The Effects of Red Blood Cell Infusion on 10-km Race Time

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The purpose of this study was to investigate the effect of infusion of 400 mL of red blood cells (RBCs) on 10-km track race time, submaximal heart rate, hematocrit, 2,3-diphosphoglycerate, and partial pressure of oxygen at 50% hemoglobin saturation. Six highly trained, male, distance runners twice donated a unit of RBCs, which was frozen for subsequent reinfusion. Eleven weeks after the second donation, they undertook a series of three competitive 10-km races on a standard 400-m track: before infusion, after 100 mL of saline solution, and after 400 mL of autologous, previously frozen deglycerolized RBCs. All subjects took all trials in this double-blind, placebo, crossover, experimental design. Running time was recorded at each 400-m split, and blood was collected prior to each trial. The data were analyzed by analysis of variance. Results following the RBC infusion showed a significantly higher hematocrit concentration, a significantly faster 10-km run, a nonsignificant decrease in submaximal heart rate (10 beats per minute), and no significant changes in either 2,3-diphosphoglycerate or partial pressure of oxygen at 50% hemoglobin saturation. Erythrocythemia induced by the infusion of 400 mL of autologous packed RBCs effectively increased performance capacity in a 10-km track race, probably due to an increase in oxygen delivery to the working muscles.

(*JAMA* 1987;257:2761-2765)

THE SUBJECT of red blood cell (RBC) infusions as an ergogenic aid has been of special interest to coaches, athletes, and scientists since Pace et al[1] first conducted a study on homologous blood infusion in 1947. The underlying theory of induced erythrocythemia is that increased oxygen-carrying capacity increases performance of working muscle by increasing oxygen supply. Studies in laboratory settings have produced conflicting results.[2]

There have been several reported instances where this practice has appeared to benefit athletes. According to the *Sunday Times* of London (Feb 5, 1984, p 30), when Italian Francesco Moser twice shattered the outdoor one-hour cycling record in Mexico City in 1984, he was assisted by an entourage of two cardiologists and eight men 18 to 20 years of age who were chosen several months previously because of their blood type compatibility with Moser. Finnish distance runner Kaarlo Maaininka freely admitted receiving 2 units of blood from team doctors shortly before he won silver and bronze medals in the 10- and 5-km events, respectively, at the 1980 Olympic games in Moscow.[3] The latest disclosure of blood boosting among several members of the successful US cycling team in the 1984 Olympics has rekindled the question of enhanced performance (*Sports Illustrated*, Jan 21, 1985, p 12).

The efficacy of induced erythrocythemia as an aid to competitive endurance performance is associated with skepticism.[4] This study determined the effects of induced erythrocythemia on highly trained, male, distance runners in a 10-km track race.

METHODS

Six male distance runners were selected to participate in a double-blind study of induced erythrocythemia. Both subjects and personnel involved in the measurements were kept unaware of treatment used. All subjects were residents of Albuquerque 18 months prior to the beginning of the study and were acclimatized to the altitude of the city (1500 to 1800 m). Their previous 10-km times prior to the study are shown in Table 1. These times and resting heart rates showed them to be relatively well trained for amateur runners. The subjects were instructed to maintain their normal daily activities and training schedule throughout the course of the study. Relative anthropometric and other data are shown in Table 1 as means ± 1 SD. Informed consent was obtained from all subjects after approval by the University of New Mexico Human Research Review Committee.

A double-blind, crossover, experimental design was utilized. The subjects were prevented from observing experimental treatments by wearing blacked-out goggles and having loud music played through headphones during all infusion processes. Those recording study results were blinded as to treatment order.

