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INFLUENCE OF A VARIABLE MAGNETIC FIELD ON THE RHEOLOGICAL PROPERTIES OF BLOOD IN TREATMENT OF RHEUMATOID ARTHRITIS

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A study has been made of the influence of a low-frequency variable magnetic field on the rheological properties of the blood of patients having rheumatoid arthritis as compared to healthy donors by means of rotational viscosimetry. To interpret the rheological properties use has been made of a three-parameter rheological model one parameter of which is sensitive to the action of the magnetic field; the other two parameters of the model have not been found to be affected by the magnetic field. These parameters are related to the hydrodynamic properties of an erythrocyte suspension. The influence of the magnetic field on the dependent rheological parameter has been revealed not in all the experiments, which is attributable to its selective action on proteins ensuring the interaction of the erythrocytes with each other.

Introduction. It is common knowledge that blood represents a concentrated dispersion formed by erythrocytes, leucocytes, and thrombocytes in the plasma. The latter in turn is a colloidal solution of proteins having different molecular weights. The constituent components of blood are dominated by erythrocytes. In the free state, they have the shape of biconcave disks with a diameter of 8 μm and they amount to approximately 93% of the total number of the elements ($\sim 5 \cdot 10^6$ cells/cm^3) and to 40–45% of the blood volume [1]. Spatial aggregates spontaneously occur in such disperse systems, as a rule, which mainly determines the structural-rheological properties of these suspensions. The surface forces of interparticle interaction are substantial, which results in aggregates that do not decompose under gravity. This is detected in rheological measurements in the nonlinear dependence of the shear stress on the rate of shear. At low τ, the dispersion is deformed almost without destroying the aggregates, while at high τ they are destroyed, which causes the viscosity to decrease [2]. As a result, we have a certain balance between the processes of aggregation and disaggregation. It is broken when the rate of shear is higher than 100 sec^{-1} [1]. The plasma of the blood (dispersive medium) is a Newtonian fluid [3].

The magnetic field has an effect on a moving erythrocyte, since the latter has a small negative charge, and on the proteins around the erythrocyte's body which participate in the formation of aggregates. Some assumptions of the action of the magnetic field on the shape elements of blood, in particular, on the erythrocytes, were discussed for the first time in the beginning of the last century in the works of Chizhevskii [4]. However there has been no accurate and reliable physical mechanism explaining the influence of the magnetic field on the state and properties of blood. Noteworthy is [5] where Turczynski et al. observed a change in the viscosity indices of the blood of experimental animals under the action of the magnetic field on it. Not only did the viscosity of the blood increase but also the viscosity of the plasma and the hematocrit, although Turczynski et al. did not interpret these facts physically.

There are fragmented data in the literature on the physical mechanism of the influence of the magnetic field on the rheological properties of blood [6]. Pauling and Coryell [7] were probably the first to report the diamagnetic susceptibility of oxidized hemoglobin and the paramagnetic susceptibility of nonoxidized hemoglobin. From their measurements, the effective magnetic moment of the Fe^{2+} complex in the erythrocyte's hemoglobin was obtained. Higashi et al. [8] have studied the orientation of normal erythrocytes in a strong magnetic field with a maximum strength of 8 T. It was found that the erythrocytes orient themselves with their flat side in the direction of the magnetic field. Yamagishi [9] has reported a similar behavior of erythrocytes for a strength of 4 T. It turned out that white blood

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cells also orient themselves for 3 T. It was noted that one protein of the plasma, i.e., fibrinogen, polymerizes and lines up in the direction of the field even for a strength of 4 T. Shalygin et al. [10] have studied the behavior of erythrocytes in high-gradient magnetic fields. According to their measurements, the susceptibility of diamagnetic erythrocytes (oxidized blood in arteries) was $-(1.6–8.2)\cdot10^{-8}$. The paramagnetic properties (nonoxidized blood in veins) were estimated at $+(1.6–4.1)\cdot10^{-6}$. Analogous results have been given by Haik et al. [11]. Motta et al. [12] have reported the orientation of human hemoglobin in the blood under the action of a strong magnetic field. Nakano et al. [13] have found that the moment required for rotation of an erythrocyte is very small (cannot be measured) if the magnetic field is directed parallel to the plane of the erythrocyte and it could be measured when the field was oriented perpendicularly to its plane. This shows that the orientation of blood cells depends on the magnetic field owing to the presence of the magnetic moment. Because of this, the blood cells and the surrounding plasma, in combination with the magnetic forces, increase the apparent viscosity of the blood.

