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# SUBARACHNOID HAEMORRHAGE DUE TO INTRACRANIAL ANEURYSMS

## RESULTS OF TREATMENT OF 249 VERIFIED CASES

BY

WYLIE McKISSOCK, O.B.E., M.S., F.R.C.S.
*Neurological Surgeon, St. George's Hospital, London*

AND

LAWRENCE WALSH, F.R.C.S.
*Research Assistant, Department of Neurosurgery, St. George's Hospital, London*

Since the advent of angiography it has been possible to subdivide cases of subarachnoid haemorrhage into three main groups: those in which an aneurysm can be displayed, those harbouring an angioma, and those in which no causal lesion can be demonstrated. We exclude, of course, all cases of subarachnoid haemorrhage due to general disease processes or to craniocerebral injury.

Before the days of angiography it was permissible to write of a series of cases of subarachnoid haemorrhage on the assumption that the majority were due to " berry " aneurysm, but we feel with others that the time has come to deal with subarachnoid haemorrhage not generally but with relation to the actual sites of the causal aneurysm in one series and the angioma in another. There will also be a third group in which it has been impossible to demonstrate any lesion by angiography or skull radiography.

Hamby (1952) has given an excellent lead in this direction in his book on intracranial aneurysms, dealing with symptomatology, signs, treatment, and prognosis according to the exact anatomical position of the aneurysm on the intracranial vascular tree. By contrast the great majority of recent papers on intracranial aneurysms and subarachnoid bleeding, particularly those relating to conservative or surgical treatment, serve only to confuse an already difficult issue. They fail to provide much relevant information regarding the selection of cases for surgical treatment, the state of the patient at the time surgery has been undertaken, and its time relationship to the last haemorrhage, to mention but a few of many similar vital factors. Norlén and Olivecrona (1953) emphasize this point. A notable exception to this general rule lies in the papers by Norlén (1952) and Norlén and Olivecrona (1953) showing that, in cases that have survived the initial two to three weeks after the first haemorrhage, direct surgical attack on the aneurysm can be undertaken with relative safety and with a lower mortality rate than that which obtains for similar patients given conservative treatment alone.

It must not be forgotten, however, that the greatest number of deaths from ruptured aneurysms occur in the first weeks following the initial haemorrhage, and Norlén and Olivecrona feel that surgical methods do not alter the prognosis during this critical period, when 30% of patients die from the disease process. An additional 20% die in the next few weeks, and it is against this mortality rate alone that the admirable results of Norlén and Olivecrona must be measured.

We feel, and indeed are convinced from personal experience, that it is possible to save some at least of those 30% dying during the first weeks following rupture of an aneurysm (who would be denied surgery by many), and have therefore instituted a system of clinical and specialized investigation which is applied to every case as soon as the patient is admitted to hospital, irrespective of how recent the haemorrhage may be. In other words, our system of investigation is applied even to patients admitted in coma only a few hours after a haemorrhage has taken place.

It has been suggested that there is danger in performing angiography in the acute phase, and we recognize that this may well be true. We are not, however, convinced that this is so, and, in any case, it has seemed to us justifiable to apply such diagnostic methods early owing to the absence of any sure method of establishing at what time a second, and possibly fatal, haemorrhage may occur.

### Method of Investigation

Our present system, which may well undergo modification as more certain knowledge becomes available, is to carry out a clinical examination of the patient immediately after admission to hospital. This clinical examination includes a ten-minute compression of each common carotid artery, and it is only as a result of this test that a divergence from the normal routine of investigation is permitted. Repeated failure to withstand consecutive compression of the common carotid arteries, a fairly rare event, causes us to refrain from further investigation and to arrange for conservative treatment unless there is evidence of an expanding intracranial haematoma.

After straight radiographs of the skull have been taken and reviewed, bilateral carotid angiography is performed

with appropriate cross-compression when an aneurysm has been demonstrated.

If the aneurysm is amenable to any method of surgical treatment, operation is proceeded with at once and under the same general anaesthetic if such has been required for angiography. The use of 25% "diagonal," or of "thorotrast" in older patients, has greatly reduced the number of cases requiring a general anaesthetic for this diagnostic procedure.

Vertebral angiography is not used as a routine, but only in a small number of selected cases. The generally accepted percentage of 15 for aneurysms on the posterior part of the circle of Willis and in the posterior fossa is thus higher than in our series, where the figure is 6%. As few of these 15% are likely to be amenable to surgical treatment we have felt it reasonable to neglect vertebral angiography as a routine measure, especially as it may lead to additional trauma to the neck, prolong the time of investigation, and possibly increase the risk to the patient. Using this system of immediate investigation and surgical treatment in practically every case, it is possible to assess the mortality rate against the generally accepted 60% reported by so many, and closely paralleled by our own series of conservatively treated cases.

## Case Material

Up to and including March 31, 1954, 461 cases of subarachnoid haemorrhage had been admitted to the Atkinson Morley Branch of St. George's Hospital, a survey of which revealed 249 cases of proved aneurysm. All patients have since been followed, in the majority of cases by letter, less often by out-patient attendance, and occasionally by reports from the patient's own doctor.

The follow-up period in the 145 survivors ranges from 6 months to 9 years and the survival periods are shown in Table I.

