Strenuous exercise: analogous to the acute-phase response?

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SUMMARY

1. It has been suggested that the physiological consequences of strenuous exercise are analogous to those of the acute-phase response.

2. In 70 male and 20 female competitive distance runners, a marked, but transient, neutrophil leucocytosis occurred immediately after these athletes completed a standard (42 km) marathon race. Concomitant significant increases were noted in the plasma cortisol levels, creatine kinase activity, C-reactive protein level, total protein level and albumin level (P<0.01).

3. The plasma fibrinogen, C-reactive protein and total protein concentrations were markedly increased both 24 h and 48 h after exercise (P<0.01). The serum haptoglobin level was significantly decreased after exercise (P<0.01), and increased 48 h later (P<0.05). There was no change in the serum iron level, total iron-binding capacity, per cent saturation of transferrin and serum ferritin level.

4. A significant increase in interleukin-1-type activity was demonstrated immediately and 24 h after exercise (P<0.01).

5. It is concluded that the metabolic sequelae of sustained exercise are similar, but not analogous, to the acute-phase response, and interleukin-1 probably plays a significant role in linking the haematological and immunological changes observed after sustained strenuous exercise.

Key words: acute-phase response, immune function, interleukin-1, sports anaemia, strenuous exercise.

Abbreviations: IMDM, Iscove's modified Dulbecco's medium; PHA, phytohaemagglutinin.

INTRODUCTION

The consequences of sustained strenuous exercise are well-documented, the most obvious being a significant, but transient, leucocytosis and lymphocytosis [1]. Concomitant metabolic changes include an increase in plasma levels of globulins and glycoproteins [2, 3], the acute-phase proteins such as ceruloplasmin and C-reactive protein [4], transferrin [3], creatine kinase [3-5], fibrinogen [6], lactoferrin [7] and ferritin [7, 8]. Trained athletes also exhibit changes in plasma protein and trace-metal levels (hypoferraemia and hypozinc-aemia) typical of the acute-phase response after sustained strenuous exercise [7, 9]. There is also evidence that long-term physical training may lead to a chronic depression of plasma iron [10], ferritin [8, 10] and zinc [11] levels.

The acute-phase response is characterized by fever, and an increase in granulocyte production, release from bone marrow and lymphokine-mediated-function [12]. Hepatic synthesis of plasma proteins, including fibrinogen, haptoglobin, C-reactive protein and ferritin, is accelerated. In contrast, plasma albumin, transferrin and glycoprotein production falls, while their catabolism increases [12]. A redistribution of amino acids and trace metals results in acute hypoferraemia and hypozinc-aemia [13]. Endocrinological changes involve increased synthesis of adrenocorticotrophin, cortisol and adrenal catecholamines [12]. All these reactions appear to be beneficial with regard to host survival by increasing resistance to infection, altering metabolism to promote wound repair and activating both cellular and immune reactivity.

The remarkable number of similarities between the acute-phase reaction and the physiological responses to exercise, together with the emerging importance of the exercise-induced modulation of the immune response, suggests an analogy between these two phenomena. Possibly the lymphokine mediators released during infection may also be produced during exercise and these pro-
tein-induced hypoferraemia, leucocytosis and modulation of the immune response. It has been further suggested that if exercise is analogous to the acute-phase response, then sports anaemia may resemble the anaemia of chronic diseases in its aetiology [7]. Although this hypothesis was recently and formally proposed by Taylor et al. [7], the concept is not new [2, 5, 14–16].

This study was therefore undertaken to further characterize the acute haematological and biochemical effects of strenuous exercise, in view of the hypothesis of Taylor et al. [7] and to investigate the possibility that interleukin-1, the synthesis of which represents a fundamental cellular response to injury [17], is the common mediator linking the immunological and haematological responses to strenuous exercise.

