Hemorheological correlates of fitness and unfitness in athletes: Moving beyond the apparent "paradox of hematocrit"?

A. Gaudard [a,*], E. Varlet-Marie [a,*], F. Bressolle [a], J. Mercier [b] and J.-F. Brun [b,**]

[a] *Laboratoire de Pharmacocinétique clinique, Faculté de Pharmacie, BP 14491,
Université Montpellier I, 34093 Montpellier Cédex 5, France*
[b] *Service Central de physiologie Clinique, Centre d'Exploration et de réadaptation des Anomalies du
Métabolisme Musculaire (CERAMM), CHU Lapeyronie 34295, Montpellier Cédex 5, France*

Abstract. Negative correlations between blood viscosity parameters and fitness have been reported, but their physiological meaning remains incompletely understood. Since rheo-active treatments are used in athletes doping, we aimed at clarifying the relationships between hematocrit (Hct), viscosity and performance by comparing aerobic capacity, overtraining questionnaire, and hemorheological parameters. *Subjects and methods*: 29 sportsmen (24.71 ± 1.05 yr; 74.90 ± 1.44 kg; 178.5 ± 1.05 cm) underwent a standardised exercise test. Physical working capacity (W_{170}), maximal power output (W_{max}) and maximal oxygen consumption ($V_{O_2 \, max}$) were calculated. Viscometric measurements were done with a MT 90 Medicatest viscosimeter. Hct was measured with microcentrifuge. All subjects answered the overtraining questionnaire proposed by the French Society for Sports Medicine. *Results*: The best correlate of maximal power output (W_{max}) was whole blood viscosity ($r = -0.383$, $p < 0.001$). The stepwise regression analysis only selected Hct as W_{170} determinant ($r = -0.66$, $p < 0.001$). Similarly the best determinant of $V_{O_2 \, max}$, expressed as a percentage of theoretical values, was Hct ($r = -0.462$, $p = 0.01$). Hct/viscosity ratio (Hct/η), a proposed index of Hct's positive influence on O_2 transfer to tissues, was positively correlated to W_{max} expressed as a percentage of theoretical values ($r = 0.487$, $p = 0.02$). The overtraining score was correlated to plasma viscosity ($r = 0.450$, $p = 0.016$). *Conclusion*: The best hemorheological correlate of fitness is a low hematocrit and the best hemorheological correlate of overtraining is increased plasma viscosity.

Keywords: Exercise, rheology, viscosity parameters, physical working capacity, fitness, unfitness, overtraining, doping

1. Introduction

While one of the most popular doping procedures, namely erythropoietin (Epo), increases performance aside with a rise in systemic hematocrit (Hct) [1,2], exercise training results in a reduction in hematocrit, this parameter being actually negatively related with fitness [3–6]. Moreover, a moderate reversal of this low Hct pattern has been described in the early stages of the overtraining syndrome, i.e. a situation where performance decreases despite adequate or even intensified training.

In a preceding study [6], we therefore pointed out the paradox of this discrepancy between the negative relationship between Hct and fitness that is constantly found in physiological conditions and the general popular belief that increasing Hct (mostly with doping procedures or perfusion of autologous blood) is

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[*]A.G. and E. V.-M. have equally contributed to this work and should both be considered as first authors.
[**]Corresponding author: Dr. J.-F. Brun, MD, PhD, Service Central de Physiologie Clinique, Centre d'Exploration et de Réadaptation des Anomalies du Métabolisme Musculaire (CERAMM), CHU Lapeyronie 34295, Montpellier-cédex 5, France. Tel.: +33 04 67 33 82 84; Fax: +33 04 67 33 59 23; Telex: CHR MONTP 480 766 F; E-mail: drjfbrun.@aol.com.

a worthwhile mean to increase performance. This issue is strongly relevant in terms of health policy in athletes. For hemorheologists, there is no doubt that Hct is an important risk factor involved in the epidemiology of stroke, brain cognitive disorders, and peripheral vascular diseases [7–10]. Accordingly, it remains very surprising to notice that athletes that should be theoretically prone to a high incidence of vascular hazards, are also the winners of extremely difficult races in condition very close from (or even beyond) the limits of human physiology.

The aim of this study was therefore to further delineate in a separate sample of athletes the boundaries between hemorheological effects of adequate training (that increases performance) and overtraining (that decreases it), in order to further understand how Hct and blood viscosity (η_{blood}) can be considered as markers of fitness or unfitness.

2. Methods

2.1. Subjects

Subjects used in this study were 29 elite athletes: 22 footballers, 4 karate professionals, 2 volleyball players and 1 cyclist. (24.71 ± 1.05 yr; 74.90 ± 1.44 kg; 178.5 ± 1.05 cm; BMI 22.7 ± 0.77 kg/m^2). They were checked to be on good health and were free of medication.