TABLE I

| Survival Period | No. of Cases |
|---|---|
| 6–12 months | 8 |
| 1–2 years | 48 |
| 2–3 ,, | 23 |
| 3–4 ,, | 26 |
| 4–5 ,, | 13 |
| 5–10 ,, | 27 |

The yearly admission rate of patients suffering from subarachnoid haemorrhage has shown, and continues to show, a steady rise as consultants and general practitioners become more alive to the possibilities of the active investigation and treatment of such patients. The advent of the percutaneous technique of angiography has also greatly facilitated the investigation, and these two factors account for the larger number of patients appearing in the upper half of Table I.

The anatomical distribution of these 249 proved aneurysms is shown in Table II and in the Diagram.

Of the 249 cases which had bled from the aneurysm many had sustained additional haemorrhage into the brain substance, ventricular system, or subdural space, and these complications are dealt with below. No case has been included in the series unless the aneurysm has been verified by angiography, operation, or post-mortem examination.

We propose to assess the results of surgical treatment against the suggested mortality rate of subarachnoid haemorrhage, generally agreed upon by Richardson and Hyland (1941), Magee (1943), Hamby (1948), Ask-Upmark and Ingvar (1950), and Walton (1952), of 50% during the 8-weeks period following hospital admission for haemorrhage. We realize, of course, that not all of their cases of subarachnoid haemorrhage were due to aneurysm. Our own series, however, of conservatively treated cases of proved aneurysm produced a similar mortality rate of about 50%, and so is in agreement with the figures of most other writers.

In trying to compare the results of operation with those of conservative treatment the greatest difficulty is to avoid the element of selection which arises in cases submitted to operation. This selection may be due, among other things,

TABLE II.—*Anatomical Distribution*

| Site | No. With Subarachnoid Haemorrhage |
|---|---|
| Anterior cerebral and anterior communicating arteries | 71 (28·5%) |
| Internal carotid at level of posterior communicating artery | 62 (25%) |
| Middle cerebral artery | 42 (17%) |
| Bifurcation of internal carotid artery | 31 (12%) |
| Multiple aneurysms | 19 (7·5%) |
| Posterior cerebral, superior cerebellar, basilar, and vertebral arteries | 15 (6%) |
| Anterior cerebral artery: distal | 7 (3%) |
| Site unverified | 2 (1%) |
| Total | 249 |

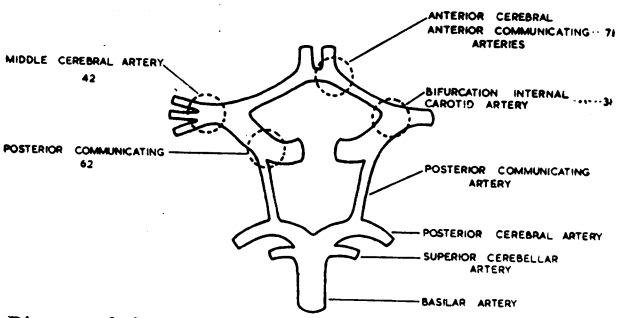


Diagram of circle of Willis showing distribution of major groups of aneurysms.

to the referring hospital or doctor, the condition of the patient, who may be so ill that he dies before an operation can be performed, or the refusal of operation by the patient. In order to try to overcome this difficulty we have decided to classify the patients according to the severity of the effects of the haemorrhage.

## Classification

*Category A: Patients who are in danger of dying in the immediate future from the haemorrhage causing admission to hospital.*—This category includes all those who are in coma or a semiconscious state with severe neurological signs.

*Category B: Patients who have completely, or in part, recovered from the haemorrhage resulting in hospital admission, are seen within 8 weeks of the last bleed, but are not in danger of dying from that initial haemorrhage.*—This category includes patients in good general condition but who may or may not still show some residual signs of haemorrhage. They are still, however, at considerable risk from a further haemorrhage.

*Category C: Patients who have recovered completely, or with residual signs in the central nervous system, from the initial bleed but are seen more than 8 weeks after the haemorrhage.*—In this category most patients were completely well and only a few had residual signs of the brain damage caused by the original haemorrhage. They, of course, are still at some risk from a further haemorrhage, but probably only to the order of about 20%.

In those who were not operated on the classification is made on the state of the patient when admitted to hospital. In those operated upon, the classification refers to the state of the patient at the time of operation. It is realized that there are difficulties in using such a classification, as different observers may vary in their assessment of the clinical state of a patient. Most patients, however, were found to be quite easy to classify, and where difficulty arose it was usually between categories A and B. In cases of doubt the patient was placed in category A.

## Outcome of Treatment

In Table III the outcome of conservative and surgical treatment is seen in relation to the time factor and the

gravity of the patient's physical state. Some explanation is required of the figure of 23.5% mortality rate in patients treated surgically who fell into category C. The aneurysms in these 4 patients were situated as follows: anterior cerebral/anterior communicating, bifurcation of internal carotid, middle cerebral, and multiple. For aneurysms in all these sites, as is mentioned below, we now feel that ligation of the common carotid artery alone provides inadequate protection. All these 4 patients died of late

TABLE III

| Category | No. of Cases | Deaths | |
|---|---|---|---|
| | | No. | Approximate Percentage |
| *Patients Treated Medically* | | | |
| A | 43 | 38 | 90 |
| B | 48 | 18 | 37·5 |
| C | 17 | 1 | 6 |
| Total | 108 | 57 | 50 |
| *Patients Treated Surgically* | | | |
| A | 52 | 34 | 65·5 |
| B | 72 | 9 | 12·5 |
| C | 17 | 4 | 23·5 |
| Total | 141 | 47 | 33·3 |

recurrence of haemorrhage at periods of 2, 1½, and 1½ years, and 6 weeks respectively after common carotid ligation. None died as a direct sequel to operation.