Different therapeutic methods based on the influence of a magnetic field on the human body are employed in medical practice. This therapeutic method was developed and used for the first time by the staff of Minsk State Medical University for treatment of rheumatoid arthritis. The positive effect of such therapy has been shown in numerous scientific and practical publications and methodological instructions but the physical mechanisms of appearance of the positive effect is discussed in none of them.

Rheumatoid arthritis is a general autoimmune disease of connective tissue with a characteristic affection of joints. Immunoglobulin disorders have an unfavorable effect on the viscous properties of plasma. Changes in the rheological properties of the plasma are accompanied by a change in the properties of the cell membrane of an erythrocyte, which leads to a decrease in the deformability of erythrocytes and an improvement in the aggregation ability of erythrocytes and thrombocytes. This is responsible for the serious microcirculation disorders [14].

One often carries out extracorporal autohemomagnetotherapy (EAHMT) for treatment of rheumatoid arthritis. This procedure implies that the patient's blood is exposed to a variable low-frequency magnetic field. According to the literature data [15–19], it acts on the cell membrane, possibly by changing such properties of the cells (in particular, erythrocytes) as deformability and aggregability, and thus exerts an influence on the rheological properties of the blood.

This work is an attempt to show the influence of a magnetic field on certain physically measured indices, in particular, the rheological behavior of the human blood in exposure to a variable magnetic field, with the example of practical use for treatment of a specific disease. Thus, we seek to study the rheological properties of blood and to evaluate the influence of a low-frequency magnetic field on them in the process of EAHMT in patients having rheumatoid arthritis.

Selection of the Rheological Model. The question of selecting the rheological model is traditional for hemorheology and it is still open. One cardinal problem is construction of the adequate rheological model of blood which would at least qualitatively reflect all the facts established reliably [20]. To describe the rheological behavior of blood one mainly employs the following models or their combinations:

(1) the power law $\tau(\dot\gamma) = k\dot\gamma^n$;

(2) the Herschel–Bulkley model $\tau(\dot\gamma) = \tau_0 + k\dot\gamma^n$;

(3) the Casson model $\sqrt{\tau} = \sqrt{\tau_0} + k\sqrt{\dot\gamma}$;

(4) the Zakharchenko model $\eta(\dot\gamma) = \eta_\infty(1 + b\sqrt{\dot\gamma})/b\sqrt{\dot\gamma}$;

(5) the Williamson model $\eta(\tau) = \eta_\infty + (\eta_0 - \eta_\infty)\tau_1/(\tau_1 + \tau)$.

The list of different rheological laws could be extended, and this suggests that no universal model can be constructed for description of the rheological behavior of blood.

Since blood is a dispersion system, the influence of structurization on the rheological properties of a suspension can be allowed for by introducing the notion of the strength of the structure (yield strength τ_0). The assumption that the structure cannot be deformed when $\tau_0 < \tau$ is a prerequisite for this. One such model for which this condition is observed is the Casson relation. Its popularity as the rheological model for blood has evolved historically, partly under the influence of the legend of its rigorous theoretical deviation, although this model assumes the presence of the limit shear stress, which is, in general, inconsistent with the physiology of blood circulation. The character of the system's behavior, described by Casson, is essentially determined by three mechanisms: first, by the disintegration of a weak spatial structure that determines pseudoplasticity, subsequently by the destruction of smaller structural elements,

which explains the presence of nonlinear viscosity, and finally, by the orientation of asymmetric aggregates forming the Newtonian viscosity.

In actual practice, it is more correct to speak of the fact that deformation is developing very slowly and the period over which it occurs (characteristic deformation time) can be much larger than the time of measurement. The viscosity also remains finite at $\tau_0 < \tau$ when the structure is deformed irreversibly but without a total destruction. The rheological models, such as those of Williamson and Zakharchenko, are applicable on condition that the system possesses fluidity at any rates of shear (the yield strength is absent). The dependence of the viscosity on the rate of shear is exceptionally due to structural changes. At low rates of shear, both models predict the presence of a Newtonian portion while at high rates of shear the viscosity decreases exponentially or by the power law.

