The value of C-reactive protein in the management of shunt infections

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Object. Shunt infections and their management remain a clinically important problem in patients with hydrocephalus. The authors evaluated, in comparison with traditional parameters, C-reactive protein (CRP) in blood/serum (S-CRP) and in cerebrospinal fluid (CSF; C-CRP) for its power to identify and treat patients with infected shunts.

Methods. On 84 different occasions, CSF and blood samples from 59 children suspected of having shunt/CSF infections were obtained and evaluated. An infection was proven by a CSF culture in 35 of 84 evaluations. Values for S-CRP in infected individuals were higher than in noninfected ones (91.8 ± 70.2 mg/L compared with 16.1 ± 28.3 mg/L, p < 0.0001). The sensitivity of S-CRP testing was 97.1%, the specificity 73.5%, the negative predictive value 97.3%, and the receiver operating characteristic area 91.6%. The probability of shunt/CSF infection—provided that the S-CRP level was greater than 7 mg/L—rose from 41.7% (prevalence) to a posttest level of 72.3%. Specificity and posttest probability were 87.8 and 87.2%, respectively, if cases with other concurrent infections were excluded. The probability of missing a CSF/shunt infection at an S-CRP lower than 7 mg/L was 2.7%. All other diagnostic parameters did not yield useful test results. The rate of reinfection was elevated in patients in whom S-CRP levels were greater than 7 mg/L at the time of shunt reimplantation.

Conclusions. Analysis of these data suggests that the S-CRP level should be included in the first-line workup of patients with suspected shunt/CSF infection. It seems justified to avoid performing a shunt tap if S-CRP levels are less than 7 mg/L. A larger multicenter trial is necessary to confirm these promising diagnostic results and to deliver hard data concerning whether or not a normalized S-CRP level is a reliable indicator of successful antibiotic therapy and whether a shunt can be safely reimplanted.

Key Words • cerebrospinal fluid • C-reactive protein • hydrocephalus • shunt infection • pediatric neurosurgery

S-hunt infections remain a clinically important problem in patients with hydrocephalus, posing a challenge for the neurosurgeon concerned with an early and accurate diagnosis and with optimization of antibiotic therapy, especially in complicated cases with multiple catheters.

The suspicion of a shunt infection arises from a history that includes recent shunt surgery and various, mostly unspecific, clinical signs and symptoms. The traditional workup to rule out or establish shunt infection includes a shunt tap. Positive CSF cultures, the final proof of infection, have a minimum waiting time of 24 hours, and a final negative result will take a minimum of 4 days. Immediately accessible CSF parameters, such as cell counts, protein/glucose levels, and Gram stain as well as WBC values, which all have limitations regarding their sensitivity and specificity, are thus used to make a preliminary diagnosis.

In cases of proven shunt infection, there are no generally accepted standards concerning the duration of antibiotic treatment and no gold-standard parameters that indicate clearance of a shunt infection. During antibiotic treatment, CSF cultures are usually negative because the presence of the drug in the CSF inhibits colony growth in the culture dish, yet these results do not indicate final clearance of the infection within the CSF compartment, the blood, the abdomen, or alongside the previous shunt track.

In both scenarios, an additional parameter with a sensi-
tivity and specificity high enough to significantly increase posttest probability for shunt infection or for clearance of an infection would be of great value. Such a parameter could save patients from unnecessary shunt taps (with the attendant risk of introducing a shunt infection), unnecessary surgeries for supposed infection, and premature reimplantation of their shunt.

The CRP is a well-known acute-phase serum protein that increases within 6 hours in response to inflammatory cytokines (mostly IL-6) but does not distinguish between the different possible causes of inflammation. Measurements of CRP are currently used in many clinical settings and are considered to be superior to measurements of erythrocyte sedimentation rate. The CRP increases within 6 hours in response to inflammatory cytokines (mostly IL-6) but does not distinguish between the different possible causes of inflammation. Measurements of CRP are currently used in many clinical settings and are considered to be superior to measurements of erythrocyte sedimentation rate. The CRP increases within 6 hours in response to inflammatory cytokines (mostly IL-6) but does not distinguish between the different possible causes of inflammation. Measurements of CRP are currently used in many clinical settings and are considered to be superior to measurements of erythrocyte sedimentation rate.