The subjects underwent two phle-

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Table 1.—Description of Subjects

Subject	Age, y	Height, cm	Weight, kg	Resting Heart Rate, Beats per Minute	Hematocrit Volume, %, Before Phlebotomy	km per Week	Years Running	10-km Time at Altitude Before Study	
								Minutes	s
Group 1 (placebo first)									
1	38	175.26	62.73	41	43 (0.43)	136.8	7	34	18
2	27	172.72	60.91	44	42 (0.42)	122.3	12	32	49
3	28	167.64	58.64	42	40 (0.40)	135.2	15	33	32
Group 2 (reinfusion first)									
4	35	177.80	61.82	39	41 (0.41)	177.0	17	32	15
5	41	167.64	58.18	45	43 (0.43)	123.9	19	33	51
6	33	182.88	65.00	40	42 (0.42)	112.7	16	33	41
$\bar{X}$	33.6	173.99	61.21	41.8	41.6 (0.416)	134.64	14.3	33	25
SD	5.2	5.96	2.57	2.3	1.4 (0.014)	22.59	4.3	...	44

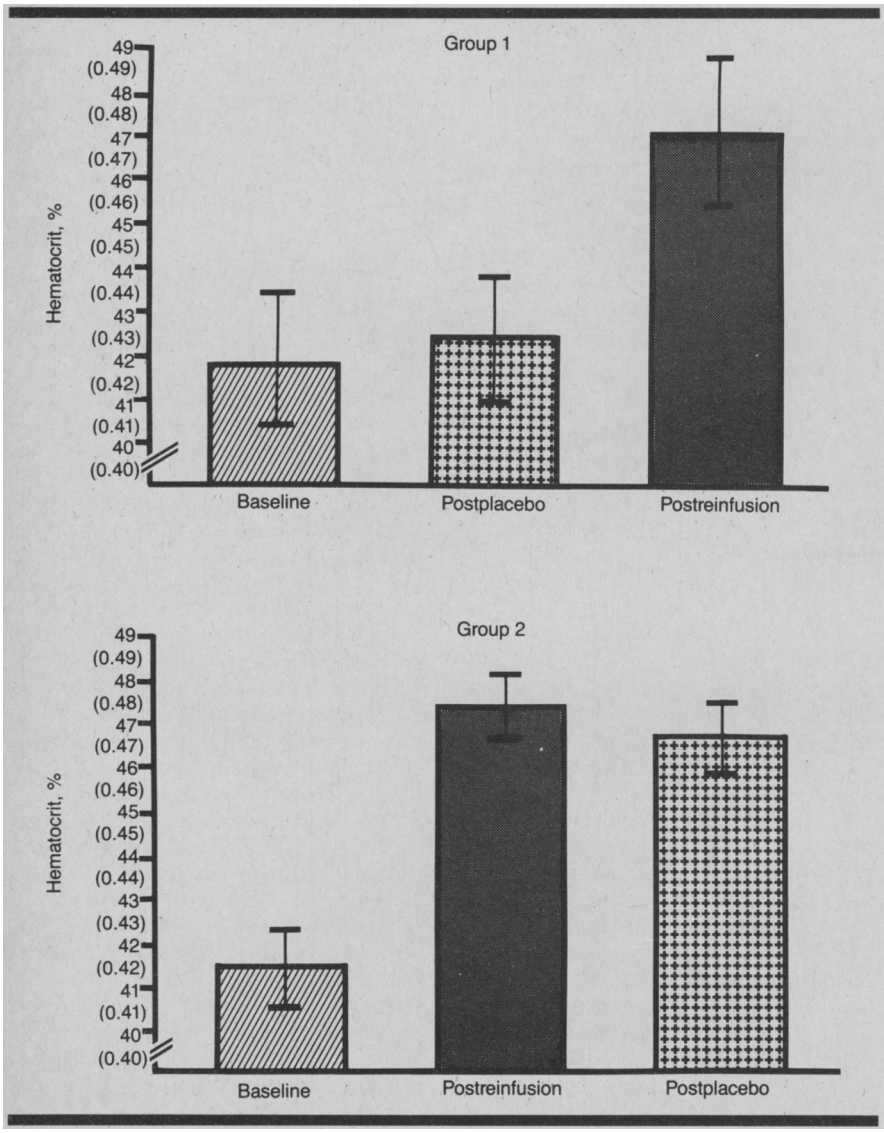

Fig 1.—Relationship between hematocrit and infusions. Hematocrit increase occurred after infusion of red blood cells and was sustained for week between 10-km race after reinfusion and 10-km race after placebo in group 2.

botomies (450 mL each) spaced eight weeks apart. Red blood cells were separated from whole blood and stored, using the high-glycerol freezing technique.[5] The subjects continued training (112 to 176 km per week) for approximately 11 weeks after the second phlebotomy before receiving the infusions.

