

## Review

# Athletes' anaemia

## A review of possible causes and guidelines on investigation†

Eric Watts, DM, MRCP, MRC Path

Michael Darmady Laboratory, Queen Alexandra Hospital, Cosham, Portsmouth, PO65 3LY

Athletes' anaemia (sports anaemia) is well recognized and there have been many suggestions for its aetiology some leading to unnecessary anxiety as well as needless investigation and treatment. This article reviews evidence on the causes of sports anaemia and suggests how to identify the few cases that require investigation and treatment.

It seems paradoxical that when most physiological parameters show improved function that the haemoglobin level should fall with training but most studies (including runners, rowers, cyclists, swimmers and walkers) show that **endurance trained athletes have a haemoglobin level about 0.5 g 100 ml lower than untrained controls**. Forty-four per cent of soldiers in basic combat training were found to have a haematocrit below 41 per cent compared with eleven per cent of soldiers not in training<sup>1</sup>.

Iron deficiency is often considered to be the cause of sports anaemia and **blood loss may occasionally occur in runners**. **Haematuria** is the most visible form of blood loss and has been well documented, particularly at distances over 10 km. Blacklock reported typical **cystoscopic findings** in these cases<sup>2</sup>. There were contusions on the bladder floor at the ureteric orifices and at the internal urinary meatus. There were mirror image lesions on the posterior bladder wall which led Blacklock to suggest that they were caused by the soft and mobile posterior bladder wall being repeatedly pressed against the firmer, fixed bladder base. In some cases the epithelium of the posterior wall may be pushed down the internal meatus by the repeated trauma of abdominal contents striking against the bladder. In all cases haematuria resolved spontaneously. He suggested that it could be avoided by ensuring that there was urine in the bladder before running but dedicated athletes have not followed this advice!

**Haemoglobinuria** is another well recognized complication of running or marching. It is distinguishable from haematuria by naked eye examination of the urine. Haematuria (unaltered blood in the urine) causes a 'smoky' opalescent appearance. Haemoglobinuria causes clear pink urine and results from **intravascular haemolysis**. Free haemoglobin normally

forms a complex with haptoglobin, but when haptoglobin is saturated, the excess haemoglobin appears in the urine. The mechanism was described in a classic experiment by Davidson in 1964<sup>3</sup>. He noticed that runners with a high, stamping gait, running on hard surfaces were prone to haemoglobinuria. He fitted tubes of blood from haemoglobinuria sufferers and non-affected runners into inserts in running shoes. After running, the haemoglobinuria sufferers showed haemolysis in all samples, whereas the unaffected individuals showed no haemoglobin of their own or the affected runners' blood. These results suggest that this haemolysis occurs in the plantar vessels and is due to a combination of running style, hard surfaces and poorly cushioned shoes.

Although blood (and haemoglobin) loss in the urine is well described, it is highly unlikely to cause an iron deficient anaemia. As little as one ml of blood in one litre of urine can cause dramatic discolouration, but this amount can easily be lost daily without causing anaemia.

**Blood loss from the gut** has also been described in runners. Fogoros reported attacks of bloody diarrhoea in a runner building up mileage for a marathon<sup>4</sup>. This was thought to be due to gut ischaemia as **splanchnic perfusion may be reduced by 80 per cent during exertion**<sup>5</sup>. Stewart measured the haemoglobin content of the stool in 24 runners before and after a marathon<sup>6</sup>. They all had normal pre-race values, but seven passed more than 3 ml of blood in the 24 hours after the race. One runner who raced on two consecutive days passed 43 ml of blood after the second day. Hence, occasional runners with very high mileage may develop significant blood loss. **Gastrointestinal blood loss may also be increased by the use of anti-inflammatory drugs and analgesics**.