This study was driven by the following three hypotheses: 1) All patients with shunt/CSF infection proven by CSF culture would have elevated S-CRP levels at the time of initial workup, whereas patients without infection in the shunt/CSF system or somewhere else would have S-CRP levels below a threshold within the so-called normal range of S-CRP. 2) The CRP determined in CSF would clearly distinguish between patients with shunt/CSF infection and inflammation somewhere else in the body. 3) Patients with an S-CRP level below the threshold at the time of shunt reimplantation would have a lower reinfection rate than those in whom S-CRP levels remained above the threshold.

Clinical Material and Methods

All patients evaluated for possible shunt infection at the Children’s Hospital of Michigan’s Pediatric Neurosurgery Service from January 2003 to June 2003 were prospectively studied. The CSF of patients evaluated for shunt obstruction served as a control reference. Patients who received antibiotic agents prior to a shunt tap were excluded from the study to minimize the likelihood of false-negative CSF culture results. The approval of the Wayne State University School of Medicine Human Investigation Committee was obtained.

Our initial routine clinical workup for suspected shunt infections (time point: initial evaluation) comprised history taking, clinical examination, and a shunt tap for determination of the following CSF parameters: glucose, protein, Gram stain, CSF culture, and cell counts (nucleated cells, erythrocytes, neutrophils, and lymphocytes). In addition, C-CRP was determined for the purpose of the study. Intravenous blood was drawn for WBC and S-CRP levels, except in control patients evaluated for shunt obstruction. In addition, the following data obtained from medical history were analyzed: type of hydrocephalus, degree of premature birth, technical shunt details, years of shunt dependency, number of previous revisions, time to last revision, and number of previous infections. All data entered into the study database were obtained from the patient’s charts and the intranet-based clinical information system of the hospital. Only a positive initial CSF culture defined infection.

Infected patients received the same diagnostic workup at the following time points: surgery (removal of shunt and placement of an external drain or externalization of distal catheter only), during antibiotic therapy on a twice-weekly basis (follow-up sessions one–six, Mondays and Thursdays), the day before planned reinternalization of a new shunt, and at internalization of the shunt. All patients were followed up for 6 months after reinternalization to determine the rate of reinfection. Patients were allowed to reenter the study in case they were reevaluated for infection, both after the initial negative workup and after their shunt infection was resolved.

Levels of S-CRP and C-CRP were determined with a routine high-sensitivity CRP assay having a functional sensitivity of 0.05 mg/L. Results for S-CRP were available within 1 to 2 hours after arrival of the sample in the laboratory. For determination of C-CRP, CSF samples were stored at −80°C, and all samples were processed at once at the end of the study period.

All concentrations were expressed as the median and mean ± SD. Differences between groups (control, suspected but negative infection, and suspected with confirmed infection) were analyzed using the Mann–Whitney U-test. A probability value of less than 0.05 was required to reject the null hypothesis of equivalence.

Results

Fifty-nine patients suspected of harboring infected shunts were included and investigated on 84 different occasions; 38 control patients were also included. Seventeen patients reentered the study for a repeated evaluation of infection, seven of them after having been infected previously during the study period. Four of those seven were infected again.

Patient Characteristics

None of the control patients was infected. In 35 of 84 evaluations, an infection was found (Group S+), leading to a pretest probability of infection (or prevalence) of 41.7% (Table 1). No infection was found in 49 evaluations (Group S−). There was no difference in age and duration of shunt dependency. A nonsignificant trend toward higher numbers of previous revisions and previous infections was seen in Groups S− and S+. Patients in whom infections were suspected had a shorter interval since the last revision than did controls. Seventy-nine percent of all control patients had VP shunts; in patients in whom infections were suspected, VP shunts were used in 44% and ventriculocisternal shunts in 17% (Table 2). Twelve percent of evaluations for CSF infection in the S− and S+ groups, respectively, were undertaken in patients with an external drain for reasons other than infection.

