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Maintenance of iron status in healthy men during an extended period of stress and physical activity[1-3]

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ABSTRACT Body weight loss and iron status of 55 male soldiers were measured during 62 d of intense physical activity and sustained stress and sleep deprivation. Body weight declined from ($\bar{x}$ ± SD) 75.9 ± 9.0 to 63.8 ± 6.7 kg ($P < 0.05$). Serum iron fell from 13.7 ± 5.6 to 8.3 ± 3.6 μmol/L by 14 d ($P < 0.05$), but returned to baseline values by 8 wk. Total iron-binding capacity declined from 53.4 ± 6.8 at baseline to 47.5 ± 6.3 μmol/L at 8 wk ($P < 0.05$). During the study, hematocrit, serum hemoglobin, and erythrocyte count did not change, whereas ferritin increased from 116 ± 84 to 202 ± 106 μg/L ($P > 0.05$). Adequate dietary iron, initiation of training with adequate body iron stores, and physical activity not in excess of pretraining workloads contributed to the maintenance of iron status during prolonged physical activity and stress. Our results suggest that some acute phase–like disturbances in iron metabolism may be a normal component of adaptation to stress and physical activity in healthy men. *Am J Clin Nutr* 1993;58:923–7.

KEY WORDS Iron status, weight loss, stress, exercise, hemoglobin, hematocrit, ferritin

Introduction

Iron-deficiency anemia is relatively rare in healthy men, but it has been reported that strenuous exercise or physical activity may adversely affect iron metabolism and contribute to a condition characterized by reduced blood hemoglobin and serum iron and ferritin concentrations in men and women (1, 2).

The mechanism by which exercise produces this apparent change in iron status is unknown, but the condition may be a result of an exercise-induced redistribution of iron stores; increased iron losses in urine, sweat, and/or feces; reduced intestinal iron absorption; hemolysis; or a higher turnover of hemoglobin and erythrocytes (2–7). Other studies suggest that changes in serum concentrations of iron and ferritin reflect a physiological response to exercise similar to a long-term adaptation to sustained stress or the acute-phase reaction (7–11). Stressors other than exercise, such as infection, inflammation, or trauma, result in biochemical and endocrine changes qualitatively similar to those caused by strenuous exercise. This acute-phase response involves reductions in plasma iron and zinc concentrations and increases in blood concentrations of transferrin, ferritin, and some other acute-phase proteins.

The exercise-induced changes in iron metabolism may persist over multiple training seasons (12, 13) but there is no consensus on the impact of these changes on other aspects of metabolism or physical performance. Some studies showed that correction of the low hemoglobin and ferritin concentrations improved physical performance (14, 15) whereas iron supplementation in other studies failed to improve performance (16, 17).

Military personnel often must perform heavy physical work for extended periods of time. Studies with Norwegian Rangers (8, 9) and Navy SEALS (10) showed that brief episodes of intense physical and mental stress induce an acute phase–like response, and reduce serum iron and ferritin concentrations. But it is unclear whether the changes in iron metabolism persist during extended periods of stress or whether they actually reflect the early stages of iron depletion in response to physical exertion.

This study was conducted to determine the effect of a sustained period of stress and heavy physical activity on iron metabolism in healthy, physically conditioned male soldiers enrolled in the US Army Ranger Course, a 62-d training program conducted under physically and mentally demanding conditions.

Subjects and methods

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Subjects

This study was reviewed and approved by the US Army Research Institute of Environmental Medicine Human Use Review Committee, and was conducted in accordance with Army Regulation 70-25 (18). All participants in the study were volunteers and gave their informed consent to participate. The volunteers were trainees participating in the US Army Ranger Course (Class 91-11, conducted from July 26 through September 26, 1991). The initial study population consisted of 190 male volunteers of 261 members of the class; 55 soldiers completed the course in 8 wk and only data from these soldiers are reported. Baseline descriptive data for these 55 soldiers are given in **Table 1.**

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TABLE 1
Descriptive data collected at baseline from soldiers who then completed the US Army Ranger Course*

Characteristic	
Age (y)	23.6 ± 2.8 (18–31)
Weight (kg)	75.9 ± 8.9 (63–100)
Height (cm)	176.6 ± 6.2 (165–192)
Body fat (%)	17.2 ± 2.9 (11–26)

* $\bar{x}$ ± SD; range in parentheses; n = 55.