There were thus 51 survivors in the medically treated patients and 94 in those treated surgically. Of the 51 medically treated patients only one is severely disabled, whilst the remainder show only slight or no disability and are regarded as having made a good recovery. There were 16 severely disabled in the 94 treated by surgical methods, and the remainder made a good recovery.

The results have also been considered in relation to the age of the patient (Table IV) and the presence or absence of hypertension (Table V). The patients have been divided into two groups—those below the age of 50 years and those 50 and over. Patients with a systolic pressure of 160 mm. Hg and over and/or a diastolic pressure of over 90 mm. Hg have been classified as hypertensive.

TABLE IV

| Age of Patients | Medically Treated | | Surgically Treated | |
|---|---|---|---|---|
| | No. | % Mortality | No. | % Mortality |
| Below 50 years .. | 61 | 44·0 | 106 | 28 |
| 50 years and over.. | 47 | 67·5 | 35 | 46 |

TABLE V

| | Medically Treated | | Surgically Treated | |
|---|---|---|---|---|
| | No. | % Mortality | No. | % Mortality |
| Non-hypertensive | 65 | 45·0 | 96 | 26 |
| Hypertensive .. | 43 | 67·5 | 45 | 47 |

We believe, as stated above, that the real issue lies in assessing the value of different forms of treatment in relation to the actual site of the aneurysm, and that it is unsatisfactory, and unrealistic, to group all aneurysms together.

We have therefore divided the aneurysms into subgroups according to their anatomical situation and endeavoured to contrast the effects of conservative and surgical treatment in this light combined with that of the time interval since haemorrhage and the gravity of the clinical state. The groups are now, of course, much smaller in numbers, but do nevertheless show a fairly consistent lowering of mortality rate in the surgically treated subgroups.

### Anterior Cerebral and Anterior Communicating

From Table VI it would appear that direct attack, particularly if the patient is dangerously ill, as in category A, is contraindicated, but that, even including these cases, surgical treatment offers a lower mortality rate than do

TABLE VI.—*Anterior Cerebral and Anterior Communicating (71 Patients, with 2 Aneurysms Treated Twice, making 73 Cases)*

| Category | Medically Treated | Deaths | % Mortality | Carotid Ligation | Deaths | % Mortality | Anterior Cerebral Clip | Deaths | % Mortality | Craniotomy and Clipping of Neck | Deaths | % Mortality |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A | 13 | 12 | 92 | 2 | 2 | 100 | 7 | 3 | 43 | 5 | 5 | 100 |
| B | 14 | 5 | 39 | 5 | 0 | 0 | 9 | 2 | 22 | 8 | 3 | 38 |
| C | 6 | 0 | 0 | 2 | 1 | 50 | 1 | 0 | 0 | 1 | 0 | 0 |
| Total | 33 | 17 | 51 | 9 | 3 | 33 | 17 | 5 | 29 | 14 | 8 | 57 |

conservative methods (50% in untreated cases and 40% in surgically treated), whilst in those treated by carotid ligation or proximal clipping of the appropriate anterior cerebral artery the combined rate is but 30%.

Most of these cases have been included in a previous publication by Logue (1956), who operated upon the majority of the patients in this subgroup.

Of the 33 conservatively treated patients 17 died. Of these deaths, 3 in category A and 5 in category B were due to a further haemorrhage—a recurrence rate of 25%. Carotid ligation was performed in 9 cases, of whom 2 (1 in category A and 1 in category C) suffered a fatal subsequent haemorrhage, a recurrence rate of 22%. Although the figures are too small to be significant there is no evidence to suggest that common carotid ligation lowers the incidence of recurrent haemorrhage.

### Middle Cerebral Aneurysms

The high mortality of these lesions when medically treated (over 50%) is again evident, and the combined mortality for all forms of surgical treatment is but 30% (Table VII). A more detailed analysis of these cases is not given here as they will form the subject of another paper in the near future.

TABLE VII.—*Middle Cerebral Aneurysms*

| Category | Medically Treated | Deaths | % Mortality | Carotid Ligation | Deaths | % Mortality | Craniotomy and Clipping of Neck | Deaths | % Mortality | Aspiration of Clot | Deaths | % Mortality |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A | 6 | 6 | 100 | 5 | 3 | 60 | 6 | 2 | 33 | 1 | 1 | 100 |
| B | 12 | 4 | 33 | 4 | 0 | 0 | 5 | 0 | 0 | | | |
| C | 1 | 0 | 0 | 1 | 1 | 100 | 1 | 0 | 0 | | | |
| Total | 19 | 10 | 52 | 10 | 4 | 40 | 12 | 2 | 17 | 1 | 1 | 100 |

### Internal Carotid Aneurysms at Level of Posterior Communicating Artery

The natural death rate in this series of aneurysms is somewhat lower than in most other situations, being only 33% (Table VIII), but again the combination of all methods

TABLE VIII.—*Internal Carotid Aneurysms at the Level of the Posterior Communicating Artery (62 Patients, 2 of Whom were Treated Twice, making 64 Cases)*

| Category | Medically Treated | Deaths | % Mortality | Carotid Ligation | Deaths | % Mortality | Craniotomy Trapping or Clipping | Deaths | % Mortality | Aspiration of Clot | Deaths | % Mortality |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A | 6 | 4 | 66 | 6 | 3 | 50 | 1 | 1 | 100 | 2 | 1 | 50 |
| B | 8 | 3 | 38 | 26 | 3 | 11 | 3 | 0 | | | | |
| C | 6 | 0 | | 6 | 0 | | | | | | | |
| Total | 20 | 7 | 33 | 38 | 6 | 16 | 4 | 1 | 25 | 2 | 1 | 50 |

of surgical treatment shows a decided improvement, there being 8 deaths in 44 treated cases, a mortality rate of only 18%.

