

# Xanthochromia after subarachnoid haemorrhage needs no revisitation

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**SUMMARY** Recently it was contended that it is bloodstained cerebrospinal fluid (CSF) that is important in the diagnosis of subarachnoid haemorrhage (SAH) and not xanthochromia, and also that a normal CT scan and the absence of xanthochromia in the CSF do not exclude a ruptured intracranial aneurysm. The CSF findings were therefore reviewed of 111 patients with a proven SAH. All patients had xanthochromia of the CSF. Lumbar punctures were performed between 12 hours and one week after the ictus. Xanthochromia was still present in all (41) patients after 1 week, in all (32) patients after 2 weeks, in 20 of 22 patients after three weeks and in 10 of 14 patients after four weeks. In six years we identified only 12 patients with sudden headache, normal CT, bloodstained CSF, and no xanthochromia. Angiography was carried out in three and was negative. All 12 patients survived without disability and were not re-admitted with a SAH (mean follow up 4 years). It is concluded that it is still xanthochromia that is important in the diagnosis of SAH and not bloodstained CSF. Furthermore a normal CT scan and the absence of xanthochromia do exclude a ruptured aneurysm, provided xanthochromia is investigated by spectrophotometry and lumbar puncture is carried out between 12 hours and 2 weeks after the ictus.

Recently MacDonald and Mendelow reviewed the case records of 100 patients with angiographically confirmed cerebral aneurysms.<sup>1</sup> Forty-six percent of the 68 patients who had undergone a lumbar puncture had bloodstained cerebrospinal fluid (CSF) but no xanthochromia. In 20 patients there was no blood on the CT scan; seven of these had blood in their CSF and again no xanthochromia. They concluded that it is bloodstained CSF that is important in the diagnosis of SAH and not xanthochromia, and also that a normal CT scan and the absence of xanthochromia in the CSF do not exclude a ruptured aneurysm. The aims of our own study were to investigate if SAH can indeed occur without the development of xanthochromia in the CSF and secondly if patients with a normal CT scan and bloodstained CSF without xanthochromia may indeed have a ruptured aneurysm.

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## Patients and methods

### *Patients with subarachnoid haemorrhage*

We reviewed the measurement of xanthochromia in the CSF of 111 patients who were admitted within 3 days after SAH to the Department of Neurology of the University Hospital, Rotterdam.

All patients had blood in the basal cisterns suggesting a ruptured aneurysm on the initial CT scan.<sup>2</sup> All patients had one lumbar puncture (LP) within 7 days after the haemorrhage, and not earlier than 12 hours after the haemorrhage. In 41 patients LP was repeated one week after the haemorrhage, in 32 patients after 2 weeks, in 22 after 3 weeks and in 14 after 4 weeks. These LPs were carried out for several other studies.<sup>3,4</sup> None of the patients had clinical symptoms of rebleeding before LP.

### *Patients with bloodstained CSF and no xanthochromia*

The records of the University Hospital, Rotterdam, were searched for patients who had been admitted with a provisional diagnosis of SAH and who had a normal CT scan, bloodstained CSF and no xanthochromia. Excluded were patients in whom the CSF was initially bloodstained but became clear during the procedure.

Between September 1981 and September 1987 we identified 12 such patients. These patients were interviewed by telephone. Any subsequent history of headache and hospital admission was evaluated.

**CSF analysis**

CSF was centrifuged immediately after LP. The supernatant was examined with a Beckman double beam spectrophotometer model 25 to record the absorption spectrum between 400 and 700 nm. The spectrophotometer was checked regularly for absorption measurement (cobaltous sulphate) and wavelength setting (holmium oxide). Xanthochromia was defined as extinctions exceeding 0.023 at wavelength 415 nm and/or a peak in the absorption curve in the 450–460 nm range.

**Results**

*CSF xanthochromia after SAH*

All 111 patients with a SAH, proven by CT scan, had xanthochromia of the CSF, between 12 hours and one week after the haemorrhage (table). The mean of the optical densities at wavelength 415 nm and at 460 nm increased up to the end of the first week. The second and third CSF samples, taken one and two weeks after the haemorrhage, showed xanthochromia in all cases. The probability of detecting xanthochromia after 3 weeks was 20/22 (91%, 95% confidence limits 71 and 99) and after 4 weeks 10/14 (71%, 95% confidence limits 42–92).

*Patients with bloodstained CSF and no xanthochromia*

We identified only 12 patients in six years with a provisional diagnosis of SAH, bloodstained CSF, no xanthochromia and a normal CT. All patients were seen within 36 hours of the ictus. In the same period, approximately 80 patients with a proven SAH were admitted each year, and 10 patients per year were seen with a provisional diagnosis of SAH, a normal CT and normal CSF findings. In three of the 12 patients with bloodstained CSF but no xanthochromia, angiography was performed. All three were negative.

