An Erythrocyte Sedimentation Rate Adjusted for the Hematocrit and Hemoglobin Concentration

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**Key Words:** Σ ESR; Erythrocyte sedimentation rate; ESR; C-reactive protein; CRP; Recent-onset arthritis; Disk-related lumbosciatic syndrome; Hyperlipidemia; Arterial hypertension

**Abstract**

The aim of the study was to simplify the first Σ erythrocyte sedimentation rate (ESR) method (manual hematocrit adjustment to 0.35, sum of 4 sedimentation levels) and to confirm its clinical relevance. The erythrocyte sedimentation rate of undiluted blood samples from 576 patients was measured simultaneously with and without manual hematocrit adjustment to 0.35 to identify an approximate expression of the area under the curve and a formula for calculating the Σ ESR.

The Σ ESR formula was based on the sum of 2 unadjusted sedimentation levels, at 30 and 60 minutes, together with the hematocrit value and the hemoglobin concentration. Σ ESR values in 274 healthy subjects showed a gaussian distribution, no difference between men and women, and no significant increase with age. In recent-onset arthritis or disk-related lumbosciatic syndrome, Σ ESR seemed to be a more reliable marker of inflammation than the Westergren ESR and C-reactive protein. We also obtained data clarifying the controversial relationship of ESR with lipid levels and arterial hypertension.

Although the erythrocyte sedimentation rate (ESR) is one of the most widely used laboratory tests, there is no universally agreed-on method. The Westergren method has been widely adopted since 1926, despite a number of shortcomings; in particular, plasma is diluted at a variable ratio according to the hematocrit value; the ESR increases as the hematocrit falls for a given degree of inflammation (and vice versa); and a given first-hour value can correspond to different S-shaped curves. Many other ESR methods, some developed in the 1930s and others more recently, were claimed to avoid some of these shortcomings but failed to gain widespread acceptance. In the 1970s, Pawlotsky et al developed a method called Σ ESR, based on undiluted blood collection, manual hematocrit adjustment to a constant value of 0.35, and characterization of the sedimentation curve by summing the values recorded at 20, 30, 40, and 50 minutes. Pawlotsky et al showed that this method could be helpful in clinical and research settings. Other authors acknowledged its clinical value, but its relative complexity and multiple manipulations hindered its widespread adoption. This led us to simplify the Σ ESR method while attempting to preserve its advantages.

**Materials and Methods**

The study population consisted of patients admitted to the Rheumatology Department of Rennes University Hospital (Rennes, France) and healthy subjects and ambulatory patients recruited at the Regional Social Security Investigations Center (Rennes) from January 1999 to December 2001, with approval from the local ethics committee. The study consisted of 3 phases: simplification of the Σ
ESR method; establishment of reference values; and validation in clinical applications.

**Simplification of the Σ ESR Method**

**Patients**

We included 576 hospitalized patients in the first phase of the study; 202 patients were males (age, 55 ± 15 years; range, 20-90 years) and 374 patients were females (age, 56 ± 16 years; range, 16-91 years). Ages are given throughout as mean ± SD.

**Procedure**

Blood was collected in lithium heparinate. The whole-blood ESR was measured simultaneously with and without manual hematocrit adjustment to 0.35. (Hematocrit values are given in Système International units [proportion of 1.0] throughout the text; to convert to conventional units [%], divide by 0.01.) For hematocrit adjustment, depending on whether the hematocrit value was more or less than 0.35, a quantity of plasma X [(Hematocrit/35) – 1/mL] was added to or withdrawn from the blood sample. For ESR measurement, the samples were transferred to glass Sedifit tube (10.25 × 120 mm; volume, 5.2 mL; Becton Dickinson Vacutainer Systems, Franklin Lakes, NJ) after removing the sodium citrate solution, washing, and drying. The tubes were placed vertically in a Sedifit tube rack (Becton Dickinson). Differential blood cell counts were performed with a multiparametric analyzer (Sysmex Counter NE 8000, Kobe, Japan). Hematocrit values ranged from 0.2 to 0.5 (mean ± SD, 0.38 ± 0.05) and hemoglobin concentrations ranged from 68 to 173 g/L (mean ± SD, 128 ± 18 g/L). (Hemoglobin concentrations are given in Système International units [proportion of 1.0]; to convert to conventional units, divide by 10.0.)