This study was conducted according to the Declaration of Helsinki as amended in the 41st World Medical Assembly (Hong Kong, 1989). According to the French regulation, this study based on statistics performed on routine measurements did not require a specific approval of the local Ethics committee.

2.2. Exercise-test

Subjects underwent a standardized sub-maximal exercise session during 25 minutes on a cycloergometer (Bodyguard, Jonas Oglaend A.S., N 4310-Sandnes, Norway). Pedal was kept constant at 60 rpm during the test. The intensity of the exercise was progressively increased during the first 15 minutes. W_{170} (w/kg) was calculated as the work in watts that subjects were able to perform at a heart rate of 170 b/min [11]. The maximal oxygen uptake ($V_{O_2\,max}$) was calculated according to Astrand and Ryhming [12] as well as the maximal power output (W_{max}) according to the following equation:

$$W_{max} = (V_{O_2\,max} - V_{O_2\,rest})/10.3.$$

During the last 10 minutes, subjects were asked to cycle at 85% of the theoretical maximal heart rate assumed to be ($220 -$ age) [13]. W_{170}, $V_{O_2\,max}$ and W_{max} were expressed both as crude values and as percentages of the theoretical value expected for age, sex and anthropometry (respectively $V_{O_2\,max}$, $V_{O_2\,maxtheor}$ and $W_{max}/W_{maxtheor}$).

The exercise-test was preceded 2 hours before by a standardised breakfast [14] and was followed by a 10 minutes recovery. The breakfast was composed of bread (80 g), butter (10 g), jam (20 g), skimmed concentrated milk (80 ml) (Gloria SA, Paris, France), sugar (10 g) and powder coffee (2.5 g). It comprised 2070 kilojoules with 9.1% proteins, 27.5% lipids, and 63.4% carbohydrates.

2.3. Measurements

Blood samples were drawn after an overnight fast in order to measure plasma ferritin, hematocrit and hemorheological parameters [15].

Plasma ferritin was measured by the solid-phase two-site immunoradiometric assay kit FER-CTRIA. Assay sensitivity, defined as the amount significantly different from zero with a probability of 95%, is 1 ng/ml. With this assay, normal values for men range between 75 and 300 ng/ml.

Samples for hemorheological measurements (7 ml) were drawn with potassium EDTA as the anticoagulant in a vacuum tube Vacutainer. Viscosimetric measurements were done at very high shear rate ($1,000$ s^{-1}) with a falling ball viscosimeter (MT 90 Medicatest, F-68280 Saint Benoît) [16,17]. Accuracy of the measurements was regularly controlled with the Carrimed Rheometer "CS" (purchased from Rheo, 91120 Palaiseau, France) [18]. The precision of this method ranges between 0.6 and 0.8% [19]. We measured with this device apparent viscosity of whole blood at native hematocrit, plasma viscosity, and blood viscosity at corrected hematocrit (45%) according to the equation of Quemada [20]:

$$\eta_{\text{blood}} = \eta_{\text{pl}}(1 - 0.5k \times \text{Hct})^{-2},$$

where η_{blood} is the whole blood viscosity, η_{pl} is the plasma viscosity, k is the index of erythrocyte rigidity of Quemada and Hct is the native hematocrit.

Hematocrit was measured with microcentrifuge. The hematocrit/viscosity (Hct/η) ratio, an index of oxygen supply to tissues, was calculated according to Chien [21] and Stoltz [22], with hematocrit (as percentage) divided by viscosity at high shear rate determined as described above.

The Dintenfass "Tk" index of erythrocyte rigidity was calculated [23,24] according the following formula:

$$\text{Tk} = \frac{\eta_{\text{r}}^{0.4} - 1}{\eta_{\text{r}}^{0.4} \times \text{Hct}},$$

where η_{r} is the ratio $\eta_{\text{blood}}/\eta_{\text{pl}}$.

RBC aggregation was measured using two well-standardized methods. The first one was the Myrenne aggregometer [25] which gives two indices of RBC aggregation: "M" (aggregation during stasis after shearing at 600 s^{-1}) and "M1" (facilitated aggregation at low shear rate after shearing at 600 s^{-1}). The second one was the SEFAM aggregometer which is based upon the experiments of Mills [26] on cell disaggregation behavior in shear flow. This device measures the changes in backscattered light which are observed when sheared RBC suspensions are abruptly brought to a full stop. The decrease in the optical signal reflects the formation of RBC aggregates. Some parameters are derived from the curve of light intensity as a function of time. The aggregation time is the reciprocal of the initial slope (calculated between 0.5 and 2 sec after the shear has stopped). The aggregation index at 10 seconds (S_{10}) is a measurement of the extent of erythrocyte aggregation and is the relative surface area above the curve calculated over the first 10 seconds. The aggregation index at 60 seconds (S_{60}) represents the same value measured at 60 seconds. This device measures also disaggregation thresholds, by submitting blood to a succession of shear rates from 600 s^{-1} to 7 s^{-1}. The total disaggregation threshold (γ_{S}) is the shear rate below which the backscattered light intensity starts to decrease, indicating that the shear stress applied to aggregates is no longer sufficient for allowing complete dispersion of RBC aggregates. The partial disaggregation shear rate (γ_{D}) is defined as the shear rate corresponding to the intersection point of the two asymptotes drawn from the extremes (maximum and minimum shear rate). Fibrinogen was assayed with the Von Clauss method.