Six days before the first infusion, collection of baseline data was initiated. Treadmill studies were done six days before infusion, blood specimens five days before, and the 10-km race three days before. Two days before the first infusion, treadmill was repeated; at three days, blood studies; and at five days, the second race. Three days after the second race, the second infusion was given, and the procedures were repeated at the same intervals. Infusion treatments consisted of an autologous infusion of 400 mL of previously frozen deglycerolyzed RBCs or a placebo infusion of 100 mL of normal saline (the approximate amount of saline used to resuspend the RBCs). The subjects were randomly divided into two groups (1 and 2) and were randomly assigned treatments, with the order of receipt of the infusion treatments reversed using a crossover double-blind design.

The subjects ran a series of three 10-km open-competition track races at nine-day intervals on a 40-m rubberized, asphalt, outdoor track located at altitude (1803 m). The first race was used as a baseline control measure, while the second and third races were run five days after the first and second infusions, respectively.

Three submaximal treadmill tests were taken three days prior to each race to determine any change in heart rate (HR), measured by recording electrocardiogram. Prior to each test, subjects performed a standard six-minute warm-up. Testing began at a velocity of 8 km/h (5 mph) and increased 1.6 km/h (1 mph) each minute until 14.4 km/h (9 mph) was reached. At that time, the treadmill speed was held constant and the grade elevated to 5%. Subjects ran at this load for six minutes, with the submaximal rate being recorded between the fifth and sixth minutes.

Blood samples (10 mL) were collected in heparinized syringes from the antecubital vein two days prior to each race. Samples were analyzed for hematocrit (Hct), red-cell 2,3-diphosphoglycerate (2,3-DPG), and partial pressure of oxygen at 50% hemoglobin saturation (P_{50}). The Hct was measured on a microhematocrit centrifuge (coefficient of variation, 1.2%). The 2,3-DPG was assayed enzymatically using a method that has a coefficient of variation of 2.0%. A device that generates an oxy-

hemoglobin dissociation curve by measuring arterial oxygen pressure through a membrane and saturation spectrophotometrically on deoxygenated blood, which is reoxygenated in stages, was used to determine P_{50} values (reproducible to 1 mm Hg).

Three subjects received the saline placebo first and were designated as group 1. The other three subjects received the RBC infusion initially and were designated as group 2.

Analysis of variance was performed for the major end points. Between-subjects effects and within-subjects effects were analyzed. Because of multiple comparisons, $P<.01$ was chosen as the determinant of significance.

RESULTS

In the three races, the temperature (18.3°C, 16.1°C, and 17.2°C), humidity (29%, 28%, and 24%), and wind velocity (8, 3.2, and 6.4 km/h [5, 2, and 4 mph]) were similar.

Figure 1 shows that Hcts were increased more than 5% by the RBC infusions. The treatment relationship with Hct was highly significant ($P=.004$). The comparisons between baseline Hct and Hct after reinfusion and between placebo and reinfusion were similarly significant ($P<.001$ and $P=.003$, respectively). In group 2, there was a carryover effect in that the Hct increase from baseline caused by the reinfusion persisted after the placebo ($P=.004$ for the interaction with order). Hematocrit after placebo was higher than baseline in group 2 (when it followed the reinfusion with RBCs) but not in group 1 ($P=.001$ for this difference), and Hct after placebo was much lower than after reinfusion in group 1 but not in group 2 ($P=.008$ for this interaction with order).