According to the literature data [21], real blood has a Newtonian portion on the flow curve in the region of low rates of shear. Therefore, for further analysis we will employ such rheological models that contain certain parameters sensitive to structural changes. One of them is the concept of Williamson (1929) [22] (consistent with the physiology of blood circulation) according to which part of the shear forces in pseudoplastic flows goes to destroy aggregates while the remaining part causes viscous flow, particularly at high rates of shear. The total shearing resistance is the sum of two independent contributions:

$$\tau\dot{\gamma} = \tau_p\dot{\gamma} + \tau_1\dot{\gamma} \ .$$

Employing the additional correcting parameter (Williamson constant), we can write this equation in the form

$$\tau = \frac{\tau_\infty\dot{\gamma}}{C_W + \dot{\gamma}} + \eta_\infty\dot{\gamma} \ . \tag{1}$$

If $\tau_\infty = 0$, we obtain the Newtonian law and if $C_W = 0$, (1) becomes the Bingham equation. We note that this concept is true when the linear (Newtonian) and nonlinear (pseudoplastic) parts of the viscosity contribution can be separated.

Such a rheological model is predicted by the momentum theory developed by Goodeve and his disciples in the 1930s [22] for moderately concentrated emulsion systems, which is easily extended to blood, which can approximately be represented as an emulsion system. Goodeve assumed that the Newtonian effects for which the shear forces are in proportion to the deformation rate and the phenomenon of thixotropy, which is independent of the deformation rate, influence the rheological behavior of emulsions and dispersions. Links between the aggregates appear only in their contact; in shear, the links are extended, broken, and transformed, which is accompanied by the transfer of the moment of momentum from one moving layer to another. Such consideration results in an equation similar to the Williamson empirical equation, with C_W being the ratio of the rate constants of Brownian motion and destruction of the aggregates. This is the only parameter related to the structural changes in shear flow. The other two parameters are compared to a purely hydrodynamic interaction of the aggregates. We note that C_W has the value of the inverse rate of destruction of the aggregates.

An analogous rheological relation was used by Sirs [23] for description of the rheological behavior of blood in its flow in capillaries. The constants of this relation have a notation different from that used in (1), and the dependence of the viscosity of the blood on the rate of shear is described by the equation

$$\eta = \eta_\infty + \frac{\tau_s}{\dot{\gamma}_* + \dot{\gamma}} \ . \tag{2}$$

The advantages of model (2) are that: a) the apparent viscosity of the blood can be subdivided into two components, one of which is related to the structural processes of interaction of the aggregates (here we can expect sensitivity to the magnetic field) and the other of which is related to the process of flow of the dispersion as a homogeneous medium; b) such a concept is consistent with the physiology of blood circulation.

Materials and Methods. The measurements were carried out on a rotational viscosimeter realizing Couette flow in the range of rates of shear of 0.5–60 $\sec^{-1}$ at a temperature of 30^oC. To describe the rheological behavior of blood we employed model (2), whose three parameters were found by fitting. The rheological properties of blood were investigated before the beginning of treatment and after a single exposure of the blood of patients having rheumatoid

TABLE 1. Change in Some Indices of Eq. (1) in Patients Having Rheumatoid Arthritis

Indices	Normal value	Blood of the patients with rheumatoid arthritis
η_∞ [1)]	2.09±0.28	3.36±0.29
τ_s	16.79±1.13	18.21±2.25
$\dot{\gamma}_*$	0.13±0.02	0.09±0.006

Note: [1)]When the standardized value of the hematocrit is Hct = 35%.