It has been claimed that iron deficiency is common amongst runners and is the main cause of athletes' anaemia<sup>7</sup>. This is mainly as a result of finding a lowered ferritin level in runners. **Although the serum ferritin is normally a good guide to iron stores it is not reliable in runners**. There are many ways to estimate iron stores but the most accurate is from bone marrow sampling, which is unpleasant. Magnusson's study of iron metabolism in 43 middle and long distance runners and 119 controls showed many familiar findings – athletes had lower haemoglobin, haematocrit and ferritin levels<sup>8</sup>. However, they all had iron present

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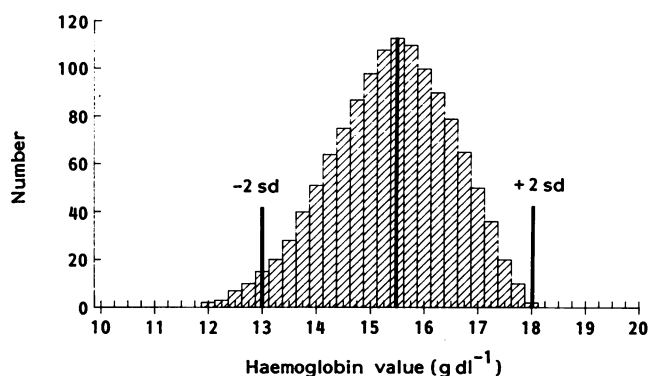


Figure 1. Normal haemoglobin values (male).

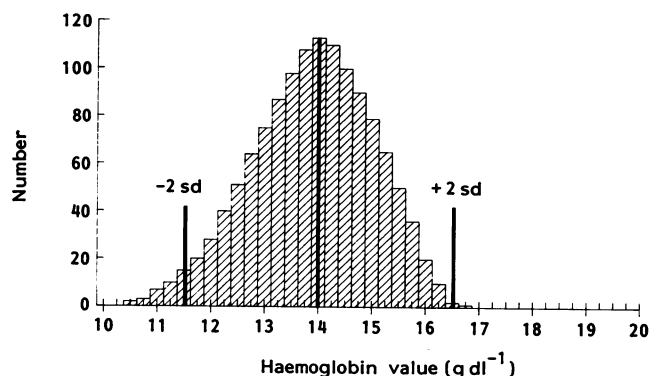


Figure 2. Normal haemoglobin values (female).

in their bone marrow stores – indicating that iron deficiency did not limit erythropoiesis. He explained the lowered ferritin levels on the basis of **altered red cell catabolism** in runners. In the normal (non-running) state, 90 per cent of red cell catabolism occurs by reticulo endothelial phagocytosis in the spleen, bone marrow and liver. The iron is then incorporated into ferritin. The other 10 per cent of red cells are lysed in the circulation, liberating free haemoglobin by haemolysis. This is then bound to haptoglobin and the resulting complex is taken up by hepatocytes. This iron is not incorporated into ferritin but released into the plasma iron/transferrin pool. In runners, however, the proportions are altered and in extreme cases the amount of intravascular haemolysis is doubled. This means that less iron is in the ferritin compartment, more in the liver/plasma iron and transferrin compartment.

This study shows that both **lowered haemoglobin and ferritin should now be accepted as normal in runners**. This is important because **unnecessary iron treatment can occasionally lead to haemosiderosis**<sup>9</sup>, but more commonly can cause gastrointestinal disturbances which may impair training and performance.

Is this 'anaemia' an adaptive response to improve performance? It is suggested that anaemic blood, by lowered viscosity, flows more easily. However, this is offset by lower oxygen carrying capacity due to reduced haemoglobin.

The fact that the anaemia may develop rapidly has led authors to speculate that haemolysis is responsible but detailed studies by Milledge<sup>10</sup> suggest otherwise. He observed a fall in haematocrit from 43.5 per cent to 37.9 per cent after five days of hill walking. This was associated with increased renin and aldosterone activity and sodium conservation. The plasma volume increased by 0.9 litres at the end of the exercise, suggesting that **volume expansion is an acute reaction to strenuous exercise**. Many studies have shown increased plasma volume in trained athletes. Endurance training commonly increases plasma volume by 10 per cent but red cell mass in unaffected or only slightly increased<sup>11,12</sup>.