The treatment effect was significant on the 10-km race time. Results are shown in Fig 2 and Table 2. Reinfusion of RBCs caused a reduction of approximately one minute in time to run the 10-km race. The comparisons of baseline to saline were not significant, but baseline to reinfusion and saline to reinfusion were both significant at $P<.001$. Order did affect the results, because of the carryover of the reduced time in group 2 from the reinfusion through to placebo. Running time after placebo was much lower than baseline in group 2 (where it followed the reinfusion with RBCs) but not in group 1 ($P=.005$ for this difference), and running time after placebo was much slower than after reinfusion in group 1 but not in group 2 ($P<.001$ for this interaction with order).

Figure 3 shows the decrease in submaximal HR of varying amounts after

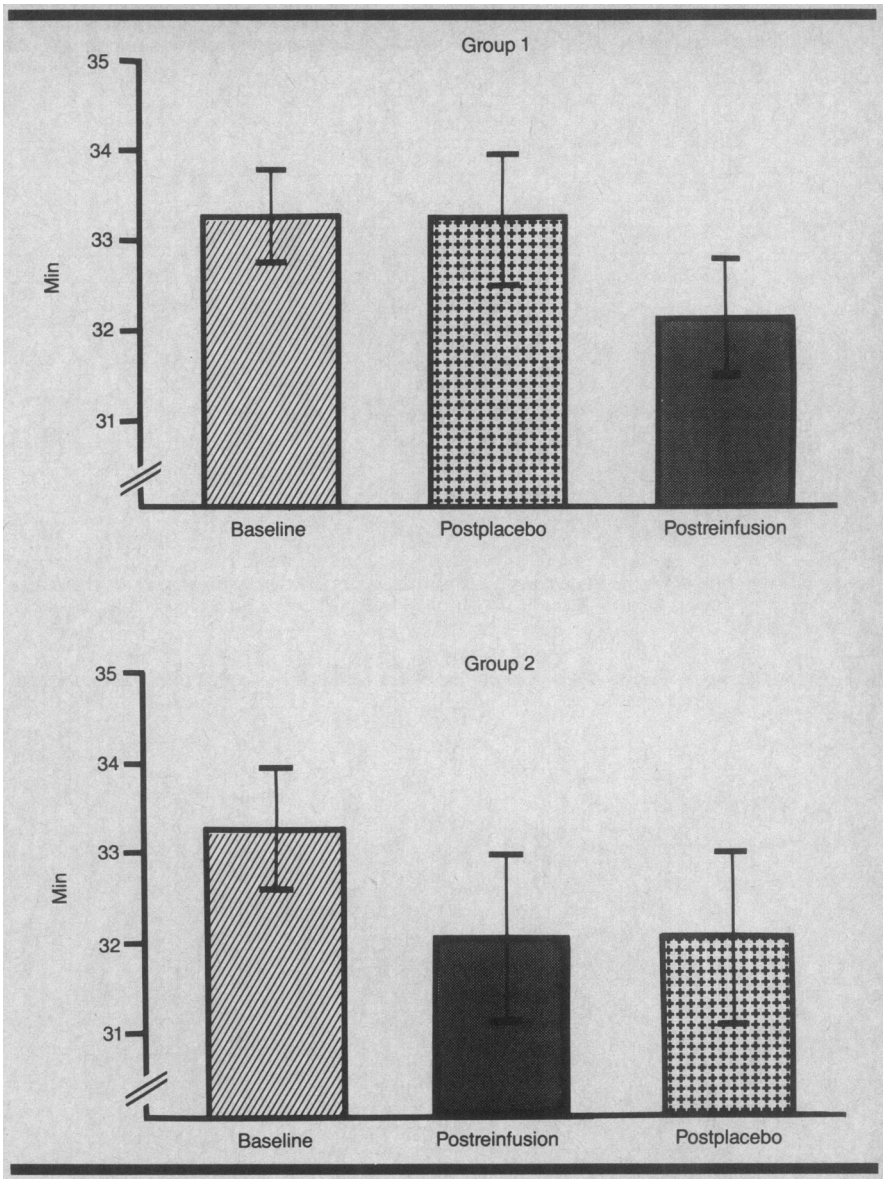

Fig 2.—Relationship between time to run 10-km race and reinfusion or placebo. In group 1, time fell after reinfusion but not after placebo. In group 2, time fell after reinfusion, and improved time was sustained for 13 days from reinfusion of red blood cells to 10-km race after placebo infusion.