The Σ ESR method was simplified in 2 steps. First, we determined the simplest reliable parameter representing the area under the S-shaped curve with its 3 phases: (1) increasing sedimentation rate corresponding to the phase of erythrocyte aggregation, (2) maximal constant sedimentation rate corresponding to the phase of the maximal size of aggregates, and (3) decreasing sedimentation rate corresponding to the phase of erythrocyte packing. Sedimentation levels were read at 20, 30, 40, 50, and 60 minutes (L20, L30, L40, L50, and L60, respectively, for samples without hematocrit adjustment; L20, L30, L40, 150, and 160, respectively, for samples with hematocrit adjustment to 0.35). Simple linear regression was used to identify correlations between the partial sums of 2 to 4 time points; the sum of all 5 time points was designated Total S for samples without hematocrit adjustment and Total Σ for samples with hematocrit adjustment to 0.35. The simplest partial sums correlating with Total S and Total Σ were designated S for samples without hematocrit adjustment and Σ for samples with hematocrit adjustment to 0.35. A simple mathematical formula then was developed to calculate Σ according to S and hematologic parameters. Correlations were tested by bivariate analysis (simple linear and polynomial regression) and multivariate analysis (multiple linear regression) between Σ on the one hand and S, hematocrit, and hemoglobin on the other hand.

**Σ ESR Reference Values**

**Subjects**

We included 274 fasting healthy subjects recruited at the Regional Social Security Investigations Center in the second phase of the study. They comprised 136 males (age, 37 ± 18 years; range, 11-75 years) and 138 females (age, 40 ± 20 years; range, 7-86 years). None of the subjects had known clinical or biologic disorders.

**Procedure**

A multiparametric analyzer (Argos ABX Counter, Montpellier, France) was used for differential blood cell counts, and a standard automatic analyzer (Kone, Espoo, Finland) was used for serum biochemical measurements. Reference values for the principal parameters are shown in **Table I**.

The distribution of the results was determined graphically by the cumulative frequency curves method. The reference limits of the Σ ESR method were determined as the mean ± 2 SD. The Kruskal-Wallis, Mann-Whitney, and t tests were used to calculate the significance of differences according to sex and according to contraceptive methods and menopausal status in women. Correlations were sought between Σ ESR and the first-hour sedimentation level with undiluted, hematocrit-unadjusted blood (L60) on the one hand, and age, the hematocrit

<table>
<thead>
<tr>
<th>Parameter*</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/L)</td>
<td>125-175</td>
<td>115-160</td>
</tr>
<tr>
<td>Hematocrit (proportion of 1.0)</td>
<td>0.4-0.5</td>
<td>0.36-0.46</td>
</tr>
<tr>
<td>Serum creatinine (µmol/L)</td>
<td>55-120</td>
<td>50-105</td>
</tr>
<tr>
<td>Serum triglycerides by age group (mmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 y</td>
<td>0.30-1.5</td>
<td>0.30-1.35</td>
</tr>
<tr>
<td>20-39 y</td>
<td>0.30-1.6</td>
<td>0.30-1.5</td>
</tr>
<tr>
<td>40-59 y</td>
<td>0.30-1.9</td>
<td>0.30-1.6</td>
</tr>
<tr>
<td>60-85 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum cholesterol by age group (mmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 y</td>
<td>5.15</td>
<td>5.15</td>
</tr>
<tr>
<td>20-39 y</td>
<td>5.7</td>
<td>5.7</td>
</tr>
<tr>
<td>40-59 y</td>
<td>6.1</td>
<td>6.1</td>
</tr>
<tr>
<td>60-85 y</td>
<td>6.5</td>
<td>6.5</td>
</tr>
<tr>
<td>γ-Glutamyltranspeptidase (U/L)</td>
<td>10-60</td>
<td>7-45</td>
</tr>
</tbody>
</table>

* Values are given in Système International units; conversions to conventional units are as follows: hemoglobin, divide by 10.0 (g/dL); hematocrit, divide by 0.01 (%); creatinine, divide by 88.4 (µmol/L); triglycerides, divide by 0.01129 (mg/dL); cholesterol, divide by 0.02586 (mg/dL); γ-glutamyltranspeptidase, divide by 1.0 (U/L).
value, and the serum cholesterol and triglyceride levels on the other hand, by using bivariate analysis (simple linear regression) and multivariate analysis (multiple linear regression).