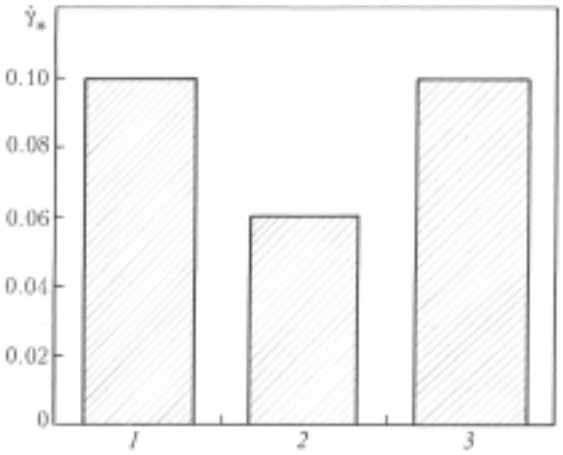

Fig. 1. Changes in the constant of the apparent kinetic rate of destruction of structural units $\dot{\gamma}_*$ in exposure to the magnetic field: 1) normal value; 2) before exposure to the magnetic field; 3) after exposure to a low-frequency magnetic field *in vitro*.

arthritis to the magnetic field *in vitro* and after four procedures of EAHMT (the blood was taken in a puncture of the peripheral vein within two days after the completion of the fourth procedure) and within a week and a month after the completion of a cycle of EAHMT procedures in the main group and accordingly before the treatment and after four days, a week, and a month in the control group.

The EAHMT cycle consisted of 4 to 5 procedures carried out daily. The volume of the irradiated blood was 1.5 ± 0.2 ml per kg of the patient's body mass. We employed a Gemospok apparatus in regime No. 8 (unipolar pulses having a repetition frequency of 10 Hz, an internal floating frequency of 60 to 200 Hz, and an induction of the magnetic field of 120 mT); the blood taken under gravity from the cubital vein into a container with anticoagulant (heparin) was exposed to a 10-min action of the magnetic field.

In the main group, there were 26 patients having rheumatoid arthritis whose cases had been diagnosed according to the criteria of the American Rheumatologic Association. All the patients underwent the course of EAHMT in combination with basis therapy and the administration of glucocorticosteroid and nonsteroid anti-inflammatory preparations. The average age was 48.3 ± 1.3 years; there were 22 females and 4 males in the group. As the control group of the analogous age and sex, we examined 12 people who took basis preparations, glucocorticosteroids, and nonsteroid anti-inflammatory preparations but had not undergone the EAHMT course.

Results and Their Discussion. As our investigations have shown, the constants η_∞ and τ_s of Eq. (2) are explicitly higher than normal ($p < 0.03$) in the patients having rheumatoid arthritis, while the constant $\dot{\gamma}_*$ is decreased ($p < 0.1$) (see Table 1). Upon exposure of the blood of such patients to a low-frequency magnetic field *in vitro*, we found no explicit changes in η_∞ for a standardized hematocrit (η was 3.32 ± 0.38 after the exposure to the magnetic field *in vitro*) and in τ_s (τ_s was 18.44 ± 2.03 after the exposure to the magnetic field *in vitro*); however, the value of $\dot{\gamma}_*$ significantly changed in a number of patients.

Depending on the initial indices $\dot{\gamma}_*$ we subdivided the main group of patients with rheumatoid arthritis into two subgroups. The initial indices $\dot{\gamma}_*$ were within the normal range in the first group (16 people), while $\dot{\gamma}_*$ was some-

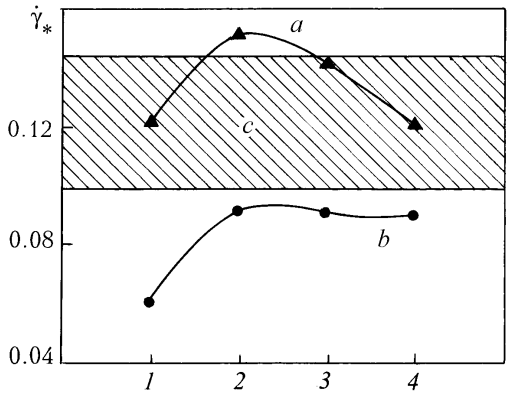

Fig. 2. Changes in the constant of the apparent kinetic rate of deformation of structural units $\dot{\gamma}_*$ during the process of EAHMT: 1) before exposure to the magnetic field; 2) after the EAHMT cycle; 3) within a week after the EAHMT cycle; 4) within a month after the EAHMT cycle; a) first subgroup; b) second subgroup; c) region of normal values.

what lower than the normal values in the second group (10 people). The exposure of the blood of the patients in the first subgroup to a low-frequency magnetic field exerted no influence on $\dot{\gamma}_*$; in the second subgroup the $\dot{\gamma}_*$ of the blood became explicitly higher after magnetic modification ($p < 0.001$), reaching the normal values (Fig. 1).