MATERIALS AND METHODS

Subjects

Seventy male distance runners and 20 female distance runners competing in a standard 42 km marathon race were recruited for the study. All had been running for at least 2 years, and had completed at least one marathon race before the study race. The demographic data are presented in Table 1. Owing to the labour-intensive nature of the data collection, the samples were obtained from different athletes at four marathon races during a single year. All races were run over undulating terrain in optimal weather conditions (18–20°C, low humidity), except for the third race when it was cold and wet (12–14°C).

Blood sample collection

At each sampling point data were collected from all the athletes participating in any one of the four studies (n = 22, 30, 20 and 20, respectively). The pre-race (baseline) blood samples were drawn in the laboratory on the day before the race at the time approximate to that when the subject would be completing the race the next day (09.00 hours), with the subject in the rested and fasted state.

The post-race sample was drawn in a locker room in the stadium at the end of the race. Within 10 min of the athlete completing the event, he/she was required to report to the assigned venue and to remain seated upright until and during venesection. Thereafter samples were taken on the subsequent 2 days (24 and 48 h after the race), again in the laboratory at 09.00 hours, with the patient fasted and not having performed any strenuous exercise subsequent to completing the marathon. In the third study, samples were also collected 6 days after the race, under the same conditions, except that the subject was not necessarily rested.

Pre- and post-race body weights were measured immediately before the start of the race and at the end, on a Seca 770 Alpha personal electronic scale (Vogel and Halke, Hamburg, Germany) with the subject in running gear including shoes, in order to assess the degree of dehydration from body weight changes.

Haematological and biochemical determinations

Full blood count. A full blood count, including haemoglobin level, packed cell volume, erythrocyte count, mean cell volume, mean cell haemoglobin and mean cell haemoglobin concentration, was performed on EDTA-blood using a Coulter Counter Model S Plus II (Coulter Electronics, Hialeah, Finland) [18]. Plasma volume shifts were calculated from the haemoglobin level and packed cell volume using the equations of Dill & Costill [19]. A differential leucocyte count was performed on a Technicon H* 1 (Technicon Instruments Co., Tarrytown, NY, U.S.A.).

Iron status and serum protein levels. Clotted blood was maintained at room temperature for at least 60 min before being centrifuged. The supernatant was divided into portions and was then stored frozen (−20°C) for later analyses. The serum iron level and the total iron-binding capacity were measured by the method described by the Iron Panel of the International Committee for Standardization in Haematology [20, 21], and the serum ferritin level was determined by r.i.a. [22] using a commercial kit (Amersham International PLC, Amersham, Bucks, U.K.). Per cent saturation of transferin was calculated from the serum iron level and the total iron-binding capacity. The serum haptoglobin level was determined on a Behring Nephelometer (Behring, Marburg, Germany).

Plasma cortisol level, creatine kinase activity and acute-phase protein levels. All heparinized blood was kept on ice until centrifugation after which the plasma supernatant was pipetted off, divided into portions and was stored frozen (−20°C) for later analyses. The plasma cortisol level was determined by r.i.a. using a commercial kit (Amerlex; Amersham International PLC, Amersham, Bucks, U.K.). Plasma creatine kinase activity was measured by an N-acetyl-L-cysteine-linked-rate reaction by the method of Rosalki [23] using a commercial kit (Boehringer, Mannheim, Germany), and the plasma C-reactive protein level was determined by standard single radial immunodiffusion [24]. The Biuret method [25] was used for total protein determination, while the
albumin level was measured on a Technicon SMAC Autoanalyzer (Technicon, Tarrytown, NY, U.S.A.) using Bromocresol Green, by the method of Rodkey [26]. The plasma globulin level was calculated by difference (total protein level minus albumin level). The plasma fibrinogen level was determined on sodium citrated blood as described by Clauss et al. [27].

