Effect of Marathon Running on Hematologic and Biochemical Laboratory Parameters, Including Cardiac Markers

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Abstract

Participants in marathon races may require medical attention and the performance of laboratory assays. We report the changes in basic biochemical parameters, cardiac markers, CBC counts, and WBC differentials observed in participants in a marathon before, within 4 hours, and 24 hours after a race. The concentrations of glucose, total protein, albumin, uric acid, calcium, phosphorus, serum urea nitrogen, creatinine, bilirubin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, total creatine kinase, creatine kinase-MB, myoglobin, and the anion gap were increased after the race, consistent with the effects of exertional rhabdomyolysis and hemolysis. The increase in WBC counts was due mainly to neutrophilia and monocytosis, with a relative decrease in circulating lymphocytes, consistent with an inflammatory reaction to tissue injury. A significant percentage of laboratory results were outside the standard reference ranges, indicating that modified reference ranges derived from marathon runners might be more appropriate for this population. We provide a table of modified reference ranges (or expected ranges) for basic biochemical, cardiac, and hematologic laboratory parameters for marathon runners.

The word *marathon* has its origin in the Greek legend of the professional runner Phidippides, who ran from Marathon to Athens to report the outcome of a battle. On arrival, Phidippides is claimed to have staggered and gasped "Rejoice! We conquer," collapsed, and died. A 42.2-km (26.2-mile) marathon race was initiated in the first modern Olympic games and in Boston in 1896, with approximately 25 and 17 runners, respectively. Physicians with emergency medications followed the runners in carriages. Modern-day marathons draw thousands of contestants (50,000 entrants took part in the 100th Boston Marathon in 1996). Contemporary recreational marathon runners are similarly challenged by the course as Phidippides, a professional runner, was 2,500 years ago. Several hundred runners require urgent medical attention during or after the race for exercise-associated collapse; several deaths have occurred in recent years.[1] At the last Boston Marathon, a runner died of hyponatremic encephalopathy; many runners were evaluated and had testing performed at the finish-line medical tent. Standard laboratory tests are performed as a part of the triage and evaluation of collapsed marathon runners and other athletes; for this reason, knowledge of expected or "normal" findings in runners is a condition for interpreting the results of laboratory tests.

Changes in laboratory parameters in marathon runners were first reported in an article edited by Blake and Larrabee[2] in 1903. Their finding of leukocytosis after a race has since been confirmed by other groups.[3-5] Reports in the literature on other laboratory parameters in marathon runners are inconsistent. For example, while one group has reported a reduction in hematocrit after a marathon,[6] other investigators found no changes in this measurement,[3] while still others

reported an increase in hematocrit after a race.[7,8] Similarly, while most investigators have found an increase in sodium concentrations after long-distance running,[7-11] at least one group was unable to reproduce this finding.[12] Some of the discrepancies in the results of the various studies may be due to differences in time intervals for sampling after the race, degrees of fitness, and environmental conditions during the race.[13] Guidelines for fluid intake and electrolyte replacement of runners during a marathon also have changed. Finally, many reports in the literature are limited by a small sample (sometimes as few as 3 runners were studied[3,14,15]) or the use of now outdated laboratory methods. It is generally accepted that to ensure comparability between reference values and observed values, the same analytic method should be used.[16] Since most studies have concentrated on selected laboratory parameters, it is difficult to collate the available information into an integrated picture.[13] A number of studies have focused on changes in cardiac, hemostatic, and inflammatory markers in marathon runners,[5,17,18] but the results for many common laboratory tests have not been reported for runners in the recent literature.

Despite the fact that blood samples from marathon runners are likely to be examined in clinical laboratories and because strenuous exercise may have a profound effect on many laboratory parameters, it is difficult to get a clear picture from the available literature of the effects of long-distance running on many common laboratory test results and the expected or normal ranges observed. On the occasion of the upcoming 100th anniversary of the first description of laboratory changes in marathon runners,[2] we report the effects of marathon running on common laboratory parameters as measured by current technologies.