During the process of EAHMT, it was found out that the exposure to a low-frequency magnetic field, despite the relatively small volume of blood (100–150 ml) irradiated in each procedure, just as the exposure of the blood of the patients with rheumatoid arthritis to a magnetic field *in vitro*, leads to an explicit increase in the index $\dot{\gamma}_*$ in the second group from 0.06 ± 0.005 before the treatment to 0.09 ± 0.017 after four procedures ($p < 0.1$) (Fig. 2).

Virtually the same values of $\dot{\gamma}_*$ are preserved in these patients within both a week (0.09 ± 0.018) and a month (0.09 ± 0.009) after the completion of the EAHMT cycle, which may suggest fairly stable changes in the membrane structures of erythrocytes in exposure to the low-frequency magnetic field. Such changes in $\dot{\gamma}_*$ were not recorded in the control group ($p > 0.3$).

CONCLUSIONS

The results obtained indicate significant changes in the rheological properties of the blood of the patients having rheumatoid arthritis, which can be due to the influence of the magnetic field on the structure of the aggregates in the dispersion. The exposure to the magnetic field leads to a normalized constant of the apparent kinetic rate of destruction of structural units $\dot{\gamma}_*$, initially decreased in a number of patients having rheumatoid arthritis, but has no influence on this index if it is within the normal values, which suggests the differentiated nature of the action of the magnetic field. This feature of the action of the magnetic field (influence exclusively on the "affected" cells or on the cells exposed to the action of a certain pathologic agent) has repeatedly been discussed in the literature [16, 18, 19, 24–26] and, in the opinion of some authors, can be due to the fact that the influence of the magnetic field is somewhat informative in character, although the action of the magnetic field, similarly to that of any other physical factors, is based on the structural change with an indirect change in the function.

A low-frequency magnetic field does not possess a sufficient quantity of energy and cannot directly affect the electric potential of the membrane, however it changes the structure and function of the membrane, probably, due to the reorientation of molecules and their vibration and rotation (that can result in resonance phenomena), thus producing changes in the kinetics of biochemical reactions. Furthermore, the induced low-frequency electric fields can affect the motion of both free ions and ions linked with the membrane surface by the forces of electrostatic interaction [17, 22–29]. In [30], it has been noted that the osmotic stability caused by the action of the magnetic field on the erythrocyte membrane increases owing to the change in the surface electric charge of the membrane even for a strength of the variable magnetic field of 0.15 T, which leads to an increase in the transmembrane ionic channel. This can have a fa-

vorable effect on the apparent kinetic rate of destruction of structural units $\dot{\gamma}_*$. A decrease in this parameter signifies a reduction in the load on the human cardio-vascular system.

It may be useful to apply the obtained effects of the action of the magnetic field to the therapy not only of rheumatoid arthritis but also of a number of other diseases in whose pathogenesis the disturbance of the structure of the components of moving blood is of importance.

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NOTATION

b, Zakharchenko constant, $\sqrt{c}$; C_W, Williamson constant, or measure of curvature of the rheological curve, 1/sec; *k*, coefficient of consistency, $(\text{Pa}\cdot\text{sec})^{1/4}$; *n*, constant in the rheological models; $\dot{\gamma}$, gradient of the rate of shear, 1/sec; $\dot{\gamma}_*$, constant of the apparent kinetic rate of destruction of structural units, 1/sec; η_0, viscosity at the zero deformation rate, Pa·sec; η, apparent viscosity of blood, Pa·sec; τ_∞, shear stress at infinite deformation, Pa; η_∞, viscosity at an infinitely high rate of shear (hydrodynamic viscosity), Pa·sec; τ, shear stress, Pa; τ_0, limit shear stress, Pa; τ, plastic resistance, Pa; τ_s, strength of the structure formed by the shape elements of blood, Pa; τ_1, shear stress on the source side of viscous flow, Pa; Hct, hematocrit. Subscripts: p, plastic; s, structure.