infusion of RBCs. These changes were not statistically significant. There were no differences for P_{50} and 2,3-DPG. Mean P_{50} at baseline was 26.8 ± 0.5 mm Hg. After RBC infusion, it was 27.4 ± 1.0 mm Hg. Mean 2,3-DPG level was 2.38 ± 0.13 μmol/mL at baseline and 2.36 ± 0.36 μmol/mL after infusion.

COMMENT

The purpose of this investigation was to determine the effects of a reinfusion of 400 mL of autologous RBCs on the 10-km track race time in highly trained, male, distance runners. Supporting data were measures of Hct, 2,3-DPG, P_{50}, and HR.

A number of important physiological changes occur in running a 10-km race. Blood volume increases with increased cardiac output and HR, working muscles experience vasodilation, sympathetic nervous system stimulation occurs, a linear increase in oxygen consumption occurs, and lactate production increases and causes increased ventilation. Endurance exercise, such as running, results in increases in maximum oxygen consumption but not in muscle hypertrophy or strength increases.[6] Thus, in the context of these complex physiological changes, this study asks the question if increased RBC mass can provide a sufficient increase in oxygen utilization to improve performance.

The RBC infusion resulted in a faster overall 10-km race time in comparison

Table 2.—Individual Performance Tests Results: Race Time in Increments of Four Laps (Minutes and s)

Subject	Race	1600 m	3200 m	4800 m	6400 m	8000 m	9600 m	10 000 m (10 km)
1	1	5.00	10.21	15.49	21.24	27.02	32.42	34.02
	2	5.03	10.26	16.01	21.43	27.24	33.08	34.32
	3*	5.03	10.16	15.32	20.54	26.18	31.45	33.02
2	1	5.00	10.13	15.32	20.53	26.21	31.40	32.51
	2	5.01	10.12	15.31	20.51	26.13	31.30	32.42
	3*	5.00	10.00	14.59	20.05	25.16	30.22	31.33
3	1	5.00	10.20	15.45	21.11	26.40	32.09	33.30
	2	5.00	10.20	15.49	21.19	26.49	32.18	33.37
	3*	5.00	10.07	15.20	20.35	25.50	31.04	32.20
4	1	5.01	10.08	15.21	20.39	26.00	31.19	32.31
	2*	5.00	10.04	15.00	19.59	25.00	29.59	31.12
	3	4.59	9.59	14.58	20.00	25.02	30.01	31.14
5	1	5.14	10.41	16.09	21.41	27.16	32.48	34.09
	2*	5.03	10.12	15.31	20.51	26.13	31.31	32.48
	3	5.03	10.16	15.32	20.53	26.13	31.35	32.51
6	1	5.07	10.28	15.56	21.30	27.05	32.31	33.46
	2*	5.00	10.12	15.31	20.55	26.28	31.51	33.04
	3	5.03	10.16	15.33	20.58	26.26	31.50	33.03

*Red blood cell infusion. Race 1 is baseline. The other race was after placebo saline infusion (2 or 3 without an asterisk).

