Although infectious complications that occur after cervical spine surgery are rare, they are potentially more perilous than those that develop after lumbar procedures. The initiation of efficient therapy after proper and timely diagnosis is difficult because laboratory tests are unspecific, clinical findings vague, initial radiographic findings inconclusive, and magnetic resonance imaging costly.

The ESR is often used for postoperative screening purposes, although it is unspecific and dependent on a number of irrelevant factors. Normalization of ESR values, even after successful treatment of an infection, is slow and irregular.

First described in 1930 by Tillett and Francis, CRP is an acute-phase protein synthesized by hepatocytes. Only trace amounts are found in the serum of healthy patients.

Following the onset of a bacterial infection, serum levels increase within 6 hours. After successful treatment of an infection, the time it takes CRP levels to normalize has been found to be much shorter than that for ESR, but CRP levels have also been found to be elevated even in the absence of infections after elective surgery for the treatment of lumbar spine disorders.

Knowledge of the normal course of inflammatory markers found after uncomplicated operations is a prerequisite to actually use these parameters as effective tools for early detection of infectious complications in a specific surgical field.

The purpose of the present study was to quantify the responses of CRP and ESR in the immediate postoperative period after cervical ventral fusion. It was also intended to analyze the impact of covariables such as the extent of surgery and hemodilution, which have been linked to changes in these parameters in previous investigations involving other surgical procedures.
Clinical Material and Methods

Following discectomy and microforaminotomy, we performed anterior cervical fusion in which we used autologous tricortical bone grafts harvested from the iliac crest and placed a titanium plate in 51 patients (22 women and 29 men). The plain radiographs shown in Fig. 1 illustrate the surgical strategy of bicortical screw fixation of the plate. The mean age of the patients was 49.2 years (range 32–76 years).

Indications for surgery were radiculopathy and/or myelopathy caused by spondylosis that was sometimes accompanied by acute disc herniation. We recorded data on duration of surgery, number of blood transfusions, and drugs administered during the postoperative course. Prophylactic antibiotic medications were not applied.

The CRP and ESR values were measured 1 day preoperatively as well as 10 days and 3 months following surgery. In addition, hemoglobin, hematocrit, red blood count, platelet count, white cell count, and axillary body temperature were checked daily at the same time. A fluorescence polarization immunoassay was used to determine serum CRP levels.

The data obtained in two cases have been excluded from statistical analysis. In the first patient, CRP values on Days 1 and 2 postsurgery could not be determined due to technical artifacts of the laboratory analyzer. In the second patient, we observed a secondary increase in CRP due to urinary infection; therefore, findings in this case will be reported separately in the result section. The data obtained in the remaining 49 patients have been grouped according to the extent of surgery: one-level fusion was performed in 18 patients (36.7%), two-level fusion in 22 (44.9%), and three-level fusion in nine (18.4%).

The mean values obtained in each group were compared using an independent t-test for statistical analysis. Paired t-test procedures were used to examine day-to-day changes in the target parameters. Pearson’s cross-correlation analysis was performed to determine interrelations among target variables, independently monitored serum parameters, and body temperature.

Results

In the 1st hour postoperatively mean ESR values increased irrespective of the number of fused cervical levels; maximum values were recorded on the 3rd postoperative day (37.2 ± 3.3 mm). For 10 days following surgery the ESRs did not significantly decrease (Fig. 2 upper). Three months postoperatively this parameter still did not significantly differ from the peak level recorded on Day 3 (19.0 ± 8.6 mm; p = 0.06).

The CRP levels did not mimic the course of ESR. The CRP increased more rapidly (Fig. 2 lower shaded area), reaching mean peak values on postoperative Day 2 (98.1 ± 9.7 mg/L). In 47 cases (95.9%) CRP levels peaked within the 1st 3 days after surgery. Maximum values ranged from 15.2 to 282.5 mg/L.

In a second phase (Fig. 3, lightly shaded) mean CRP values displayed a steep decline. A highly significant decrease
occurred between the 2nd and 3rd postoperative day (98.1 compared with 80.3 mg/L, respectively; t = 4.24, p < 0.001).

