

# Letters to the Editor

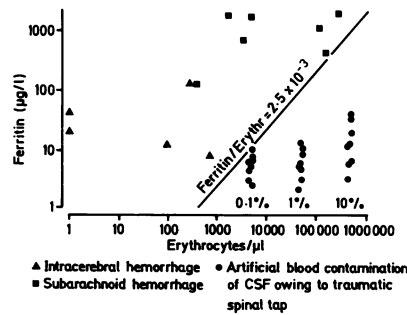
## Ferritin in cerebrospinal fluid differentiation between central nervous system haemorrhage and traumatic spinal puncture

Observations by Hällgren *et al*<sup>1</sup> and Sindic *et al*<sup>2</sup> made us investigate to what extent ferritin in cerebrospinal fluid (CSF) may serve as an indicator of central nervous system haemorrhage and facilitate its differentiation from artificial blood contamination of CSF due to traumatic spinal puncture.

Artificial blood contamination of CSF was simulated by the addition of 0.1, 1.0, and 10% (v/v) of fresh edetic acid blood (which equals an average erythrocyte content of roughly 4 500, 45 000, or 450 000/ $\mu$ l CSF) of eight patients to their cerebrospinal fluids. These were compared with seven from patients with subarachnoid haemorrhage and five from patients with intracerebral haemorrhage, all confirmed by cranial computed tomography scan or angiogram. All determinations of ferritin concentration were performed by a commercial enzyme immunoassay (Enzymun-Test Ferritin, Boehringer Mannheim, West Germany), the suitability of which for measurement of ferritin in CSF was confirmed by precision and recovery studies.

Cerebrospinal fluids with moderate or even considerable artificial blood contamination of up to 1% (v/v) or an erythrocyte count of 45 000/ $\mu$ l did not show any significant increase of ferritin concentrations compared with those found before blood was added. Only in grossly contaminated CSF, which rarely occurs in clinical practice (10% v/v or 450 000 erythrocytes/ $\mu$ l) was a significant increase exceeding the imprecision of the method observed, which corresponded to the expected carry-over from the plasma ferritin concentrations of each patient. Haemolysis of erythrocytes in grossly contaminated CSF after one week's incubation, however, causes a further increase of CSF ferritin concentration, depending on intracellular ferritin pools.

In contrast to CSF artificially contaminated with blood, all patients after subarachnoid haemorrhage showed grossly raised (by several orders of magnitude) CSF ferritin concentrations (figure). Even after intraparenchymatous cerebral haemorrhage moderate to pronounced increases of CSF ferritin concentrations were observed, which were clearly distinguishable from commonly encountered degrees of artificial blood con-



tamination (up to 1% v/v). In all cases CSF ferritin was disproportionately raised with regard to the amount of blood present in CSF (figure).

Our findings indicate that ferritin concentrations in CSF may facilitate the differentiation of blood contamination of CSF due to traumatic puncture from genuine central nervous system haemorrhage. While this is quite obvious from the grossly raised concentrations encountered in subarachnoid haemorrhage, even cases of intraparenchymatous haemorrhage could be distinguished by CSF ferritin concentrations, increased disproportionately to the amount of red blood cells present.

In contrast to many other CSF proteins, the interpretation of CSF ferritin concentrations does not require the taking into account of plasma ferritin or the permeability of the blood-CSF barrier. CSF ferritin can be considered to be derived almost exclusively from sources within the central nervous system itself, as even in cases of severely impaired blood-CSF barrier function, the amount of ferritin present in CSF by far exceeds the amount explicable by its molecular size (450 000).<sup>3</sup>

While the precise sources of ferritin within the central nervous system are not known, degradation of haemoglobin by macrophages after central nervous system haemorrhage seems to be the most obvious origin.

CSF ferritin seems to offer a more specific and sensitive discrimination than the assessment of xanthochromia. Whereas CSF samples from all seven patients with subarachnoid haemorrhage were xanthochromic, only one CSF sample from five patients with intracerebral haemorrhage showed this discoloration.

The fact that xanthochromia occurs in all central nervous system diseases with a considerable blood-CSF barrier dysfunction is well documented and was confirmed in our

study. This also applies to artificial blood contamination from 1%. CSF xanthochromia may serve as an indicator of central nervous system haemorrhage, only in the absence of severe impairment of the blood-CSF barrier (albumin CSF: serum ratio less than  $15 \times 10^{-3}$  or CSF protein less than 100 mg/dl) and in the absence of jaundice.

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### New type of staphylococcal endocarditis

We report a case of natural valve endocarditis caused by a previously undescribed penicillin sensitive *Staphylococcus*. The strain was positive for clumping factor (slide coagulase positive) but was tube coagulase negative. The clinical picture resembled *Staphylococcus aureus* endocarditis with a rapid course and gross valve destruction.