Experimental design

The Ranger Course comprises four 2-wk phases taught under different environmental and geographical conditions over a 62-d period. After a preliminary testing period to determine whether trainees meet physical and technical skill standards, they complete training in the four phases: general subjects training at Fort Benning, Columbus, GA (phase 1); mountain training at Camp Merrill, Dahlonega, GA (phase 2); jungle training at Eglin Air Force Base, Walton Beach, FL (phase 3); and desert training at Fort Bliss, El Paso, TX (phase 4). Each phase consists of 3–7 d of subject-matter training followed by a 7–10-d field training exercise.

The field training consisted of simulated combat infantry patrols with weapons and basic equipment load (average weight per soldier, 34 kg). Trainees averaged 3–4 h sleep/d (19).

Hunger is an important stressor during Ranger training and is created by imposing food restriction during certain periods of training. During the field-training exercises (35 d of the study period) soldiers were provided one Meal, Ready-to-Eat (MRE) field ration daily (20). During other training periods (27 d of the study period) they were provided the equivalent of two or three meals daily. Trainees were not permitted to save food items from an individual meal and were unable to obtain food from outside sources during the entire 8-wk training course.

The average daily energy and protein intakes, determined by menu analysis, were 11.7 MJ (2800 kcal) and 80 g, respectively. The average energy expenditure determined by the doubly labeled water technique was 16.8 MJ (4010 kcal)/d (21).

Blood specimens and anthropometric measurements were collected before beginning the course (baseline) and at the completion of each training phase. The measurements were made on fasted subjects as they returned from the field-training exercises between 0430 and 0900.

Methods

Body weight and body composition measurements were made at baseline and at the end of each training phase. Nude body weights were determined by using an electronic balance (model 708; SECA Instrument Co, Columbia, MD). Skinfold-thickness measurements were made at four sites (biceps, triceps, suprailiac, and subscapula) as described by Durnin and Womersley (22). Body fat is typically overestimated (3–4% body fat) by anthropometric equations in lean men relative to criterion methods such as hydrostatic weighing (23) and dual-energy x-ray absorptiometry (21). The predictions from skinfold thickness reported here are nevertheless useful as relative markers of the change in fat stores.

Fasting blood samples (35 mL) were collected into untreated, heparinized, and EDTA-treated evacuated tubes between 0430 and 0900 from soldiers in a seated position. Blood samples were kept cool (15 °C) until processed (within 5 h). Erythrocytes collected into EDTA-treated tubes were separated from plasma and washed two times with ice-cold 0.15 mol NaCl/L and then frozen (−20 °C). The separated serum, plasma, and cells were frozen (−20 °C) until analyzed. Except where specifically noted, all specimens were shipped frozen on dry ice to the Pennington Biomedical Research Center, Baton Rouge, LA, for analysis.

Serum iron and total iron-binding capacity (TIBC) were analyzed by using a Synchron CX5 automated chemistry analyzer (Beckman Instruments, Inc, Fullerton, CA) according to manufacturer-recommended procedures (24). Percent iron saturation was calculated as the ratio of serum iron concentration to TIBC. Ferritin was determined in duplicate serum aliquots by using an IRMA kit (BioRad, Richmond, CA).

Erythrocyte aspartate aminotransferase (EAST) activity was determined on erythrocyte hemolysates by using an AST reagent cartridge (Beckman Synchron CX5 automated chemistry analyzer) according to the method developed by Bayoumi and Rosalki (25) and Vuilleumie2r et al (26).

At each testing site, hematocrit values were determined by using the capillary tube microhematocrit method, and hemoglobin concentrations were determined on aliquots of whole blood by the cyanomethemoglobin method by using a cooximeter (Instrumentation Laboratories, Lexington, MA). The same technician performed these tests at each site, using the same instruments and controls.