On the 5th postoperative day the mean CRP level had returned to a value below 50% of the peak (43.8 ± 5.6 mg/L). This decline was observed in all groups independent of the number of fused spinal levels.

In the absence of secondary complications CRP remained low throughout the 10-day period of observation. In one patient symptoms of a urinary tract infection were observed 7 days after surgery, and CRP levels responded to the inflammation with a secondary increase after a regular decline until the 7th postoperative day. The ESR had not significantly declined before and did not respond adequately (Fig. 3).

Mean CRP peak values were higher after two-level operations (124.5 ± 15.6 mg/L) than those after one-level procedures (95.3 ± 13.4 mg/L). The same was true for ESR peak values (49.8 ± 5.5 compared with 41 ± 4.5 mm), respectively, but these differences did not reach statistical significance in both parameters. Mean CRP peak values in patients who underwent three-level fusion (98.2 ± 16.3 mg/L) almost equaled those in patients who underwent one-level procedures (Fig. 4).

In the Pearson’s cross-correlation analysis we did not find any significant correlation coefficients between CRP levels and axillary body temperature, hemoglobin, hematocrit, red blood cell count, platelet count, or white blood cell count (Table 1).

Maximum CRP levels were not correlated to preoperatively recorded levels, bleeding, number of blood transfusions, operative time, administered drugs, age, or sex.

There have been no cases of wound infection during the study period. Since shortly after its conclusion, however, we have observed such a complication in a 52-year-old woman who underwent C5–7 fusion in which titanium plates and screws were placed for the treatment of cervical disc herniations and spondylosis. At this time, according to the results of the recently concluded study, we had just altered the standard laboratory routine, measuring CRP and ESR only on the 2nd and 5th postoperative days in inconspicuous cases. The patient had complained of persistent wound-related pain and swallowing difficulties 5 days after surgery. On that same day, the wound itself felt somewhat hardened and swollen, but it neither appeared reddish nor felt hot. When these symptoms occurred in combination with febrile body temperature on the 7th postoperative day,
antibiotic treatment was initiated. During the next 5 days clinical signs gradually resolved.

The graph in Fig. 5 demonstrates the course of CRP levels and ESRs obtained in this patient during the postoperative period. When CRP levels had not declined properly on the 5th postoperative day, an infection was suspected, and we continued to acquire blood samples daily. When clinical symptoms became apparent on Day 7, the ESR was still only slightly elevated compared with uncomplicated cases (see Fig. 2), whereas CRP was clearly elevated (117 mg/l) above its normal postoperative range (see Fig. 3). The CRP level also started to decline rapidly from the 1st day after antibiotic treatment had been initiated, whereas the ESR even increased during the first 2 days after commencement of antibiotic treatment.

Discussion

Because of its relatively slow response, the efficacy of ESR as an early detector of postoperative infections has been questioned.24 Our results confirm the validity of this skepticism and disqualify this parameter for monitoring purposes, because it did not show a significant decline within 10 days following ventral fusion and failed to respond in a timely and adequate manner in a case of cervical spine wound infection.

As in studies involving lumbar procedures,13,15,24 CRP level has been proven clearly superior to ESR as a marker for early detection of postoperative infection following cervical ventral fusion. After an initial increase, which has been interpreted as an effect of tissue affection,1,12,13,24 CRP levels decreased rapidly in all patients. In one patient this decline was disrupted by a secondary increase that paralleled a symptomatic urinary bladder infection.