Body composition was assessed with a multifrequency bioelectrical impedancemeter Dietosystem Human IM Scan that uses low intensity (100–800 μA) at the following frequencies: 1, 5, 10, 50, and

100 kHz. Analysis was performed with the software Master 1.0 that gives the choice among 25 published equations for body composition calculations (body water, fat mass...) [27,28].

Handgrip and adductor isometric strength were measured using home-made dynamometers [29,30].

2.4. Overtraining questionnaire

All subjects answered a standardised questionnaire developed by the French consensus group on overtraining proposed by the French Society for Sports Medicine in order to quantify the early clinical symptoms of the overtraining syndrome [31]. This questionnaire includes 54 items; the number of positive items gives a numerical "score" that helps to evaluate the degree of exercise overload in sportsmen submitted to a heavy training program.

2.5. Statistics

Values are presented as mean value ± standard error (SE). We used the software package Statview (Jandel Corporation, San Rafael, USA).

In a first step, a stepwise analysis was performed. In a second step, we chose the better model that rely the correlation found in first step. Correlations were performed by Pearson analysis and multiple regression analysis. The relationship between different variables and the choice of the best model were determined on the basis of the correlation coefficient value and the statistical significance. Significance level was defined as $p < 0.05$. The relationship between hemorheologic parameters (Hct, η_{pl}, and η_{blood}) and (i) power output (W_{max} and W_{170}) (ii) $V_{O_2 max}$ and (iii) overtraining score (OTS) were explored.

Normality of parameters was assessed with the normality test of Kolmogorov and Smirnov. This test gives a K–S distance and a p value that allow to conclude that the test "passes" or "fails". A test that fails indicates that the data varies significantly from the pattern expected if the data was drawn from a population with a normal distribution. A test that passes indicates that the data matches the pattern expected if the data was drawn from a population with a normal distribution. When the distributions is not normal, corresponding values are log-transformed. Distribution of viscosity factors and OTS was performed by means of the box-and-whisker plot (BWP) procedure. Box and whisker plots combine statistical techniques and graphical displays for studying symmetry, checking distribution assumptions and for detecting outliners. Box-plots divide the data into three classes according to its quartiles. A central line inside the box indicates the median value. The central box (second quartile) encloses the middle 50% of the data values between the lower and upper quartiles. The underline (called whisker) extends from the lower end of the box (lower quartile or first quartile) or to the smallest data point. The other whisker extends from the highest end of the box (upper quartile or third quartile) to the largest data point. Lower and upper quintiles were compared using the Student's t-test. A value of $p < 0.05$ was considered as significant.

3. Results

3.1. Parameters values

Parameters values are presented as mean ± standard error (SE) in Table 1.

Table 1
Values (mean value $\pm$ SEM) of parameters in studied subjects

Parameters[*]	Values $\pm$ SEM
W_{170} (watt/kg)	2.93 ± 0.11
$V_{O_2\,max}$ (ml.min^{-1}.kg^{-1})	50.01 ± 2.20
W_{max}	343.10 ± 22.22
Ferritin (ng/ml)	78.51 ± 9.53
Whole blood viscosity (mPas.s)	2.84 ± 0.05
Plasma viscosity η_{pl} (mPas.s)	1.37 ± 0.02
Corrected viscosity η_{45} (mPas.s)	3.10 ± 0.05
Hct (%)	41.43 ± 0.45
H/viscosity	14.71 ± 0.32
RBC rigidity Tk	0.60 ± 0.02
RBC aggregation "M"	4.62 ± 0.38
RBC aggregation "M1"	9.13 ± 0.46
TA (s)	3.45 ± 0.39
S_{10}	21.21 ± 1.13
S_{60}	38.42 ± 1.01
γ_S (s^{-1})	65.06 ± 5.48
γ_D (s^{-1})	96.91 ± 9.88
Fibrinogen (g/l)	2.39 ± 0.101
Z 1 kHz (Ω)	595.69 ± 13.35
Z 5 kHz (Ω)	558 ± 11.33
Z 10 kHz (Ω)	534.71 ± 11.73
Z 50 kHz (Ω)	461.78 ± 9.22
Z 100 kHz (Ω)	425 ± 9.25
Total water (l)	46.91 ± 0.921
Fat (%)	12.74 ± 0.336
Strength (handgrip) (N)	520.60 ± 24.84
Strength (adductors) (N)	793.69 ± 125.53
Overtraining score	7.24 ± 1.39

[*]Hematological and hemorheological parameters have been measured at rest before exercise. Aerobic capacity and strength have been measured after a standardised test-exercise. The overtraining score is the result of a standardised questionnaire proposed by the French Society of Sport Medicine.