**Interleukin-1-type activity.** Interleukin-1-type activity was measured using the murine thymocyte assay [28,29]. Briefly, $2 \times 10^6$ mononuclear cells harvested from the peripheral blood on a Ficoll–Hypaque gradient (Lympho-prep; Nycomed, Gotenburg, Norway) and suspended in Iscove’s modified Dulbecco’s medium (IMDM; Gibco, Gibco Ltd, Paisley, Scotland, U.K.) supplemented with 10% (v/v) AB serum (Western Province Blood Transfusion Service, Cape Town, South Africa) were enriched by adherence to plastic ($2 \times 10^6$ cells/ml). After stimulation with 1% (w/v) phytohaemagglutinin (PHA; Wellcome Diagnostics, Dartford, Kent, U.K.) in IMDM/AB serum were distributed in 96-well microtitre plates (Nunclon, Roskilde, Denmark) at $10^6$ cells/well, and were cultured for 72 h. Proliferation incorporation was assessed by overnight incubation with 0.5 $\mu$Ci of $[^3H]$thymidine (Amersham, Bucks, U.K.)/well followed by liquid scintillation of incorporated radioactivity using a Beckman LS 1801 counter (Beckman Instruments Inc, Fullerton, CA, U.S.A.). Results were expressed as c.p.m. $\times 10^3$.

**Statistical analyses**

The data were analysed using the general linear models procedure and repeated measures analysis of variation, with the baseline (pre-race) value as the dependent variable. Univariate hypothesis for within-subject effects and the multiple analysis of variance test criteria for the hypothesis of no time effect were also applied [30]. In all cases, $P<0.05$ was the accepted level of significance.

### RESULTS

#### Full blood count

The blood haemoglobin level, packed cell volume, erythrocyte count and mean cell volume did not change significantly after exercise. The plasma volume shift calculated from changes in the haemoglobin level and packed cell volume [25] was $<5\%$, and the degree of dehydration calculated from body weight change was 3.03% and 2.36% for the male and female athletes, respectively, so that a haemoconcentration effect could be negated (Table 2).

There was a transient, but highly significant, increase (160%; $P<0.01$) in the leucocyte count immediately after the race. This involved a marked rise in the absolute neutrophil, monocyte and basophil counts ($P<0.01$), while the absolute lymphocyte and eosinophil counts were reciprocally decreased ($P<0.01$; Table 2).

#### Iron status and serum protein levels

There was no change in the serum iron level, total iron-binding capacity, per cent saturation of transferrin or serum ferritin level after exercise (Table 3). The serum haptoglobin level was significantly decreased immediately after exercise ($P<0.01$), and was similarly increased 48 h later ($P<0.05$) (Table 3).

#### Plasma cortisol level, creatine kinase activity and acute-phase protein levels

Immediately after exercise, 50% of the athletes had a plasma cortisol level greater than 1600 nmol/l, which is the upper limit detected by this assay. At 24 h and 48 h, the plasma cortisol level was significantly lower than baseline ($P<0.01$, $P<0.05$, respectively; Table 4). The plasma creatine kinase activity was markedly increased immediately, 24 h and 48 h ($P<0.01$) after the race, but had returned to baseline after 6 days (Table 4). A significant increase ($P<0.01$) was measured in the plasma C-reactive protein level 24 h after the race ($P<0.01$), and likewise at 48 h after the race ($P<0.01$; Table 4). The plasma fibrinogen level was increased ($P<0.01$) over baseline at

### Table 2. Erythrocyte and leucocyte indices measured in 70 male and 20 female distance runners before and after completing a standard 42 km marathon race