Validation of Σ ESR Reliability in Clinical Applications

These clinical applications were validated retrospectively in 2 populations: some of the hospitalized patients included or not included (because of missing data) in the first phase of the study and some ambulatory patients excluded from the second phase of the study.

Sensitivity, Specificity, and Predictive Values of Σ ESR, Westergren ESR, and C-Reactive Protein in Patients With Onset Unclassified Polyarthritis or Monarthritis Compared With Patients With Noninflammatory Articular Disorders

Of 26 patients with unclassified polyarthritis, 7 were men (age, 64 ± 10 years; range, 49-76 years), and 19 were women (age, 48 ± 16 years; range, 25-79 years). Of 22 patients with monarthritis, 7 were men (age, 47 ± 12 years; range, 22-57 years), and 15 were women (age, 44 ± 17 years; range, 23-81 years). The 26 patients with noninflammatory articular disorders comprised 14 men (age, 50 ± 11 years; range, 37-76 years) and 12 women (age, 44 ± 15 years; range, 18-76 years). Twelve patients had osteoarthritis, 9 had complex regional pain syndrome type I, and 5 had a frozen shoulder. None of these patients had other known clinical or biologic disorders.

Normal and elevated Σ ESR, Westergren ESR, and C-reactive protein (CRP) values were counted in each group of patients. The standard ESR was measured by using the Westergren method, with 4 volumes of well-mixed blood to 1 volume of 3.8% sodium citrate solution; a vertical glass tube 300 mm long and about 2.55 mm in internal diameter was used; the sedimentation level was read at 60 minutes. In the absence of consensus, 2 reference ranges were used: (1) according to the Royal College of Pathologists of Australasia (RCPA); for subjects 17 to 50 years old: men, 1 to 10 mm/h; women, 3 to 12 mm/h; for subjects older than 50 years: men, 2 to 14 mm/h; women, 5 to 20 mm/h; (2) according to Bottiger and Svedberg: subjects 17 to 50 years old: men, 0 to 15 mm/h; women, 0 to 20 mm/h; subjects older than 50 years: men, 0 to 20 mm/h; women, 0 to 30 mm/h. CRP was measured by means of nephelometry (N Latex CRP OQI Y21, Behring, Marburg, Germany). In the absence of consensus, 2 reference limits were used: less than 5 mg/L and 10 mg/L.

Σ ESR Values in Patients With Disk-Related Lumbosciatic Syndrome Compared With Sex- and Age-Matched Healthy Subjects

We compared 42 patients comprising 24 men (age, 39 ± 8.5 years; range, 25-56 years) and 18 women (age, 45 ± 10 years; range, 28-66 years) who had disk-related lumbosciatic syndrome and no other known clinical or biologic disorders with 42 sex- and age-matched healthy subjects. A first group of 32 patients had received only medical treatment; the 10 patients in the second group had undergone disk surgery. In the 2 groups of patients, we compared the Σ ESR, the first-hour sedimentation level with undiluted blood and unadjusted hematocrit (L60), and the hematocrit, using Wilcoxon and t tests.

Σ ESR Values in Ambulatory Patients With Untreated Hyperlipidemia

Of 80 ambulatory patients with untreated hyperlipidemia, 40 were males (age, 46 ±14 years; range, 17-79 years), and 40 were females (age, 36 ± 17 years; range, 16-74 years).

The prevalence of elevated Σ ESR values was established. Correlations between Σ ESR and serum cholesterol and triglycerides and between the first-hour sedimentation level with undiluted blood and unadjusted hematocrit (L60) and serum cholesterol, triglycerides, and hematocrit value were sought by bivariate analysis (simple linear regression) and multivariate analysis (multiple linear regression).

Σ ESR Values in Ambulatory Patients With Arterial Hypertension

Of 62 ambulatory patients with arterial hypertension (>150 mm Hg systolic; >90 mm Hg diastolic), 26 were men (age, 64 ± 8 years; range, 42-77 years), and 36 were women (age, 63 ± 10 years; range, 28-79 years). Thirteen patients had other manifestations of atherosclerosis, and 16 had hyperlipidemia.

The procedure was exactly the same as for the group of ambulatory patients with untreated hyperlipidemia.

Results

All data are expressed as mean ± SD. Differences and correlations were considered significant if the P value was less than .05.