Materials and Methods

Specimens

Participants were 37 runners (mean ± SD age, 49 ± 10 years; 32 men, 5 women) attending the premarathon scientific symposium of the American Medical Association as entrants in the 105th Boston Athletic Association Marathon in 2001. Medical and running histories obtained by questionnaire indicated no smoking or known coronary heart disease, an average of 25 training miles per week, and 5 previous marathons completed, including a qualifying race of less than 4 hours during the previous year. Blood samples were obtained the day before and within 4 and 24 hours after the race, without stasis, from an antecubital vein using a 21-gauge butterfly needle. Samples were obtained before the race and within 4 hours after the race from 37 participants. Additional samples obtained 24 hours after the race were available from 11 runners (8 men, 3 women). The protocol was approved by the institutional review board of the hospital.

Clinical Chemistry Assessment

Serum samples were analyzed on the Roche/Hitachi 917 system (Roche Diagnostics, Indianapolis, IN) using reagents supplied by the manufacturer. The instrument uses ion-selective electrodes to determine sodium, potassium, and chloride concentrations. Glucose, total protein, albumin, uric acid, calcium, inorganic phosphorus, magnesium, total carbon dioxide, creatinine, total and direct bilirubin, and cholesterol are assayed spectrophotometrically. Alkaline phosphatase, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total creatine kinase, and serum (blood) urea nitrogen (BUN) are determined with a kinetic method. Globulin and anion gap are calculated by the analyzer. Osmolality was measured with freezing point depression on an Advanced Osmometer Model 3900 (Advanced Instruments, Norwood, MA).

Cardiac Markers

Whole blood samples were tested immediately for creatine kinase-MB (CK-MB), myoglobin, and cardiac troponin I (cTnI) by a rapid quantitative fluorescence immunoassay using a Triage Cardiac Panel point-of-care testing instrument with reagents supplied by the manufacturer (Biosite Diagnostics, San Diego, CA).

CBC Counts and WBC Differentials

CBC counts and WBC differentials were performed with an ADVIA 120 Hematology System (Bayer, Tarrytown, NY) on whole blood samples anticoagulated with EDTA. This analyzer uses a cyanmethemoglobin method for the measurement of hemoglobin, isovolumetric sphering and light scatter for all other RBC and platelet parameters, and peroxidase staining and light scatter for the WBC measurements. The CBC parameters included WBC count, hematocrit, hemoglobin, RBC count, platelet count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width. The WBC differential consisted of the percentages of neutrophils, lymphocytes, monocytes, eosinophils, and basophils. No specimens were flagged by the automated cell counter for manual review.

Statistical Analysis

A 2-tailed paired *t* test was used to evaluate differences between premarathon and postmarathon samples. Statistical analysis was performed using Microsoft Excel software (Microsoft, Redmond, WA).

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Results

The 2001 Boston Marathon was run under overcast skies, at a temperature of 53°F to 56°F (11.7°C-13.3°C), with a light northeasterly wind of 1 to 5 mph. Of 13,408 runners who started the race, 97.5% completed it. The mean finishing time for the runners participating in our study was 4.0 hours ± 30 minutes, representing the middle third of the pack. Weight change of the runners was –6.6 ± 2.5 lb (–3.0 ± 1.1 kg), or a 4% decrease in average body weight. None of the subjects experienced an adverse medical event requiring medical attention during or after the race.

The mean values for routine biochemistry and cardiac parameters obtained from samples obtained before, within 4 hours after, and 24 hours after the marathon are given in **Table 1**. Samples drawn before and within 4 hours after the marathon were available for 37 runners. There was a statistically significant ($P < .05$) increase in the values for glucose, albumin, total protein, calcium, phosphorus, uric acid, anion gap, BUN, creatinine, direct and total bilirubin, alkaline phosphatase, ALT, AST, and total CK in the specimens obtained within 4 hours after the marathon compared with the premarathon specimens. No statistically significant difference was observed between premarathon samples and those obtained within 4 hours after the race for sodium, potassium, triglycerides, cholesterol, and osmolality. The concentrations of magnesium, chloride, carbon dioxide, and globulin were significantly lower in the postmarathon specimens than in the premarathon specimens ($P < .05$).

