Current Practice

PRACTICAL NEUROLOGY

Subarachnoid Haemorrhage

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In cases of proved subarachnoid haemorrhage how should one proceed?

Clearly the answer will depend on the nature of the lesion, the risk involved if it remains untreated, the possibilities of treatment in relation to the lesion itself, and, finally, the clinical features of the individual patient.

An analysis of the cases admitted to Atkinson Morley's Hospital with a diagnosis of subarachnoid haemorrhage in the last 10 years shows the incidence of the various responsible lesions (Table I).

TABLE I.—Incidence of Lesions Causing Subarachnoid Haemorrhage

Aneurysm	...	...	...	1,571
Angioma	...	...	...	142
Primary intracerebral haemorrhage	...	...	...	626
Unexplained	...	...	...	604
Cerebellar and brain stem	...	...	...	99
Total				3,042

It will be seen from this that more than a half of such patients have a ruptured aneurysm, about one-fifth have suffered a primary haemorrhage into the cerebral or cerebellar hemispheres or brain stem, and that in a similar number no source for the bleeding is demonstrated. The proportion of this latter group, however, in more recent years has showed a steady diminution. Angiomatous malformations are seen to account for about 5% of all cases of spontaneous intracranial bleeding. Taking all the available clinical information into account, is it possible to arrive at a reliable diagnosis of the cause of the haemorrhage without the aid of angiography? The answer in almost every case is no, for the age incidence of subarachnoid haemorrhage, which is 40-65 years, covers the range in which any of the responsible lesions could be present. This is not to deny that clinical features may strongly suggest a deeply placed hemisphere lesion, which would be more indicative of a primary arteriosclerotic haemorrhage or a lesion involving the cerebellar hemispheres, but at the same time it is important to remember that rupture of an intracranial aneurysm or angiomatous malformation may well give rise to features indistinguishable from these other lesions, a point well made by Fisher *et al.*¹

Angiography

Given that inspired guesswork can be no basis for deciding treatment, brief consideration must be given to the question of angiography, which at the moment is our only method for accurate diagnosis and for assessing the possibilities of treatment. Should it then always be performed, and, if so, when? The decision is influenced by other factors, the most important of which is whether the damage inflicted is so severe that treat-

ment of the responsible lesion, even if accompanied by a haematoma, will not help or may indeed be harmful. Secondly, even if this is not the case then the relative risks of treatment by surgery as opposed to non-operative methods have to be considered. The most important guide to initial management must remain the patient's clinical features. Regardless of the nature of the lesion, the prognosis in a general way is related to the level of consciousness. It is generally accepted that unremitting coma carries a very poor prognosis regardless of the treatment given, and if to this is added advanced age then the potential for treatment is very limited indeed. If the patient is not in coma then advanced age of itself may be a clear contraindication to further investigation, as the performance of angiography must be predicated by the intention to undertake surgical treatment. Similar considerations must also apply to those patients who also have an unrelated lesion apt to prove fatal very rapidly, or who by virtue of it constitute a totally unacceptable anaesthetic or surgical risk. With modern methods of anaesthesia and intensive care this latter group is steadily diminishing in size.

In all other circumstances the case for angiography at an early stage when the patient's state has stabilized is irrefutable if we assume, as we must, that the nature of the lesion is obscure before angiography and that the most likely lesion in the common age group is a ruptured aneurysm. Such lesions in general carry the highest rate of preventable death from recurrent bleeding, and it can be assumed that this eventuality will account for a mortality rate of 40-50% within the first six months after the initial ictus if untreated. Moreover, the tendency to recurrent haemorrhage is maximal in the second week after the haemorrhage, this risk diminishing sharply after the first month. With this high statistical probability, therefore, there is some urgency in the performance of angiography consistent with the patient's clinical state; in general the younger the patient and the better his clinical state the more urgent is his need for investigation.

Management of Individual Lesions

Once angiography has been performed the responsible lesion will be identifiable in over 80% of cases, and the further management will depend on its precise nature and the total clinical circumstances of the case.