*Patients Treated Medically.*—Of 20 patients, 13 survived. Of the survivors, 2 in category A had only slight residual disability after 18 and 24 months respectively; 5 in category B showed slight disability in one case and none at all in 4 cases after 1–3 years; and of 6 in category C, 2 cases showed slight disability and 4 no disability after 1–6 years. Seven patients died: 3 in category A gradually deteriorating and dying within 3 weeks of the haemorrhage causing admission to hospital. Post-mortem examination showed haemorrhage into the temporal lobe in 2 cases, in one of which rupture into the ventricle had occurred. The fourth death in category A was due to recurrent haemorrhage in hospital proving fatal 18 days later. The remaining 3 deaths, all occurring in patients in category B, were due to recurrent haemorrhage at intervals of 10 days, 5 weeks, and 6½ years.

*Patients Treated Surgically.*—Three out of the four treated by craniotomy survived, 1 having had the aneurysm packed with muscle and 2 the neck of the aneurysm clipped. At follow-up 5–6 years later 1 had severe and 2 only slight residual defects. In the fatal case nothing was done to the aneurysm, but a temporal clot was evacuated and the patient slowly deteriorated until his death 11 days after operation. Of the 38 cases subjected to carotid ligation, only 2 had the internal carotid artery tied; in the remainder the common carotid vessel was ligated. Thirty-two of the patients survived—3 in category A, 23 in category B, and 6 in category C. Of the 3 in category A, followed for a few weeks (when craniotomy was performed) to 2½ years, 2 had severe disability and 1 no residual defect. The 23 survivors from category B, followed up from a few weeks (when craniotomy was performed) to 9 years, showed 14 perfect recoveries, 8 had slight disability, and only 1 was severely handicapped. Of the 6 patients surviving in category C, 4 were in normal health and 2 had slight residual signs. Six patients died—3 in category A of slow deterioration in 5 days, 8 days, and 2½ months, showing at post-mortem examination subdural blood in one, bronchopneumonia in another, and subarachnoid blood only in the third. Three others from category B died: one died on the fourth post-operative day, and at the post-mortem examination blood was found in the subarachnoid space; one died of coronary thrombosis 15 months later at the age of 70, whilst the third died of carcinoma of the colon 7½ years after operation.

### Comparison of the 38 Patients Treated by Carotid Ligation for Posterior Communicating Aneurysm with the 20 Patients Treated Medically

*Category A.*—There is no significant difference between the small numbers in both groups.

*Category B.*—The results with carotid ligation were very good, and only one patient, out of 26 patients, died as a result of the aneurysm. In patients not operated on, 3 out of 8 died, all with a recurrence of haemorrhage. In the 20 cases not operated on, 4 (20%) had a fatal recurrence of haemorrhage. In the 38 cases treated by carotid ligation there was no certain recurrence of haemorrhage, but 2 (5%) had a possible fatal recurrence. None of the patients treated by carotid ligation has suffered a recurrence of subarachnoid haemorrhage after discharge from hospital. It is therefore submitted that common carotid ligation affords a high degree of insurance against a further haemorrhage in aneurysms of the internal carotid artery at the level of the posterior communicating artery. In patients in category A, many of whom have an intracerebral, intraventricular, or subdural haemorrhage, the operation has not been beneficial. This is to be expected, and it seems that if any treatment can help it will have to be directed against the intracerebral haemorrhage when it exists.

TABLE IX.—*Aneurysm of Internal Carotid Bifurcation*

| Category | Medically Treated | Deaths | Mortality | Carotid Ligation | Deaths | Mortality | Craniotomy | Deaths | Mortality |
|---|---|---|---|---|---|---|---|---|---|
| A | 6 | 4 | 66% | 8 | 4 | 50% | | | |
| B | 7 | 2 | 29% | 5 | 0 | 0% | 1 | 0 | 0% |
| C | 2 | 1 | 50% | 2 | 1 | 50% | | | |
| Total .. | 15 | 7 | 50% | 15 | 5 | 33% | 1 | 0 | 0% |

### Aneurysm of Internal Carotid Bifurcation (Table IX)

*Patients Treated Medically.*—Of the 8 survivors in this series of 15, 2 came from category A, and follow-up at 5 and 7 years showed slight disability in 1 and none in the other case. In category B, 5 patients survived and at a 1–7 year follow-up 1 was severely and 2 were slightly disabled. The remaining patients were perfectly well. Four of the 7 dying had been included in category A, and 2 of these died in a few hours, 1 in 4 weeks and 1 from a recurrence at 4 weeks. Post-mortem examinations carried out in 3 of the 4 revealed temporal-lobe softening in 1, subarachnoid haemorrhage in 1, and subdural and intraventricular haemorrhage in the third. Two patients in category B died of recurrent haemorrhage in 1 and 3½ weeks respectively: the post-mortem examinations revealed subdural bleeding in 1 and subarachnoid blood in the other. The seventh death took place in a category C patient from a recurrent haemorrhage 4 years later.