Additional blood samples obtained 24 hours after the marathon were available for analysis from 11 of 37 study participants. The increases in CK, BUN, creatinine, uric acid, anion gap, direct bilirubin, ALT, and AST remained statistically significant in these specimens. Values for glucose, total protein, albumin, globulin, calcium, phosphorus, total bilirubin, triglycerides, alkaline phosphatase,

Table 1
Basic Biochemical and Cardiac Parameters: Mean Values, SD, and *P* Values for Differences in Premarathon vs Postmarathon Samples*

	Mean (SD)				
		Postmarathon		*P* Premarathon vs Postmarathon	
Analyte	Premarathon	4 h	24 h	4 h Post	24 h Post
Sodium (mmol/L)	142.4 (1.58)	141.5 (4.04)	139.0 (3.21)	.17	**.003**
Potassium (mmol/L)	4.5 (0.41)	4.5 (0.52)	4.3 (0.24)	.35	**.04**
Chloride (mmol/L)	105.8 (1.96)	101.0 (4.02)	102.8 (3.32)	**<.0001**	**.0002**
Carbon dioxide (mmol/L)	29.3 (1.38)	27.6 (1.35)	28.4 (0.96)	**<.0001**	**.003**
Anion gap (mmol/L)	11.8 (1.25)	17.5 (1.85)	13.3 (1.56)	**<.0001**	**.01**
Glucose (mg/dL)	99.4 (26.54)	110.3 (24.18)	116.8 (25.42)	**.05**	.34
Total protein (g/dL)	7.1 (0.34)	7.4 (0.39)	7.1 (0.44)	**<.0001**	.33
Albumin (g/dL)	4.0 (0.23)	4.5 (0.30)	4.1 (0.20)	**<.0001**	.83
Uric acid (mg/dL)	4.8 (1.15)	5.7 (1.23)	5.8 (1.57)	**<.0001**	**.03**
Globulin (g/dL)	3.1 (0.27)	2.9 (0.28)	3.0 (0.34)	**<.0001**	.09
Calcium (mg/dL)	9.2 (0.34)	9.4 (0.51)	9.4 (0.35)	**.005**	.48
Phosphorus (mg/dL)	2.8 (0.44)	3.2 (0.80)	3.0 (0.45)	**.001**	.11
Magnesium (mEq/L)	1.7 (0.13)	1.5 (0.16)	1.7 (0.12)	**<.0001**	1
Serum urea nitrogen (mg/dL)	16.0 (5.52)	19.5 (4.35)	20.7 (7.50)	**<.0001**	**.002**
Creatinine (mg/dL)	1.0 (0.16)	1.3 (0.32)	1.2 (0.24)	**<.0001**	**.001**
Bilirubin (mg/dL)					
Direct	0.2 (0.10)	0.3 (0.16)	0.4 (0.20)	**<.0001**	**.01**
Total	0.5 (0.27)	0.8 (0.44)	0.8 (0.59)	**<.0001**	.22
Triglycerides (mg/dL)	114.2 (58.13)	109.5 (60.43)	73.1 (56.07)	.5	.11
Cholesterol (mg/dL)	194.9 (29.09)	196.5 (29.44)	169.1 (32.64)	.6	**.0008**
Alkaline phosphatase (U/L)	66.9 (16.00)	70.3 (16.97)	60.2 (12.37)	**.01**	.69
Alanine aminotransferase (U/L)	21.8 (14.40)	24.8 (11.49)	29.8 (13.45)	**.04**	**.02**
Aspartate aminotransferase (U/L)	29.3 (12.76)	51.6 (17.98)	106.9 (55.65)	**<.0001**	**.0007**
Total creatine kinase (U/L)	131.9 (57.80)	843.8 (782.3)	2,470.0 (1,950)	**<.0001**	**.002**
Osmolality (mOsm/kg H_2O)	293.9 (6.86)	295.8 (11.42)	295.0 (9.53)	.27	.78
Creatine kinase-MB (ng/mL)	2.3 (1.61)	23.8 (25.17)	56.2 (46.54)	**<.0001**	**.003**
Troponin I (ng/mL)	0 (0)	0.02 (0.04)	0 (0)	**.004**	Identical†
Myoglobin (µg/L)	83.1 (28.3)	>500 (0)	379.3 (142.3)	**<.0001**	**<.0001**

