hemorrhage. Repeated bouts of bleeding are even more common with angiomatous malformation but they appear to be less lethal.
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These differences in susceptibility to and mortality from repeated episodes of hemorrhage exemplify the necessity for separate consideration of each of the major causes of subarachnoid bleeding.

**Primary Intracerebral Hemorrhage with Subarachnoid Extension**

Intracerebral hematomas rupture into the cerebral ventricles or subarachnoid space in as many as 75 per cent of cases. Two types of intracerebral hemorrhage are now recognized: one that is apparently secondary to hypertension and arteriosclerosis, and a rarer "spontaneous" variety of bleeding in which the cause is not always apparent.

Hypertensive hemorrhage usually occurs deep within the cerebral hemispheres, particularly in the basal ganglia. Arterial degeneration and sustained systemic hypertension are presumed to be the important factors giving rise to this type of bleeding. Why the arteries of the brain are more prone to rupture than the extracranial vessels, and what the exact nature of the arterial degeneration is, are questions as yet unanswered. No form of therapy is currently available to reverse the worsening course of the patient who is rendered immediately or rapidly unconscious by brain hemorrhage and who develops signs of brain stem compression shortly thereafter.

Within this hypertensive-arteriosclerotic group, a less virulent form of the illness is occasionally seen. Here the patient is at first only transiently unconscious or perhaps only slightly obtunded. There is, however, a definite neurologic defect that usually progresses over a period of 2 or 3 days, during which time the state of consciousness gradually deteriorates. Lumbar puncture reveals the cerebrospinal fluid to be under increased pressure, and red blood cells are present in varying concentration. Finally, within 3 to 7 days, death usually ensues as a result of midbrain compression from the intracerebral clot. These hematomas frequently originate in the white matter of the frontal, temporal, or parietal lobes. Evacuation prior to the onset of signs of midbrain compression can be life-saving. It is our opinion that wider recognition of this variety of hypertensive bleeding might have some beneficial influence on a mortality rate that is more than 90 per cent.

**Spontaneous Intracerebral Hematoma**

This condition is usually seen in younger patients (fig. 1) and the diagnosis implies the absence of a history of significant hypertension. The course is similar to that described above for the more benign form of hypertensive hemorrhage, with gradually progressing neurologic signs, deepening coma, and death in 3 to 7 days from brain stem compression if no treatment is instituted. At postmortem examination the bleeding point is difficult to identify. With careful histologic preparation, however, some of these cases of "spontaneous" hemorrhage can be demonstrated to originate from minute, deeply seated vascular malformations. It is reasonable to believe that in many more cases the small malformation has been obliterated by its own bleeding.11 Odom et al.12 reported 14 cases of this syndrome; in 10 patients the hematoma was evacuated and all 10 survived. The 4 patients who were not operated upon died. These hematomas are as uniformly fatal as those produced by hypertension if "conservatively" handled.

**Cerebral Angiomatous Malformation**

While this entity has certain well-defined clinical and pathologic features, its origin and developmental history are disputed. As a result many descriptive terms have been used for the same basic entity: arterial, arteriovenous, or venous angioma or hemangioma; telangiectasis; arteriovenous hamartoma, aneurysm, or malformation; anastomotic aneurysm or angioma.13 These lesions are nearly always made up of rather large, tortuous arteries and veins with multiple cross-communications, fed and drained through a lesser number of widely dilated vessels. The lesion may be quite superficial. Frequently, however, it is deeply seated in the cerebrum and wedge-shaped, extending
from a ventricle to the cortex. Hemorrhage from these lesions can be intracerebral with or without subarachnoid extension, or primarily subarachnoid.

Common symptoms prior to bleeding include unilateral recurrent headache, epileptiform seizures (usually focal), and localized weakness. Any combination or sequence may be seen; the first manifestation most commonly appears in the second and third decades of life. In 110 cases described by Paterson and McKissock, 70 per cent developed their first symptom before the age of 30 years.