Simplification of the Σ ESR Method

The correlation study between the partial sums of 2 to 4 time points and the sums of all 5 time points showed that the sum of 2 time points, ie, S = L30 + L60 and Σ = 130 + 160, met the dual conditions of simplicity and valid replacement of the sum of all 5 time points, ie, Total S and Total Σ (bivariate analysis, respectively, R = 0.995; P = .0001; and R = 0.998; P = .0001). Figure 1 shows the correlation between Σ and Total Σ. As shown in Figure 2, a given first-hour sedimentation level 160 could correspond to very different values of Σ and Total Σ, which correlated with each other.

Bivariate analysis (simple linear regression) identified correlations between Σ and S, hematocrit, and hemoglobin.
Table 2. Multiple linear regression showed that S, hematocrit, and hemoglobin were all independent explanatory variables for $\Sigma$ (Table 2). A first equation thus was established: $\Sigma = [S \times 1.038] + [\text{Hematocrit} \times 802.526] - [\text{Hemoglobin} \times 0.92] - 176.316$. Polynomial regression identified a second-degree correlation between $\Sigma$ and S (Table 2). A second equation thus was established: $\Sigma = [S^2 \times -0.005] + [S \times 1.504] + 11.615$. The following formula results from the combination of these 2 equations (sum of the left-hand and right-hand sides of the two equations):

$$\Sigma = \frac{- [0.005 \times S^2] + [2.542 \times S] + [802.5 \times \text{Hematocrit}] - [0.92 \times \text{Hemoglobin}] - 164.701}{2}$$

These results showed that $\Sigma$ ESR could be determined by a simple method consisting of the following steps:
1. Blood collection in glass Seditainer tubes (10.25 × 120 mm; 5.2 mL) containing lithium heparinate instead of sodium citrate solution.
2. Reading of sedimentation levels at 30 and 60 minutes.
3. Summing of these 2 levels.
4. Determination of hematocrit and hemoglobin with a multiparametric analyzer.
5. Calculation of $\Sigma$ ESR values in mm/h (whole numbers):

$$\Sigma_{\text{ESR}} = \frac{- [0.005 \times S^2] + [2.542 \times S] + [802.5 \times \text{Hematocrit}] - [0.92 \times \text{Hemoglobin}] - 164.7}{2}$$

The results of the $\Sigma$ ESR calculation with this formula are graphed in Figure 3 for hematocrit values of 0.30, 0.35, 0.40, 0.45, and 0.50.

Determination of the $\Sigma$ ESR Reference Range

In the 274 healthy subjects, the distribution of $\Sigma$ ESR values was gaussian. No significant difference ($t = -0.713; P = .4763$) was found between males (n = 136; $\Sigma$ ESR = 34.512 ± 7.783 mm/h) and females (n = 138; $\Sigma$ ESR = 35.279 ± 8.971 mm/h), and the mean ± SD of all $\Sigma$ ESR values was 34.898 ± 8.888 mm/h. In females, no significant difference was found according to contraceptive methods or menopausal status. Bivariate analysis (simple linear regression) identified correlations between $\Sigma$ ESR and age ($R = 0.193; P = .0013$), serum cholesterol level ($R = 0.258; P = .0001$), and triglyceride level ($R = 0.144; P = .0171$), but multiple linear regression showed that the serum cholesterol level was the only independent explanatory variable for the $\Sigma$ ESR value.

In 144 subjects with serum cholesterol levels of 5 mmol/L or less, the $\Sigma$ ESR did not increase significantly with the serum cholesterol concentration, and the mean ± SD of all its values was 33.041 ± 8.26 mm/h. (Cholesterol values are given in Système International units [mmol/L] throughout the text; to convert to conventional units [mg/dL], divide by 0.02586.) In 112 subjects with serum cholesterol concentrations of more than 5 mmol/L and 6 mmol/L or less, the $\Sigma$ ESR did not increase significantly with the serum cholesterol concentration, and the mean ± SD of all its values was 36.253 ± 9.045 mm/h. In 18 subjects with serum cholesterol levels of more than 6 mmol/L and 6.5 mmol/L or less, the $\Sigma$ ESR value was 41.329 ± 8.682 mm/h. It was deduced from these results that, as a first estimate, the $\Sigma$ ESR normal range was 17 to 53 mm/h in both sexes, regardless of age. When taking the serum

![Figure 1](image1.png)  
Blood with hematocrit adjustment to 0.35. Correlation between $\Sigma$ (sum of sedimentation levels at 30 and 60 minutes) and total $\Sigma$ (sum of sedimentation levels at 20, 30, 40, 50, and 60 minutes); n = 576; $R = 0.998; P = .0001$.  