<table>
<thead>
<tr>
<th></th>
<th>Before race</th>
<th>After race</th>
<th>24 h after race</th>
<th>48 h after race</th>
<th>6 days after race</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haemoglobin concn.</strong> (males) (g/l)</td>
<td>153.9 ± 8.9</td>
<td>156.3 ± 8.7</td>
<td>152.7 ± 10.5</td>
<td>149.6 ± 9.1</td>
<td>153.4 ± 6.9</td>
</tr>
<tr>
<td>Packed cell volume (males)</td>
<td>0.45 ± 0.0</td>
<td>0.46 ± 0.0</td>
<td>0.43 ± 0.0</td>
<td>0.42 ± 0.1</td>
<td>0.44 ± 0.0</td>
</tr>
<tr>
<td>Haemoglobin concn. (females) (g/l)</td>
<td>137.1 ± 6.8</td>
<td>142.1 ± 17.4</td>
<td>129.5 ± 5.7</td>
<td>131.8 ± 8.1</td>
<td>137.0 ± 15.0</td>
</tr>
<tr>
<td>Packed cell volume (females)</td>
<td>0.41 ± 0.0</td>
<td>0.41 ± 0.0</td>
<td>0.38 ± 0.0</td>
<td>0.38 ± 0.0</td>
<td>0.38 ± 0.0</td>
</tr>
<tr>
<td>$10^9$ × Total leucocytes (l$^{-1}$)</td>
<td>5.73 ± 1.3</td>
<td>14.91 ± 4.5 $^\dagger$</td>
<td>6.65 ± 1.5</td>
<td>5.87 ± 1.4</td>
<td>5.70 ± 1.3</td>
</tr>
<tr>
<td>$10^9$ × Lymphocytes (l$^{-1}$)</td>
<td>3.30 ± 0.1</td>
<td>10.31 ± 0.3 $^\dagger$</td>
<td>3.65 ± 0.0</td>
<td>3.46 ± 0.0</td>
<td>3.25 ± 0.0</td>
</tr>
<tr>
<td>$10^9$ × Monocytes (l$^{-1}$)</td>
<td>2.32 ± 0.1</td>
<td>2.09 ± 0.1</td>
<td>2.33 ± 0.0</td>
<td>2.11 ± 0.0</td>
<td>1.71 ± 0.0</td>
</tr>
<tr>
<td>$10^9$ × Eosinophils (l$^{-1}$)</td>
<td>0.24 ± 0.0</td>
<td>0.46 ± 0.0 $^\dagger$</td>
<td>0.44 ± 0.0</td>
<td>0.46 ± 0.0</td>
<td>0.42 ± 0.0</td>
</tr>
<tr>
<td>$10^9$ × Basophils (l$^{-1}$)</td>
<td>0.02 ± 0.0</td>
<td>0.00 ± 0.0 $^\dagger$</td>
<td>0.22 ± 0.0</td>
<td>0.21 ± 0.0</td>
<td>0.21 ± 0.0</td>
</tr>
<tr>
<td>$10^9$ × Neutrophils (l$^{-1}$)</td>
<td>0.04 ± 0.0</td>
<td>0.03 ± 0.2</td>
<td>0.04 ± 0.0</td>
<td>0.04 ± 0.0</td>
<td>0.04 ± 0.0</td>
</tr>
</tbody>
</table>

Data are presented as means ± s.d. Statistical significance: $^\dagger$ $P<0.01$ compared with before race (baseline).
Table 3. Iron status and serum protein levels in 52 male and 20 female distance runners before and after completing a standard 42 km marathon race

<table>
<thead>
<tr>
<th></th>
<th>Before race</th>
<th>After race</th>
<th>24 h after race</th>
<th>48 h after race</th>
<th>6 days after race</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum iron concn. (µmol/l)</td>
<td>19.5 ± 6.3</td>
<td>20.7 ± 6.0</td>
<td>21.7 ± 8.0</td>
<td>17.5 ± 7.0</td>
<td>16.5 ± 5.3</td>
</tr>
<tr>
<td>Total iron-binding capacity (µmol/l)</td>
<td>57.8 ± 8.2</td>
<td>58.8 ± 8.6</td>
<td>52.6 ± 7.5</td>
<td>48.6 ± 6.0</td>
<td>52.6 ± 6.3</td>
</tr>
<tr>
<td>Saturation of transferrin (%)</td>
<td>33.5 ± 9.0</td>
<td>35.7 ± 7.7</td>
<td>40.4 ± 11.9</td>
<td>38.1 ± 12.5</td>
<td>30.6 ± 7.1</td>
</tr>
<tr>
<td>Serum ferritin concn. (males) (µg/l)</td>
<td>8.19 ± 55.2</td>
<td>100.5 ± 107.7</td>
<td>108.9 ± 68.2</td>
<td>76.2 ± 48.9</td>
<td>70.0 ± 38.0</td>
</tr>
<tr>
<td>Serum ferritin concn. (females) (µg/l)</td>
<td>3.10 ± 23.6</td>
<td>34.2 ± 29.2</td>
<td>44.1 ± 35.5</td>
<td>38.0 ± 38.1</td>
<td>37.3 ± 39.2</td>
</tr>
<tr>
<td>Serum haptoglobin concn. (g/l)</td>
<td>0.89 ± 0.44</td>
<td>0.69 ± 0.39†</td>
<td>0.89 ± 0.62</td>
<td>1.12 ± 0.73*</td>
<td>1.09 ± 0.78</td>
</tr>
</tbody>
</table>