In 30 to 40 per cent of patients, unfortunately, the first signs will be those of intracranial hemorrhage, the majority with subarachnoid extension. In such cases the diagnosis is made arteriographically. A bruit has been observed with as many as 50 per cent of angiomatous malformations, but is remarkably less common (9 to 12 per cent) when hemorrhage has occurred.

Spontaneous subarachnoid hemorrhage in a young patient suggests the diagnosis. Suspicion should be strong if there is a prior history of hemorrhage, epilepsy, or localized weakness. A bruit over the skull is confirmatory.

A single hemorrhage from an angiomatous malformation appears to carry a mortality of 10 to 20 per cent, much lower than the other causes of subarachnoid bleeding. However, bleeding frequently recurs over a period of years and each episode adds its risk of morbidity and death. Potter has noted the course of 58 patients with this condition from less than 5 to more than 50 years (average 13 years) from the first symptom. In 38 patients treated conservatively there were 6 deaths from hemorrhage, all within 10 years of the first symptom. One other death resulted from hydrocephalus produced by the lesion. Eighty-two per cent of the entire group had 1 or more bleeding episodes during the follow-up. Over shorter periods of observation, other series show 30 to 60 per cent of patients to have had 1 or more hemorrhages at some time. If the malformation is surgically accessible, it may be excised, or if this is not possible, feeding vessels may be occluded. Surgical mortality at the present time is about 5 to 10 per cent for excision; Paterson and McKissock report 16 cases wherein feeding vessels were occluded, with no deaths and good results. The location of the lesion is the prime factor influencing the surgical result. Cases must be carefully selected.

When hemorrhage causes an intracerebral hematoma with acute compressive symptoms, evacuation must be performed immediately.

Aneurysms

These lesions fall into 3 distinct groups: mycotic, as a result of softening of the arterial wall at the site of lodging of a septic embolus; arteriosclerotic fusiform dilatations of the internal carotid, vertebral or basilar arteries; and congenital saccular, or "berry" aneurysms. The first group is rare and seldom causes subarachnoid hemorrhage. The arteriosclerotic variety also ruptures only rarely but produces neurologic signs and symptoms by pressing upon neighboring structures. The congenital saccular type occurs most commonly and ruptures most frequently. It is, therefore, with this group of aneurysms that we are primarily concerned.

The developmental fault leading to the formation of congenital aneurysms is not definitely known. Defects in the tunica media can be demonstrated at the points of bifurcation of the arteries at the base of the brain, which is the usual location of aneurysms. Such defects can also be found in patients without aneurysm. It has been postulated that congenital aneurysms may arise from remnants of the rich vascular network of the embryonic brain, a portion of which undergoes atresia during later stages of development. An increased incidence of aneurysm has been noted with other congenital defects such as polycystic kidney and coarctation of the aorta.

Aneurysms are not uniformly dispersed throughout the circle of Willis and its branches. From a series of 1,023 cases,
McDonald and Korb\textsuperscript{10} reported a distribution as noted in table 2. More than 1 aneurysm is found in 7 to 15 per cent of cases,\textsuperscript{18, 20, 21} and as many as 5 have been found in the same patient.\textsuperscript{18}

Hemorrhage from these lesions can occur at any age although it is most common between 30 and 60 years (fig. 1). In the unruptured state they may compress neighboring structures. One syndrome occurring after rupture is so diagnostic that it deserves special mention: sudden third nerve palsy (manifested by pupillary dilatation and oculomotor paralysis), when associated with the typical signs and symptoms of subarachnoid hemorrhage, is pathognomonic of bleeding from an aneurysm of the internal carotid artery at or near the origin of the posterior communicating branch.

Treatment of patients with saccular aneurysms is directed toward (1) prevention of rupture, (2) assisting the patient to overcome the immediate effects of hemorrhage, and (3) prevention of recurrent bleeding. To reach a conclusion concerning the wisdom and efficacy of any therapeutic regimen, the following facts relative to the "natural history" of the condition are necessary: A. What proportion of aneurysms rupture? B. What is the mortality and morbidity from initial hemorrhage? C. What is the probability of and the mortality and morbidity from recurrent hemorrhage? D. What is the most likely time for recurrent hemorrhage to take place? E. What are the effects of the age of the patient, the presence of hypertension and arteriosclerosis, and the size and location of the aneurysm on the factors listed above?