![Figure 2](image2.png)  
Blood with hematocrit adjustment to 0.35. In 17 patients, the l60 level of 80 mm (triangles) corresponds to very different values of total $\Sigma$ (ranging from 232 to 372 mm/h) (squares) and $\Sigma$ (ranging from 108 to 152 mm/h) (circles), the latter 2 values correlating with each other ($R = 0.989; P = .0001$). Total $\Sigma$, sum of sedimentation levels at 20, 30, 40, 50, and 60 minutes; $\Sigma$, sum of sedimentation levels at 30 and 60 minutes; l60, sedimentation level at 60 minutes.
Table 21  
Correlations Between Σ and S,* Hematocrit, and Hemoglobin Concentration in Bivariate and Multivariate Analyses and Between Σ and S in Bivariate Analysis (Polynomial Regression) in 576 Hospitalized Patients

<table>
<thead>
<tr>
<th>Statistical Analysis /Parameter</th>
<th>Σ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bivariate analysis (simple linear regression) S</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>0.81</td>
</tr>
<tr>
<td>P</td>
<td>.0001</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>0.219</td>
</tr>
<tr>
<td>P</td>
<td>.0001</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>0.285</td>
</tr>
<tr>
<td>P</td>
<td>.0001</td>
</tr>
<tr>
<td>Multivariate analysis (multiple linear regression) S</td>
<td></td>
</tr>
<tr>
<td>SC</td>
<td>1.157</td>
</tr>
<tr>
<td>P</td>
<td>.0001</td>
</tr>
<tr>
<td>SC</td>
<td>0.944</td>
</tr>
<tr>
<td>P</td>
<td>.0001</td>
</tr>
<tr>
<td>SC</td>
<td>0.92</td>
</tr>
<tr>
<td>P</td>
<td>.0001</td>
</tr>
<tr>
<td>Bivariate analysis (polynomial regression) S²</td>
<td></td>
</tr>
<tr>
<td>SC</td>
<td>-0.918</td>
</tr>
<tr>
<td>P</td>
<td>.0001</td>
</tr>
<tr>
<td>S</td>
<td>1.677</td>
</tr>
<tr>
<td>P</td>
<td>.0001</td>
</tr>
<tr>
<td>SC</td>
<td>0.863</td>
</tr>
<tr>
<td>P</td>
<td>.0001</td>
</tr>
</tbody>
</table>

SC, standardized coefficient.  
* Σ, sum of the sedimentation levels at 30 and 60 minutes with hematocrit adjustment to 0.35; S, sum of the sedimentation levels at 30 and 60 minutes without hematocrit adjustment.

cholesterol concentration into account, the Σ ESR normal ranges were 17 to 50 mm/h for serum cholesterol levels of 5 mmol/L or less and 18 to 54 mm/h for serum cholesterol concentrations of more than 5 mmol/L and 6 mmol/L or less. The lower and upper limits of the reference range would be 24 and 59 mm/h in healthy subjects with serum cholesterol levels more than 6 mmol/L and 6.5 mmol/L or less.

In contrast, the distribution of the first-hour sedimentation level with undiluted blood and unadjusted hematocrit (L60) was not gaussian, and L60 was significantly lower in males than in females (7 ± 6 mm/h vs 14 ± 6 mm/h; Z = -9.072; P = .0001), with a significantly higher hematocrit value in males than in females (0.43 ± 0.02 vs 0.39 ± 0.02; t = 17.408; P = .0001). In addition, in males, L60 correlated positively with age (R = 0.318; P = .0002) and serum cholesterol level (R = 0.357; P = .0001) and negatively with the hematocrit value (R = -0.514; P = .0001). Multivariate analysis showed that the serum cholesterol concentration and the hematocrit value were the only explanatory independent variables for L60 (R = 0.576; P = .0001; standardized coefficient [SC] = 0.266; P = .0003; and SC = -0.461; P = .0001, respectively). In females, L60 did not increase significantly with age, but also was dependent on the serum cholesterol concentration and the hematocrit value in bivariate analysis (R = 0.222; P = .0089; and R = -0.242; P = .0043, respectively) and multivariate analysis (R = 0.331; P = .0004; SC = 0.227; P = .006 and SC = -0.246; P = .0029, respectively).