3.2. Correlations

The stepwise analysis only selected Hct as determinant of W_{170}. Hct/η, η_{blood}, η_{pl} and Tk were not added to the ability of the equation to predict W_{170} and were not included in the final equation. $V_{O_2\,max}$ can be predicted from a linear combination of Hct. Hct/η, η_{blood}, η_{pl} and Tk were excluded by the stepwise analysis. Hct was conserved by the analysis as determinant of $V_{O_2\,max}$ expressed as percentage of theoretical values.

In the whole group of 29 subjects, we found negative correlations between W_{170} and Hct ($r = -0.66$, $p < 0.001$) (Fig. 1a), and $V_{O_2\,max}$ (expressed as a the percentage of theoretical values, $V_{O_2\,max}/V_{O_2\,maxtheor}$) and Hct ($r = -0.462$, $p = 0.01$) (Fig. 1b). The best correlations were found with
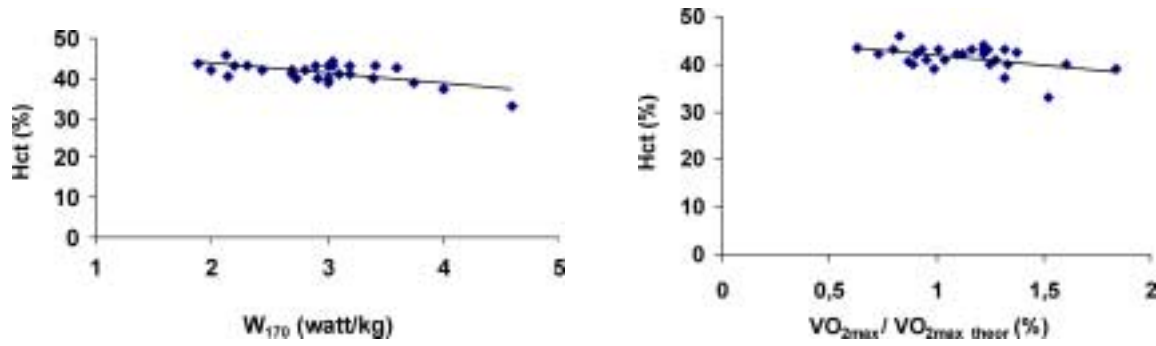
Fig. 1. Correlations in athletes, during an exercise-test, between hematocrit (Hct) and (a) the work in watts that subjects are able to perform at a heart rate of 170 b/min (W_{170}) ($r = -0.66$, $p < 0.001$) and (b) the ratio between maximal oxygen uptake and its theoretical value ($V_{O_2 max}/V_{O_2 maxtheor}$) ($r = -0.462$, $p = 0.01$). These correlations show that fitness is negatively related to Hct.
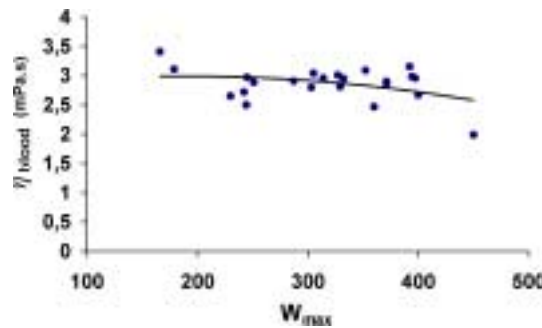

Fig. 2. Negative correlation between the aerobic working capacity (W_{max}) and whole blood viscosity (η_{blood}) in athletes while training ($r = -0.385$, $p = 0.01$).

linear relationship corresponding to the following equations:

$$\text{Hct} = 49.2 - 2.65W_{170},$$

$$\text{Hct} = 46.71 - 4.173V_{O_2 max}/V_{O_2 maxtheor}.$$

A correlation between W_{max} and η_{blood} was performed by linear regression analysis ($r = -0.393$, $p = 0.05$) (Fig. 2) The best correlation was found with a polynomial relationship corresponding to the following equation:

$$\eta_{blood} = 2.7727 + 6 \times 10^{-6}W_{max}^2 + 0.0023W_{max}.$$

We found also a correlation between W_{max} expressed as a percentage of theoretical values ($W_{max}/W_{maxtheor}$) and Hct/η with a linear relationship (Fig. 3):

$$\text{Hct}/\eta = 10.7555 + 3.3413W_{max}/W_{maxtheor} \quad (r = 0.487, \ p = 0.02).$$

