Blood doping

$\dot{V}O_2MAX$, blood doping, and erythropoietin

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Methods (legal and illegal) of increasing total body haemoglobin and thereby $\dot{V}O_2MAX$ are discussed

By the 1930s it was clear that champion endurance athletes had remarkably high maximal O_2 uptake ($\dot{V}O_2MAX$).[1] In the 1950s, 1960s, and 1970s, classic studies were performed on the physiological determinants of $\dot{V}O_2MAX$ and on its key role in endurance performance.[2–4] During this time there was much debate on O_2 delivery versus O_2 extraction as the "limiting factor" for $\dot{V}O_2MAX$.[5 6] Observations during this era clearly established the role of maximal cardiac output as a determinant of $\dot{V}O_2MAX$, and very high maximal cardiac output values were seen in champion endurance athletes.[2] In addition, the important role of blood volume and total body haemoglobin as determinants of $\dot{V}O_2MAX$ also emerged (fig 1).[2 7–9] In an effort to better understand the physiological determinants of $\dot{V}O_2MAX$, studies were then conducted that attempted to manipulate O_2 delivery using a variety of approaches including altered concentrations of inspired O_2, drugs that speed or slow the heart, and, as will be discussed here, techniques that altered total body haemoglobin and haemoglobin concentration.[10 11]

In general, by the 1970s it was clear that manoeuvres that increased total body haemoglobin increased $\dot{V}O_2MAX$ and manoeuvres that reduced total body haemoglobin reduced $\dot{V}O_2MAX$.[9] These changes in $\dot{V}O_2MAX$ appeared to be somewhat independent of total blood volume because volume loading per se had little impact on $\dot{V}O_2MAX$, and likewise manoeuvres that cause haemoconcentration did not increase $\dot{V}O_2MAX$. Therefore, the importance of total body haemoglobin as a primary determinant of $\dot{V}O_2MAX$ was emphasised.

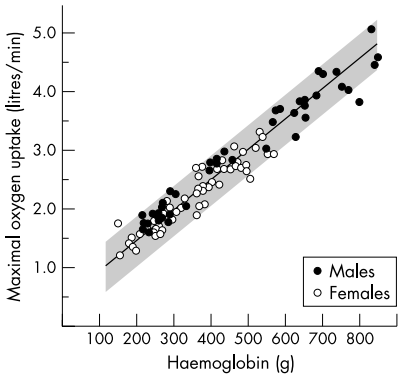

Figure 1 Classic data showing the relation between total body haemoglobin and whole body maximal oxygen uptake ($\dot{V}O_2MAX$) for 94 subjects age 7–30 years.[7] The subjects were all fit and none were overweight. Information such as this set the stage for much of the work that was to come on the relation between total body haemoglobin and $\dot{V}O_2MAX$ in humans.

In parallel with these mechanistic studies on the determinants of $\dot{V}O_2MAX$, applied observations on athletic performance and the role of $\dot{V}O_2MAX$, lactate threshold, and running economy emerged.[3 4] As $\dot{V}O_2MAX$ was seen as a key determinant of performance, the next obvious question was whether or not manoeuvres that increased total body haemoglobin and $\dot{V}O_2MAX$ would also increase performance. A number of studies confirming the positive impact of increased total body haemoglobin on performance were then conducted.[12 13] In addition, a variety of rumours and innuendo suggested that at least some endurance athletes were using this technique in an effort to gain a competitive advantage in international competition.[13–15] Thus, the term "blood doping" was coined. Although it is clear that blood doping improves performance, it is unclear how widespread it was in the 1970s and 1980s as detection was difficult because athletes received a reinfusion of their own red blood cells.

By the late 1980s recombinant erythropoietin (EPO), a hormone secreted by the kidney which is an important regulator of red blood cell production by the bone marrow, became available to treat patients with anaemia. Early studies in patients with renal failure, severe anaemia, and poor exercise tolerance showed that this hormone and the associated increase in whole body haemoglobin and packed cell volume could have profound effects on exercise tolerance in these patients.[16] Studies were also conducted in trained subjects and athletes that showed the expected increase in $\dot{V}O_2MAX$ when total body haemoglobin was increased.[13 16]

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By the early 1990s it was clear that EPO was the "drug of choice" for athletes illegally seeking to increase their endurance performance.[13] From a technical perspective, EPO had a number of advantages including no need for complex logistically challenging manoeuvres such as blood withdrawal, storage, and reinfusion. In addition, there was no reduction in performance or training after a period of blood withdrawal, and there was limited "detectability" because EPO is a "naturally occurring" peptide hormone. The use of EPO in international competition has been highlighted by a variety of scandals in events such as the Tour de France. In addition to EPO, there are several EPO analogues that are also effective—for example, darbypoietin. Fortunately these substances, which have a longer half life, are more easily detectable, and several athletes were suspended for darbypoietin use at the 2002 Winter Olympics.[15] So, where does this leave us in the early 21st century as we consider efforts by athletes to increase their circulating haemoglobin and improve their endurance performance?