It is unfortunate that no absolute answers to these questions are available. Prior to the advent of angiography most aneurysms were discovered post mortem in patients who had died from their rupture. The era of angiography so quickly led to surgical intervention that the "natural course" described in current writings on this subject is often for patients adjudged too ill to withstand surgical attack.

\begin{table}[h]
\centering
\begin{tabular}{|l|c|}
\hline
Artery & Relative incidence (per cent) \\
\hline
Intracranial portion of internal carotid and its point of division & 19 \\
Anterior cerebral—anterior communicating complex & 23 \\
Middle cerebral & 28 \\
Posterior communicating & 3.5 \\
Posterior cerebral & 3 \\
Arteries of the posterior fossa & 23.5 \\
\hline
\end{tabular}
\caption{Distribution of Aneurysms in the Circle of Willis and Its Radicals as Noted by McDonald and Korb in 1023 Cases\textsuperscript{9}}
\end{table}

According to the figures presented by McDonald and Korb\textsuperscript{19} from a study of 1,023 cases, approximately 77 per cent of aneurysms will eventually rupture. Thus the incidental finding of aneurysm in the living patient indicates a grave but not hopeless prognosis for longevity. For this reason we have recently advised no surgical therapy for a 70-year-old woman whose unruptured internal carotid aneurysm was producing facial pain.

The surgery of intracranial aneurysms is a comparatively new field. Carotid ligation was performed successfully in cases of "pulsating exophthalmos" (carotid-cavernous fistula) as early as 1808, but it was not until 1936 that Dandy\textsuperscript{21} performed the first successful intracranial operation for nonfistulous aneurysm; concerted attack on these lesions has been carried out for the most part only since 1945. As with any new field of surgery, early results were frequently disappointing and the surgical mortality was high. Safer percutaneous angiography, the utilization of hypotension and hypothermia, and increasing surgical experience have, however, resulted in an improvement in the surgical outcome. In a recent series of 141 surgically treated patients operated upon by McKissock and Walsh\textsuperscript{22} the over-all mortality was 33 per cent in contrast to 53 per cent deaths in their patients who were not operated upon. Norlen and Olivecrona\textsuperscript{23} reported 78 patients operated upon with 10 deaths, a 13 per cent mortality. Jefferson and his co-
workers subjected 142 patients with ruptured aneurysm to carotid ligation. There were 12 early and 8 late deaths, a mortality of 14 per cent. Poppen, using several types of surgical approach, reports a mortality of 8 per cent in 226 cases.

It has been suggested, however, that the surgeons have chosen patients who have survived the high initial mortality and who would have lived if left alone. It becomes necessary, therefore, to examine such reports as have included the time interval from bleeding to operation and to compare these with a similar prognostic figure for conservatively managed patients seen at the same interval after hemorrhage.

We have mentioned the difficulty in obtaining an unselected series of angiographically proved aneurysms, observed without surgery, with which to compare the results of operation. McKissock and Walsh reported a group of 108 such patients treated without surgery and followed from 6 months to 10 years after aneurysmal rupture. Bjorkesten and Troupp reported a similar series of 40 cases. The basis for patient selection is not definitely stated for either series. It is nevertheless most interesting that a total mortality of 53 per cent was noted in the first series and a 55 per cent mortality in the second. These figures are in remarkable agreement with Walton's report of 55 per cent mortality within an average of 5 years of spontaneous subarachnoid hemorrhage where the cause of bleeding is unspecified, except for an attempt to exclude the hypertensive and arteriosclerotic group. From the literature to date it is not possible to construct a curve of progressive mortality for proved aneurysms conservatively managed after subarachnoid hemorrhage. However, since aneurysms produce about 80 per cent of subarachnoid hemorrhage as defined for Walton's series (fig. 2), and since the mortality after bleeding from aneurysm as derived from the data of McKissock and Walsh and Bjorkesten and Troupp would seem to correspond to that shown by Walton's series, figure 2 represents the best curve of mortality available for the study of aneurysms alone. It is probable, however, that Walton's series shows a higher early mortality (and therefore a lower mortality from recurrent bleeding) due to the inclusion of cases of spontaneous intracerebral hematoma. Also, as mentioned above, a number of Walton's patients had not been observed for a full 5 years after hemorrhage. In this respect, the mortality figures derived from Walton's report would seem to present the most optimistic picture of late mortality from recurrent subarachnoid hemorrhage due to ruptured aneurysm. We have adopted Walton's data for comparison with the results of operations for aneurysm in the opinion that it represents the most critical (if not the most accurate) standard available for such a comparison.

