Perimesencephalic haemorrhage occurs in 10% of all patients with subarachnoid haemorrhage, and in two thirds of the patients with an initially negative angiogram.[9 10]

*"Preoperative medication includes administration of anticonvulsants [and] corticosteroids [in patients with aneurysmal as well as patients with nonaneurysmal subarachnoid haemorrhage]."*

Neither medication has proved of value in patients with subarachnoid haemorrhage, and neither should therefore be given as a routine. These medications should be withheld from patients with perimesencephalic haemorrhage, who never have serious complications.

*"Preoperative medication includes . . . antihypertensives [since] strict attention to blood pressure control before aneurysm surgery has been shown to reduce the rate of . . . rebleeding."*

A relation has been found between an increased rebleed rate and drug induced hypotension. In another study, patients with blood pressures within the normal range had more rebleeds than patients with high blood pressure.[11 12]

*"The effect of calcium channel blockers is less clear."*

Calcium channel blockers reduce the occurrence of poor outcome by 40%.[13]

*"Epsilon-aminocaproic acid . . . functions to inhibit the conversion of plasminoid into plasmin."*

Epsilon-aminocaproic acid blocks the lysine sites of plasminogen and consequently prevents the binding to fibrin.[14]

*"The administration of antifibrinolytic agents . . . may be of value if an operative procedure is delayed longer than 48 hours."*

The reduced risk of rebleeding is offset by an increased risk of cerebral infarction.[2]

*". . . continuous external ventricular drainage [in patients with acute hydrocephalus] can usually be performed with little additional morbidity and mortality."*

After ventricular drainage, patients have an increased risk of rebleeding.[15 16]

*"Hypernatraemia [has] the highest mortality rate . . ."*

Hypernatraemia is extremely rare in subarachnoid haemorrhage.[17]

*"Hyponatraemia can be due to either inappropriate secretion of antidiuretic hormone or true natriuresis due to cerebral salt wasting."*

Hyponatraemia in subarachnoid haemorrhage is caused by cerebral salt wasting in most patients.[17]

*"Thick layers of blood in the basal cisterns carries a higher risk of vasospasm than diffuse or focal [locations]."*

Measurement of thickness of layers of blood or of clots at a single site depends as much on the dimension of the cisterns as on the overall severity of the haemorrhage.

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*Kopitnik and Samson reply:*

Our lengthy review article on the management of subarachnoid hemorrhage was elicited by the *Journal of Neurology, Neurosurgery and Psychiatry* and was intended to be a general overview of subarachnoid hemorrhage, with a specific request to discuss how we manage this condition.[1] It is unfortunate that Drs Vermeulen and Rinkle have interpreted it as being *the* definitive treatise on subarachnoid haemorrhage, which is not the purpose or scope of an article on such a complicated subject.

The article addresses many controversial management issues, which are as yet not definitively understood, from a non-biased and non-specific viewpoint. It was our purpose to assemble relevant references and write an article that addressed the major points. Statistics and concepts were quoted in a general sense, not as dogma. It was our opinion that biased, exacting statements regarding a specific point would only confuse practitioners, residents, and students who may use such a review article as a source of reference, and that such statements would falsely imply that the diagnosis and management of subarachnoid haemorrhage is a clearly understood, exact science.

Many of the refutations submitted by Vermeulen and Rinkle are criticisms of general statements taken out of the context in which they were written. For example, an issue was made of a brief discussion of the Fisher grading system for the CT appearance of subarachnoid haemorrhage.[2] Reading our review article carefully makes it clear that we merely define what the grading system entails in four sentences. We make no statements as to the utility or the facility of such a scale.

The same holds true for statements regarding the Hunt-Hess grading scale for the clinical presentation of patients with subarachnoid haemorrhage.[3 4] We find it interesting that the reviewers are critical of the very mention of grading scales such as these, but incorporate them into their own published clinical studies. In fact, Dr Vermeulen was lead author on a publication in 1984 in which the Hunt-Hess clinical grade was listed in a table referred to for "important prognostic factors."[5]

Some of the other refutations are controversial only if the medical literature is misunderstood. Our statement that loss of consciousness occurs in most patients with subarachnoid haemorrhage is realistic. The reviewers again cite the same article, in which 46% of their patients lost consciousness during ictus.[5] Although this figure is true for that particular series, it fails to consider the patients who died immediately, during their initial haemorrhage, and never reached the hospital, or were misdiagnosed elsewhere. Many studies have estimated the rate of sudden death from subarachnoid haemorrhage to approach 40%.[6-10] When these two factors are considered, most people suffering a haemorrhage will have a depression in their level of consciousness if death is also considered.

Similarly, there is overwhelming evidence in the medical literature that some patients experience a warning leak or "sentinel haemorrhage". This point was discussed only to bring this to the attention of practitioners who may be less familiar with subarachnoid haemorrhage and merits *no* further discussion.

Controversy continues over the usefulness and safety of lumbar puncture in the diagnosis of subarachnoid haemorrhage, and we have rarely found it to play any role. Because practitioners and students have uniformly learned that this technique is needed for diagnosis, the focus of the paragraph that discusses it is meant to downplay the usefulness, and emphasise the unnecessary risk, of its indiscriminant use.

Drs Vermeulen and Rinkle state that visual examination of CSF is unreliable. We would point out that the term "xanthochromia" (*xanthochromie*) was first used in 1902 to describe a yellow colouration of CSF on visual examination. Dr Vermeulen has

apparently modified the definition in the reference he both cited and authored to be as follows: "Xanthochromia was defined as extinctions exceeding 0·023 at wavelength 415 nm and/or a peak in the absorption curve in the 450–460 range."[11] We sincerely doubt that in 1902 Milian used a double-beam spectrophotometer when he coined the term.