All 12 patients survived without disability and were not re-admitted for a SAH. The mean follow up period was 4 years and 4 months: one year in one patient, between 2 and 3 years in one, between 3 and 4 in four, between 4 and 5 in two, between 5 and 6 in two and between 6 and 7 in two patients.

Table CSF xanthochromia after SAH

Delay since ictus	No of patients xanthochromia		Mean optical density in patients with xanthochromia at wavelength	
	absent	present	415 nm	460 nm
12–24 hours	—	34	0.184	0.107
1–2 days	—	37	0.388	0.164
3–4 days	—	27	0.382	0.223
5–6 days	—	13	0.951	0.380
1 week	—	41	0.825	0.323
2 weeks	—	32	0.562	0.239
3 weeks	2	20	0.122	0.081
4 weeks	4	10	0.063	0.052

**Discussion**

We found xanthochromia of the CSF in all 111 patients with SAH examined between 12 hours and one week after admission. The concentration of oxyhaemoglobin and bilirubin increased during the first week and decreased thereafter. Two weeks after the haemorrhage xanthochromia was still present in all patients, and at three weeks the probability of detecting xanthochromia was still over 70%. Even after 4 weeks the probability of detecting xanthochromia was more than 40%.

The occurrence of the combination of (1) signs and symptoms suggestive of SAH, (2) bloodstained CSF without xanthochromia and (3) a normal CT-scan, is very rare. Only 12 such patients were identified in a 6 year period, whereas in the same period we admitted approximately five times this number of patients with a provisional diagnosis of SAH but with normal CSF findings and a normal CT, and 40 times as many patients with a proven SAH. All 12 patients with a normal CT and bloodstained CSF without xanthochromia survived without disability during a mean follow up of 4 years, and they were not re-admitted with a SAH. Therefore, a ruptured aneurysm in these patients is unlikely. Moreover, in three of these 12 patients angiography was done and in none an aneurysm was demonstrated. The most probable explanation is that these patients had a non-haemorrhagic thunderclap headache and a traumatic LP.

Our finding that all patients with a proven SAH have xanthochromia between 12 hours and 2 weeks after the haemorrhage is in agreement with the study of Walton,<sup>5</sup> but not with the study of MacDonald and Mendelow, who found no xanthochromia in 31 of 68 patients.<sup>1</sup> Thirteen of their patients were punctured on the day of the ictus, 10 on the following day, 7 on day 2 to 5, and one on day 11. How can these different results be explained? A true absence of xanthochromia on the day of the ictus can be explained only if all CSF samples were taken within 12 hours of the ictus. Xanthochromia may not have developed within this 12 hour period, as demonstrated by Walton.<sup>5</sup> The failure to detect xanthochromia in the other patients in the series of MacDonald and Mendelow should probably be attributed to the method used for the detection of xanthochromia. They examined the supernatant of the CSF by direct vision, which is an insensitive method. This was demonstrated by Söderström who found that xanthochromia detected by spectrophotometry in a series of 32 CSF samples was visible with the naked eye in only half of these samples.<sup>6</sup> The finding of MacDonald and Mendelow that xanthochromia may fail to develop after several days of the haemorrhage is the more unlikely as the milieu of the CSF is favourable for the process of

haemolysis. The rapid lysis of red cells in the CSF results in the formation of oxyhaemoglobin and bilirubin, the pigments that cause xanthochromia of the CSF.<sup>7</sup> We therefore contest the conclusion of MacDonald and Mendelow that a normal CT and the absence of xanthochromia in the CSF do not exclude a ruptured aneurysm. If CT is performed on the day of the ictus, the probability of detecting blood is almost 100%.<sup>8</sup> Unless LP is carried out within 12 hours or later than 2 weeks, xanthochromia is bound to be present on spectrophotometric analysis after true SAH.

CT scanning should be the investigation of choice in patients who present with symptoms of SAH. If CT is normal the probability of SAH is very low, provided scanning has been done within 48 hours of the ictus.<sup>8</sup> If, in addition, CSF findings are normal, a SAH is excluded and angiography is not indicated.<sup>9</sup> If the patient presents after more than 48 hours after the ictus, the probability of detecting blood on CT becomes lower and CSF analysis is increasingly important. The probability of detecting blood on CT is 50% after one week, 30% after 2 weeks and almost nil after 3 weeks,<sup>8</sup> whereas CSF xanthochromia is present in all patients up to two weeks and is still present in over 70% of the patients after 3 weeks.

We conclude that it is xanthochromia that is important in the diagnosis of SAH and not blood-stained CSF, and that a normal CT-scan and the absence of xanthochromia do exclude a ruptured aneurysm, provided xanthochromia is investigated by spectrophotometry, a technique which is available in almost every hospital, and provided the lumbar puncture is done not earlier than 12 hours after the ictus and not later than 2 weeks.

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