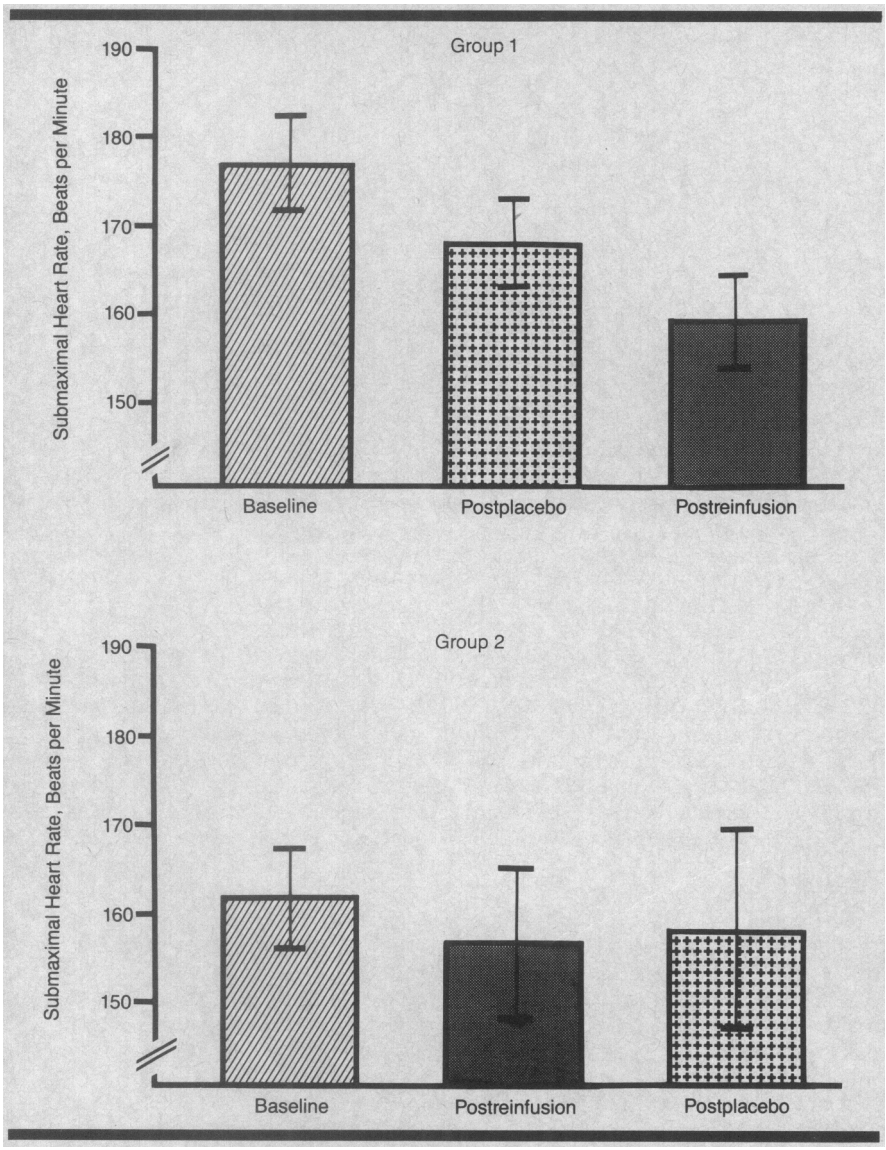

Fig 3.—Submaximal heart rate decreased after both placebo and reinfusion in group 1 and after reinfusion in group 2. There was greater fall after reinfusion than placebo.

with the preinfusion race or the race after saline when saline was first. In group 1, there was no change after saline infusion but an improvement after the RBC infusion. In group 2, the change was seen after infusion and remained throughout the rest of the study (ie, persisted after the second infusion of saline). In either case, it was the RBC infusion that caused the decrease, and it lasted at least 13 days. The improved performance was related to increased Hct, facilitating aerobic metabolism in the working muscles. The identical pattern of interaction between RBC reinfusion and order seen for Hct and 10-km race time effectively excludes a psychological effect. Thus, only with elevation in Hct was the improvement in the 10-km running time seen.

Astrand and Rodahl[7] note that maximal performance in events of approximately 30 minutes' duration represents an energy output of 95% from aerobic and 5% from anaerobic sources. Following induced erythrocythemia, the mean performance time for the 10-km track race was 69 s faster, ie, an average of almost 7 s/km. Similar results have been reported by Goforth et al,[8] who found that runners improved an average of 9 s per mile in a 3-mile time trial. The environmental conditions for the track races showed little variation and are unlikely to have affected performance time. Questioning prior to the two postinfusion races revealed that the subjects did not know exactly what they had received, ie, saline or RBCs.