Blood Investigations

Levels of S-CRP were not determined in control patients. Figure 1 upper demonstrates S-CRP values in the group of
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TABLE 1
Characteristics of evaluated patients by group*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Patients</th>
<th>Group S−</th>
<th>Group S+</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (yrs)</td>
<td>15 (15.3 ± 10.7)</td>
<td>12.5 (12.3 ± 8.4)</td>
<td>14 (14.2 ± 10.7)</td>
</tr>
<tr>
<td>shunt dependency (yrs)</td>
<td>13 (13.8 ± 10.7)</td>
<td>6 (10.3 ± 9.0)</td>
<td>13 (11.1 ± 6.6)</td>
</tr>
<tr>
<td>previous revisions (no.)</td>
<td>5 (10.4 ± 14.7)</td>
<td>10 (17.9 ± 23.6)</td>
<td>14.5 (24.1 ± 31.4)</td>
</tr>
<tr>
<td>time since last revision (days)</td>
<td>100 (293 ± 390)</td>
<td>15 (116 ± 206)</td>
<td>12.5 (107 ± 316)</td>
</tr>
<tr>
<td>previous infections (no.)</td>
<td>0 (0.4 ± 0.8)</td>
<td>0 (0.8 ± 1.5)</td>
<td>0 (1.2 ± 1.9)</td>
</tr>
</tbody>
</table>

* Patients who reentered the study were counted only once. Abbreviation: VAr = ventriculoatrial.

patients who were suspected to have an infected shunt. The median CRP was 4.3 mg/L in this group without infection and 76.2 mg/L in those with infection. Mean values for these groups (± SD) were 16.1 ± 28.3 mg/L and 91.8 ± 70.2 mg/L (p < 0.0001), respectively. Figure 1 center demonstrates the distribution of the individual S-CRP levels in patients of both groups around the threshold of 7 mg/L that was considered to mark the upper limit of normal.

One patient with a positive CSF culture had an S-CRP level less than 7 mg/L. She was a 7-year-old girl who had a lumboperitoneal shunt implanted 4 weeks previously. She presented with slight fever (38.2°C), headaches, irritability, vomiting, and belly pain for 1 day. Her S-CRP level was 1.29 mg/L, her CSF glucose and CSF protein levels were normal, and her CSF cell count revealed six erythrocytes per TCC. The WBC count was slightly higher in Group S− compared with those in Group S+ (54.8 ± 10.9, 54.5 ± 14.9, and 59.8 ± 12.7 mg/dL, respectively). Protein levels in control patients were less scattered and lower than those in Group S− and S+ patients (54.8 ± 10.9, 54.5 ± 14.9, and 59.8 ± 12.7 mg/dL, respectively). Protein levels in control patients were less scattered and lower than those in Group S− and S+ patients (p < 0.02 but p < 0.005) but did not differ between the latter two (47.6 ± 43.1, 127.3 ± 202.7, and 143.6 ± 227.9, respectively).

Table 3 gives the results for distribution of S-CRP levels in both groups. The ability of S-CRP to discriminate between the two groups, estimated using the area under the ROC curve, was 91.6% (Fig. 1 lower). Sensitivity was 97.1%, specificity 73.5%, positive predictive value 72.3%, and negative predictive value 97.3%. Accordingly, the posttest probability of detecting a shunt infection in patients with a CRP level greater than 7 mg/L was 72.3%. Compared with the pretest prevalence of 41.7%, this was an increase of 73%. The probability of missing a shunt infection in patients with a CRP level less than 7 mg/L was 2.7%.

In 13 evaluations, an S-CRP level greater than 7 mg/L was seen; however, CSF cultures remained negative. An obvious reason for infection, other than shunt infection, existed in eight of these 13: two cases of sinusitis, one positive blood culture for streptococcus pneumonia 3 days prior to evaluation (a patient with a VP shunt), one case of pneumonia, two urinary tract infections, one skin infection, and one case of peritonitis in a dialysis patient.

Two further evaluations came from a patient who received a diagnosis of a shunt infection in a third evaluation. Only three patients showed no indication of a concurrent infection at the time of initial workup. If the eight evaluations in which there was another reason for a CRP elevation are excluded, then specificity and posttest probability for S-CRP testing were 87.8 and 87.2%, respectively.

The WBC count was slightly higher in Group S+ than in Group S− patients (11,800 ± 4500/TCC compared with 8800 ± 3300/TCC, p = 0.001); however, data ranges overlapped too much to allow for diagnostic separation between groups.