This correlation must be considered carefully because one subject is an outliner. If we exclude him, we do not longer found the Pearson product moment correlation ($r = 0.078$, $p = 0.735$). This subject is a
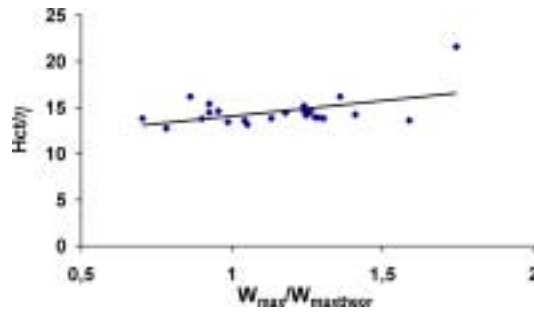
Fig. 3. Negative correlation between hematocrit/blood viscosity ratio (Hct/η) and the ratio between aerobic working capacity W_{max} and its theoretical value ($W_{max}/W_{maxtheor}$) ($r = -0.4872$, $p = 0.02$).
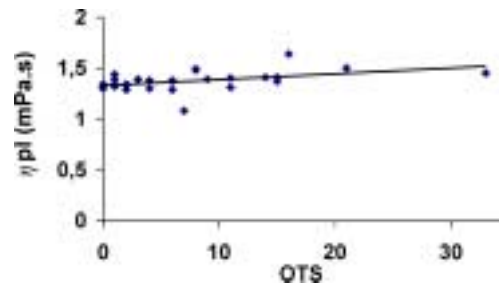

Fig. 4. Correlation between plasma viscosity (η_{pl}) and overtraining score (OTS) ($r = 0.450$, $p = 0.016$) showing that over-training is positively related to plasma viscosity.

football player (29 years old; 61 kg; 170 cm; 21.5 kg/m^2). He presents the following hematological and biological characteristics: Hct 43%, η_{blood} 1.99 mPa.s, W_{max} 450, W_{170} 3.2, $V_{O_2 max}$: 49, Hct/η 21.61, $V_{O_2 max}/V_{O_2 maxtheor}$: 1.23. We have no particular reason to exclude him from the test.

OTS was also found to be correlated to η_{pl} according to a linear relationship (Fig. 4):

$$\eta_{pl} = 1.331 + 0.057 \text{ score} \quad (r = 0.450, \ p = 0.016).$$

3.3. Box-and-Whisker Plot (BWP) procedure

η_{blood} exhibits a normal distribution with the Kolmogorov–Smirnov test (K–S distance = 0.1305, $p = 0.2286$, passed). By contrast, most hemorheological parameters as well as OTS exhibit a non-normal distribution: Hct (K–S distance = 0.0785, $p = 0.0189$, failed), Hct/η (K–S distance = 0.2058, $p = 0.0029$, failed), Tk (K–S distance = 0.2005, $p = 0.0054$, failed), TA (K–S distance = 0.1865, $p = 0.001$, failed), γ_D (K–S distance = 0.2545, $p = 0.0015$, failed), ferritin (K–S distance = 0.1706, $p = 0.0306$, failed) and OTS (K–S distance = 0.1679, $p = 0.0357$, failed). η_{pl}, M, M1, S$_{10}$, S$_{60}$, γ_S and fibrinogen exhibit a normal distribution: η_{pl} (K–S distance = 0.1590, $p = 0.0677$, passed), M (K–S distance = 0.1216, $p = 0.448$, passed), M1 (K–S distance = 0.1401, $p = 0.3950$, passed), S$_{10}$ (K–S distance = 0.1193, $p = 0.5837$; passed), S$_{60}$ (K–S distance = 0.0984; $p = 0.7944$; passed), γ_S (K–S distance = 0.1770, $p = 0.1178$, passed) and fibrinogen (K–S distance = 0.1239, $p = 0.5342$, passed). W_{max}, W_{170} and $V_{O_2 max}$ were also normally distributed: W_{max} (K–S distance = 0.1310, $p = 0.4889$, passed), W_{170} (K–S distance = 0.1219, $p = 0.3163$, passed), $V_{O_2 max}$ (K–S distance = 0.1742, $p = 0.0960$, passed) and $V_{O_2 max}/V_{O_2 maxtheor}$ (K–S distance = 0.1025, $p = 0.5599$, passed).
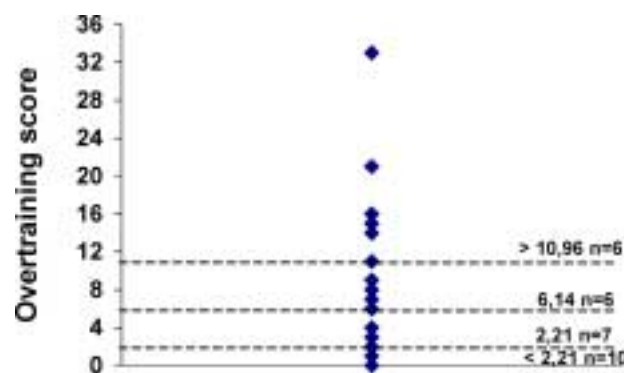
Fig. 5. Distribution of the overtraining score (OTS) among the 29 athletes included in the study and divided into quartiles after log-transformation. When OTS is superior or equal to 6, subjects are tired and, above 11, they are overreached. n: number of subjects of the quartile.