REFERENCES

1. V. A. Levtov, S. A. Regirer, and N. Kh. Shadrina, *Rheology of Blood* [in Russian], Moscow (1983).
2. N. B. Ur'ev and A. A. Potanin, *Fluidity of Suspensia and Powders* [in Russian], Moscow (1992).
3. G. R. Cokelet, Y. C. Fung, N. Perrone, and M. Anliker, *Biomechanics. Its Foundations and Objectives*, New York (1972).
4. A. L. Chizhevskii, *Electric and Magnetic Properties of Erythrocytes* [in Russian], Kiev (1973).
5. B. Turczynski, G. Cieslar, A. Sieron, and M. Adamek, *The Effect of Variable Magnetic Field on Rheological Properties of Blood in Experimental Animals*, in: *Trans. 2nd Congr. Eur. Bioelectromagnetics Association*, December 9–11 (1993), pp. 79–80.
6. Y. Haik, V. Pai, and C.-J. Chen, *J. Magnetism Magn. Mater.*, **225**, No. 180b, 180–186 (2001).
7. L. Pauling and C. Coryell, *Proc. Natl. Acad. Sci.*, **22**, 210 (1936).
8. T. Higashi, A. Yamagishi, T. Takeuchi, N. Kawaguchi, S. Sagawa, S. Onishi, and M. Date, *Blood*, **82**, 1328 (1993).
9. A. Yamagishi, *J. Magn. Mater.*, **90**, 43 (1990).
10. A. N. Shalygin, S. B. Norina, and E. I. Kondorsky, *J. Magn. Mater.*, **31**, 555 (1983).
11. Y. Haik, V. Pai, C. J. Chen, W. Shyy, and R. Narayanan, *Fluid Dynamics at Interfaces*, Cambridge (1999).
12. M. Motta, Y. Haik, A. Gandahari, et al., *Bioelectrochem. Bioenerg.*, **47**, 297 (1998).
13. N. Nakano, J. Ostuka, and A. Tasaki, *Biochem. Biophys. Acta*, **278**, 355 (1972).
14. V. A. Nasonova and N. V. Bunchuk, *Rheumatic Diseases* [in Russian], Moscow (1997).
15. S. S. Bessmel'tsev, K. M. Abdulkadyrov, and Yu. L. Katsadze, *Efferent. Terap.*, **5**, No. 1, 34–40 (1998).
16. N. Bordyushkov, I. A. Goroshinskaya, and E. M. Frantsiyants, *Vopr. Med. Khim.*, **46**, No. 1, 72–80 (2000).
17. V. V. Lednev, *Bioelectromagnetics*, Vol. 12, 71–75 (1991).
18. R. de Seze, C. Bouthet, and S. Tuffet, *Bioelectromagnetics*, **14**, 405–412 (1993).
19. J. Walleczek and Th. F. Budinger, *Bioelectromagnetics*, **11**, 71–75 (1990).
20. S. A. Seleznev, G. I. Nazarenko, and V. S. Zaitsev, *Clinical Aspects of Microcirculation* [in Russian], Leningrad (1985).
21. A. L. Copley and C. R. Haung, *Biorheology*, **10**, 325 (1973).
22. P. Sherman (ed.), *Emulsion Science*, London–New York (1968).
23. J. A. Sirs, *J. Physiol.*, **442**, 569–583 (1991).
24. E. E. Sagalovich and E. V. Kil'chevskaya, *Information Leaflet of the Belarusian Scientific-Research Institute of Maternity and Childhood of the Ministry of Public Health of the Republic of Belarus, Scientific-Research Insti-*

tute of Radiobiology of the Academy of Sciences of Belarus, Belarusian State Polytechnic Academy [in Russian], Minsk (1998).
25. L. Bonhomme-Faivre, A. Mace, and Y. Benzie, *Life Sci.*, **62**, No. 14, 1271–1280 (1998).
26. A. Ubeda, M. Diaz-Enriquez, M. Martinez-Pascual, and A. Parreno, *Life Sci.*, **61**, No. 17, 1651–1656 (1997).
27. M. Blank, *Biosystems*, **35**, 175–178 (1995).
28. E. Lindstrom, A. Berglund, K. H. Mild, et al., *FEBS Lett.*, **370**, 118–122 (1995).
29. S. Paradisi, G. Donelli, M. T. Santini, et al., *Bioelectromagnetics*, **14**, 247–255 (1993).
30. M. A. Motta, A. M. Peixoto, Y. Haik, and C. Y. Chen, *Blood J.*, **35**, 321–326 (2000).