As a patient lives through successive days after the first subarachnoid hemorrhage, an increasing proportion of the statistical mortality is survived, and the mortality yet to be faced decreases. A curve of simple death rate (fig. 2) does not give a true picture of changing prognosis, since the mortality yet to be faced at any given time after the ictus must be absorbed by a steadily shrinking population. Walton's patients alive 1 week after the original hemorrhage had already lived through a 26 per cent population loss, and according to figure 2, 29 per cent of the entire population remained to die between 1 week and 5 years. But this 29 per cent toll now fell upon a population reduced to 74 per cent of the original, giving a mortality expectancy of 39 per cent for survivors at this point. Similar prognostic figures can be calculated from figure 2 for patients seen on any given day after the bleeding episode, and the prognostic curve formed by these points is shown in figure 4.

For comparison with prognosis on conservative management (fig. 4) there are, unfortunately, only a few surgical reports in which the operative mortality can be precisely determined for each interval from time of hemorrhage to time of surgery. A definite trend in the surgical results is nevertheless quite evident. Botterell et al. reported 73
consecutive cases of ruptured aneurysm operated upon under hypothermia. Surgery was carried out in 44 within 1 week after the last episode of bleeding, and 16 of these patients died (36 per cent). Of the other 29 patients, 6 were operated upon 8 to 14 days after bleeding, and 23 thereafter, with no deaths. In the series reported by Norden and Olivecrona,23 15 patients were operated upon within 3 weeks of bleeding, and 8 died. Of 63 patients operated upon 3 weeks or longer after the last hemorrhage, only 2 (3 per cent) died. It can be seen from figure 4 that in a similar group of patients not operated upon there is a 20 per cent chance of fatality within 5 years, even 8 weeks after the bleeding episode. All surgical procedures do not protect equally well against the possibility of recurrent hemorrhage, and adequate studies of the late results of aneurysmal surgery are lacking. It is probable, nevertheless, that obliteration of the aneurysms as reported above results in a “cure” if the patient survives the immediate postoperative period.

It is seen that at this writing very early surgery carries a mortality that may be higher than that for the natural history of the disease. This is due to the frequent presence of vasospasm, cerebral edema, and a severe neurologic defect in many of the patients undergoing surgery at this time. After a week or 2 have passed, vasospasm and cerebral edema have subsided and the patients with severe brain damage are dead. However, if this natural selection is allowed to operate until a time when surgery is completely safe, the fundamental purposes of surgery are defeated. If surgical intervention is to prevent the large morbidity and mortality from recurrence of bleeding in the second and third weeks (fig. 3), it must be performed before this time.

There is good evidence that the condition of the patient rather than a specific waiting period after bleeding should indicate the optimum time for intervention. Botterell et al.20 noted that in 7 poor-risk patients, operated upon 4 hours to 7 days after bleeding, 3 died, 2 were classified as “bad results,” and 2 as

![Fig. 4. Prognosis for patients with spontaneous subarachnoid hemorrhage based on figure 2. The survivors at any stated time after the initial hemorrhage are subjected to the indicated mortality risk for the remainder of a 5-year period. (Derived from Walton.)](image)
scioussness, all patients are classified as alert (A), blunted (B), or comatose (C). Improvement or stability in category, coupled with falling or stable cerebrospinal fluid pressure, indicates the proper time for operation. As a rule, surgery is not performed if this pressure is greater than 220 mm. of water; in our experience a high pressure bodes ill for surgical intervention.