Firstly, it is clear that the studies that led to blood doping were not designed to improve athletic performance; they were, however, designed to study the determinants of $\dot{V}O_2MAX$ in humans. Studies on the determinants of $\dot{V}O_2MAX$ then led to the realisation that blood doping could be a powerful ergogenic aid, and, in the modern "commercial" era of sport where national prestige and financial benefits to the athlete were "on the line" during major competitions, it is not surprising that blood doping became a factor in international competition. The emergence of EPO just made these strategies easier and reduced the medical infrastructure needed to manipulate whole body haemoglobin. In both cases, it is unclear how widespread the use of these techniques has been, but it is clear that at least some organisations and countries have doped in a systematic manner and that an "arms race mentality" has developed which contributes to a cycle of suspicion of use by non-users and subsequent increased use by those fearful of a competitive disadvantage.

More recently, ideas about how altitude training may affect total body haemoglobin and the optimal combination of training and living at altitude has been investigated, and the so-called "live high, train low" concept has emerged.[17] Whether the increases in performance associated with this approach are due

solely to increased haemoglobin levels or other factors is unclear, but there has been an emergence of strategies ranging from the construction of "nitrogen houses" or decompression dormitories to the commercial availability of hypoxic tents to facilitate the non-medical/non-pharmacological manipulation of total body haemoglobin.[15] At the same time, the governing bodies of many sports federations and the Olympic Committee have set upper limits for haemoglobin and packed cell volume so that any competitive advantage associated with doping would be eliminated or at least regulated.

So, athletes and those interested in improving their performance now have a variety of "choices" related to increasing whole body haemoglobin. Traditional blood doping and EPO use are illegal, whereas the approaches that result in hypoxic sleeping or sojourns to high altitude are permitted. In this context, the era of "doping" to manipulate haemoglobin and packed cell volume may be over, but the search for "legal" approaches to raise whole body haemoglobin are likely to continue.

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REFERENCES

1 **Robinson S**, Edwards HT, Dill DB. New records in human power. *Science* 1937;**85**:409–10.
2 **Ekblom B**, Hermansen L. Cardiac output in athletes. *J Appl Physiol* 1968;**25**:619–25.
3 **Costill DL**, Thomason H, Roberts E. Fractional utilization of the aerobic capacity during distance running. *Med Sci Sports* 1973;**5**:248–52.
4 **Farrell PA**, Wilmore JH, Coyle EE, *et al*. Plasma lactate accumulation and distance running performance. *Med Sci Sports* 1979;**11**:338–44.
5 **Rowell LB**. *Human circulation regulation during physical stress*. New York: Oxford University Press, 1986:1–416.
6 **Saltin B**, Strange S. Maximal oxygen uptake: "old" and "new" arguments for a cardiovascular limitation. *Med Sci Sports Exerc* 1992;**24**:30–7.
7 **Åstrand P-O**. *Experimental studies on physical working capacity in relation to sex and age*. Copenhagen: Ejnar Muksgaard, 1952.
8 **Åstrand P-O**, Rodahl K. *Textbook of work physiology*. New York: McGraw-Hill Book Company, 1977.
9 **Kanstrup I**, Ekblom B. Blood volume and hemoglobin concentration as determinants of maximal aerobic power. *Med Sci Sports Exerc* 1984;**16**:256–62.
10 **Ekblom B**, Goldberg AN, Gullbring B. Response to exercise after blood loss and reinfusion. *J Appl Physiol* 1972;**33**:175–80.
11 **Ekblom B**, Wilson G, Åstrand P-O. Central circulation during exercise after venesection and reinfusion of red blood cells. *J Appl Physiol* 1976;**40**:379–83.
12 **Berglund B**, Hemmingsson P. Effect of reinfusion of autologous blood on exercise performance in cross-country skiers. *Int J Sports Med* 1987;**8**:231–3.
13 **Sawka MN**, Joyner MJ, Miles DS, *et al*. American College of Sports Medicine position stand: the use of blood doping as an ergogenic aid. *Med Sci Sports Exerc* 1996;**28**:i–viii.
14 **Berglund B**, Hemmingsson P, Birgegard G. Detection of autologous blood transfusions in cross-country skiers. *Int J Sports Med* 1987;**8**:66–70.
15 **Joyner MJ**. News brief: altitude training, erythropoietin, and blood doping. *Exerc Sport Sci Rev* 2002;**3**:97–8.
16 **Ekblom B**, Berglund B. Effect of erythropoietin administration on maximal aerobic power. *Scand J Med Sci Sports* 1991;**1**:88–93.
17 **Stray-Gundersen J**, Chapman RF, Levine BD. "Living high-training low" altitude training improves sea level performance in male and female elite runners. *J Appl Physiol* 2001;**91**:1113–20.