*Patients Treated Surgically.*—Carotid ligation was performed in 15 cases and 9 patients survived, 4 of them from category A at 2–6½ years, with severe defect in 2, mild disability in 1, and no sequel in the remaining patient. Five patients from category B recovered, and at periods of 1–8 years showed mild disability in 2 cases and none whatever in 3. One patient in category C has survived for 4 years with only slight residual sequelae. Four of the 5 deaths came from category A—3 within 2 hours of operation and one 2 months later. In the 2 upon whom a post-mortem examination was performed there was intracerebral haemorrhage with rupture into the ventricle. The remaining death was in a category C patient, and occurred 1½ years later from recurrent haemorrhage. The mortality rate in conservatively treated cases again appears as 50%, whilst the cases treated surgically show 5 deaths in 16 cases—a mortality rate of 30%.

### Comparison of 15 Patients Treated by Carotid Ligation for Aneurysms of Internal Carotid Bifurcation with 15 Patients Treated Medically

*Category A.*—There is no great difference between the small numbers in each group.

*Categories B and C.*—Of patients not operated on, 3 out of 9 died. Out of 7 patients treated by carotid ligation, 1 died. Of the 15 patients not operated on 4 had a fatal recurrence of the haemorrhage. Of the 15 patients treated by carotid ligation, 1 had a fatal recurrence of haemorrhage and 1 may have had a recurrence of haemorrhage in the post-operative period that was not fatal. Thus it seems that common carotid ligation affords some insurance against further haemorrhage in patients with an aneurysm at the termination of the internal carotid artery. There have been,

TABLE X.—*Multiple Aneurysms*

| Category | Medically Treated | Deaths | Mortality | Carotid Ligation | Deaths | Mortality |
|---|---|---|---|---|---|---|
| A .. | 2 | 2 | 100% | 3 | 2 | 67% |
| B .. | 6 | 3 | 50% | 3 | 0 | 0% |
| C .. | 2 | 0 | 0% | 3 | 1 | 33% |
| Total .. | 10 | 5 | 50% | 9 | 3 | 33% |

however, one and possibly two recurrences in the 15 patients, and it may well be that ligation of the internal carotid artery will provide greater safety.

### Multiple Aneurysms (Table X)

*Patients Treated Medically.*—In this series 5 patients survived: 3 in category B for 1, 2, and 3 years respectively with minor disability in 2 and no disability in the other; and 2 in category C who survived for 1 and 2 years with minor sequelae in each instance. Of the 5 deaths in the series (2 in category A and 3 in category B), 4 were the result of recurrent haemorrhage at 1 day, and 2, 3½, and 5 weeks after the original bleed. The fifth patient, in category A, gradually deteriorated and died 5 weeks after the initial haemorrhage.

*Patients Treated Surgically.*—Common carotid ligation was the surgical treatment offered in 9 cases, and death occurred in 3. One patient from category A has survived 5 years with severe disability, 3 from category B were alive at 1, 2, and 3 years, with minor defect in one case and none in the other two. The other 2 survivors were alive at 2 and 5 years, one severely and the other only slightly disabled. Two of the 3 patients who died were placed in category A; one slowly deteriorated until death 4½ weeks after the haemorrhage from internal carotid thrombosis and the other of recurrent haemorrhage 6 weeks later. The third death, in a patient from category C, was due to recurrent haemorrhage 6 weeks after operation from rupture of a middle cerebral aneurysm on the side opposite to that on which the common carotid artery had been tied.

Again the consistent lowering of mortality rate over that of the natural history of rupture of an aneurysm is displayed in the reduction of death rate from 50% in cases treated conservatively to 33% for those patients submitted to surgery.

TABLE XI.—*Anterior Cerebral Aneurysms Distal to Anterior Communicating Artery*

| Category | Medically Treated | Deaths | Mortality | Aspiration of Clot | Deaths | Mortality | Craniotomy and Clipping of Neck | Deaths | Mortality |
|---|---|---|---|---|---|---|---|---|---|
| A | 2 | 2 | 100% | 1 | 1 | 100% | 1 | 1 | 100% |
| B | | | | | | | 2 | 0 | 0% |
| C | | | | | | | 1 | 0 | 0% |
| Total.. | 2 | 2 | 100% | 1 | 1 | 100% | 4 | 1 | 25% |

### Anterior Cerebral Aneurysm Distal to Anterior Communicating Artery (Table XI)

*Patients Treated Medically.*—Both of these patients died in 2 and 3 weeks respectively, one from recurrent haemorrhage. Each patient was gravely ill on admission and was included in category A: at post-mortem examination each had intracerebral and intraventricular haemorrhage in addition to subarachnoid blood.

*Patients Treated Surgically.*—The one patient treated by aspiration of intracerebral clot had been submitted to prefrontal leucotomy 24 hours before, and naturally was thought to have developed an intracerebral haemorrhage from the operation. At post-mortem examination, however, death was found to be due to spontaneous rupture of an aneurysm producing intraventricular haemorrhage as well as intracerebral and subarachnoid bleeding. One patient out of the 4 subjected to major operation, with clipping of the aneurysmal neck, died two months later after slow deterioration and was a category A patient. Two patients in category B were alive at 1 and 1½ years after operation—one severely crippled, the other quite well and without signs or symptoms. The other survivor in this group had no disability 2 years after operation.