### TABLE 1

Mean and standard deviation of body temperature and serum parameters recorded 1 day before and 10 days following anterior cervical fusion.*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preop</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
<th>Day 8</th>
<th>Day 9</th>
<th>Day 10</th>
</tr>
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<tr>
<td>body temperature (°C)</td>
<td>36.3 ± 0.34</td>
<td>37.0 ± 0.65</td>
<td>36.6 ± 0.51</td>
<td>36.8 ± 0.48</td>
<td>36.3 ± 0.70</td>
<td>36.6 ± 0.46</td>
<td>36.4 ± 0.44</td>
<td>36.5 ± 0.43</td>
<td>36.7 ± 0.46</td>
<td>36.9 ± 0.43</td>
<td>36.6 ± 0.28</td>
</tr>
<tr>
<td>WCC (p/nl)</td>
<td>7.9 ± 3.31</td>
<td>11.4 ± 3.22</td>
<td>10.4 ± 2.95</td>
<td>10.1 ± 2.49</td>
<td>9.0 ± 1.83</td>
<td>8.5 ± 2.00</td>
<td>8.4 ± 1.87</td>
<td>7.6 ± 1.85</td>
<td>8.0 ± 2.24</td>
<td>8.5 ± 2.11</td>
<td>8.5 ± 2.08</td>
</tr>
<tr>
<td>hematocrit (%)</td>
<td>44.1 ± 6.44</td>
<td>37.5 ± 5.92</td>
<td>37.4 ± 5.11</td>
<td>37.4 ± 5.87</td>
<td>37.4 ± 5.37</td>
<td>37.2 ± 5.41</td>
<td>37.2 ± 5.37</td>
<td>37.2 ± 5.37</td>
<td>37.2 ± 5.37</td>
<td>37.2 ± 5.37</td>
<td>37.2 ± 5.37</td>
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<tr>
<td>hemoglobin (g/dl)</td>
<td>14.9 ± 5.06</td>
<td>20.4 ± 4.92</td>
<td>20.1 ± 4.02</td>
<td>20.1 ± 4.01</td>
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<td>20.1 ± 4.01</td>
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<td>20.1 ± 4.01</td>
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</tbody>
</table>

* All values are presented as the means ± standard deviation. Abbreviation: WCC = white cell count.

FIG. 4. Bar graph demonstrating the mean and standard error of maximum CRP (white bars) and ESR (gray bars) values grouped by number of fused levels.
Blood parameters following cervical fusion

In the majority of patients, peak CRP values were reached on the 2nd postoperative day, independent of the extent of the operation performed. In similar investigations following abdominal\textsuperscript{23} and lumbar spine surgery,\textsuperscript{15,21} peak CRP levels were sometimes found to be higher in patients in whom more extensive procedures had been performed. It was assumed that this phenomenon might be due to the larger amount of tissue being injured. Based on differences in CRP levels observed during anterior and posterior lumbar procedures, it has also been suggested that the type of tissue injured and hemodilution effects caused by transfusion may be factors influencing postoperative CRP values.\textsuperscript{24}

In our study we could not confirm any of these suggestions. First, there was no clear correlation between the extent of surgery (number of fused levels) and maximum CRP values. On the contrary, mean CRP values did not differ between the groups of patients who underwent three- or two-level procedures. Note, however, that incision and exposure for a one- and a three-level fusion also often do not differ significantly. Second, because the type of tissue affected is generally similar in single- and multi-level anterior cervical fusion, this factor could not possibly account for peak-level variability. Last, hemodilution effects as indicated by a decreased hematocrit persisted for 10 days postsurgery and did not show any correlation to the course of CRP levels.

Although there was no indication that any of the above-mentioned factors could explain the variability of peak CRP values, this parameter was shown to have striking individual differences. In extreme cases, peak values were almost 19 times higher than those in other cases. Individual response should be considered as a likely contributing factor to CRP level variance in the present investigation. Therefore, even in future studies involving larger numbers of patients, it will remain difficult to determine normative CRP ranges 1 week after cervical fusion. It is conceivable that it will be necessary to calculate a ratio or percentage based on individual peak levels.

Conclusions

Present data suggest that if on the 5th postoperative day CRP has decreased to 50\% of its peak level, no surgery-related infection has been introduced. Because peak values are usually reached on the 2nd postoperative day, a safe postoperative protocol may include the obtaining of blood samples on postoperative Days 2 and 5. Provided that CRP levels decline regularly, secondary infections may be easily detected and monitored by this parameter.

On basis of present data, the level of CRP may be used as a cost-effective serum marker for screening purposes after ventral cervical fusion.

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