Once the patient has achieved the appropriate clinical state, surgery should be undertaken directly. Delay can offer only further opportunity for recurrence of hemorrhage, and a patient’s good progress on one day is no guarantee against fatal rebleeding on the next.

Aneurysmal hemorrhage quite frequently results in secondary intracerebral hematoma. Five authors,\textsuperscript{12, 18, 27-29} reported a total of 79 such instances in 204 cases of ruptured aneurysm—an incidence of 39 per cent. If signs indicate such a process with progression, immediate operation must be performed, regardless of the above factors.

Other considerations are also of prime importance to the outcome, whether management be conservative or surgical. McKissock and Walsh\textsuperscript{22} noted a 47 per cent mortality among hypertensive patients subjected to surgery, while that for normotensive subjects was 26 per cent. For patients over 50 years of age, the mortality with surgery was 46 per cent; of the younger patients, 28 per cent died. Nearly identical differences in mortality were found for conservatively managed patients in the same categories. Furthermore, there is general agreement that both conservative and surgical prognosis will vary with the location and configuration of the aneurysm, but good statistical evidence is lacking at the present time.

The ideal operative procedure for aneurysm is occlusion of the aneurysmal neck by suture or clip, excluding the sac from the circulation without disturbance to circulatory dynamics. Unfortunately, some aneurysms are found to be nodular outpouchings, with no definite neck. Many are inaccessible to direct attack. Nearly all are tense and friable, and respond to enthusiastic manipulation with massive hemorrhage. A variety of procedures has been proposed and attempted in a large number of aneurysms varying widely in location and size. Clipping and ligation of the aneurysm neck, trapping procedures (occlusion of the feeding vessel on both sides of the lesion), muscle packing in and about the aneurysm, and cervical carotid occlusion are the most frequently described. We prefer an intracranial approach whenever possible, since in our opinion carotid ligation is not so certain to produce a permanently good result. Moreover, the sacrifice of one carotid artery in a younger patient would mean dire circulatory embarrassment if thrombosis of the second carotid artery should occur at a later date, and it has become increasingly evident that carotid thrombosis is an important cause of cerebrovascular accident in older patients. In some cases carotid ligation may be quite definitely preferable, and in some situations it may be the only procedure possible. One of us (H.T.B.) has recently performed such a ligation upon a 53-year-old woman who developed dysphasia and hemiparesis following hemorrhage from an aneurysm located in the terminal branching of the middle cerebral artery. It was considered that a direct surgical approach in this situation might increase the chances of permanent hemiparesis.

Angiography

It can be seen from the foregoing discussion that early angiography is an absolute necessity. Unless the exact size, shape, location, and nature of the offending lesion is determined, no rational plan of management can be formulated. The dynamics of collateral circulation, abnormalities of cerebral blood supply, and multiplicity of lesions must also be carefully considered before proper therapy can be instituted. Carotid injection should be done bilaterally whenever possible. Only a small proportion of aneurysms and anomalies are found in the vertebral-basilar portion of the circle of Willis, and these are usually not accessible to surgery. Because of this low yield and the difficulty of performing verte-
bral angiography, we believe that this procedure should be done only in special circumstances.

When bilateral carotid angiography fails to show a lesion, prognosis is relatively good and surgical intervention is usually precluded. Parkinson reported 22 cases in which bilateral carotid angiograms were negative. None of these patients suffered a recurrence of bleeding during the subsequent 1 to 5 years. A similar group of 61 patients was observed by Bjorkesten and Troupp for an average of 3 years. There were only 3 fatal recurrences (5 per cent). Angiography will miss a certain proportion (possibly 20 per cent) of aneurysms, especially if performed soon after hemorrhage. In some cases the presence of an aneurysm is suggested by vasospasm in the surrounding vasculature, and a later repetition of the study will demonstrate the lesion. Thrombosis within the aneurysm, developing after a bleeding episode, may prevent filling. The negative arteriogram in this circumstance still correctly indicates medical management and a relatively good prognosis.