* All *P* values are for 2-tailed paired *t* tests. Bold type indicates significant values. Values for sodium, potassium, chloride, carbon dioxide, and anion gap are given in Système International (SI) units; conventional values are in mEq/L, and the conversion factor is 1.0. Other values given are conventional; SI units and conversion factors are as follows (multiply by the conversion factor to determine SI units): alanine aminotransferase, U/L, 1.0; albumin, g/L, 10; alkaline phosphatase, U/L, 1.0; aspartate aminotransferase, U/L, 1.0; bilirubin, direct and total, µmol/L, 17.1; calcium, mmol/L, 0.25; cholesterol, mmol/L, 0.02586; creatine kinase, total, U/L, 1.0; creatinine, µmol/L, 88.4; globulin, g/L, 10; glucose, mmol/L, 0.05551; magnesium, mmol/L, 0.50; osmolality, mmol/kg H_2O, 1; phosphorus, mmol/L, 0.3329; protein, total, g/L, 10.0; triglycerides, mmol/L, 0.01129; troponin I, µg/L, 1.0; urea nitrogen, serum, mmol/L, 0.357; uric acid, mmol/L, 0.0595.

† Before and 24 hours after the race, all runners had cardiac troponin I values less than 0.01 ng/mL (0.01 µg/L), the lower limit of detection of the assay.

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and osmolality in these samples were not significantly different from the premarathon specimens. Levels of sodium, potassium, chloride, carbon dioxide, and cholesterol were significantly lower in the samples obtained within 24 hours after the marathon compared with premarathon specimens.

As previously reported,[18] myoglobin and CK-MB levels were higher in all runners at both time points after the race. Troponin I concentrations were slightly higher in some runners at 4 hours after the marathon; at 24 hours after the event, all troponin I levels had returned to below the level of sensitivity of the assay.

Mean results for the CBC parameters are shown in **Table 2**. There were statistically significant differences in all parameters between the premarathon samples and those obtained within 4 hours after the marathon. We observed the previously reported increase in WBC counts. In addition, there were increases in hemoglobin, platelet count, MCH, MCHC, and red cell distribution width. There was a significant decrease in hematocrit, RBC count, and MCV. All changes were sustained in the samples obtained 24 hours after the race, with the exception of the increase in hemoglobin.

WBC differential counts performed on postmarathon specimens within 4 hours showed an elevated percentage of neutrophils **Table 3** and decreased percentages of lymphocytes and eosinophils, while the percentage of monocytes was unchanged. As shown in Table 2, the total WBC count was dramatically higher in the postmarathon specimens than before the marathon. It therefore was possible that the lower percentage of lymphocytes in the postmarathon specimens

Table 2
CBC Count: Mean Values, SD, and *P* Values for Differences in Premarathon vs Postmarathon Samples*