At each measurement period, automated complete blood counts and white blood cell differential counts were obtained on a blood sample drawn into EDTA-containing evacuated tubes by using either an H-6000 analyzer (Technicon, Inc, Tarrytown, NY) at Martin Army Community Hospital, Fort Benning, GA (baseline and phases 1 and 2 samples), or model STKR analyzers (Coulter Electronics, Inc, Hialeah, FL) at either US Air Force Regional Hospital, Eglin Air Force Base, FL (phase 3) or William Beaumont Army Medical Center, El Paso, TX (phase 4). Differential counts were not done at the end of phase 1.

Statistical methods

The data were analyzed by using a one-way repeated-measures analysis of variance. Individual means were compared across time periods by using paired t tests on the *SPSSx* statistical software program (27). Tabular data is reported as mean ± SD.

Results

Trainees lost an average of 12.1 ± 3.4 kg body wt (range 6.5–20.6 kg) during the course. Percentage body fat estimated from skinfold-thickness measurements fell from 17.2 ± 2.9% (range 6–26%) at baseline to 9.5% ± 2.2% (range 4–12%) at 8 wk. Body weight and anthropometric data are given in **Table 2.**

Serum iron concentration was lower at the end of the first 2 wk of training (**Table 3**) than at baseline. However, serum iron increased to low-normal values by 4 and 6 wk and had returned to baseline values at the end of the 8-wk course. Hemoglobin and hematocrit (Table 3) measurements remained within normal limits throughout the study and did not change over the course of the training.

Ferritin concentration (Table 3) gradually increased over the course of the study ($P < 0.01$) but because of the large variation

TABLE 2
Body composition of soldiers completing the US Army Ranger Course*

Variable	Baseline (n = 55)	Phase 1 (n = 52)	Phase 2 (n = 52)	Phase 3 (n = 52)	Phase 4 (n = 55)
Body weight (kg)	75.9 ± 9.0	71.0 ± 8.0†	68.9 ± 7.6†	66.4 ± 7.2†	63.8 ± 6.7†
Body fat (%)	17.2 ± 2.9	13.5 ± 2.7†	11.7 ± 2.2†	9.9 ± 2.1†	9.5 ± 2.2†

* $\bar{x}$ ± SD.
† Significantly different from baseline, $P < 0.05$.

in individual values, post hoc comparisons vs baseline were not significant. Sample variances were similar at each measurement period even though there was a moderate amount of skewing associated with the data. Logarithmic transformation of the data produced a similar level of significance ($P < 0.01$, F value = 10.90) compared with the raw data ($P < 0.01$, F value = 8.74), and therefore we only reported the arithmetic means in Table 3. Ferritin concentration was within normal limits throughout the study. TIBC was lower than baseline at the end of each phase.

Erythrocyte counts, mean corpuscular hemoglobin (MCH), MCH concentration (MCHC), and mean cell volume (MCV) fluctuated during the study, but the changes were not clinically significant. There were small increases in EAST activity during the course, but EAST activity returned to baseline values by phase 4. White blood cell counts were higher than baseline values at 4 wk, but returned to baseline values by the end of the course (**Table 4**).

Discussion

The present study demonstrated no significant adverse impact of sustained, strenuous physical work on indicators of iron status in men. Although there was a temporary decline in serum iron concentration at 2 wk, this condition resolved without intervention by 8 wk. These results are in contrast to most studies on exercise and iron metabolism in men and women that have demonstrated that blood iron, hemoglobin, and ferritin concentrations are generally lower in trained athletes or are reduced in response to strenuous physical exercise (1, 2, 28–31).

The most significant change that occurred in trainees in the present study was a transient decline in serum iron at 2 wk, which gradually returned to baseline concentrations by 8 wk. This response is characteristic of an acute-phase response (7, 32). Other studies have observed acute phase–like changes in markers of iron status after single bouts of exercise (11) or after extended (5-d) periods of intense physical activity (7–9). In contrast to the studies of Lindemann et al (8) and Vidnes and Opstad (9) in Norwegian Ranger trainees after 5 d of complete food and sleep deprivation combined with intense physical activity, trainees in our study were subjected to continuous stress and sleep and food deprivation for 62 d. Yet, the only significant indicator of an acute-phase response, the lower serum iron at 2 wk, resolved itself during this period, which suggests that some changes in iron metabolism that occur early during exercise may be transitory physiological adaptations to stress and probably do not represent the early signs of iron deficiency. Dressendorfer et al (29) also showed that plasma indicators of iron status stabilized after ≈6 d during a 20-d road race.