Aneurysms

The common sites for these lesions are at vessel junctions or branchings. Table II shows the incidence in our recent cases. Thus the commonest sites are at the level of the anterior cerebral-anterior communicating artery complex, the point of division of the middle cerebral artery, and the point of origin

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of the posterior communicating artery from the internal carotid. It will be noted that there is also a high incidence of multiple lesions. Having demonstrated such a lesion by angiography we also require from the method further information regarding size, shape, direction of pointing, and accessibility, as well as guidance on the presence of accompanying haematoma, vascular spasm, or anatomical anomalies. Armed with this information we can apply the results from controlled trials of different treatments to decide the most suitable mode of management. Apart from the earlier broad statement that unconsciousness in general is a bar to surgical treatment, other than in very young persons, the treatment will depend largely on the location of the lesion in the first instance. It will simplify discussion if the various lesions are considered in relation to their sites.

TABLE II.—Incidence of Sites of Aneurysms

Anterior cerebral/anterior communicating complex	29%
Internal carotid/posterior communicating origin ...	23%
Middle cerebral artery ...	23%
Multiple lesions ...	15%
Basilar/vertebral system ...	5%
Internal carotid artery bifurcation ...	3%
Distal portion of anterior cerebral artery ...	2%

Posterior Communicating Aneurysms.—In patients not in coma the superiority of common carotid ligation as opposed to bed rest was established² in 1959. Treatment in this group of patients was allocated at random and the two methods of treatment were of six weeks' bed rest as compared with immediate surgical intervention. The mortality of the surgically treated cases was 10%, and the corresponding figure for those treated by bed rest was 42%, the latter all from recurrent haemorrhage. Complications in the form of hemiplegia or hemiparesis occurred in about one-third of the patients treated by surgery, but more than half of these showed a good recovery. These results both in terms of mortality and morbidity are perfectly acceptable, though this trial did not consider the relative merits of common carotid ligation as opposed to direct intracranial surgery. A recent publication³ shows a similar mortality rate in 77 cases treated by direct clipping of the neck of the aneurysm, and in this paper the author makes the comment that "for patients in good clinical condition direct attack gives results similar to those for carotid ligation; for the seriously ill patient direct attack is superior." Though perhaps the best methods of surgical treatment in individual cases may not have been yet completely clarified, it is clear that either method is accompanied by a low mortality in relation to natural history and that therefore surgical management is the treatment of choice.

Middle Cerebral Aneurysms.—The early results of our trial⁴ in these cases confirmed that patients in coma did not benefit from surgery. Of those conscious at the time of admission it was found that male patients fared better with operation with direct clipping or investment of the aneurysm than they did with bed rest. The surgical mortality was of the order of 11% and the bed rest mortality was 36%, this again being due mainly to recurrent haemorrhage. At this time female patients showed little difference in mortality between the two treatment groups, but subsequently, possibly related to some changes in surgical technique, it has been shown that they also benefit by direct surgical intervention as opposed to those cases treated non-surgically. The timing of surgery in such patients is important, and a little delay in undertaking operative treatment is more than justified by the markedly improved surgical results.

Anterior Communicating Aneurysms.—In a recent review of the cases in our clinical trial it was impossible to find any consistent superiority for current surgical methods as opposed to bed rest when due allowance was made for the important prognostic factors of age, blood pressure, state of consciousness, and time interval from the haemorrhage. This does not carry the implication that surgery must be abandoned, but merely indicates the need for a more cautious and thoughtful approach to cases harbouring such a lesion, and for repeated critical

appraisal of surgical results in controlled clinical studies wherein treatment is randomly allocated. There is growing evidence that the use of measures designed to improve the clinical state prior to surgical intervention may very considerably improve the surgical results without unduly increasing the risk of further haemorrhage in the interval prior to operation.

Multiple Lesions.—As shown in Table II, aneurysms are multiple in over 15% of cases, and increasing improvement in diagnostic technique may in time well show that the actual incidence is even higher. Management resolves itself into consideration of three groups of cases:

(1) Those in which the responsible lesion is clearly identifiable.

(2) Those where only two lesions are present and they are on the same side of the circle of Willis or accessible by one surgical approach.

(3) The patient harbours scattered lesions.