Data are expressed as means ± sd. Statistical significance; *P<0.05, †P<0.01 compared with before race (baseline).

Table 4. Plasma cortisol concentration, creatine kinase activity, acute-phase reactant concentrations and interleukin-1-type activity in male distance runners before and after completing a standard 42 km marathon race

<table>
<thead>
<tr>
<th></th>
<th>Before race</th>
<th>After race</th>
<th>24 h after race</th>
<th>48 h after race</th>
<th>6 days after race</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol concn. (nmol/l)</td>
<td>731.0 ± 223.0</td>
<td>1465.9 ± 221.7†</td>
<td>393.7 ± 133.0*</td>
<td>525.5 ± 152.5†</td>
<td>552.6 ± 172.6</td>
</tr>
<tr>
<td>Creatinine kinase activity (units/l)</td>
<td>88.5 ± 28.9</td>
<td>212.7 ± 75.1†</td>
<td>801.7 ± 558.9†</td>
<td>522.1 ± 481.7†</td>
<td>131.8 ± 99.6</td>
</tr>
<tr>
<td>C-reactive protein concn. (mg/100 ml)</td>
<td>0.11 ± 0.44†</td>
<td>0.40 ± 0.83</td>
<td>2.27 ± 1.59†</td>
<td>0.97 ± 1.41†</td>
<td>0.0 ± 0.00</td>
</tr>
<tr>
<td>Fibrinogen concn. (g/l)</td>
<td>2.61 ± 0.44</td>
<td>2.50 ± 0.66</td>
<td>5.22 ± 1.42†</td>
<td>5.42 ± 1.63†</td>
<td>4.93 ± 1.48†</td>
</tr>
<tr>
<td>Total protein concn. (g/l)</td>
<td>61.6 ± 29.0</td>
<td>77.7 ± 6.0</td>
<td>54.3 ± 20.7*</td>
<td>72.9 ± 4.0‡</td>
<td>75.1 ± 5.6</td>
</tr>
<tr>
<td>Albumin concn. (g/l)</td>
<td>50.0 ± 1.6</td>
<td>53.5 ± 1.9†</td>
<td>49.6 ± 1.4</td>
<td>49.6 ± 1.9</td>
<td>49.5 ± 2.6</td>
</tr>
<tr>
<td>Globulin concn. (g/l)</td>
<td>23.9 ± 3.5</td>
<td>24.2 ± 5.2</td>
<td>23.8 ± 4.1</td>
<td>24.3 ± 3.8</td>
<td>25.8 ± 4.1</td>
</tr>
<tr>
<td>10^–6 × Interleukin-1-type activity (c.p.m.)</td>
<td>13.57 ± 4.3</td>
<td>18.85 ± 9.7†</td>
<td>20.05 ± 7.2†</td>
<td>19.69 ± 14.9</td>
<td>—</td>
</tr>
</tbody>
</table>

Data are expressed as means ± sd. Statistical significance: *P<0.05, †P<0.01 compared with before race (baseline).

24 h, with the mean level peaking at 48 h, but was still significantly elevated (P<0.01) 6 days after the race (Table 4). The total protein level rose markedly 24 h after the race (P<0.05) but dropped below the basal level after 48 h (P<0.01). The plasma globulin level, calculated by difference, remained unchanged after exercise, whereas the plasma albumin level rose immediately after the race (P<0.01).