	Mean (SD)				
		Postmarathon		*P* Premarathon vs Postmarathon	
Variable	Premarathon	4 h	24 h	4 h Post	24 h Post
WBC count (× 10^9/L)	5.6 (0.98)	17.0 (3.18)	9.5 (2.59)	**<.0001**	**.0002**
Hematocrit (%)	44.0 (2.60)	43.0 (2.35)	40.8 (2.65)	**.01**	**.001**
Hemoglobin (g/dL)	14.8 (0.91)	15.1 (0.94)	14.5 (0.94)	**.03**	.19
RBC count (× 10^6/μL)	5.0 (0.31)	4.9 (0.30)	4.6 (0.34)	**.03**	**.003**
Platelet count (× 10^3/μL)	227.6 (50.31)	267.7 (60.30)	233.1 (47.93)	**<.0001**	**.006**
Mean corpuscular volume (fL)	88.8 (3.59)	88.5 (3.69)	88.8 (3.46)	**.009**	**.0006**
Mean corpuscular hemoglobin (pg)	29.9 (1.27)	31.0 (1.23)	31.5 (0.97)	**<.0001**	**<.0001**
Mean corpuscular hemoglobin concentration (g/dL)	33.6 (0.67)	35.1 (0.77)	35.5 (0.59)	**<.0001**	**<.0001**
Red cell distribution width (%)	13.1 (0.49)	13.4 (0.45)	13.7 (0.49)	**<.0001**	**<.0001**

* All *P* values are for 2-tailed paired *t* tests. Bold type indicates significant values. Values for WBC count and mean corpuscular volume are given in Système International (SI) units; conventional units and the conversion factors are as follows: mean corpuscular volume, μm^3, divide by 1.0; WBC count, /μL, divide by 0.001. Other values given are conventional; units and conversion factors are as follows (multiply by the conversion factor to determine SI units): hematocrit, proportion of 1.0, 0.01; hemoglobin, g/L, 10.0; mean corpuscular hemoglobin, pg, 1; mean corpuscular hemoglobin concentration, g/L, 10; platelet count, × 10^9/L, 1.0; RBC count, × 10^{12}/L, 1.0.

Table 3
WBC Differential: Mean Values, SD, and P Values for Differences in Premarathon vs Postmarathon Samples*

	Mean (SD)				
		Postmarathon		*P* Premarathon vs Postmarathon	
WBC count	Premarathon	4 h	24 h	4 h Post	24 h Post
Percentage of total WBC count					
Neutrophils	57 (10.6)	85 (10.9)	63 (14.9)	**<.0001**	**.004**
Lymphocytes	30 (6.6)	7 (2.4)	21 (5.4)	**<.0001**	**.002**
Monocytes	7 (6.1)	7 (10.4)	11 (14.8)	.6	.3
Eosinophils	3 (1.5)	1 (0.2)	2 (1.3)	**<.0001**	.2
Basophils	1 (0.3)	1 (0.3)	1 (0.2)	**.001**	.8
Absolute count (× 10^9/L)					
Neutrophils	3.2 (0.9)	14.4 (3.0)	5.8 (1.9)	**<.0001**	**<.0001**
Lymphocytes	1.7 (0.4)	1.1 (0.4)	1.9 (0.4)	**<.0001**	**.01**
Monocytes	0.4 (0.3)	1.3 (2.7)	1.3 (2.4)	**.03**	.2
Eosinophils	0.2 (0.1)	0.1 (0.0)	0.2 (0.1)	**<.0001**	.2
Basophils	0.0 (0.0)	0.1 (0.0)	0.1 (0.0)	**<.0001**	**<.0001**

* All *P* values are for 2-tailed paired *t* tests. Bold type indicates significant values. Values for the differential as a percentage of the total WBC count are conventional values; for Système International (SI) values (proportion of 1.0), divide by 0.01. Values for the absolute count are given in SI units; for conventional units (/μL), divide by 0.001.

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was due to an increase in the absolute number of neutrophils, not a change in the number of circulating lymphocytes. We therefore also examined the absolute numbers of WBC types. This analysis showed that while the absolute number of neutrophils and monocytes was elevated in the postmarathon specimens, the absolute number of lymphocytes was lower after the marathon than before the marathon (Table 3).