We are also in complete disagreement with Dr Vermeulen's series in 1989 in which all patients with proven subarachnoid haemorrhage underwent multiple lumbar punctures with potential morbidity and little demonstrable benefit.[11] We disagree with the concept stated in this series that the absence of xanthochromia, despite patient history consistent with subarachnoid haemorrhage eliminates the need for angiography. Dr Vermeulen states that "xanthochromia" (spectrophotometrically measured) can be detected three weeks after haemorrhage with a probability of 70%. In his series, only 20 of 111 patients had xanthochromia demonstrated after three weeks, and no mention was made of the timing of aneurysm repair or the amount of blood on the initial CT scan. Unlike Dr Vermeulen, we would not conclude that nine patients with blood stained CSF, histories consistent with subarachnoid haemorrhage, and no xanthochromia were not candidates for cerebral arteriography. We would also not conclude that, because nine such patients did not present again to the same institution with subarachnoid haemorrhage within four years of discharge, this represents the ideal standard of care, as inferred in his paper.

Similar points can be made when discussing subarachnoid haemorrhage of unknown aetiology and the need for repeat angiography. The pattern of haemorrhage on CT can be overemphasised with regard to the necessity of repeat cerebral arteriography. We stand by our statements that repeat angiography is strongly considered if the first angiogram shows significant vasospasm, fails to completely visualise the entire vascular tree, or the CT scan demonstrates a large amount of subarachnoid blood.

Articles cited by the reviewers (and authored by them) show the CT scans of patients demonstrating what they refer to as "perimesencephalic" subarachnoid haemorrhage.[12 13] In fact, these scans show interpeduncular and suprasellar haemorrhage consistent with what we have frequently found to be aneurysmal haemorrhage, proven by surgical exploration. They further state that all such patients did well at long term follow up. We challenge their contention that two years is long term.

In their series it was also noted that five patients deteriorated from acute hydrocephalus and two of these patients remained severely disabled. This explains the criticisms leveled at our use of external ventricular drainage in patients with acute hydrocephalus. We agree that there is a small risk of aneurysm rebleeding, although we have found this to be extremely rare in our practice, and consider permanent disability from untreated hydrocephalus to be unacceptable.

The final segment of our paper that merits rediscussion is the issue of medications. Drs Vermeulen and Rinkle are critical of the use of anticonvulsants, corticosteroids, antihypertensives, and antifibrinolytic medications. As far as anticonvulsants are concerned, studies have shown a 10–25% incidence of epilepsy in patients with subarachnoid haemorrhage.[14–16] We believe that the morbidity of seizures in patients with acutely ruptured aneurysms outweights the minimal side effects of anticonvulsant medication, and believe that these medications are warranted.

In a similar fashion, judicious treatment of hypertension immediately after haemorrhage has been clearly shown to decrease the incidence of aneurysm rebleeding. In the study referred to by Drs Vermeulen and Rinkle (their ref 11) 11% of patients rebled when mean arterial blood pressure was less than 110 mmHg. Contrast this with a rebleed rate of 19·6% when arterial pressure is over 130 mmHg. Considering that most of our patients undergo surgery within 48 hours of admission, and that aneurysm rebleeding carries significant morbidity, we judiciously use antihypertensives to maintain normotensive blood pressure until the aneurysm is repaired, which is typically only several days. At no time in our review article do we advocate drug induced hypotension as a preoperative treatment for subarachnoid haemorrhage.

We have found that a short course of preoperative corticosteroids relieves many patients of the symptoms of blood induced aseptic meningitis and helps to decrease the oedema associated with the trauma of aneurysm surgery.

Antifibrinolytic therapy merits little further discussion. We only mention its use for completeness, but rarely use it in our practice. We agree that routine use of antifibrinolytic medications results in an increased incidence of ischaemic complications. Dr Vermeulen is misleading when he cites his own study to corroborate his negative bias on these medications.[5] He only studied one dosage regimen for tranexamic acid, not episilon-aminocaproic acid (AMICAR), the drug referred to in our article,—as he stated: "The effects of antifibrinolytic therapy are likely to depend on the dose and the agent used."[5] It should also be mentioned that, although a high incidence of ischaemic complications was noted in his study, all patients underwent delayed surgery and no patients were treated with intravascular volume expansion at the onset of ischaemic symptoms. This is a very different patient population to that of our patients, who are operated on as early as possible, and aggressively treated postoperatively with volume expansion, should ischaemic vasospasm develop. Comparisons between the two patient populations would be nonsensical.

Other critical statements are merely a matter of semantics and do not merit further exhaustive discussion. It appears as though comments regarding blood electrolyte imbalances are referred to by the reviewer to cite a paper on which Dr Vermeulen is a participating author.[17] Finally, the management, both medical and surgical, of subarachnoid haemorrhage is a complex endeavour which has many areas of controversy. The nature of our review article was to present a general overview without interjecting significant personal bias in areas that are not definitively understood. Dogmatic and exacting statements such as those made by Drs Vermeulen and Rinkle are prevalent in the medical literature. We do not believe that the pathophysiology and treatment of subarachnoid haemorrhage lends itself to such statements. Our review article is a good reference source for those interested in an informed general discussion of the topics. Judging by the large number of reprint requests for our article, it must have served its purpose well.


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