Σ ESR Reliability in Some Clinical Applications

Sensitivity, Specificity, and Predictive Values of Σ ESR, Westergren ESR, and CRP in Patients With Recent-Onset Unclassified Polyarthritis or Monarthritis Compared With Patients With Noninflammatory Articular Diseases

Of 26 patients with polyarthritis, 18 had elevated Σ ESR values (>53 mm/h), while 12 and 6 had elevated Westergren ESR values determined according to the RCPA24 and Bottiger and Svedberg,25 respectively; and 16 and 9 had elevated CRP values (≥5 mg/L and ≥10 mg/L, respectively).

Of 22 patients with monarthritis, 21 had elevated Σ ESR values (>53 mm/h), while 15 and 8 had elevated Westergren ESR values determined according to the RCPA24 and Bottiger and Svedberg,25 respectively; and 16 and 9 had elevated CRP values (≥5 mg/L and ≥10 mg/L, respectively).

Of 26 patients with noninflammatory articular disorders, 25 had normal Σ ESR values (<53 mm/h), while 25 and 26 patients had normal Westergren ESR values according to the RCPA24 and Bottiger and Svedberg,25 respectively; 24 and 26 patients had normal CRP values (<5 mg/L and <10 mg/L, respectively).

The sensitivity, specificity, and predictive values for Σ ESR, Westergren ESR, and CRP for 26 patients with polyarthritis...
and 22 patients with monarthritis compared with 26 patients with noninflammatory articular disorders are given in Table 3 and Table 4.

**ESR Values in Patients With Disk-Related Lumbosciatic Syndrome Compared With Sex- and Age-Matched Healthy Subjects**

ESR values for 32 patients with no history of disk surgery were not significantly different from those for control subjects (36 ± 11 mm/h vs 34 ± 8 mm/h; \( t = 0.702; P = .4881 \)), but a significant difference was found between 10 patients who had undergone disk surgery and control subjects (39 ± 5 mm/h vs 32 ± 7 mm/h; \( t = 2.969; P = .0157 \)). The opposite results were found with the measurement of the first-hour sedimentation level with undiluted blood and unadjusted hematocrit (L60): no significant difference in L60 (12 ± 5 mm/h vs 7 ± 4 mm/h; \( t = 1.768; P = .1109 \); and \( Z = -1.601; P = .01094 \)) and the hematocrit value (0.42 ± 0.03 mm/h vs 0.42 ± 0.03 mm/h) between 10 patients who had undergone disk surgery and control subjects, but a trend toward a significant difference in L60 between 32 patients with no history of disk surgery and control subjects (13.5 ± 8.5 mm/h vs 9 ± 6.5 mm/h; \( t = 2.05; P = .0492 \); and \( Z = -1.894; P = .0583 \)), owing to a significantly lower hematocrit value in the patients (0.4 ± 0.03 mm/h vs 0.42 ± 0.03 mm/h; \( t = -2.762; P = .0097 \)).

**ESR Values in Ambulatory Patients With Untreated Hyperlipidemia**

In 80 ambulatory patients with untreated hyperlipidemia (hypercholesterolemia, \( n = 52 \); hypertriglyceridemia, \( n = 10 \); mixed hyperlipidemia, \( n = 18 \)), ESR values ranged from 16 to 78 mm/h (44 ± 15 mm/h). Based on the normal upper limit of 53 mm/h, without adjustment for the serum cholesterol concentration, values were elevated in 20 (25%) of 80 cases; however, based on the cholesterol-adjusted normal upper limits of 49 mm/h, 54 mm/h, and 59 mm/h, respectively, values were elevated in only 15 (19%) of 80 cases.

ESR values trended toward positive correlations with serum cholesterol and triglyceride levels in bivariate analysis (\( R = 0.212; P = .0587 \); and \( R = 0.217; P = .0533 \), respectively) and correlated positively with these parameters in multivariate analysis that included the hematocrit value (Table 5).