Interleukin-1-type activity

The interleukin-1-type activity from peripheral blood monocytes was significantly enhanced immediately and 24 h (P<0.01) after exercise (Table 4).

DISCUSSION

The athletes who participated in this study were highly trained and competitive, and it can therefore be assumed that they were all performing at a similar exercise intensity (65–70% of maximal oxygen consumption) [31]. Furthermore, these competitors were well-educated, and were aware of the importance of maintaining adequate hydration. This is confirmed by the minimal loss of body weight immediately after the race. Calculation of plasma volume changes [19] (Table 1) indicated that the athletes were fully rehydrated within 24 h of completing the race. We did not feel it justifiable to collect data during the running event, both from a logistical point of view, and because it would have impeded the performance of these seriously competitive athletes.

The transient, primarily neutrophilic, leucocytosis observed to the same degree immediately after exercise in all four studies (Table 2) is entirely consistent with the reported literature [1, 7, 8]. It was not possible to quantify lymphocyte sub-populations in this study and we can only speculate on the immunological consequences of strenuous exercise in these athletes. The precise mechanisms of this transient neutrophilia are not known, but may be related to increased levels of circulating catecholamines [32] and corticosteroids, including cortisol [7, 33]. A concomitant elevation of the latter hormone was measured in this study (Table 3). However, as this neutrophilia was such a transient and immediate effect, preceding the measured increase in interleukin-1-type activity, a demargination effect, particularly in the lungs and spleen, as the result of accelerated systemic blood flow could be implicated [34].

The data obtained in this study both support and contradict the analogy of exercise as an acute-phase response. Evidence in the former category includes the following. [i] A marked increase in the plasma concentration of the prototypic acute-phase reactant, C-reactive protein, was seen 24 h after exercise, although mean levels before and 6 days after exercise were almost zero.
Exercise as an acute-phase response

A delayed increase in the plasma fibrinogen level, peaking only after 48 h (107% over baseline) and remaining markedly elevated after 6 days, was demonstrated (Table 4). Fibrinogen is known to be stimulated by interleukin-1, with plasma concentrations remaining elevated for several weeks after an inflammatory stimulus [35]. A significant increase in the serum haptoglobin level was seen 48 h after exercise. Similar decreases in the serum concentration of this protein 24 h after exercise are consistent with previous reports of erythrocyte destruction as a consequence of prolonged exercise [36]. A marked increase in plasma creatine kinase activity was seen 24 and 48 h after exercise (805.9% and 523.8% over baseline, respectively, \( P < 0.01 \)). This is consistent with previous studies as regards both the time course and degree of change [2, 4, 5] (Table 4). It is more likely that muscle injury contributed to the apparent inflammatory response and not vice versa, as the evidence that sustained exercise causes a degree of muscle necrosis is unequivocal [5, 37]. However, it is possible that this necrotic event is exacerbated by concomitant prosta-glandin-stimulated proteolysis [38].

The following observations in the present study are inconsistent with the exercise and acute-phase response analogy. First, no evidence of hypoferraemia was seen. Secondly, no significant change in the serum ferritin level was measured in either sex, possibly because of the large sors in mean concentrations (Table 3). However, when calculated as a per cent change from pre-race values (both sexes combined), the immediately post-race serum ferritin level was 58.2% higher, and was still 46.9% above the pre-exercise value 48 h later. It has been repeatedly implied that serum ferritin levels in exercising subjects may be constantly falsely elevated, due to the role of this protein as an acute-phase reactant. Therefore the real incidence of iron deficiency in athletes, based on this single index of iron status, could be greater than reported [8]. This claim is not borne out by these data, as the change in the mean serum ferritin level of the study group was non-significant and transitory. Furthermore, the mean serum ferritin concentration (13.8 \( \mu g/l \)) of the 14 athletes (six males and eight females) with baseline concentrations of 20 \( \mu g/l \) was not elevated into the ‘normal range’ (20–300 \( \mu g/l \)) at any point after exercise (Table 3). Thirdly, the plasma concentration of albumin, a negative acute-phase reactant, increased significantly immediately after exercise, while the globulin fraction remained unchanged (Table 4). Similar changes in plasma protein concentrations have been reported previously [2, 3].