These are fairly rare aneurysms lying along the course of the artery beyond the anterior communicating vessel, and the numbers are probably too few to be significant.

### Exact Site of Aneurysm Unverified

There were 2 cases in this group—one in category B and one in C. The former patient was well one and a half years after ligation of the common carotid artery. The latter patient underwent exploratory craniotomy and, elsewhere two years later, ligation of the common carotid artery, owing to further haemorrhage. Three weeks later he had a fatal recurrence.

### Aneurysms on the Posterior Cerebral, Basilar, Vertebral, and Superior Cerebellar Arteries (17 Cases)

*Posterior Cerebral Artery Aneurysms (10 Cases).—Patients treated medically (6 cases, 6 died):*—In 2 of these the aneurysm was shown by angiography and in the remaining 4 it was shown at necropsy. Five of these cases were in category A, 4 gradually deteriorating until death, while one died of a fatal recurrent bleed 4 weeks after the initial haemorrhage. One patient, in category B, died 9 months later of a fatal recurrence. *Patients treated surgically (4 cases, 4 died):*—In 2 of these the aneurysm was shown by angiography. One was in category A and one in B. In one case a proximal clip was placed on the posterior cerebral artery; in the other, exploration only was performed. Both died a few days after operation. In the remaining two patients, both of whom were placed in category A, the aneurysm was not shown by angiography. In one the posterior fossa was explored, as a tumour was suspected, and the patient died 5 days later. In the other the common carotid artery was ligated on clinical signs alone when the patient was moribund, and she died a few hours later.

*Basilar Aneurysms (3 Cases, 3 Died).*—No patient was operated upon, and in every case the aneurysm was shown at necropsy.

*Aneurysm on the Superior Cerebellar Artery (1 Case).*—This patient, in category B, had the aneurysm excised and 3 years later was quite well.

*Aneurysm in Cerebellum (1 Case).*—In this category A case an angiogram showed a suspected aneurysm of the carotid artery. The common carotid artery was ligated, and one month later there was a fatal recurrence. The brain was found to be bathed in blood, with a possible aneurysm in the cerebellar hemisphere.

This series of aneurysms on the posterior half of the circle of Willis and in the posterior fossa is by no means representative of aneurysms in this situation. As we have mentioned previously, vertebral angiography is not performed routinely, and these patients were exceptional in that vertebral angiography was indicated by repeated and severe haemorrhage, or, alternatively, they died and the aneurysm was revealed at necropsy.

### Frequency of Intracerebral, Intraventricular, and Subdural Haemorrhage in Association with Subarachnoid Haemorrhage from an Aneurysm

Only post-mortem or operation evidence is included as proof of haemorrhage in these situations. This list (Table XII), therefore, is incomplete, as not all patients who died

TABLE XII

| Site of Aneurysm | No. of Cases | Intracerebral Haemorrhage | Intracerebral and Intraventricular Haemorrhage | Subdural Haematoma | Intracerebral and Subdural Haemorrhage | Total |
|---|---|---|---|---|---|---|
| Anterior communicating artery .. | 71 | 11 | 10 | — | 3 | 24 |
| Middle cerebral artery .. | 42 | 10 | 5 | — | 5 | 20 |
| Internal carotid at level of posterior communicating | 62 | 3 | 2 | 1 | — | 6 |
| Internal carotid artery termination | 31 | 2 | 3 | 1 | — | 6 |
| Multiple aneurysms | 19 | — | 2 | 1 | — | 3 |
| Total .. | 225 | | | | | 59 |

were subjected to post-mortem examination, and many who were surgically treated and survived did not have a craniotomy. This is particularly the case in patients with an aneurysm on the internal carotid artery. Patients with an anterior communicating or middle cerebral aneurysm more commonly had a craniotomy, and so the opportunity for determining the presence of haemorrhage was greater. The presence of displacement of the cerebral arteries, as seen at angiography, affords valuable evidence of intracerebral clot, but we have not regarded this as conclusive, for such displacements may be caused by cerebral oedema alone. The classic appearances of subdural haematomas in angiograms are, however, quite conclusive.

### Multiple Haemorrhages

Of the 249 cases of subarachnoid haemorrhage, 155 had more than one incident of bleeding. The evidence of a further haemorrhage was in many cases clinical, and only 84 of the 155 cases had the second haemorrhage confirmed by lumbar puncture, operation, or post-mortem examination. The time and relative incidence of the first recurrence of bleeding is shown in Table XIII.

Thus at the end of the eighth week 123 patients (80% of the total suffering recurrence) had sustained a second bleed.

TABLE XIII.—*Time and Incidence of First Recurrent Haemorrhage*

| Period | No. of Patients | Percentage Recurrence | Deaths |
|---|---|---|---|
| 1st week | 33 | 20 | 6 |
| 2nd ,, | 42 | 28 | 8 |
| 3rd ,, | 11 | 8 | 3 |
| 4th ,, | 15 | 10 (80) | 2 |
| 5th ,, | 7 | 4 | 1 |
| 6th ,, | 9 | 6 | 1 |
| 7th ,, | 2 | 1·5 | 0 |
| 8th ,, | 4 | 2·5 | 2 |
| 3rd month | 5 | | 1 |
| 3–6 months | 2 | | 0 |
| 6–12 ,, | 5 | | 1 |
| 1–2 years | 4 | | 0 |
| 2–3 ,, | 4 | | 1 |
| 3–4 ,, | 3 | | 1 |
| 4–5 ,, | 4 | | 1 |
| 5–10 ,, | 3 | | 1 |
| Over 10 years | 2 | | 0 |
| | 155 | | 29 |

Analysis of the time of occurrence of the third haemorrhage after the second shows a similar pattern, with the maximum incidence in the first and second weeks.