Investigations of CSF

Concerning CSF investigations, no single parameter with a diagnostic potential for infection came close to S-CRP results. Glucose levels in control patients were not different from those in Group S− and S+ patients (54.8 ± 10.9, 54.5 ± 14.9, and 59.8 ± 12.7 mg/dL, respectively). Protein levels in control patients were less scattered and lower than those in Group S− and S+ patients (p < 0.02 and p < 0.005) but did not differ between the latter two (47.6 ± 43.1, 127.3 ± 202.7, and 143.6 ± 227.9, respectively).

Table 4 demonstrates that counts of nucleated cells in CSF were highest in S+ patients, compared with those in the S− and control groups; however, as Fig. 2 upper demonstrates, there was an enormous overlap between groups, and no threshold could be defined that would have allowed for a separation of the S− and S+ groups. The ratio of erythrocytes to nucleated cells, calculated to correct for contamination of CSF with blood, was lower in Group S+ than in Group S−, but it was not different from the control group. Again, there was a large overlap between Groups S− and S+ (Table 4 and Fig. 2 lower).
In control patients, C-CRP concentrations were low, and none exhibited values above the assay minimum threshold of 0.05 mg/L. Levels of C-CRP could be determined in 12 (24%) of 49 evaluations in Group S− and in 24 (69%) of 35 evaluations in Group S+. Furthermore, in patients in whom C-CRP levels were above the assay threshold, there was no difference between Groups S− and S+ (0.59 ± 1.04 mg/L compared with 0.66 ± 0.88 mg/L).

Forty-six percent of Gram stains in Group S+ were negative, leading to a sensitivity of only 54.3%, with a specificity of 100%. Forty percent of CSF cultures took longer than 1 day to become positive, and 20% did not turn positive until Day 4. Table 5 shows the distribution of bacteria cultured in our 35 infected patients. Approximately 50% of these positive cultures were S. epidermidis.

**Other Indices of Shunt Infection**

No parameter obtained from patients’ medical history and symptoms was diagnostic to distinguish between Group S+ and Group S− patients. Forty percent of Group S+ patients had no fever. The temperatures of the febrile S+ patients and the febrile S− patients were the same (38.97 ± 0.70°C compared with 39.01 ± 0.61°C). Group S− and Group S+ patients had an equal distribution of headache (33% compared with 30%), irritability (13% compared with 18%), increased fatigue (13% compared with 13%), vomiting (7% compared with 11%), and belly pain (11% compared with 10%). Only 26% of Group S− patients and 37% of Group S+ patients had specific signs and findings on examination. Fifty-eight percent of findings in Group S+ patients were not diagnostic of infection: abdominal mass or distension and abdominal pain on palpation were even more common in the S− group (18% compared with 9% and 27% compared with 4%, respectively). Decreased level of consciousness (14% compared with 9%) and drainage from the incision (14% compared with 13%) were equally common in both Group S− and S+ patients.

Three findings were present in Group S+ patients only: positive blood cultures in those with ventriculoatrial shunts (21%), erythema alongside shunt track or incision (17%), and nuchal rigidity (4%).

In four patients in Group S−, the shunt system was removed because the strong clinical impression of infection led the surgeon to action, despite negative initial S-CRP levels (median 0.93 mg/L, mean 1.4 ± 1.6 mg/L). None of these patients exhibited an infection.

**Time Course of S-CRP Levels During Treatment of Infection**

The time course of S-CRP levels in Group S+ is shown in Fig. 3. Initial S-CRP levels increased to a maximum at the time of initial surgery and then decreased gradually during antibiotic treatment until reternalization of a new shunt system (median 14 days, mean 15 ± 6.6 days after initial evaluation). At the time of reternalization of a new shunt system, 26 (79%) of 33 patients had an S-CRP level less than 7 mg/L (median 2.8 mg/L, mean 3.5 ± 2.5 mg/L); seven patients, however, still had an elevated S-
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CRP level (median 12 mg/L, mean 16 ± 12.3 mg/L; Fig. 3 lower). In the first group, three (11.5%) of 26 patients presented with a shunt reinfection at 11, 48, and 89 days after internalization, respectively. In contrast, three (43%) of seven in the second group presented with a shunt reinfection at 3, 3, and 46 days after internalization, respectively. The patient who received a diagnosis of infection 46 days later was never well during this time, and his S-CRP level remained higher than 7 mg/L throughout that period; however, two consecutive CSF cultures remained sterile until infection was finally proven in a third sample.