Many factors may contribute to the reduction in hemoglobin and ferritin concentrations observed in response to exercise. During long-term training or initial fitness training, there is a reduction in hemoglobin concentration and hematocrit resulting from a greater expansion of blood volume relative to increases in erythrocyte mass (4, 33). The soldiers in our study were in excellent physical condition at the beginning of the course and the physical effort of Ranger training was not substantially more intense than that of their normal activities, which may account for the lack of a dilutional effect of Ranger training on blood-constituent concentrations.

Iron depletion could occur in persons engaged in exercise if metabolic demand increased above the available iron provided from body iron stores or the diet. Serum ferritin concentrations < 60 μg/L reflect minimal body iron stores and values < 20 μg/L indicate substantial depletion of body iron stores (34). Schobersberger et al (6) showed that hemoglobin concentration, serum ferritin, MCHC, and MCH decreased in untrained men (ferritin concentrations < 75 μg/L) during 6 wk of weight training and Diehl et al (12) reported that serum ferritin concentration (initial concentration 25 μg/L) progressively decreased in female athletes over three training seasons. In contrast to these studies

TABLE 3
Hematologic markers of iron status, serum iron, total iron-binding capacity (TIBC), and ferritin concentrations in Ranger trainees*

Iron-status marker	Baseline (n = 51)	Phase 1 (n = 48)	Phase 2 (n = 48)	Phase 3 (n = 45)	Phase 4 (n = 49)
Hematocrit (l)	0.423 ± 0.022	0.427 ± 0.029	0.423 ± 0.023	0.418 ± 0.019	0.437 ± 0.029
Hemoglobin (g/L)	143 ± 8	140 ± 8	146 ± 9	142 ± 7	146 ± 8
Iron (μmol/L)	13.7 ± 5.6	8.3 ± 3.6†	10.6 ± 4.2†‡	10.8 ± 3.5†	13.4 ± 5.5‡
TIBC (μmol/L)	53.4 ± 6.8	50.6 ± 6.7†	50.0 ± 6.0†	47.4 ± 5.6†‡	47.5 ± 6.3†
Ferritin (μg/L)	116 ± 84 [53]	112 ± 53 [50]	153 ± 82 [50]	159 ± 89 [45]	202 ± 106 [41]

* $\bar{x}$ ± SD; (n) number of observations for ferritin only in brackets.
† Significantly different from baseline, $P < 0.05$.
‡ Significantly different from preceding phase, $P < 0.05$.

TABLE 4
Erythrocyte (RBC) counts and characteristics and white blood cell (WBC) counts of Ranger trainees*

Blood characteristics	Baseline	Phase 1	Phase 2	Phase 3	Phase 4
RBC count ($\times 10^{12}$/L)	4.71 ± 0.27 [51]	4.62 ± 0.35 [48]	4.78 ± 0.29 [48]	4.64 ± 0.26 [45]	4.76 ± 0.38 [49]
MCHC (%)	33.7 ± 1.4	32.8 ± 1.0†	34.4 ± 0.9†	33.9 ± 0.5†	33.4 ± 1.0†
MCH (pg)	29.9 ± 1.8	30.5 ± 1.8†	30.5 ± 1.6†	30.6 ± 1.6†	30.7 ± 2.0†
MCV (fL)	90.0 ± 2.8	92.7 ± 3.7†	88.5 ± 3.7†	90.5 ± 3.8	91.9 ± 4.2
RBC AST (IU/g Hb)	5.99 ± 1.75	6.39 ± 1.54†	6.41 ± 1.66†	6.59 ± 1.87	5.83 ± 1.79
WBC count ($\times 10^{12}$/L)	6.65 ± 2.39 [49]	5.39 ± 1.41 [43]†	8.17 ± 3.01 [46]†	7.42 ± 2.04 [44]†	6.97 ± 1.95 [51]

