

References

1. Browne A, Lachance V, Pipe A. The ethics of blood testing as an element of doping control in sport. *Med Sci Sports Exerc* 1999; 31:497-501.
2. Macdougall IC. Novel erythropoiesis stimulating protein. *Semin Nephrol* 2000; 20:375-81.
3. Chang MSC. Blood substitutes. Switzerland: Karger AG. 1997.
4. Parisotto R, Gore CJ, Emslie KR, Ashenden MJ, Brugnara C, Howe C, et al. A novel method utilizing markers of altered erythropoiesis for the detection of recombinant human erythropoietin abuse in athletes. *Haematologica* 2000; 85:564-72.
5. Parisotto R, Wu M, Ashenden MJ, et al. Detection of recombinant human erythropoietin abuse in athletes utilizing markers of altered erythropoiesis. *Haematologica* 2001; 86:128-37.
6. Lasne F, de Ceaurriz J. Recombinant erythropoietin in urine. *Nature* 2000; 405:635.
7. Berglund B, Hemmingsson P, Birgegard G. Detection of autologous blood transfusions in cross-country skiers. *Int J Sports Med* 1987; 8:66-70.

Further concerns about the medical risks of blood doping

This journal and its editor strongly oppose the spreading phenomenon of blood doping in sport.¹⁻³ Some time ago we wrote: «As hematologists, over the next years we could face problems related to blood doping with increasing frequency: atypical cases of iron overload, erythrocytosis of unknown origin, unexplained anemias, atypical thromboembolic complications, and so on».¹

Recent observations emphasize the medical risks of blood doping, in particular those related to the abuse of recombinant human erythropoietin (rHuEpo). Casadevall *et al.*⁴ have recently identified 22 cases of pure red-cell aplasia in patients with chronic renal failure who were receiving rHuEpo. These individuals develop anti-erythropoietin antibodies that neutralize both rHuEpo and endogenous erythropoietin, thus producing severe PRCA. These patients become totally transfusion-dependent and apparently do not respond to erythropoietin molecules other than that used before development of PRCA.⁴ Additional cases have been independently reported.⁵

It must be clearly said that this risk is very low in renal patients (less than 1:10,000), and probably even lower in patients with anemia of malignancy

receiving chemotherapy, so that this adverse event should be borne in mind by clinicians but should not prevent the vast majority of patients from benefiting from a treatment that can improve quality of life and prolong survival.

Doping with erythropoietin is a totally different issue. Athletes are healthy individuals who do not need any treatment. They abuse rHuEpo or related drugs to win games unfairly and earn money illicitly. Any medical risk related to drug abuse is unacceptable by definition: to realize this, simply consider to the drama of a (theoretical) young vigorous man who abuses rHuEpo to increase his red cell mass and athletic performance, develops PRCA and becomes transfusion-dependent for the rest of his life. According to current rumors, endurance athletes have started abusing darbepoetin alpha (Aranesp): since this molecule differs markedly from endogenous erythropoietin, the risk of developing cross-reacting antibodies on long-term abuse cannot be excluded *a priori*.⁶

Finally, we totally agree with the conclusion of Casadevall *et al.*⁴ that the severity of rHuEpo-induced PRCA argues also against the use of this drug for unlicensed indications.

Mario Cazzola, M.D.
Department of Hematology,
University of Pavia Medical School,
27100 Pavia, Italy

References

1. Cazzola M. A global strategy for prevention and detection of blood doping with erythropoietin and related drugs. *Haematologica* 2000; 85:561-3.
2. Parisotto R, Gore CJ, Emslie KR, Ashenden MJ, Brugnara C, Howe C, et al. A novel method utilizing markers of altered erythropoiesis for the detection of recombinant human erythropoietin abuse in athletes. *Haematologica* 2000; 85:564-72.
3. Parisotto R, Wu M, Ashenden MJ, Emslie KR, Gore CJ, Howe C, et al. Detection of recombinant human erythropoietin abuse in athletes utilizing markers of altered erythropoiesis. *Haematologica* 2001; 86:128-37.
4. Casadevall N, Nataf J, Viron B, Kolta A, Kiladjian J-J, Martin-Dupont P, et al. Pure red-cell aplasia and antierythropoietin antibodies in patients treated with recombinant erythropoietin. *N Engl J Med* 2002; 346:469-75.
5. Important safety message: Epex (epoetin alpha): reports of pure red cell aplasia (PRCA). Bucks, United Kingdom: Janssen Cilag, 2001 (memorandum).
6. Bunn HF. Drug-induced autoimmune red-cell aplasia. *N Engl J Med* 2002; 346:522-3.