The performance of cerebral angiography is not without its risk. With every large series of angiograms there is an occasional transient or permanent complication: hemiparesis, convulsions, internal carotid thrombosis, cervical trauma, and sensitivity to the injected contrast medium are reported. More rarely, death can result. However, as with the surgery in aneurysm, angiographic technic is steadily improving and these unfortunate complications are seen in decreasing number. In a recent series of 104 angiograms performed in this hospital there have been only 1 major complication and no deaths. When the tremendous mortality from undiagnosed and untreated subarachnoid hemorrhage is in the offing, carotid angiography seems well worth the risk.

**Care of the Patient Who Has Recently Bled**

In the comatose patient there is no substitute for a patent airway and adequate oxygenation, careful fluid balance, and prevention of urinary sepsis. Periodic observations of vital signs and state of consciousness should be recorded. The conscious patient should be kept at bed rest, and possible sources of exertion should be eliminated.

The recent development of hypothermia may prove of great value to the nonoperative management of these patients. With body temperature lowered to 30 C., the basal metabolic rate in human beings is reduced to about 60 per cent of normal. In experimental dogs, Lougheed and Kahn found a reduction of cerebral metabolic rate to between 23 and 35 per cent of normal when body temperature was lowered to 25 C., with no pathologic changes on sectioning the brain 6 months later. This reduction in cerebral metabolic rate will markedly lessen the damaging effects of local ischemia, as created experimentally and as seen clinically. Hypothermia is thus valuable in combating the ischemic effects of vasospasm and also appears to reduce cerebral edema. The use of prolonged hypothermia in the conservative treatment of acute bleeding has not yet been reported in a statistically significant number of cases; its ultimate place in conservative management is yet to be determined. Hypothermia is of particular value in the surgery of aneurysms, when carotid or vertebral blood flow must be occluded to facilitate the operation.

Hypotensive agents have been used to reduce the danger of "rebleeding" in both conservative and surgical management. We think that the use of these agents is accompanied by a definite risk, however: the ischemic effect of local vasospasm is accentuated by a severe drop in blood pressure, and infarction is more likely to occur in those areas affected by vasospasm when hypotensive drugs are administered. The combination of hypotension and hypothermia would seem to be ideal from this point of view; unfortunately this combination is apparently conducive to cardiac arrhythmias, particularly ventricular fibrillation. The future holds promise of greater use for these agents as their properties become better understood.
SUMMARY AND CONCLUSIONS

Spontaneous intracranial subarachnoid hemorrhage is an emergency, to be approached carefully but aggressively. If specific etiology is not established and appropriately attacked, more than half of the patients so afflicted will be dead, and only 1 in 5 well, within 5 years from the ictus.

Nearly all subarachnoid hemorrhage results from 1 of 4 basic conditions: intracranial aneurysm, angiomatous malformation, hypertensive-arteriosclerotic cerebral hemorrhage, and "spontaneous" intracerebral hematoma. A specific surgical approach in selected cases may considerably lower the mortality in each of these categories.

Because of the diagnostic, prognostic, and therapeutic significance of subarachnoid blood, lumbar puncture should be performed in all cases where intracranial vascular accident is suspected. If blood is found on lumbar puncture, bilateral carotid angiography should be performed as soon as possible, except in those cases in which a diagnosis of hypertensive hemorrhage can be clearly established on clinical grounds.

Evacuation of a rapidly expanding intracerebral hematoma is a simple, often lifesaving procedure.

When hypertensive hemorrhage is excluded, the most common single cause of spontaneous subarachnoid hemorrhage is intracranial aneurysm. If the maximum number of patients with aneurysm is to be saved from fatal recurrent hemorrhage, definitive surgery must be performed at the earliest relatively safe time after the first hemorrhage. This time is found to coincide with the patient's earliest clinical improvement and stabilization. Immediate advantage should be taken of this improved state, since recurrence of hemorrhage may follow at any time. There can be no substitute for judgment and experience in choosing the proper course of action for each patient.