* $\bar{x}$ ± SD; n in brackets. MCHC, mean corpuscular hemoglobin concentration; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; RBC AST, erythrocyte aspartate aminotransferase activity.
† Significantly different from baseline, $P < 0.05$.

the soldiers in the present study began training with adequate iron stores (ferritin concentration > 100 μg/L) and thus may have been better able to meet increased iron demand and resist developing lower serum hemoglobin and ferritin concentrations and hematocrit compared with athletes or persons with minimal body iron reserves.

Roberts and Smith (35) showed that serum ferritin concentrations decreased from 80 to 46 μg/L in male swimmers during 3 wk of heavy training at high altitude, but returned to pretraining concentrations when they returned to pretraining altitude even though training intensity did not change. Their data and ours show that iron stores can be maintained during heavy physical work or training provided adequate dietary iron is consumed and initial iron stores are adequate to meet short-term changes in metabolic iron demand.

Typical iron losses in adult males are ≈ 1 mg/d (36) and higher urine, sweat, and fecal losses could increase losses to ≈2–2.5 mg Fe/d (2). In our study, iron intakes averaged 13 mg/d, but were as low as 6 mg/d during the 35 d when soldiers were given one ration per day. Assuming an apparent absorption of dietary iron of 20% (2), the diet provided between 1.2 and 2.6 mg available Fe/d, sufficient to meet metabolic requirements during Ranger training. The combination of an adequate iron intake and sufficient pretraining body iron stores probably accounts for much of the ability of the soldiers in the present study to maintain iron status during sustained exercise compared with subjects described elsewhere who engage in physical training with low reserves and marginal dietary iron intakes (6, 12, 28, 29).

Exercise increases erythropoiesis and erythrocyte turnover (5, 6). Schobersberger et al (6) suggested that the decline in MCHC, MCH, and ferritin during 6 wk of weight training indicated the presence of a prelatent iron deficiency. TIBC declined during our study; transferrin concentrations are accurately reflected by serum TIBC (37), and the apparent decline in transferrin concentrations probably reflects the mild protein-energy malnutrition during the course (38). The percentage saturation of transferrin gradually increased during the course, reflecting the recovery of serum iron concentration, and MCHC, MCH, hemoglobin, and ferritin concentrations did not change or increased slightly. These data indicate that even if sustained physical activity and stress increased iron turnover, the magnitude of the increase did not exceed the amount of replacement iron available from iron stores and the diet.

Some forms of endurance exercise, such as marathon running or swimming, consistently induce rapid declines in blood iron and ferritin concentrations (1, 2), which has been attributed to increased intravascular erythrocyte hemolysis (6, 39, 40). Weight et al (5) showed that erythrocyte turnover was higher in endurance-trained athletes than in sedentary control subjects and Vidnes and Opstad (9) reported an increase in serum ferritin concentration similar in magnitude to what we observed, which they attributed to increased ferritin synthesis and release by the reticuloendothelial system in response to iron release due to hemolysis. We did not measure haptoglobin concentration and cannot rule out that erythrocyte hemolysis increased during the course. However, erythrocyte AST activity increased by 2 wk, but then remained constant for the remainder of the course. The specific activity of AST is higher in young erythrocytes (41) and the increase observed may indicate that erythrocyte turnover was slightly increased during the course. But the relatively modest changes in EAST activity and absence of change for other markers of hemolysis and cell iron metabolism (hematocrit, MCH, and MCHC) suggest that any changes in erythrocyte turnover were within the capability of the body to adapt (6, 39–41).

Our data demonstrate that intense physical exertion over an extended period of time does not necessarily lead to impaired iron metabolism. Soldiers were able to maintain normal iron status because of high pretraining iron stores, a physical workload similar in magnitude to pretraining workload, and consumption of a diet that met metabolic iron needs. The transient changes in serum iron suggest that some acute phase–like disturbances in iron metabolism may be normal adaptations to stress and physical activity in healthy men.

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