In the first group it is reasonable to treat the responsible lesion if surgically indicated, and in group 2 one would consider either proximal ligation of the appropriate carotid artery or simultaneous direct surgical neutralization of both lesions demonstrated. The patients in group 3 are usually treated conservatively, at least initially, though it must be mentioned that a more aggressive surgical approach to these lesions is emerging since the natural mortality in multiple lesions is about 60% in the first six months as opposed to approximately 40% for single aneurysms. The very high untreated mortality in this total group is attracting attention to more refined methods of determining the responsible lesion in multiple aneurysm complexes, which include a more careful evaluation of the arteriographic features and the use in appropriate cases of electroencephalography.^{5 6}

Basilar-Vertebral Aneurysms.—The relatively low incidence of these lesions naturally restricts the number of suitable cases seen by any one surgeon. There is, however, a growing literature⁷ in relation to the management of aneurysms on the basilar and vertebral arteries and their branches, in which the results of surgical treatment in suitable cases are encouraging. In particular Drake⁷ reports a series of 20 cases of aneurysm at the basilar bifurcation treated surgically with six deaths, which is an acceptable surgical mortality when it is remembered that the natural mortality in this particular lesion is of the order of 60%. My own experience in 23 such similar cases has resulted in seven deaths, and this coincides clearly with the results achieved by Drake. It is obviously too early to make a plea for surgical intervention in all cases, but it is at the same time clear that operative management is relevant in a high proportion of them.

Angiomatous Malformations

Vascular malformation as a cause of subarachnoid haemorrhage is common in the age group 20–40 years, though almost one-third of the patients seen are aged more than 40. Their presenting features on the whole are indistinguishable from aneurysmal rupture, but the younger age and the history of preceding unilateral headache or epilepsy or both may suggest the diagnosis. Angiography will confirm the presence and nature of the lesion and also indicates its size, site, and source of arterial supply, and may also demonstrate the size of the commonly accompanying haematoma. Though these lesions are also prone to recurrent haemorrhage their behaviour is rather different from that of ruptured aneurysms. The likelihood of further haemorrhage is possibly of the order of 20% measured over periods of 10–15 years, though as yet no statistically valid studies have been conducted comparing surgery and conservative treatment in a random trial structure. The major point, however, is clear; unlike the intracranial aneurysms, angiomas tend to bleed again less often, and where

recurrence does occur it is likely to be after a long interval which is measured in months and years as opposed to days or weeks. Most authors are agreed that where possible surgical excision should be undertaken, but that the advisability or otherwise of surgery has to be decided on the total circumstances of the case, which will include not only all the patient's clinical features but necessarily all the information provided by angiographic study. Where the lesion is surgically accessible, and it is likely that a neurological deficit will not follow surgical removal, and, finally, the patient's clinical condition is good there can be no doubt that surgery is the treatment of choice. The surgical mortality in such cases would be about 5%, and most of the survivors in this group will have a virtually normal existence.

Intracerebral and Cerebellar Haemorrhage

Haemorrhage into the cerebral or cerebellar hemispheres accounts for over 20% of patients with subarachnoid haemorrhage, the ratio of the former to the latter being 10:1. The diagnostic and surgical problems are slightly different in the two lesions and will therefore be considered separately.

Cerebral Haemorrhage.—Surgical enthusiasm has waxed and waned, but our controlled study⁸ comparing surgery with conservative treatment in non-comatose patients showed that the mortality rate in patients treated by bed rest was 21 out of 58 or 40% as opposed to a surgical mortality of 31 out of 57 or 54% when treatment was randomly allocated. This clearly suggested no overall advantage to surgical treatment, but further analysis of the data suggested that very early surgery might worsen the prognosis, that if the patient's state was deteriorating at the time of operation surgery was unhelpful, and that in particular elderly, hypertensive female patients fared badly with operation. Again these results did not indicate that surgery was inappropriate in these conditions but simply suggested that more critical evaluation of the patient was necessary before deciding whether or not to proceed with surgery. A more recent study⁹ has suggested certain more definite guide lines.

In general, patients who have become unconscious following the incident and have remained so do not benefit by urgent surgery. On the other hand, in such cases if consciousness is subsequently regained the question of surgery arises under similar circumstances to those cases in which consciousness was never seriously impaired. The first requirement is that the haematoma should be accessible and not be deeply situated—in the region of the internal capsule, for example. Secondly, it is important that the patient's neurological state, particularly in relation to his conscious level, should be stable at the point of accessibility. Thirdly, and it is most important in this group of patients in whom either hypertension or atherosclerosis are the rule, there should be no co-existing disease sufficiently severe to compromise the safety of anaesthesia or surgical intervention.