Classic *Staphylococcus epidermidis* endocarditis occurs in patients with prosthetic valves and is usually low grade with few embolic phenomena.<sup>1</sup> *S aureus* endocarditis is aggressive and fulminant and is often associated with intravenous self-administration of drugs.<sup>2</sup>

Our case highlights a problem if staphylococci are speciated by means of tube coagulase alone. We therefore suggest that staphylococci causing serious sepsis be identified by means of clumping factor and free coagulase tests and that anomalous strains be sent to the reference laboratory.

## Case report

A 67 year old woman presented with a two week history of fever, weight loss, malaise and increasing shortness of breath. There were no predisposing factors for endocarditis; she was pale with severe dyspnoea. Her pulse was 120 and temperature 38°C. Splinter haemorrhages were evident but no other peripheral stigmata of endocarditis were present. She had the murmurs of mixed mitral valve disease. Staphylococci were isolated after 24 hours' incubation from six sets of blood cultures. All the isolates were penicillin sensitive and all showed positive clumping factor in the slide test, were Staphaurex positive, but tube coagulase was negative. Biochemical tests were carried out.<sup>3</sup> The closest identification was as *S hominis* or SV in the Baird Parker 1963 scheme, but unusual results were seen with very strong DNase activity, positive phosphatase, and ornithine decarboxylase. Acetoin was positive but acid production from mannitol and ribose was absent.

The table<sup>5</sup> compares the standard biotyping profile of the isolate with those of closely related staphylococcal species: *S hominis*, *S intermedius*, and *S aureus*.

Echocardiography showed a thickened aortic valve compatible with endocarditis. Initial treatment consisted of intravenous benzyl penicillin 1.2 g two hourly and gentamicin 80 mg twice a day. Both a deterioration in cardiac and renal function and multiple emboli necessitated emergency mitral valve replacement.

At operation there was gross mitral valve destruction and vegetations, and a Carpentier Edwards prosthesis was inserted. The valve was sterile.

Postoperative treatment was changed to benzyl penicillin 1.2 g five times a day and rifampicin 600 mg twice a day (in vitro synergy was demonstrable). She made a good recovery and after two weeks was changed to oral amoxycillin 1 g three times a day for four further weeks. Peak and trough serum bactericidal titre were adequate (1/64, 1/16, respectively). She was discharged and remained well on follow up at five months.

## Comment:

The anomalous results of tube coagulase, clumping factor and Staphaurex latex agglutination and the clinical course strongly suggest an association with *S aureus*. The strong DNAase production also supports this, but the lack of acidification of mannitol by two methods, combined with ribose negativity and the positive maltose and Voges Proskaver reaction, prevent identification as either *S aureus* or *S intermedius*. The carbohydrate reactions suggest *S hominis*.

Overall, the results would be compatible with an anomalous variety of the *S aureus*/*S intermedius*/*S hyicus* species group.

This case raises the question of which tests should be used in the routine laboratory to identify staphylococci. Tube coagulase testing alone may misidentify strains that share characteristics of different staphylococci. We therefore feel that clinically important staphylococcal isolates should also be identified

by clumping factor tests, irrespective of their coagulase reaction. The Staphaurex latex agglutination method is more sensitive than the slide technique<sup>4</sup> and in this case would have highlighted the anomaly. We believe that isolates of coagulase negative staphylococci from patients with serious sepsis deserve detailed identification so that the epidemiology and natural history can be further elucidated.

One case is merely interesting, two form an anecdote, and three a series, so we ask for contributions.

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Glycocalyx in virulent and avirulent strains of *Shigella flexneri*

External polysaccharidic coats (glycocalyx) in bacteria have been largely overlooked as

Table Biotyping profile<sup>5</sup> of blood culture isolate compared with those of closely related staphylococci

Test	Blood culture isolate	<i>S hominis</i>	<i>S intermedius</i>	<i>S aureus</i>
Acid (aerobically) from:				
Arabinose	-	-	-	-
Lactose	+	v	+	+
Maltose	+	+	-	+
Mannitol	-	-	+	+
Fructose	+	+	+	+
Ribose	-	-	+	+
Sucrose	+	+	+	+
Trehalose	+	+	+	+
Xylitol	-	-	-	-
Phosphatase	+	-	+	+
Acetoin (VP)	+	+	-	+
Thermolabile DNAase	+	-	+	+
Nitrate reduction	+	v	+	+
Ornithine decarboxylase	+	-	-	-
Coagulase human plasma	-	-	v	+
Coagulase rabbit plasma	-	-	+	v
Clumping factor	+	-	+	+
Staphaurex	+	-	+	+

Key: + positive, - negative, v variable