For many laboratory parameters examined in our study, the average results before and after the marathon were not dramatically different, while the statistical analysis of the paired samples showed a number of statistically significant changes. Therefore, we examined the percentage of runners with laboratory results outside the standard reference range in use at our hospital.[19] As shown in **Table 4**, for 100% of the participants, the values for anion gap, myoglobin, and WBC, neutrophil, and lymphocyte counts were outside the standard reference range within 4 hours after the race. At this time, at least 30% of the runners had albumin, chloride, glucose, phosphorus, creatinine, cholesterol, AST, total CK, CK-MB, and osmolality values outside the standard interval.

A crucial component in the establishment of normal values for laboratory tests is the selection of the appropriate reference population.[20] Although none of the participants in our study experienced an adverse medical event, many laboratory parameters were outside the standard reference range. This indicates that the standard reference ranges derived from healthy, resting volunteers do not apply to marathon runners before or after competition. Therefore, we used the data obtained in our study to establish modified reference ranges (expected values) for marathon runners before and after a marathon. **Table 5** shows the 95% confidence intervals for basic biochemical, cardiac, and hematologic parameters in the general population and in marathon runners before and after a race.

Table 4
Percentage of Runners With Laboratory Results Outside the Standard Reference Range*

Variable	Before Marathon (n = 37)	After Marathon 4 h (n = 37)	After Marathon 24 h (n = 11)
Clinical chemistry			
Sodium	0	5	0
Potassium	14	16	0
Chloride	5	30	9
Carbon dioxide	0	0	0
Anion gap	24	100	82
Glucose	22	46	45
Total protein	0	5	0
Albumin	3	59	9
Uric acid	3	3	9
Globulin	0	16	18
Calcium	0	0	0
Phosphorus	19	32	18
Magnesium	0	16	0
Serum urea nitrogen	3	11	18
Creatinine	0	30	9
Bilirubin			
Direct	3	11	18
Total	3	19	9
Triglycerides	24	16	55
Cholesterol	49	41	9
Alkaline phosphatase	0	3	9
Alanine aminotransferase	5	5	0
Aspartate aminotransferase	11	70	91
Total creatine kinase	3	81	91
Osmolality	27	54	36
Creatine kinase-MB	11	95	100
Troponin I	0	3	0
Myoglobin	89	100	100
CBC count			
WBC count	3	100	18
Hematocrit	0	0	0
Hemoglobin	0	0	0
RBC count	19	8	0
Platelet count	5	11	0
Mean corpuscular volume	0	0	0
Mean corpuscular hemoglobin	0	0	0
Mean corpuscular hemoglobin concentration	0	3	0
Red cell distribution width	0	3	9
WBC differential			
Neutrophils	3	100	27
Lymphocytes	3	100	18
Monocytes	11	14	18
Eosinophils	0	0	0
Basophils	0	0	0

* Standard reference ranges for the general population were from Kratz and Lewandrowski,[19] with the exception of the ranges for the cardiac markers myoglobin, creatine kinase-MB, and cardiac troponin I, for which the instrument manufacturer's recommendations for reference ranges were used.

Discussion

We report the proximate and short-term (within 24 hours) changes in basic biochemical and hematologic parameters associated with marathon running. Our sample of 37 runners is one of the largest data sets reported in the literature. Many of the changes observed in our runners confirm the findings of previous investigations that used smaller samples or technologies no longer in use. For example, increases in glucose, plasma proteins, albumin, BUN, creatinine, uric acid, and creatine phosphokinase[7,9,11,13,21] and decreases in magnesium[10,22] immediately after participation in a marathon have been reported by other investigators. Similarly, increases in WBC count, platelet count, hemoglobin, MCH, MCHC, and MCV have been described in other studies.[4,8,13,14,23]

Several groups reported a significant increase in serum sodium and potassium concentrations immediately after completion of a marathon.[7,8,10,22] An increase in the potassium concentration but not in the sodium concentration was described by Dancaster and Whereat[12]; in contrast, Whiting and coworkers[23] found an increase in the sodium concentration but not in the potassium concentration. Our findings indicated no changes in the sodium and potassium concentrations