While Table XIII is an accurate guide to the time of recurrent haemorrhage in the cases under review it is not accurate with regard to fatality of recurrence of haemorrhage. If, for example, a patient with recurrent bleeding were subjected to operation his death would be listed under operative mortality and not included in this table.

In Table XIII the maximum incidence of recurrence of haemorrhage is seen to be in the first and second weeks. This is earlier than in most of the published series, and an attempt was made to determine any possible factor that might have contributed to this discrepancy. First, the 84 cases of recurrent haemorrhage proved by lumbar puncture or post-mortem examination were reviewed, and again the major incidence was found in the first two weeks as obtained in the total series of 155 patients. Secondly, the number of cases in which the second haemorrhage occurred within two weeks of an angiogram were considered. Of the 155 cases only 17 had had the second haemorrhage within 2 weeks of angiography, and only one of these had the second haemorrhage in the first week after angiography, so that the performance of this investigation was not felt to be an important factor precipitating the first recurrent haemorrhage.

Of these 155 cases, 113 cases had 2 incidents, 34 had 3 incidents, and 8 had more than 3 (Table XIV).

TABLE XIV

| Site of Aneurysms | No. of Cases | 2 Haemorrhages | 3 Haemorrhages | More than 3 Haemorrhages | Total with Recurrent Haemorrhage |
|---|---|---|---|---|---|
| Anterior communicating artery | 71 | 31 | 9 | 3 | 43 (60%) |
| Middle cerebral artery | 42 | 19 | 6 | 0 | 25 (60%) |
| Internal carotid artery—termination | 31 | 15 | 9 | 0 | 24 (80%) |
| Internal carotid artery at level of posterior communicating artery | 62 | 28 | 4 | 0 | 32 (50%) |
| Multiple aneurysms | 19 | 7 | 5 | 3 | 15 (79%) |
| Others | 24 | 13 | 1 | 2 | 16 (67%) |
| Total | 249 | 113 | 34 | 8 | 155 |

### Review of Carotid Ligation in this Series

Of 249 patients, 85 were subjected to carotid artery ligation in the neck, 83 having the common vessel tied and 2 the internal. Of these 85, 30 were operated on within 10 days of the subarachnoid haemorrhage.

TABLE XV

| Site of Aneurysm | No. of Patients Treated by Carotid Ligation | No. of Cases with Complications | Time after Last Haemorrhage that Carotid was Ligated |
|---|---|---|---|
| Anterior communicating artery | 9 | 1 | 5 days |
| Middle cerebral artery | 10 | 0 | — |
| Internal carotid artery—level of post. communicating | 38 | 3 | 1: 1 day—fatal<br>2: 8 days<br>3: 3 years |
| Internal carotid—termination | 14 | 1 | 6 days |
| Multiple aneurysms | 9 | 1 | 1 day |
| Others | 4 | 0 | 0 |

Under "complications" (by which we mean the development of contralateral signs) only patients who were definitely made worse by operation are included. Most of the cases were in category B or C. Patients who were very ill before operation, and whose downward course seemed uninfluenced by operation, were not included.

All the patients who developed complications had had a haemorrhage less than 10 days before the operation, except one who had bled 3 years before. This patient had the internal carotid artery ligated. In only one of the above patients was the outcome fatal. The others suffering complications recovered from the hemiparesis and were left with little or no disability as a result of it. These figures confirm the view, often previously expressed, that ligation of the carotid artery is more dangerous when performed shortly after a haemorrhage than when it is performed later. As has been previously mentioned, we have found that the operation of common carotid ligation has been very effective in preventing recurrence of haemorrhage from an aneurysm on the internal carotid artery at the level of the posterior communicating artery, and effective, but less so, in preventing haemorrhage from aneurysms at the termination of the internal carotid artery.

The question arises concerning when carotid ligation should best be performed. Whilst it would seem to be safer, from the point of view of avoiding complications, to wait 10 to 14 days after a haemorrhage before operating, it is in this very period that the greatest danger of recurrent haemorrhage exists.

Table XIII shows that 20% of those suffering recurrent haemorrhage do so in the first week after the initial haemorrhage. In the second week a further 28% bleed again, so that at the end of two weeks from the time of the haemorrhage causing hospital admission, 75 patients of the 155 suffering more than one bleed have had the second haemorrhage. Therefore, if surgery is to be withheld for 14 days in order to avoid the risk of complications, almost half of the patients destined for a second bleed would have already sustained that bleed. As the death rate for a second bleed is even higher than for the initial one we feel that the greater risks of complication should not be allowed to prevent early operation.

Comparison of the risks of death from a second haemorrhage with those of carotid ligation in the first 2 weeks redounds greatly to the credit of carotid ligation.