Plasma protein changes cannot be dissociated from the plasma volume shifts which occur during exercise and in the recovery phase after exercise [39]. Previous studies have shown that the plasma volume is well maintained during marathon running [39]. The measured increase during the recovery phase is due primarily to a large influx of serum albumin and the associated increase in the plasma sodium content. These data would support this observation. However, while the calculated decrease in the plasma volume immediately after exercise in the present study was not sufficient to account for a haemo-

concentration effect [7], rather greater changes on the recovery days could result in a discrepancy between the concentration of plasma constituents and their actual content in the expanded plasma volume [39]. This would make any increase in a given biochemical parameter even more significant (for example, in haptoglobin and fibrinogen), while minimizing any marked decreases, for example in total protein levels.

Although Taylor et al. [7] did not measure interleukin-1 levels in their study, they claim that all the metabolic sequelae of sustained exercise are attributable to the release of this protein from tissue monocytes and phagocytes. Evans et al. [15] report that although interleukin-1 activity was significantly increased in five untrained male subjects after eccentric exercise, no consistent change was demonstrated in the four trained males after the same degree of exercise. Thus an attempt was made to measure interleukin-1-type activity in peripheral blood monocytes before and after sustained exercise. Cognizance is given to the fact that the traditional mouse thymocyte assay [28, 29] fails to distinguish between interleukin-1 and interleukin-6, and is also subject to contamination with interleukin-2. Furthermore, obtaining suitable samples for assay (supernatant from PHA-stimulated peripheral blood monocytes) is extremely labour-intensive, so that the sample size is relatively small \( n = 14 \). Thus the intention was only to demonstrate the presence of interleukin-1-type activity in peripheral blood monocytes subsequent to endurance exercise. This was achieved, with a significant increase being measured immediately and 24 h after exercise \( P < 0.01 \). Although there was an absolute increase in circulating monocyte number after exercise (Table 3), the levels remained at about 6% of the total leucocyte count. The possibility that monocyte function is altered by strenuous exercise is recognized [1]. However, we found that monocyte adherence to plastic remained unchanged, before and after exercise, so that the number of monocytes stimulated with PHA can be assumed to be constant. In other words, any change in interleukin-1-type activity could be attributed to an increased production of this cytokine by a constant number of monocytes, and not to an increase in monocyte numbers per se.

Analysis of the cellular effects of interleukin-1 are complicated, as this polypeptide can induce the proliferation of other cytokines, particularly interleukin-2 and interleukin-6 [40]. The former, a powerful autocrine and paracrine T-cell growth factor, plays a pivotal role in the immune response [40], whereas the latter influences the hepatic production of the acute-phase proteins, a role formerly attributed to interleukin-1 alone. Thus, the ‘contaminating’ presence of both lymphokines in the demonstrated increase in interleukin-1-type activity would therefore serve to confirm the mediatory role of the lymphokines in the haematological and immunological response to strenuous exercise. Increased plasma concentrations of fibrinogen, haptoglobin and C-reactive protein paralleled the increase in interleukin-1 activity. However, in this study, the negative acute-phase reactants albumin and transferrin respectively increased and
remained unchanged after exercise. The contradictory rise in the former could, as well as denying the analogy of exercise as an acute-phase response, be attributed to large plasma volume shifts associated with prolonged exercise, in which albumin plays a critical homeostatic role [37]. As studies of immune function after exercise have produced conflicting results, it is possible that the individual differences in interleukin-1-type activity after exercise could account for this variability.

To conclude, these data suggest that although the metabolic sequelae of strenuous exercise may be similar to those of the inflammatory response, there are several inconsistencies, particularly as regards iron metabolism and plasma protein levels. These would deny then the analogies of strenuous exercise as an acute-phase response per se and of sports anaemia as being aetologically comparable with the anaemia of chronic disorders.

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