

# Why Shouldn't We Determine the Erythrocyte Sedimentation Rate?

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A test that is meant to measure a given parameter is more likely to detect changes in that parameter if it is not affected by factors other than those which it is intended to quantitate. The clinical use of the laboratory test for determining the erythrocyte sedimentation rate is backed by nearly a century of experience. Although its nonspecificity is acknowledged, it has been used to quantitate the inflammatory process that underlies infectious, inflammatory, and neoplastic disorders. I believe that this venerable test is affected by too many factors in addition to that which we think we are measuring, to the point that its clinical usefulness is severely compromised.

The major influence on the rate of sedimentation of erythrocytes suspended in plasma is the degree to which they aggregate with one another [1]. There are 3 major factors that influence erythrocyte aggregation: the surface-free energy of the cells, the charge of the cells, and the dielectric constant. The latter is a property of the plasma related to the concentration of asymmetric molecules. An increase in these proteins leads to greater cohesion of erythrocytes, which leads to agglutination and stacking (*rouleaux*) and a more rapid rate of decrease.

A moderate increase in the concentration of 1 of 2 classes of plasma proteins can cause an elevated erythrocyte sedimentation rate (ESR): extremely asymmetric proteins (fibrinogen) or moder-

ately asymmetric proteins (immunoglobulins). Because fibrinogen is an acute-phase positive reactant, the increase in its level in the face of infection, inflammation, or non-plasma cell neoplasms is the basis for an elevated ESR in those disorders. The nonspecificity of the ESR is widely acknowledged. Nonetheless, it is frequently overlooked that many other factors besides the presence and degree of inflammation affect the ESR, which, in my opinion, renders it useless.

## VARIABLES THAT SPURIOUSLY ELEVATE THE ESR

There are numerous factors that can elevate the ESR.

1. Anemia with normal RBC morphology. This effect is mediated by the change in the ratio of erythrocytes to plasma, which favors *rouleaux* formation, independent of the changes in fibrinogen concentration (less friction to keep the RBCs suspended caused by changes in the ratio).

2. Elevated serum concentrations of nonfibrinogen proteins: M proteins, macroglobulins, and RBC agglutinins.

3. Renal failure [2–4]. In stable patients, renal failure is probably due to elevated serum fibrinogen levels.

4. Heparin [5]. Sodium citrate and EDTA do not affect the ESR.

5. Hypercholesterolemia [6].

6. Extreme obesity, which is probably the result of elevated fibrinogen levels [7, 8].

7. Pregnancy (testing for which was the first medical use of the ESR) [9].

8. Female sex [10].

9. Advanced age [11, 12]. As a rule of thumb, for men, the upper limit of the normal ESR is age divided by 2; for women, it is age plus 10, divided by 2.

10. Technical factors. Tilting the test tube accelerates the ESR. The RBCs aggregate along the lower side while plasma rises along the upper side. Consequently, the retarding influence of the plasma is diminished. An angle of even 3° from the vertical may accelerate the ESR by as much as 30 points [13].

Received 22 September 2000; revised 17 January 2001; electronically published 11 July 2001.

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**Clinical Infectious Diseases** 2001;33:548–9

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1058-4838/2001/3304-0019\$03.00

## VARIABLES THAT SPURIOUSLY DECREASE THE ESR

There are numerous factors that can decrease the ESR.

1. Morphological abnormalities of the RBCs. Commonly seen abnormalities of the RBCs can interfere with RBC pellet formation, thus affecting the ESR. Red cells with an abnormal or irregular shape, such as sickle cells, hinder rouleaux formation, which decreases the ESR. Spherocytes, anisocytosis, and poikilocytosis also interfere with the stacking of erythrocytes, thus decreasing the ESR [14, 15].

2. Polycythemia. This will have the opposite effect that anemia has on RBC pellet formation.

3. Extremely elevated WBC count [16].

4. Diffuse intravascular coagulation (due to hypofibrinogenemia).

5. Dysfibrinogenemia and afibrinogenemia.

6. Extremely high serum bile salt levels (via alteration of the RBC membrane properties).

7. Congestive heart failure.

8. Valproic acid [17].

9. Low-molecular-weight dextran [18].

10. Cachexia.

11. Feeding [19].

12. Technical factors. Inasmuch as the ESR increases as the temperature increases, refrigerated blood samples cannot be used. If the blood has been refrigerated, it should be allowed to reach room temperature before the test is run. It is important that the test be performed using blood samples that were obtained within 2 h of testing. In standing blood, eryth-

rocytes tend to become spherical, an RBC shape that interferes with rouleaux [6].

## DISCUSSION

In contrast to the multitude of confounding factors that affect the ESR, the level of C-reactive protein (CRP) is not affected by any factor other than the presence and degree of inflammation. The plasma half-life and catabolic rate of CRP are constant under virtually all conditions. Therefore, its level of plasma is determined only by its synthesis rate, which depends solely on the presence and severity of the noxious stimulus. CRP is a group III acute-phase-reactant protein, and its level increases from 100-fold to 1000-fold during inflammation; fibrinogen is of group II, and its level increases from 2-fold to 4-fold. These 2 facts make the CRP level more discriminatory for gauging the intensity of the inflammatory response. Serum CRP levels also increase and decrease faster than serum fibrinogen levels; therefore, determination of the CRP value has a chronological advantage as a marker of inflammation [20].

It is true that it is simpler and faster to determine the ESR (it takes 1 h to determine the ESR); determination of the CRP level requires the use of EIA or radioimmunoassay methodology. Nonetheless, I respectfully submit that those health care professionals who still use the ESR determination in clinical practice adhere more to the traditions of medicine than to its scientific basis and simple logic.

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