Table 2

Comparison of anthropometric characteristics of study subjects (mean $\pm$ SEM) classified in 4 quartiles of overtraining score (OS)

Quartile of OS	Age (years)	Weight (kg)	Height (m)	BMI (kg/m^2)	Fat mass (%)
Lowest <2.21 ($n = 10$)	25.1 ± 2.29	75.23 ± 2.68	178.7 ± 1.76	23.52 ± 0.49	12.89 ± 0.48
2.21–6.14 ($n = 7$)	24.29 ± 1.52	74.6 ± 2.60	177.6 ± 2.36	23.61 ± 0.33	12.76 ± 0.86
6.14–10.96 ($n = 6$)	23.69 ± 2.29	74.6 ± 2.21	179.2 ± 2.98	23.27 ± 0.57	12.07 ± 0.76
Highest >10.96 ($n = 6$)	25.58 ± 2.33	74.96 ± 4.48	178.67 ± 2.78	23.45 ± 0.91	13.15 ± 0.78
Statistical comparison	NS	NS	NS	NS	NS

n: number of subjects in the quartile; NS: no statistical difference between the quartiles.

The non-normal distribution pattern of OTS prompted us to use a log transformation prior to define quartiles of distribution. The distribution became normal using the log transformation procedure (K–S distance = 0.1321, $p = 0.2776$, passed). Thus, the limit of the upper quartile was 10.96, and the limit of the lower quartile was 2.21 (Fig. 5).

Comparison of general characteristics of study subjects is shown Table 2. They remained the same whatever the quartile.

Comparison of hemorheological parameters across the quartiles of distribution of OTS are presented Table 3. When the subgroup with high OS (OS > 10.96) was compared with the subgroup with low OS (OS < 2.21), subjects in the high OS subgroup were shown to have a higher Hct (42.67 ± 0.60 vs 40.4 ± 1.02, $p = 0.02$), a lower η_{pl} (1.46 ± 0.04 vs 1.34 ± 0.01, $p < 0.006$), a lower Tk (0.5 ± 0.05 vs 0.65 ± 0.01, $p = 0.02$) and a lower ferritin concentration (48.3 ± 9.29 vs 98.1 ± 17.3, $p = 0.04$) (Fig. 6).

Since η_{pl} is the only hemorheological parameter positively related to OTS, we tried to defined also quartiles of distribution of η_{pl}. The boundary of the upper quartile of η_{pl} was 1.41 mPa.s. OTS was higher (14.5 ± 4.67) in the 6 subjects whose η_{pl} was > 1.41 mPa.s than in the 23 others (5.35 ± 1.03) ($p < 0.037$).

These results can also be expressed in terms of sensitivity and specificity of η_{pl} for predicting the overtraining syndrome. As 10.96 is the lower limit of the higher quartile, we take this value as an indicator of overreaching. When OTS is superior or equal to 6, we talk about tiredness, above 11 about overreaching, and above 32 about stillness. Among 8 "overeached subjects", there were 3 subjects with η_{pl} > 1.41 mPa.s and 5 with η_{pl} < 1.41 mPa.s. Among the 21 others with "normal" OTS, there were only

Table 3
Comparison of hemorheological parameters of study subjects (mean $\pm$ SEM) classified in 4 quartiles of viscosity sensitivity

Quartile of OS	Hct	Ratio Hct/viscosity	η_{blood}	η_{45}	Plasma viscosity	Tk	M
Lowest <2.21	40.4 ± 1.02	13.97 ± 0.27	2.89 ± 0.05	3.27 ± 0.07	1.34 ± 0.01	0.65 ± 0.01	5.43 ± 0.56
2.21–6.14	41.43 ± 0.65	14.12 ± 0.29	2.94 ± 0.05	3.16 ± 0.08	1.35 ± 0.02	0.64 ± 0.09	3.98 ± 0.84
6.14–10.96	42.42 ± 0.89	15.16 ± 0.69	2.82 ± 0.15	2.87 ± 0.12	1.36 ± 1.46	0.58 ± 0.03	4.35 ± 0.84
Highest >10.96	42.67 ± 0.60	16.19 ± 1.12	2.47 ± 0.15	2.94 ± 0.07	1.46 ± 0.04	0.5 ± 0.05	4.47 ± 0.81
Comparison highest quartile vs lowest	$p = 0.02$	$p = 0.015$	NS	NS	$p < 0.006$	$p = 0.02$	NS