With continued clinical experience and rapidly advancing technics, such as hypothermia and hypotension, it is probable that an even greater saving of patients will soon be realized by surgery in the earlier period after bleeding.

SUMMARIO IN INTERLINGUA

Spontane hemorrhagias intracranial subarachnoide representa un situation de urgentia que debe esser attaccate caute- sed agressivamente. Sie le etiologia specific non es identificata e attaccate per medios appropriate, plus que un medietate del patientes assi affligite va esser morte e solmente 1 inter 5 va esser ben al fin de 5 annos post le icto.

Quasi omne hemorrhagias subarachnoide re- sulta ab 1 de 4 conditiones fundamental: (1) Aneurysmo intracranial, (2) malformation angiomatose, (3) hemorrhagia cerebral hypertensive-arteriosclerotic, e (4) "spontane" hematoma intracerebral. Un specific tactica chirurgic in seligite cases es forsae capace a reducere le mortalitate de maniera considerabile in cata un del mentionate categorias.

A causa del signification diagnostic, prognostic, e therapeutic de sanguie subarach- noide, un punctura lumbar debe esser effectuate in omne cases in que il existe le suspicion de un accidente vascular intracranial. Si le punctura lumbar revela le presentia de sanguie, angiographia carotic bilateral debe esser effectuate le plus promptemente possibile, excepte in cases in que un diagnose de hemorrhagia hypertensive pote esser establite clarmente super le base de datos clinic.

Le evacuation de un hematoma intracerebral a expansion rapide es un simple manovra que sucede frequentemente a salvar le vita del patiente.

Post que le possibilitate de hemorrhagia hypertensive es excludite, le plus commun causa individual de spontane hemorrhagias subarachnoide es aneurysmos intracranial. Si on vole salvar le plus grande numero possibile de patientes con aneurysma ab le effectos mortal de hemorrhagias recurrente, un definitive intervention chirurgic debe esser effectuate al prime momento post le hemorrhagia initial ubi illo es possible con libertate relative de hasardos. Il ha essite constatate que iste mo- mento coincide con le tempore del prime melioration e stabilisation clinic del patiente.
Le opportunitate de un tal melioration debe esser utilizate immediatamente, proque un recurrentia del hemorrhagia pote sequer a non importa qual tempore. Nihil equivalde judicio sitate e experientia in le selection del mejor curso de action pro le patiente individual.

Con le continuation del experientia clinic e le rapide progresso additional in le technicas applicabile—per exemplo hypothermia e hypotension—il es probable que un percentage ancora plus alte de patientes va tosto poter esser salvate per intervention chirurgic promptemente post le sanguination.

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Observations on 6 patients with penicillin-susceptible streptococcal endocarditis who were treated with at least a 4-week course of large doses of penicillin V (2,000,000 units every 4 hours by mouth) and a streptomycin dihydrostreptomycin parenterally are presented. Clinical and bacteriologic cures were observed in all patients with no signs of relapse during follow-up periods ranging from 3 to 10 months. In 5 patients the serum penicillin levels were maintained above 1.6 units per ml throughout the 4-hour interval between doses. Penicillin V serum levels, however, were consistently lower and less uniform than those obtained in other patients receiving equal doses of aqueous penicillin G intramuscularly, but were higher than those obtained with equal doses of penicillin G orally. Higher penicillin levels were found when the penicillin V was taken after meals. Simultaneous administration of aluminum hydroxide gel was found to depress the subsequent penicillin levels. Two patients developed nausea and vomiting of sufficient severity to interfere with therapy. One patient failed to obtain an adequate penicillinemia until probenecid was administered concurrently. Because the absorption of penicillin V taken orally is not predictable nor uniform enough to assure an adequate penicillinemia in this disease, the authors conclude that parenteral administration of penicillin still remains the preferred treatment for the majority of patients with subacute bacterial endocarditis.

Sagall
Management of Spontaneous Intracranial Subarachnoid Hemorrhage
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