Fever After Aneurysmal Subarachnoid Hemorrhage
Relation With Extent of Hydrocephalus and Amount of Extravasated Blood

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Background and Purpose—Fever after aneurysmal subarachnoid hemorrhage is associated with poor outcome. Because hydrocephalus and extravasated blood may influence thermoregulation, we determined whether these factors increase the risk for fever after subarachnoid hemorrhage.

Methods—Fever within 14 days (subdivided into infectious and noninfectious) was defined as a mean daily body temperature above 38.0°C for at least 2 consecutive days in a prospectively collected cohort of 194 patients with subarachnoid hemorrhage. Hazard ratios were calculated to assess the impact of hydrocephalus (bicaudate index) and cisternal and intraventricular blood (Hijdra score) on the occurrence of fever. Adjusted hazard ratios were calculated in one multivariate model, including other possible confounding factors.

Results—Infectious fever occurred in 34% of patients and noninfectious fever in 9%. Adjusted hazard ratios of intraventricular blood were 2.2 (95% CI, 1.3 to 3.8) for any fever, 2.4 (95% CI, 1.3 to 4.4) for infectious fever, and 2.0 (95% CI, 0.7 to 5.9) for noninfectious fever. Adjusted hazard ratios of cisternal blood and hydrocephalus for infectious and noninfectious fever ranged from 0.6 to 1.5, all with wide CIs.

Conclusion—Intraventricular blood is an independent risk factor for the development of fever. In this study, noninfectious fever was rare and not related to extravasated blood or hydrocephalus. (Stroke. 2008;39:2141-2143.)

Key Words: fever ■ hydrocephalus ■ subarachnoid hemorrhage

Many patients with aneurysmal subarachnoid hemorrhage (SAH) develop fever during their clinical course, which is associated with poor outcome. In some patients with fever after SAH, no infection is identified. Fever in absence of infection can be attributed to a systemic inflammatory reaction or to loss of central temperature control. Central thermoregulation is a process that involves several neuronal pathways, most extending from the hypothalamus and limbic system. Some patients with SAH develop hydrocephalus within the first days after the event. Hydrocephalus may influence the thermoregulation process, for example, from pressure on the hypothalamus or limbic system. Also, presence of hemoglobin in the basal cisterns can increase body temperature. We assessed the hypothesis that fever after SAH is associated with the extent of hydrocephalus and the amount of extravasated blood in the subarachnoid space.

Patients and Methods

We included patients admitted within 4 days after onset of aneurysmal SAH to the University Medical Center Utrecht and who were randomized for the MASH-1 trial. Patients were excluded when their medical records were incomplete with regard to temperature measurements. The clinical condition on admission by means of the World Federation of Neurological Surgeons scale, the amount of ventricular and the amount of cisternal blood on initial CT scan by means of the Hijdra score, were prospectively collected, blinded for the temperature data. The Hijdra score assesses the amount of blood on a semiquantitative scale (range, 0 to 3) for 10 cisterns and 4 ventricles and yields total sum scores for cisternal (range, 0 to 30) and intraventricular (range, 0 to 12) blood. Hydrocephalus was quantified by measuring the greatest value of the bicaudate index on any CT scan performed within 3 days after the SAH.

Rectal body temperatures were retrieved from the medical records and were measured at least 4 times a day. We calculated daily mean body temperatures for each patient during 14 days after the SAH. Fever was defined as a mean daily body temperature above 38.0°C for at least 2 consecutive days. In patients with more than one fever episode, only the first episode was used in the analysis. Bacterial cultures, chest x-rays, and extraventricular drainage were obtained from the patients’ medical records. Infectious fever was defined as the presence of fever in combination with a positive bacterial culture in blood, urine, cerebrospinal fluid, or sputum. All fever without an infection in accordance with this definition was classified as a noninfectious fever.

All patients were treated according to a standard protocol, including 6 doses of 500 mg acetaminophen on a daily basis. In case of fever, patients were thoroughly examined for an infectious focus.
### Data Analysis

Crude hazard ratios (HRs) with corresponding 95% CIs for the occurrence of any fever, infectious fever, and noninfectious fever in the first 14 days after the SAH were calculated for bicaudate index and amount of cisternal and intraventricular blood on initial CT scan dichotomized at their median values by means of the Cox proportional hazard model. All analyses were censored for death. Adjusted HRs were calculated in one model, adjusting for the clinical condition at admission (World Federation of Neurological Surgeons scale), age, sex, cerebrospinal fluid drainage, and intensive care unit (ICU) admittance.

### Results

In our hospital, 200 patients were included in the MASH-1 trial; 6 were excluded because the daily temperature curves could not be retrieved. An episode of fever occurred in 82 (42%) of the 194 included patients (Table 1). Infectious fever occurred in 34% of patients and noninfectious fever in 9%. Infectious fever occurred in 33 (56%) of the 59 patients who had been admitted to the ICU and in 31 (23%) of the 135 patients who had not been admitted to the ICU.

Intraventricular blood was related to any fever (adjusted HR, 2.2; 95% CI, 1.3 to 3.8) and infectious fever (adjusted HR, 2.4; 95% CI, 1.3 to 4.4), and a trend was shown for noninfectious fever (adjusted HR, 2.0; 95% CI, 0.7 to 5.9; Table 2). Cisternal blood and the bicaudate index were not related to any type of fever.

### Discussion

The amount of intraventricular blood is an independent risk factor for the development of any fever and infectious fever, and a trend was shown for noninfectious fever. There was no relationship between cisternal blood or hydrocephalus and infectious or noninfectious fever.

We do not have a clear explanation why ventricular blood is associated with infectious fever. Because we adjusted for cerebrospinal fluid drainage, clinical condition at admission, and ICU admittance, these factors cannot explain this relationship.

Other studies on fever in patients with SAH found similar proportions of infection underlying fever. Several studies have shown that fever in patients with SAH is related to poor clinical outcome. In one of these studies, the occurrence of fever was related to the presence of blood in the ventricles and large amounts of subarachnoid blood, which is in line with our finding.

Our study has the advantage that the study population covers both patients admitted to the ICU and patients admitted to the medium-care unit, whereas in other studies, the study population consisted only of patients admitted to the ICU. Also, patients were prospective collected and temperature measurement was performed rectally. A limitation of our study is our strict definition of fever. Episodes shorter than 2 days of fever or episodes with less increased temperature were not taken into account. It is possible that these less severe episodes of increased temperature are more associated with blood degradation products in the basal cisterns without concomitant infection. A second point of concern might be the definition of infection, in which we had to rely on the medical records instead of daily prospective assessment of episodes of fever. A third issue is that all patients were treated with acetaminophen, which also has antipyretic properties and that in case of fever, more aggressive methods of cooling such as cooling blankets were used. Thus, our study reflects fever that did not respond rapidly to antipyretic or antibiotic treatment.

From a clinical point of view, our results warrant a thorough examination for infection in patients with SAH and fever, even if these patients have intraventricular blood. Because most episodes of fever were related to infection, we think it unlikely that aggressive treatment of hydrocephalus or clearing of subarachnoid blood by lumbar drainage will lead to less episodes of fever.
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Disclosures
None.

References
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