**ESR Values in Ambulatory Patients With Arterial Hypertension**

In 62 patients with arterial hypertension, ESR values ranged from 19 to 110 mm/h (54 ± 21 mm/h). Based on the

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**Table 3**

<table>
<thead>
<tr>
<th>Reference Range</th>
<th>( \Sigma ) ESR</th>
<th>Westergren ESR*</th>
<th>CRP</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-53 mm</td>
<td>0.69</td>
<td>0.46</td>
<td>0.23</td>
<td>0.62</td>
<td>0.92</td>
<td>0.89</td>
<td>0.71</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.96</td>
<td>0.96</td>
<td>1.00</td>
<td>0.92</td>
<td>0.92</td>
<td>1.00</td>
<td>0.70</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.95</td>
<td>0.92</td>
<td>1.00</td>
<td>0.89</td>
<td>0.92</td>
<td>1.00</td>
<td>0.70</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>0.76</td>
<td>0.64</td>
<td>0.56</td>
<td>0.71</td>
<td>0.60</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

* Westergren ESR normal range: A, according to the Royal College of Pathologists of Australasia: for 17-50 y, men, 1-10 mm; women, 3-12 mm; for >50 y, men, 2-14 mm; women, 5-20 mm. B, according to Bottiger and Svedberg: for 17-50 y, men, 0-15 mm; women, 0-20 mm; for >50 y, men, 0-20 mm; women, 0-30 mm.

**Table 4**

<table>
<thead>
<tr>
<th>Reference Range</th>
<th>( \Sigma ) ESR</th>
<th>Westergren ESR*</th>
<th>CRP</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-53 mm</td>
<td>0.95</td>
<td>0.68</td>
<td>0.36</td>
<td>0.68</td>
<td>0.92</td>
<td>0.88</td>
<td>0.77</td>
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<tr>
<td>Sensitivity</td>
<td>0.96</td>
<td>0.96</td>
<td>1.00</td>
<td>0.92</td>
<td>0.92</td>
<td>1.00</td>
<td>0.70</td>
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<tr>
<td>Specificity</td>
<td>0.95</td>
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<td>1.00</td>
<td>0.88</td>
<td>0.92</td>
<td>1.00</td>
<td>0.70</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>0.96</td>
<td>0.78</td>
<td>0.65</td>
<td>0.77</td>
<td>0.70</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

* Westergren ESR normal range: A, according to the Royal College of Pathologists of Australasia: for 17-50 y, men, 1-10 mm; women, 3-12 mm; for >50 y, men, 2-14 mm; women, 5-20 mm. B, according to Bottiger and Svedberg: for 17-50 y, men, 0-15 mm; women, 0-20 mm; for >50 y, men, 0-20 mm; women, 0-30 mm.

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normal upper limit of 53 mm/h, without adjustment for the serum cholesterol concentration, values were elevated in 24 (39%) of 62 cases; however, based on the cholesterol-adjusted normal upper limits of 49 mm/h, 54 mm/h, and 59 mm/h, respectively, values were elevated in only 20 (32%) of 62 cases. In these patients, \( \Sigma \) ESR and L60 values did not correlate with serum cholesterol or triglyceride level.

### Discussion

The Westergren ESR and CRP remain the most widely used laboratory tests for monitoring the course of infections, inflammatory diseases, and some types of cancer, but false-negative results can lead to a risk of overlooking an inflammatory disorder, and false-positive results expose patients to unnecessary diagnostic tests that might be costly and even harmful. There is no ideal biologic marker of inflammation. In some cases, combination of the Westergren ESR and CRP can yield useful information, but our results suggest that the complementarity between ESR and CRP could be improved significantly by using the simplified \( \Sigma \) ESR method described herein.

The first method of \( \Sigma \) ESR measurement, with blood collection in lithium heparinate, manual adjustment of the hematocrit value to 0.35, and expression in terms of the area under the time-sedimentation curve, proved helpful in internal medicine, pulmonaryology, cardiology, and rheumatology. In the research setting, interesting data were obtained on the biologic effect of nonsteroidal anti-inflammatory drugs, the circadian rhythm of the \( \Sigma \) ESR and its sensitivity to these drugs, the reduction in indomethacin activity under the influence of aspirin, the anti-inflammatory activity of a benzodiazepine, and the influence of the severity of chronic joint diseases on the pharmacokinetics of nonsteroidal anti-inflammatory drugs. These data could not have been obtained with the Westergren method.