Intensive medical management of such patients is often a prerequisite to any consideration for surgical intervention, as in many cases pulmonary infection supervenes rapidly after even short periods of disturbed consciousness, and in the same way fluid and electrolyte depletion may occur promptly. Adequate management of these two complications may do much to improve the patient's clinical state, and in more than 10% of such cases as a result of this regimen the patient's neurological recovery may continue uninterrupted so that the question of surgical treatment never arises. Assuming the lesion to be accessible, the decision for or against surgery is usually made in the 10 days following the incident, during which time the patient's level of recovery becomes clear. In those cases where coma has supervened and remains unremitting surgical intervention is of no value. Where good recovery, as far as conscious level is concerned, has taken place but the patient remains with a serious neurological deficit surgical

evacuation of the haematoma will, in about half the cases, increase either the speed or extent of recovery. In a further small percentage of cases it will become evident that satisfactory recovery is occurring without further intervention. This regimen was followed in a total of 115 patients, in whom 66 were treated by surgery and 49 were not subjected to operation. It is clear that one was not comparing one method of treatment with another but was concerned with evolving an overall regimen calculated to produce as small as possible mortality and morbidity rate. Of these 115 patients 22 died, a mortality rate of 20%, and of the survivors 44 made a recovery that was judged to be excellent by an uncommitted neurologist. It is always difficult to compare different series of cases treated in various centres, but these results at the moment would appear to be satisfactory and acceptable.

Cerebellar Haemorrhage.—Early recognition of haemorrhage into the cerebellar hemisphere plays a vital part in the success or otherwise of surgical treatment. It may be difficult to differentiate the condition from the more common forms of "stroke," but the more slowly progressive onset of disturbance of level of consciousness, associated with constricted, unreactive pupils and with gaze palsy or irregular respiration, should arouse the suspicion of indirect brain stem involvement.

In such cases one should withhold lumbar puncture in the first instance, as it may be dangerous, and proceed to more benign investigations, such as the use of ultrasonography, by which the diagnosis may be implied by the absence of a midline displacement and the presence of dilatation of the ventricular system—which often ensues as rapidly as three hours after the haemorrhage. In these particular cases time is of the utmost importance—rapid deterioration may occur, and with increasing obtundition the patient's chance of a successful outcome progressively diminishes. In a recent series of 67 such patients admitted to this department the patients' dire clinical state precluded active surgical treatment in nearly one half of the cases, so that surgery was undertaken in only 32 of them with 20 survivors. Three patients made a spontaneous and satisfactory recovery, but such spontaneous recovery is obviously very much the exception rather than the rule. The high incidence of patients whose state becomes irretrievable at the time of admission underlines the urgency with which this lesion must be managed, for in a high proportion of these cases it was clear that for many hours, or in some cases several days, the patient's clinical condition was such that intervention would have been successful, and equally clear that the clinical features strongly suggested the diagnostic possibility. For those interested in a more comprehensive review of this problem, with particular relation to its clinical aspects, reference should be made to the excellent article by Fisher *et al.*¹

Unexplained Haemorrhage

Somewhat fewer than 20% of patients suffering subarachnoid haemorrhage prove on angiography to have no obvious causal or associated lesion. In a small percentage of these subsequent events prove that they in fact harboured an intracranial aneurysm which for various reasons was not demonstrated. Perhaps the commonest explanation is that the lesion was filled with recent thrombus and therefore was not visualized by the radio-opaque contrast. In a further small number there is no doubt clinically that a small, strategically placed haematoma or localized area of destruction must be present, but the assumption has to be that the size of the lesion is such that it is not angiographically demonstrable. These two situations possibly account only for about 10% of all cases in which angiographic investigation proves negative. In a recent analysis of some 650 cases of this type I found that only 37 patients were definitely known to have died subsequently, giving a late undirected mortality rate of 6%, this being in terms of follow-up periods varying from 1–10 years. Much speculation has