Erythrocythemia may have influenced submaximal performance in this study, as evidenced by lower HRs, but the finding was not statistically significant. During a constant level of submaximal steady-state exercise, HRs were 10 beats per minute lower at 48 hours after RBC reinfusion. Buick et al[9] reported comparable results and claimed that erythrocythemia, through an elevation in arterial oxygenation, permits submaximal aerobic metabolism to be attained at a lower cardiac output.

Infusion of 400 mL of RBCs did not cause a compensatory shift in P_{50}, and this agrees with findings by Williams et al[10] and Goforth et al.[8]

The concentration of 2,3-DPG in the RBCs is important relative to the affinity of oxygen to hemoglobin. An increased level of 2,3-DPG is associated with a reduced affinity of oxygen to hemoglobin, thereby facilitating the release of oxygen from hemoglobin when

the blood reaches the muscles. On the other hand, hemoglobin affinity for oxygen is increased when the level of 2,3-DPG is decreased.[11,12] Frozen RBCs maintain 2,3-DPG[5]; thus, there were no significant differences in 2,3-DPG levels in this study. Oxygen affinity of the RBCs was not adversely affected. Comparable findings have been reported by Buick et al[9] and Goforth et al.[8]

Increases in blood viscosity could affect oxygen delivery following an elevation in Hct. Research indicates that the ideal Hct for the delivery of oxygen to contracting muscle is between 50% and 60% volume (0.50 and 0.60). This finding differs from the generally accepted optimal Hct of 45% volume (0.45) at rest.[13] In this study, the mean Hct after RBC infusion was only 47.4% volume (0.474), one not likely to compromise blood flow due to increased viscosity.

The results of this study are in agreement with those of a number of previous investigations[8,9,14-18] that reported significant increases in endurance performance. On the other hand, the results were at odds with those of a number of former studies[10,19-22] that reported no significant effect of erythrocythemia on endurance performance. The decisive elements seem to be the quantity of RBCs infused and an appropriate time span to allow the Hct and blood volume to stabilize between phlebotomy and 10-km race.

Within the limitations of this study, it appears that the infusion of 400 mL of RBCs into a distance runner with stable Hct will significantly increase the total RBC concentration, which, in turn, will contribute to a significant decrease in the time required to run a 10-km track race. The effect of the infusion and the subsequent increase in RBC mass may also relate to the observation that runners usually experience some element of hemolysis and iron depletion, which keeps their Hct at a lower level than they would have if not running.[23] The RBC infusion thus increases the runners' Hct to a level that might be their normal value if not running. In this study, the Hcts were within accepted normal range but below mean levels seen in men acclimated to altitude in Albuquerque.[24] The subjects in this study, although good-caliber runners, were not elite distance runners, and the results obtained in this study may or may not be applicable to the latter.

This procedure of "blood doping," or induced erythrocythemia, is controversial in sports medicine (*Sunday Times* [London], Feb 5, 1984, p 30; *Sports Illustrated*, Jan 21, 1985, p 12).[2-4] Done with autologous reinfusion under careful medical supervision, as in this study, the procedure is safe. Homologous blood and autologous blood without these careful controls are not safe. Overtransfusion to polycythemia could result in ischemic episodes due to decreased flow in vessels.

Autologous transfusion has raised ethical questions. It is regarded by the International Olympics Committee as dishonest.[3] Our purpose was not to encourage dishonesty in sports but rather to explore the effects of increase in RBC mass on runners' performance. Well-trained individuals appear to utilize the additional oxygen carried by the increased RBC mass advantageously in athletic performance. Increased RBC mass can improve performance even in runners at a stable, presumably normal Hct level.

This study was supported by grants from General Clinical Research Center Program DRR, National Institutes of Health M01-RR00997-09, and Public Health Service Transfusion Medicine Academic Award 5 K07 HL01252-03 from the National Heart, Lung, and Blood Institute, National Institutes of Health, and Blood Systems Research Foundation.

Statistical consultation was provided by Richard Harris, PhD. The authors also thank Lee Gates, MD, of the Lovelace Medical Center Laboratory and the staffs of the Clinical Research Center and United Blood Services.

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