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Table 5
Reference Ranges for Most Frequently Assayed Laboratory Parameters in the General Population and in Marathon Runners Before, Immediately After, and 24 Hours After a Marathon*

Parameter	Reference Range in			
		Runners		
	General Population†	Before Marathon‡	Immediately After Marathon‡	24 h After Marathon‡
Clinical chemistry				
Sodium (mmol/L)	135-145	139-146	134-149	133-145
Potassium (mmol/L)	3.5-5.0	3.7-5.3	3.5-5.5	3.8-4.8
Chloride (mmol/L)	100-108	102-110	93-109	96-109
Carbon dioxide (mmol/L)	24-30	27-32	25-30	27-31
Anion gap (mmol/L)	3-11	9-14	14-21	10-16
Glucose (mg/dL)	70-110	47.4-151.4	63-158	67-167
Total protein (g/dL)	6.0-8.0	6.4-7.8	6.6-8.2	6.2-8.0
Albumin (g/dL)	3.1-4.3	3.5-4.5	3.9-5.1	3.7-4.5
Uric acid (mg/dL)	3.6-8.5	2.5-7.1	3.3-8.1	2.7-8.9
Globulin (g/dL)	2.6-4.1	2.6-3.6	2.4-3.4	2.3-3.7
Calcium (mg/dL)	8.5-10.5	8.5-9.9	8.4-10.4	8.7-10.1
Phosphorus (mg/dL)	2.6-4.5	1.9-3.7	1.6-4.8	2.1-3.9
Magnesium (mEq/L)	1.4-2.0	1.4-2.0	1.2-1.8	1.5-1.9
Serum urea nitrogen (mg/dL)	8-25	5-27	11-28	6-35
Creatinine (mg/dL)	0.6-1.5	0.7-1.3	0.7-1.9	0.7-1.7
Bilirubin (mg/dL)				
Direct	0.0-0.4	0.0-0.4	0.0-0.6	0.0-0.8
Total	0.0-1.0	0.0-1.0	0.0-1.7	0.0-2.0
Triglycerides (mg/dL)	40-150	0-228	0-228	0-183
Cholesterol (mg/dL)	<200	138-252	139-254	105-233
Alkaline phosphatase (U/L)	45-115	36-98	37-104	36-84
Alanine aminotransferase (U/L)	10-55	0-50	2-47	3-56
Aspartate aminotransferase (U/L)	10-40	4-54	16-87	0-216
Total creatine kinase (U/L)	60-400	19-245	0-2377	0-6292
Osmolality (mOsm)	280-296	281-307	273-318	276-313
Creatine kinase-MB (ng/mL)	0-4.3	0-5.5	0-73.1	0-147.4
Troponin I (ng/mL)	0-0.19	0	0-0.1	0
Myoglobin (ng/mL)	0-52	28-138	>500§	101 to >500§
CBC count				
WBC count (× 10^9/L)	4.5-11	3.7-7.5	10.8-23.2	4.4-14.6
Hematocrit (%)	37-49	39-49	38-48	36-46
Hemoglobin (g/dL)	13-18	13-17	13-17	13-16
RBC count (× 10^6/μL)	4.5-5.3	4.4-5.6	4.3-5.5	3.9-5.3
Platelet count (× 10^3/μL)	150-350	129-326	150-386	139-327
Mean corpuscular volume (fL)	78-100	81-96	81-96	82-95
Mean corpuscular hemoglobin (pg/RBC)	25-35	27-32	29-33	30-33
Mean corpuscular hemoglobin concentration (g/dL)	31-37	32-35	34-37	34-37
Red cell distribution width (%)	11.5-14.5	12.1-14.1	12.5-14.3	12.7-14.7
WBC differential (%)				
Neutrophils	45-75	36-78	64-100	34-92
Lymphocytes	16-46	17-43	2-11	10-31
Monocytes	4-11	0-19	0-27	0-40
Eosinophils	0-8	0-6	0-1	0-5
Basophils	0-3	0-1	0-1	0-1