Quartile of OS	M1	TA	S_{10}	S_{60}	γ_S	γ_D	Ferritin	Fibrinogen
Lowest <2.21	9.91 ± 0.84	2.65 ± 0.22	22.1 ± 1.95	38.71 ± 0.97	64.59 ± 9.26	85.5 ± 23.66	98.1 ± 17.3	2.33 ± 0.11
2.21–6.14	8.37 ± 0.98	4.52 ± 1.05	18.83 ± 1.97	36.7 ± 1.88	83.88 ± 12.4	46.45 ± 2.28	95.8 ± 25.31	2.35 ± 0.41
6.14–10.96	9.27 ± 0.98	3.25 ± 0.86	24.22 ± 2.36	41.5 ± 2.95	56.9 ± 5.49	76.75 ± 22.6	55.8 ± 9.64	2.62 ± 0.19
Highest >10.96	8.27 ± 0.26	3.41 ± 0.60	19.9 ± 3.17	37.13 ± 2.77	46.2 ± 5.78	44.66 ± 9.26	48.3 ± 9.29	2.26 ± 0.17
Comparison highest quartile vs lowest	NS	NS	NS	NS	NS	NS	$p = 0.04$	NS

Hct: venous hematocrit; η_{blood}: whole blood viscosity; η_{45}: corrected viscosity at Hct 45%; Tk: erythrocyte rigidity index; M and M1: erythrocyte aggregation indices calculated respectively at stasis and low shear rate with the Myrenne; TA, S10 and S60: parameters quantifying erythrocyte aggregability with the SEFAM AFFIBIO erythroaggregometer; γ_S: total disaggregation threshold; γ_D: partial disaggregation threshold. NS: no statistical difference between the quartiles.

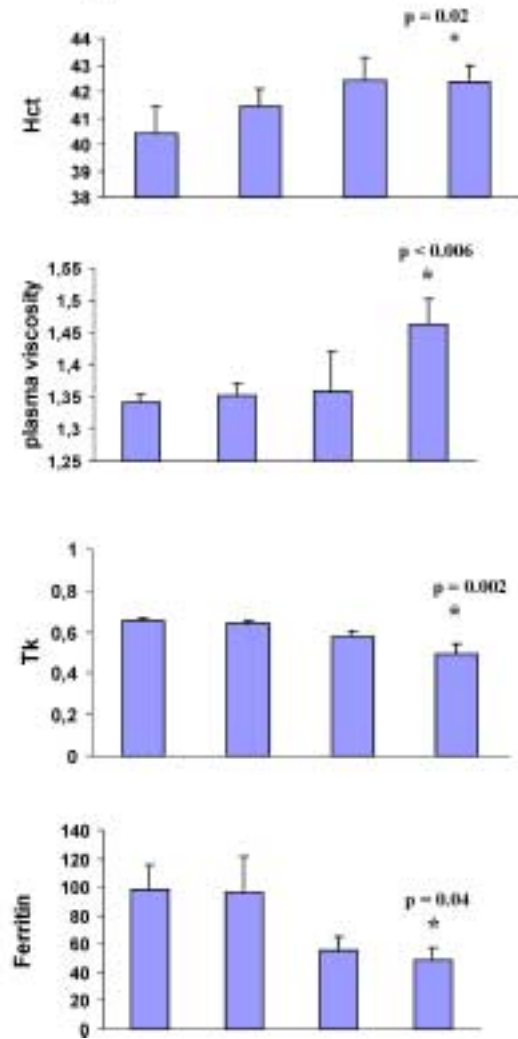**Overtraining score   2.21   2.21/6.14   6.14/10.96   10.961**

Fig. 6. Comparison of mean values ($\pm$SEM) of hemorheological parameters in the 4 quartiles of distribution of overtraining score (*comparison of parameters between the highest quartile of overtraining score and the lowest one).

3 with $\eta_{pl} > 1.41$ mPa.s and 18 with $\eta_{pl} < 1.41$. Thus, the sensitivity of η_{pl} for detecting overtraining syndrome is $3/8 = 37.5\%$, the specificity $18/21 = 85.7\%$, the positive predictive value $3/(3+3) = 50\%$ and the negative predictive value $18/(5 + 18) = 78.2\%$.

4. Discussion

This study analyses the relationship between various measurements of aerobic working capacity and factors of blood viscosity. It shows that all these parameters are negatively correlated with viscosity factors. While the analysis only selects η_{blood} as a predictor of maximal aerobic power, Hct is the best correlate of both $V_{O_2 \, max}$ and W_{170}. Besides, there is a positive correlation between η_{pl} and OTS.

