

Reprint from

RECENT ADVANCES
IN DOPING ANALYSIS
(7)

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Sport und Buch Strauß, Köln, 1999

K.I. BIRKELAND, K. FISKUM, B. BJERKE, E. HAUG, P. HEMMERSBACH:
Physiological and non-Physiological Variations in Serum Levels of Soluble Transferrin
Receptor - Implications for Use as Indicator of Doping with rhEPO
In: W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (eds.) Recent advances in doping
analysis (7). Sport und Buch Strauß, Köln, (1999) 289-290

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Physiological and non-physiological variations in serum levels of soluble transferrin receptor - implications for use as indicator of doping with rhEPO.

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We and others have previously shown that administration of recombinant erythropoietin (rhEPO) to healthy athletes increase serum levels of soluble transferrin receptors (sTfR) significantly due to the effect of rhEPO on erythropoiesis. In search for indirect markers of doping with rhEPO, sTfR is therefore a possible candidate.

If sTfR is to be used as an indicator of doping with rhEPO, it is important to investigate the effect on this parameter of various physiological and pathological conditions. It is particularly important to measure sTfR in a large number of athletes presumably free from doping with rhEPO.

In the present study we measured serum levels of EPO with an immunochemoluminometric method (Nichols Inst. Diagnostics, San Juan Capistrano, CA, USA) and sTfR with an immunoenzymometric method (Orion Diagnostica, Espoo, Finland) in 1) a subset of athletes that was tested in doping control in Norway during the last year (n=172), 2) in 26 athletes during high altitude training, 3) in 12 athletes repeatedly tested during one week in a low-oxygen-pressure chamber, and 4) in a small group of patients with anaemia (n=5).

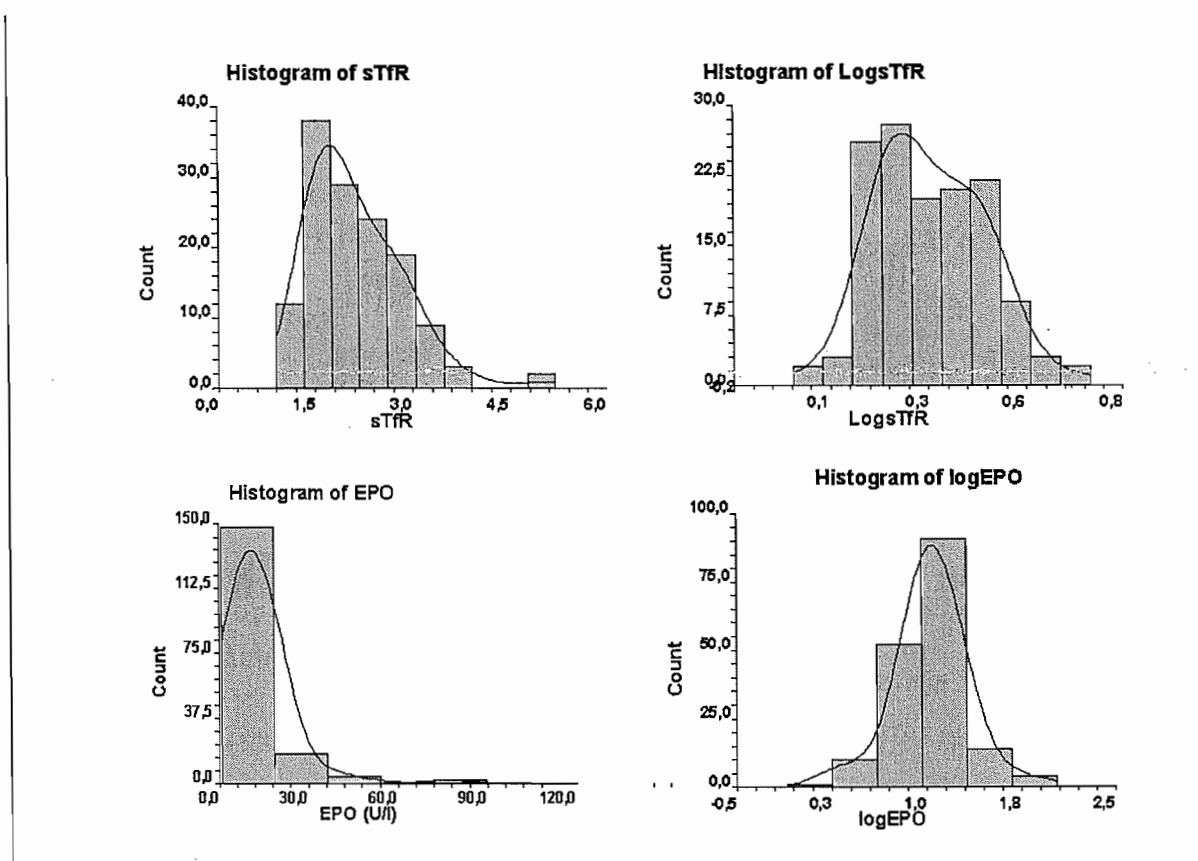
In healthy athletes the distributions of EPO and sTfR were log-normal, with a geometric mean of EPO that was 10.9 U/l, and of sTfR 2.0 mg/l (fig 1). Using the geometric mean +3SD as a cut-off limit, we defined a normal upper limit that was 86 U/l for EPO and 5.3 mg/l for sTfR. None of the athletes had a sTfR value that was above this limit, and only one had an EPO-level that exceeded this limit.

During training in high altitude, repeated measures of EPO and sTfR showed increasing values in most subjects and two athletes achieved sTfR ≥ 5.3 mg/l.

During seven days in a low-oxygen chamber, the median level of EPO increased from 7.4 to 11.8 U/l and sTfR from 1.8 to 2.1 mg/l (both $p < 0.05$), and the one with the highest level of sTfR had an increase from 2.3 to 3.0 mg/l.

Finally, to illustrate the magnitude of the response in these parameters of serious illness, we measured sTfR and EPO in a small group of patients with anaemia, and found EPO-levels between 40.4 and 1067 U/l and sTfR between 6.0 and 14.7 mg/l.

In conclusion, we find that the use of sTfR alone is not sufficiently specific as a marker for doping with rhEPO, mainly because training in high altitude might increase serum levels of sTfR to a similar degree as doping with moderate doses of rhEPO.



Figur 1. Distribution of soluble transferrin receptor (sTfR) and erythropoietin (EPO) in normal athletes measured during doping control.