Hence, the term 'anaemia' is inappropriate because the red cell mass is actually normal or increased. 'Dilutional pseudo-anaemia' is a more accurate term. Other training changes include increases in the muscle vas-

cular bed and ventricular volume. Mean blood pressure and total peripheral resistance are reduced, i.e. training leads to vasodilatation. Increased stroke volume and the blood volume reflect this.

Detraining leads to a fall in stroke volume and blood volume<sup>11</sup>. One experiment, on four athletes after two to four weeks inactivity, showed a nine per cent drop in blood volume. Their haemodynamic response to sub-maximal exercise on a cycle ergometer was largely restored to trained levels by infusion of 700 ml dextran<sup>10</sup>, suggesting that the most important requirement in exercise is for an adequate blood volume.

Further training change occurs within the red cell itself, increased oxygen extraction by exercising muscle altering the oxygen affinity of the haemoglobin. This is similar to the compensatory changes of chronic anaemia which facilitate oxygen delivery to the tissues. It is mediated by increased 2–3 diphosphoglycerate levels in the red cell. Oxygen uptake in the lungs is maintained but more oxygen is released at lower levels of oxygen tension, i.e. in the tissues. This improved function of the erythrocyte has earned the term 'super cell' from Uddin<sup>13</sup>.

In summary, the **dilutional pseudo-anaemia of training is only of concern when the haemoglobin level alone is compared with the untrained state**. The changes in blood occur in concert with those in other organs and as a result of this the blood volume and oxygen delivery to the tissues is increased<sup>14</sup>. An excellent demonstration that this pseudo-anaemia is not a pathological abnormality but part of an improved physiological state comes from the study by Dressendorfer<sup>15</sup>. He studied 12 marathon runners in The Great Hawaiian Footrace – a 20-day, 312 mile event. Over the 20 days the mean haemoglobin fell from 16 g/dl to 13.6 g/dl but the running speed increased as the haemoglobin fell.

**In practical terms all that is necessary is to determine whether the athlete is iron deficient**. The law of averages dictates that 2.5 per cent of normal men will have a haemoglobin below 13 g/l and 2.5 per cent of women below 11.5 g/bl. (See *Figures 1 and 2*).

The most useful information is obtained from the red cell indices. Iron deficiency is likely if the mean cell volume (MCV) is below 75 fl (normal range: 77–93 fl) and the mean cell haemoglobin below 25 pg (normal range: 27–32 pg). From Magnusson's study'

lower levels of ferritin apply to runners and truly iron deficient levels are probably 5 µg/l lower than in normals\*. If the red cell indices or ferritin are in the equivocal or borderline low range then a trial of iron for one month is quite reasonable. If the haemoglobin does not rise by at least 1 g then iron deficiency has been excluded.

If iron deficiency is identified in a high mileage runner, then a reduction in mileage is indicated as investigations at this stage are unrewarding<sup>4</sup>.

Only if iron deficiency continues and is not associated with NSAID or other drug-induced bowel loss of blood, menstrual loss, or dietary deficiency, should further investigation be considered for intestinal blood loss.

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\*The normal range is 12-300 µg/L but there is some variation between laboratories according to the method used. Below 7 µg/L is clearly iron deficient.

### DUTCH MEDICAL JOGGERS ASSOCIATION



The Dutch Medical Joggers Association is organizing the first international Medical Marathon in September 1989. They seek contact with all interested medical running groups to whom they will send full details of the event.

The Marathon Medical Symposium will be held on Friday 15 September, and the full Marathon as well as a Half-Marathon Race and a 10 km Race will take place on Saturday 16 September 1989.

All races are open to running doctors, dentists, veterinarians and physiotherapists.

Venue: all events take place at the National Sports Centre, Papendahl, Arnhem, Netherlands. There is accommodation available at the centre itself.

Full details from: Dr Jacob A. Du Boeuff, President, Dutch Medical Joggers Association, PO Box 8153, NL-3503 RD, Utrecht Netherlands.