Discussion

The study showed that a simple blood test, which can be made available in most laboratories at any time within 1 hour, increased the probability of detecting a shunt infection through a shunt tap by 73%. The probability of missing a shunt infection would have been 2.7% if only patients with an elevated S-CRP had been tapped to have their CSF cultured. If patients with other obvious causes for an elevated S-CRP (such as concurrent sinusitis, urinary tract infection, and pneumonia) are excluded, then the specificity of S-CRP testing rises and posttest probability approaches the 90% range. Therefore, our first hypothesis, concerning the sensitivity and specificity of using S-CRP measurements in testing for shunt/CSF infection, seems to be valid according to these data (albeit they are limited by the relatively small number of patients).

Using S-CRP Testing as an Infection Marker

Using tests of S-CRP levels in the differential diagnosis of bacterial, viral, and aseptic meningitis began in 1966 and continued until recently. All authors concluded that the CRP level was a most useful parameter in making a diagnosis of meningitis and in differentiating bacterial meningitis from other forms. Beginning in the 1980s, this topic also stimulated the evaluation of C-CRP. All authors concluded that the C-CRP level was superior to all other CSF parameters in differentiating bacterial meningitis from viral meningitis and that C-CRP levels were higher in cases of bacterial meningitis than in the viral or tubercular forms.

This sufficient body of literature for meningitis was the rationale for our study. In contrast, a Medline search regarding CRP and shunt infection yielded just two initial investigations from the late 1970s and early 1980s. At that time, precipitation tests could detect only the presence or absence of CRP and found a high rate of positive results in cases of shunt infection. A third, very recent paper, published after our study was performed, compared 10 children with shunts and positive CSF cultures and 28 such children without positive cultures. The authors found significantly higher S-CRP levels in the first group of patients (p < 0.05); however, their results had a much lower diagnostic power compared with our analysis. Using an S-CRP threshold of greater than 100 mg/L, their sensitivity was 40%, specificity 95%, positive predictive value 36%, and negative predictive value 95%. Direct comparison with our results is inhibited by their study’s retrospective character, different selection criteria, much smaller cohort size, and lack of detailed information.

We had one patient with a positive CSF culture (S. epidermidis) and an S-CRP level less than 7 mg/L. Two possible scenarios can explain the failure of S-CRP measuring to detect the shunt infection in this case: 1) contamination caused by the shunt tap; or 2) a very early stage of infection, before S-CRP levels began to rise. The median initial S-CRP level in the remaining 17 S. epidermidis infections was 92 mg/L (range 9–281 mg/L). Therefore S. epidermidis—our most common germ—does seem to be capable of eliciting an inflammatory response strong enough to be discovered by measuring the S-CRP level at the time of symptoms. Thus, a de novo infection caused by the shunt tap has to be considered seriously, which constitutes a morbidly rate that is preventable if an elevated S-CRP level is a prerequisite for a shunt tap.

A “CRP First” Policy

Overall, we performed 84 shunt taps, of which 49 were in patients who turned out not to be infected (36 of the 49 had a normal CRP reading). A policy that makes determination of S-CRP elevation mandatory before a shunt is tapped could therefore reduce the number of shunt taps by approximately 45%. These findings correlate well with recent experiences of using S-CRP testing in predicting bacterial meningitis in children with meningeal signs. Using a multivariate logistical prediction model that incorporated clinical signs and symptoms, S-CRP was the only independent laboratory test that improved the ROC area. The model including S-CRP testing identified 35% of all suspected patients in whom a lumbar puncture could be withheld without missing a single case of bacterial meningitis.