naturally been forthcoming about the source of haemorrhage in these patients, and numerous possibilities have been put forward, notably the rupture of minute aneurysms or minute angiomas which in the process of haemorrhage destroy themselves and therefore neither leave evidence of their presence nor are they a source of future potential danger. Whatever the truth may be, the fact remains that the long-term prognosis in such cases is extremely favourable, particularly as compared with the natural history of patients in whom an intracranial aneurysm is demonstrated. Worthy of consideration in relation to this group of cases are episodes of subarachnoid haemorrhage which may follow the administration of antidepressant drugs, particularly the monoaminoxidase inhibitors, where perhaps insufficient warning has been given about the possible harmful effects of ingesting foodstuffs with a high tyramine content. Cheese is notorious in this respect, but in addition a miscellany of foods such as meat extracts, beans, peas, and even some well-known Italian wines have been implicated. There is no doubt that the ingestion of such foodstuffs during a course of treatment or within a fortnight of its termination may produce hypertensive crises, and the number of cases associated with subarachnoid haemorrhage is undoubtedly increasing. In these cases, as with all others of unexplained haemorrhage, the future prognosis if the patient survives is extremely good; but, of course, it is necessary that the further administration of such drugs should either be discontinued or more carefully monitored thereafter.

Conclusions

It is difficult to give a meaningful and brief summary of all the problems associated with the management of subarachnoid haemorrhage, but perhaps the most significant points may be summarized as follows.

In any case of proved subarachnoid haemorrhage within the common age period of 40–65 years the most likely causal lesion is an aneurysm of the circle of Willis. It is only in the very young patients that an angioma becomes the more likely diag-

nosis. On this basis, therefore, one must suspect in every case the presence of an intracranial aneurysm unless the features are so specific as to suggest a haemorrhage into the cerebellar hemisphere or a deeply placed lesion involving the region of the internal capsule in the cerebral hemisphere. There are no consistent reliable features or signs to indicate the possible site of location of an aneurysm, and the clinical state of the patient may vary from unremitting coma to the so-called mild cases, in which the patient is neurologically completely intact but simply suffering from headache and perhaps neck stiffness. Such mild cases may well, nevertheless, harbour a potentially lethal aneurysm, and, far from being a reason for not pursuing investigation, the good clinical state of the patient represents an indication for urgent investigation—for if a responsible lesion is demonstrated the probability that surgery will be successful in preventing further haemorrhage is extremely high. It cannot be overemphasized that with all lesions the poorer the patient's clinical state at the time of investigation or treatment then the less promising are the results of any treatment either surgical or medical. As a corollary to this it is important that if the patient's neurological deficit is severe following such a haemorrhage, and in particular if his conscious level is disturbed, then preliminary energetic non-surgical measures may be necessary in order to try to improve the patient's condition prior to investigation or more commonly surgery.

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TODAY'S DRUGS

With the help of expert contributors we print in this section notes on drugs in common use.

Systemic Corticosteroid Therapy

A corticosteroid is a 21-carbon steroid hormone made in the adrenal cortex. This includes several substances ranging from cortisol (hydrocortisone) to aldosterone. Virtually all of them possess the same basic physiological actions, but to strikingly different degrees, so that their net effects are very diverse. Their basic actions are the promotion of renal sodium retention, liver glycogen deposition accompanied by increased protein catabolism, and an anti-inflammatory effect. Their presence is also necessary for certain processes to occur—for example, fat mobilization by adrenaline, or osmotically “free” water excretion.

The net effect of a corticosteroid depends upon its structure and the dose given to the patient, both daily and in aggregate. *Structural differences* ensure that the compound will predominantly affect carbohydrate metabolism with some anti-inflam-

matory potency as well (the glucocorticoid group of hormones), or will chiefly promote sodium retention and potassium excretion (the mineralocorticoid group). By “chemical tailoring” new molecules have been devised so as partly to separate the anti-inflammatory and salt-retaining properties of glucocorticoids so that some of the new drugs (e.g., prednisone or betamethasone) have a more favourable therapeutic ratio than cortisol (or corticotrophin). The relative potencies of different compounds to produce these effects are summarized in Table I.

Confusingly, the term “corticosteroid” has become attached by usage to the glucocorticoid group, together with synthetic substances which mimic their action, and even quite wrongly to the hormones such as corticotrophin, which promote their release. This grouping has practical significance but is inaccurate.

The *dose* of a compound determines whether its action will be in the physiological or pharmacological range. When adrenal hormones are deficient (Addison's disease or hypopituitarism) they are replaced using small doses of drugs whose