### Comment

It will be observed that when aneurysms causing subarachnoid haemorrhage are reviewed according to their anatomical site there is a consistently lower mortality rate in the groups dealt with conservatively. It should be pointed out that selection of cases has played little, if any, part; the control series was largely drawn from material acquired during a period of time when little good was thought likely to accrue from surgical methods of treatment. It is during the last few years that surgery has been attempted in almost every case. No attention has been paid to the presence of other disease processes present at the time of the patient's admission to hospital. Such factors are, of course, important and must be taken into consideration when larger numbers of case records dealing with specially sited aneurysms become available for study.

In assessing the state of survivors of treatment, whether medical or surgical, "slight" indicates the presence of abnormal neurological signs which do not, however, hamper the patient in leading his normal life. The term "severe" is self-explanatory.

### Conclusions

We feel that a case has been made out for the very early investigation and treatment of cases of bleeding aneurysm, for a lower mortality has been shown to occur in cases handled in such a manner than is to be expected from the natural course of the disease, as evidenced by our conservatively treated cases and by the existing literature on the subject.

It would seem desirable that the subject of subarachnoid haemorrhage due to aneurysm should be dealt with not as a whole but in relation to the actual situation of the lesion, thus making for much easier comparison of results of differing treatment practised in a variety of centres. The time factor in relation to the haemorrhage and the physical condition of the patient must surely be very important details of which to be fully informed when attempting to assess the relative values of different lines of therapy.

It seems to us that little information of real value can be obtained from series of cases in which the situation and nature of the aneurysm have not been established by angiography; for we know, to take but one example, that about 10% of cases of subarachnoid haemorrhage are due to intracranial angiomas, which have a totally different natural history from that of aneurysms.

We feel convinced that surgical methods of treatment offer a definite lowering of the mortality rate when compared with purely conservative measures. For example, in medically treated patients with anterior communicating or middle cerebral aneurysms whose clinical state is so bad that they are included in category A we find the natural death rate to be over 90%. If even a few patients in this category can be restored to reasonable health by surgical measures the operative mortality rate should surely be assessed against the natural death rate of 90%, and so even a 50% operative mortality rate would be acceptable.

### Summary

A review of 249 cases of proved intracranial aneurysm associated with subarachnoid haemorrhage is given.

These cases are considered in relation to the severity of the effects of the haemorrhage and the site of the aneurysms.

The results of various forms of surgical treatment in these cases are compared with the results in patients who had received medical treatment.

The frequency of associated intracerebral, intraventricular and subdural haemorrhage is given.

The frequency and time of occurrence of repeated haemorrhage is considered.

The operation of carotid ligation is discussed.

We should like to record our gratitude to Mr. Valentine Logue for permission to use many of his case records, particularly those relating to anterior cerebral/anterior communicating aneurysms. We also thank the Board of Governors of St. George's Hospital for the research grant made to one of us (L. W.), which has made the collection of this material possible.

#### REFERENCES

Ask-Upmark, E., and Ingvar, D. (1950). *Acta med. scand.*, **138**, 15.
Hamby, W. B. (1948). *J. Amer. med. Ass.*, **136**, 522.
—— (1952). *Intracranial Aneurysms*. Thomas, Springfield.
Logue, V. (1956). *British Medical Journal*, **1**, 473.
Magee, C. G. (1943). *Lancet* **2**, 497.
Norlén, G. (1952). *Proc. roy. Soc. Med.*, **45**, 291.
—— and Olivecrona, H. (1953). *J. Neurosurg.*, **10**, 404.
Richardson, J. C., and Hyland, H. H. (1941). *Medicine (Baltimore)*, **20**, 1.
Walton, J. N. (1952). *British Medical Journal*, **2**, 802.

# FREEZE-DRIED B.C.G.

## VACCINATION OF NEWBORN INFANTS WITH A BRITISH VACCINE

BY

**MARGARET I. GRIFFITHS, M.D., M.R.C.P.**

AND

**WILFRID GAISFORD, M.D., F.R.C.P.**

*St. Mary's Hospital, Manchester, and the Department of Child Health, University of Manchester*

The recent report of the Medical Research Council (1956) trials of B.C.G. and vole bacillus vaccines in school-leavers has confirmed the value of such vaccination as protection against tuberculosis for the children of this country at the present time. From the point of view of child health the most significant periods of risk of tuberculous infection are earliest infancy and puberty, but both of these groups were omitted in the Medical Research Council trial. One of the significant features of this investigation was the high percentage of children (40%) who had already had their primary infection. In girls the risk of genital tuberculosis following a flare-up of their primary infection at puberty makes it highly desirable that those not already infected should be protected *before the onset of puberty*, because genital involvement is a common cause of subsequent sterility. It would seem more logical, therefore, to vaccinate girls at an earlier age—10 or 11 years—rather than to wait until they are about to leave school, when many of them have already passed puberty.

### Optimal Age for Vaccination

If the prophylactic value of B.C.G. in paediatrics is generally accepted, the question of the optimal age for vaccination should be seriously considered. The ideal procedure would surely be a single vaccination in infancy, using a vaccine of sufficient antigenicity to provide protection until after puberty. This may or may not prove possible. It is certainly generally agreed now that infants can be safely and successfully vaccinated with B.C.G., but the duration of the protection afforded is as yet undetermined. In a recent five-year follow-up we found that only 7 of more than 1,000 infants who had been vaccinated in the newborn period with Danish vaccine had reverted and required revaccination. Furthermore, the degree of sensitivity showed little, if any, diminution at the end of the fifth year (Fig. 1). It remains to be seen whether this state will persist for a further seven or eight years.

Although the duration of allergy depends on a variety of conditions, undoubtedly the most important single factor