A “CRP first” policy requires that all children need blood to be drawn, which might in some cases be more difficult and also more painful than merely tapping the shunt; how-

**TABLE 4**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Patients Median (mean ± SD)</th>
<th>Group S− Median (mean ± SD)</th>
<th>Group S+ Median (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>nucleated cells/TCc</td>
<td>1 (19.3 ± 97.0)†‡</td>
<td>8 (58.2 ± 206.9)†‡</td>
<td>30.5 (187.6 ± 342.7)†‡</td>
</tr>
<tr>
<td>erythrocytes/nucleated cells</td>
<td>5.5 (77.5 ± 262.6)†</td>
<td>34.6 (118.1 ± 297.2)†‡</td>
<td>5.3 (66.7 ± 187.5)†‡</td>
</tr>
</tbody>
</table>

* Values in Groups S− and S+ were widely scattered; therefore, the median gives a more realistic impression of the average parameter levels.  † p < 0.008 compared with both other groups.  ‡ p < 0.05 compared with both other groups.
ever, drawing blood carries no risk for inducing a shunt infection or a proximal obstruction. In our experience, parents accepted this change in policy quite readily when they were properly informed and instructed and thus could recognize the benefit for their child.

**Low Diagnostic Power of Traditional Shunt Infection Parameters**

During the study period, the shunt was replaced by an extraventricular drain because of “convincing” clinical symptoms and “pathological” CSF parameters in four children, despite a negative S-CRP result. None of those children subsequently was found to be infected, but one child returned 3 months after placement of the new shunt system with a true shunt infection.

This example highlights the clinical significance of our findings concerning the value of all diagnostic information obtained from patients’ medical history or symptoms and of all other CSF parameters. We only identified truly diagnostic (100% sensitivity) positive blood cultures in patients with ventriculoatrial shunts, erythema adjacent to the shunt track or incision, and nuchal rigidity; however, in the vast majority of infected patients, none of these signs was present. All other data obtained from these sources can be misleading, and no parameter had a useful diagnostic power. Consequently, clinical signs and CSF testing results, especially because there is no clear-cut threshold for pathological CSF cell counts, contribute to an experience-based but not an evidence-based decision-making process that—as we all know—varies from surgeon to surgeon and even from patient to patient.

This interpretation of CSF results correlates well with data on S-CRP levels in patients with bacterial meningitis who test negative for a CSF Gram stain. All traditional CSF parameters did not distinguish between bacterial and viral infection; however, S-CRP did so with a sensitivity of 96%, a specificity of 93%, and a negative predictive value of 99%.27

We had two infections with *Propionibacterium acnes*, a germ known to cause low-grade infection for which CSF cultures typically turn positive late, in both of our cases on Day 4. All other CSF parameters in these children, including Gram stains, were normal; however, their S-CRP levels were 21.6 and 45.29 mg/L at the time of the shunt tap, respectively, clearly indicating the presence of an infection. The number of *P. acnes* infections that are missed because CSF cultures have not turned positive in time is unknown; however, an elevated S-CRP level and exclusion of other infectious foci should prompt the clinician and the microbiologist to continue cultures longer than usual.

**Concentrations of CRP in CSF as an Additional Marker**

Our second hypothesis—that, in cases of elevated S-CRP levels, C-CRP is able to distinguish between true shunt/CSF infections and an infection outside the CSF compartment—was proven wrong. The results were disappointing and were in clear contrast to those found in bacterial meningitis, which formed the rationale for investigating C-CRP. In one of the earlier meningitis studies, a qualitative latex agglutination test for C-CRP was used. This test distinguished bacterial meningitis from nonbacterial meningitis with a 100% sensitivity and a 94% specificity and was superior to all other CSF testing parameters.8 A more recent metaanalysis concerning C-CRP testing from 1981 to 1995 found a high odds ratio of 241 (95% confidence interval 59–980) and a sensitivity of 94% for rendering a diagnosis of bacterial meningitis.13 Another recent review concluded that C-CRP is a reliable marker of bacterial meningitis and

### Table 5

<table>
<thead>
<tr>
<th>Bacteria cultured in CSF samples from patients in Group S+</th>
<th>No. of Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus epidermidis</em></td>
<td>18</td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td>7</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>3</td>
</tr>
<tr>
<td><em>Propionibacterium acnes</em></td>
<td>2</td>
</tr>
<tr>
<td><em>S. coagulase negative</em></td>
<td>2</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Corynebacterium diphtheriae</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Neisseria meningitides</em></td>
<td>1</td>
</tr>
</tbody>
</table>