Therefore, we further confirm the "paradox of hematocrit". In physiological conditions, fitness is associated with a low Hct, while overtraining is associated with a mild hyperviscosity syndrome. Obviously, this finding does not rule out the fact that anaemia may frequently occur in athletes as a consequence of iron depletion and be associated with a low Hct/low performance pattern [32]. By contrast, a high Hct/high performance pattern is clearly a non-natural situation which can probably not result from normal training and is likely to reflect, most of the time, doping procedures. As pointed out in a preceding paper of our group [6], when Hct reaches the upper quintile of distribution, i.e. values close from 50%, performance is likely to decrease.

Actually, the "paradox of hematocrit" is no longer a paradox if we try to understand it with the new paradigms proposed by H. Schmid-Schönbein [33] and based upon the percolation theory. If we assumed, according to classical circulatory physiology, a linear relationship between viscosity factors and muscle hemodynamics, it is very surprising to notice that doped athletes, with high Hct and presumably increased blood viscosity, are actually able to achieve remarkable performances. By contrast, the concept of a non-linear influence of viscosity factors described by the percolation theory makes all this very easy to understand.

Briefly, the application of the percolation theory to hemorheology means that (a) whole blood viscosity by its own is not a relevant factor in microcirculation; (b) in high shear/high flow situations, Hct and erythrocyte rheology do not markedly influence circulatory parameters; (c) by contrast, these parameters are critical in low flow/low shear conditions. In others terms, in the exercising muscle, blood rheology has little circulatory influence, and the most relevant hemorheological factor that is able to increase local resistance is plasma viscosity. By contrast, at rest, high Hct is likely to promote a self-potentiating viscidation process that may markedly impede local flow. It is interesting to point out that this theoretical description is in agreement with the clinical picture of Epo-doped athletes that are both extremely fit at exercise and prone to venous insufficiency [34].

We think that this new theoretical background gives a new interest to the large body of hemorheological literature that supports the concept of the "paradox of hematocrit". This paradox would be in fact explained by the strong influence of flow conditions on the circulatory effects of Hct. Hct would be, according to this theory, a factor of viscosity at rest and a factor of increased O_2 transfer to tissues in the high flow/high shear conditions of exercise. Although further studies are needed to fully demonstrate this interpretation, we think that it provides a satisfactory explanation of what was previously presented as a paradox.

In addition, we confirm our previous finding [35] of a mild hyperviscosity syndrome in the early stage of overtraining. As previously reported [35–38], the self-administered questionnaire developed in French language by the consensus group on overtraining of the French Society for Sports Medicine (SFMS) is able to detect early stages of this complex situation where performance begins to decrease despite maintained or even intensified training, i.e. a situation usually referred as "overreaching". This questionnaire gives a "score" which is correlated to various biological parameters [36,37,39]. Interestingly, in the current study, the best correlate of this score is plasma viscosity.

Plasma viscosity may be linked to overtraining by several ways. First, as stated above, it is, according to a physiological interpretation of muscle circulatory physiology based on the percolation theory, the most relevant factor of blood viscosity for muscle, with an effect which can be expected both at rest and during exercise. In addition, it is clearly the mirror of plasma composition, and thus reflects both the hydration status and the inflammatory response, two important sides of the overtraining syndrome [35].

Interestingly, red cell rigidity, which is increased in most hyperviscosity syndromes, is not increased in overreaching and actually appears to be significantly decreased. Perhaps a different picture would be

found in more severe conditions of overtraining. Our subjects exhibiting a score higher than 11 represent a rather moderate situation of overtraining, yet they already have higher plasma viscosity and higher Hct. Thus, a higher red cell deformability index may indicate that they are more intensively trained than the other athletes, and that this level of intense training is still beneficial for erythrocyte deformability. A beneficial effect of intense training on erythrocyte deformability has already been reported in several studies [40–42].

On the whole, this study further confirms that fitness is physiologically associated with a low Hct, a condition which is perhaps not critical for optimal blood supply in exercising muscle, but which is likely to be beneficial in the resting athlete and possibly to play a role in the protective effects of regular exercise. Given the new theoretical background provided by the percolation theory, these aspects will require specific studies that will help to resolve the so called "paradox of hematocrit in athletes". In addition, blood rheology is impaired when athletes report signs of overreaching; the factor of viscosity that appears the most clearly related to this situation is plasma viscosity, i.e. a factor of viscosity which is likely to influence microcirculation both at rest and during exercise.

To summarise all this more briefly, the hemorheological correlate of high aerobic working capacity is low hematocrit and the hemorheological correlate of overtraining is high plasma viscosity.

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