Retaining lithium heparinate as the anticoagulant because it better preserves erythrocyte morphologic features, the new variant procedure described herein notably simplifies \( \Sigma \) ESR determination. Only 2 sedimentation levels at 30 and 60 minutes need to be read; their sum correlates with a rounded-down value of the area under the S-shaped first-hour erythrocyte sedimentation curve (Figures 1 and 2). The erythrocyte sedimentation rate is calculated at a constant hematocrit value of 0.35, minimizing sample manipulations with the use of a Vacutainer system. The tubes used in the Seditainer ESR system have the advantage of wide diameter and the disadvantage of short length. In our study, this disadvantage was most problematic in major inflammatory syndromes, with a decrease in the variation range of the highest \( \Sigma \) ESRs (Figure 3). The value of CRP variations in this situation is well established.

\( \Sigma \) ESR values in healthy subjects had a gaussian distribution. The normal range established herein is 17 to 53 mm/h, with no significant difference between males and females and no significant age-related increase. If the serum cholesterol concentration is known, more precise upper limits of \( \Sigma \) ESR values can be used, as follows: 50 mm/h, 54 mm/h, and 59 mm/h for serum cholesterol levels of 5 mmol/L or less, more than 5 mmol/L and 6 mmol/L or less, and more than 6 mmol/L and 6.5 mmol/L or less, respectively. These characteristics are interesting compared with unadjusted techniques such as the Westergren and Wintrobe methods, in which the distribution of normal values is not gaussian and values increase significantly with age and are significantly lower in men than in women. We confirmed these data, studying the results of the first-hour sedimentation level with undiluted blood and unadjusted hematocrit (L60). We found that the age-related increase in the sedimentation rate in healthy men, when measured without hematocrit adjustment, could be due to an increase in the cholesterol level and a fall in the hematocrit.
value. Other authors have reported a significant age-related reduction in the hemoglobin level in healthy men or a trend toward a fall in the hemoglobin and hematocrit values.25,31

The results of our study confirm the value of the Σ ESR method in the clinical setting. The sensitivity, specificity, and predictive values of Σ ESR, Westergren ESR, and CRP in 26 patients with unclassified recent-onset polyarthritis and in 22 patients with monarthritis compared with 26 patients with noninflammatory articular disorders (Tables 3 and 4) showed that Σ ESR might be a more reliable marker of inflammation in this setting. The previous Σ ESR method was particularly helpful in recent-onset rheumatoid polyarthritis16 and rheumatic diseases with minimum activity.21

In patients with disk-related lumbosciatic syndrome, compared with sex- and age-matched healthy subjects, we were surprised to find elevated unadjusted blood sedimentation in patients with no history of disk surgery and no elevation in patients with such a history. Σ ESR gave the opposite results, showing that the former results were falsely positive (due to a significant fall in the hematocrit value) and the latter were falsely negative.

The relationship between ESR values and serum lipid levels is controversial. Only some investigators have reported correlations.32 In patients with isolated hyperlipidemia, we found a possible role of the hematocrit value in these contradictory results and showed that Σ ESR could overcome these problems. The unadjusted blood sedimentation rate did not correlate with serum cholesterol or triglyceride level in bivariate analysis or in multivariate analysis that did not include the hematocrit value, but it was significantly dependent on these parameters and on the hematocrit value in multivariate analysis including the latter. In contrast, Σ ESR values trended toward a positive correlation with the serum cholesterol and triglyceride concentrations in bivariate analysis and correlated positively with these parameters in multivariate analysis. Σ ESR values were high in 25% of cases (20/80) using a normal upper limit of 53 mm/h but in only 19% of cases (15/80) when the serum cholesterol concentration was taken into account.

The Westergren ESR has been described as a possible marker of atherosclerosis and a strong predictor of coronary death among subjects in apparently good health.33 Because it is not influenced by the hematocrit value, Σ ESR could be a better marker of inflammation than Westergren ESR in atherosclerosis. The prevalence of elevated Σ ESR values in patients with arterial hypertension is noteworthy (39% [24/62] using a normal upper limit of 53 mm/h and 32% [20/62] of cases when the serum cholesterol concentration was taken into account). It also is important to emphasize that this elevation of Σ ESR was not influenced by lipid disorders and, thus, seems directly related to the inflammatory component of atherosclerosis.

Undiluted blood, a hematocrit value adjusted to 0.35, and calculation of the area under the first-hour sedimentation curve are important conditions for accurate Σ ESR determinations. These conditions are met in the simplified Σ ESR method described herein. This new variant procedure is easy to apply in clinical laboratories. Σ ESR can be very helpful in some circumstances in which Westergren ESR and CRP are unreliable.

References


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