FIG. 2. *Upper:* Graphic representation of results of cell counts for nucleated cells in CSF. Patients with infection (S+) and without infection (S−) cannot be separated in the relevant range of 0 to 200 nucleated cells per TCC (n/cumm), although mean and median cell counts of both groups are statistically different (see Table 4). A significant number of infected patients have a cell count less than 100 nucleated cells per TCC. This finding results in a loss of diagnostic power for this parameter. *Lower:* Graphic representation of results of the ratio of erythrocytes to nucleated cells (E/N) in CSF, computed to correct for blood contamination during the tap procedure. Groups are not separated.
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**Serum CRP as a Marker During Treatment of Infection**

Finally, we investigated with our third hypothesis the ability of S-CRP to determine the point at which infection has cleared and reimplantation of a new shunt system is safe. Our small cohorts of seven patients with shunts and on elevated CRP and six with reinfections (three in patients with elevated CRP and three in patients with normalized CRP at shunt surgery) certainly limit conclusions. All patients underwent shunt reimplantation in the absence of fever, received antibiotic agents according to sensitivity testing up to the day of surgery, had at least three consecutive negative CSF cultures, and had a cell count in CSF that seemed acceptable. Group A (elevated S-CRP) and Group B (normalized S-CRP) have different characteristics: in Group A, patients presented again after a shorter time (median 3 days) than did the patients in Group B, who returned with infections rather late (median 48 days). Although these data have no statistical power at present, it can be anticipated that an elevated S-CRP level at the time of shunt implantation, which signifies an active inflammation (with IL-6 production somewhere in the body), increases the risk of having a shunt/CSF reinfection earlier rather than later. Similar results have been published concerning preoperative S-CRP levels and postoperative infections in almost 600 patients after cardiac surgery. Those with postoperative infections had a significantly higher preoperative S-CRP level (17.8 mg/L compared with 7.7 mg/L, p < 0.001), and an elevated CRP level greater than 8 mg/L was the most important predictor of postoperative infection.

Responsible medical practice therefore suggests that an existing inflammatory condition is a contraindication for any elective surgery in which foreign bodies are implanted with a permanent perspective. This contraindication becomes even more evident if an infected foreign body had been explanted just 10 to 14 days previously.

Our antibiotic treatment regimens were applied for a median of 14 days before the shunt was reimplanted. Consequently, the possibility exists that several patients were treated longer than necessary to clear infection.

In conclusion, our study data are insufficient to validate our third hypothesis. A larger clinical trial that investigates the power of S-CRP testing to guide antibiotic treatment and to determine the day of reinsertion of a new shunt system seems justified to answer these demands and questions scientifically.

**Conclusions**

According to our data, measuring S-CRP levels, not C-CRP levels, significantly increased the precision of making a diagnosis of shunt infection in a fashion superior to any other clinical or laboratory data; however, the number of patients included in the study and the single-institution setting limits our results somewhat. Nevertheless, we suggest assigning this parameter a first-line priority in the diagnostic workup to help the clinician make the decision of whether or not to tap a shunt. A larger randomized multicenter trial evaluating a “CRP first” diagnostic approach to suspected shunt infection as well as a CRP-based decision about when to reinsert a new shunt system should help to finally establish the predictive value of S-CRP measurements for the diagnosis of shunt infection and for deter-

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**Figure 3.** Upper: Box plot representation of the time course of S-CRP levels in patients with infection at initial evaluation (ini), at surgery (S1: explantation/externalization of shunt system), during follow up (fu1–fu6), the day before implantation of new shunt system (dbi), and at the time of implantation/internalization (int). Lower: Data distribution of S-CRP levels at the time of internalization of the new shunt system. In the majority of 26 cases, the S-CRP level was below 7 mg/L, compared with seven patients with still elevated S-CRP values. The horizontal line inside the box is the median; black boxes represent the interval between the 25th and 75th percentiles of the variable; small horizontal lines mark the 10th and 90th percentiles; white circles mark values above the 90th and below the 10th percentile.

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mining the time point of shunt reinsertion that carries the lowest risk of recurrent shunt infection.

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References


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