* Values given are 95% confidence intervals. For information about Système International (SI) units and conversions between conventional and SI units, see the footnotes for Tables 1-3.
† Reference ranges for the general population are from Kratz and Lewandrowski,[19] with the exception of the ranges for the cardiac markers myoglobin, creatine kinase-MB, and cardiac troponin I, for which the instrument manufacturer's recommendations for reference ranges are indicated.
‡ Reference ranges were calculated as the mean ± 1.96 SD.
§ The upper limit of detection for myoglobin was 500 ng/mL. At 4 hours after the race, all runners had myoglobin concentrations >500 ng/mL; 5 of 11 runners had myoglobin concentrations >500 ng/mL 24 hours after the race.

immediately after the race; the levels of both electrolytes were decreased 24 hours after the race in the population studied by our group. While other groups found no change in chloride levels after a marathon,[10,11,22] we found significantly lower chloride levels in the postmarathon specimens. These discrepancies might be due to methodological differences or to the smaller samples of some of these studies. A likely explanation also may be differences in fluid intake during the marathon. The importance of adequate fluid intake to prevent dehydration in athletes has led to progressively stronger recommendations for athletes to increase fluid intake before and during participation in major sporting

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events.[24,25] Our data indicate that these recommendations are leading to the desired effect, and that the biochemical markers of dehydration (increased protein, albumin, and BUN) can be largely mitigated during marathon running. The mild dehydration seen in our runners, as indicated by the loss of 4% of body weight, was offset by adequate and appropriate fluid intake as shown by the stable values for serum sodium. Decrease in renal perfusion also is indicated by the increase in BUN and creatinine at both time points after the marathon. The postmarathon increase in albumin and total protein concentrations that we observed might be due to a combination of mild dehydration and an increased flow of lymph, with a high protein content, from contracting muscle into the vascular compartment.[3,9,26]

The elevations in myoglobin, total CK, CK-MB, and AST after the marathon indicate exertional rhabdomyolysis and leakage from skeletal muscle,[18,27,28] while ALT as a more specific marker for hepatic injury showed little change. The slight elevation of cTnI in some runners may indicate similar injury to the myocardium in some runners. Elevation of markers of hemolysis after a marathon has been well documented in the literature[29] and explains the increase in total bilirubin, which was more marked for the unconjugated than for the conjugated form. The significantly increased anion gap immediately after the race can be explained mostly by an increased lactic acid level with a reciprocal decrease in chloride concentration. Increases in the lactate level after a marathon have been described by other investigators.[13] The increase in lactate level, in conjunction with hyperventilation and reduced bicarbonate regeneration by the renal tubules due to a decreased glomerular filtration rate, might be responsible for the decrease in carbon dioxide we observed after the race.[23]

Our data confirm the well-documented leukocytosis after a marathon.[2-4] In addition, we confirm the finding of Davidson and coworkers[4] that while the absolute numbers of neutrophils and monocytes are increased shortly after a race, the number of circulating lymphocytes is not. These increases were sustained 24 hours after the race, although owing to the smaller sample analyzed at this time point, the difference was not statistically significant for monocytes. It is generally assumed that leukocytosis after a race is mainly caused by demargination of WBCs induced by increased blood flow; however, our observation of an increase of the absolute numbers of neutrophils and of monocytes but not of lymphocytes argues that some of the leukocytosis observed in runners might be due to the inflammatory response caused by tissue injury.[3] This is consistent with the increase in C-reactive protein in marathon runners as described recently[5]; studies are underway to determine the upstream mediators of this inflammatory response.

Discussions about optimal reference populations and cutoff values are taking place for a variety of laboratory markers, perhaps most notably prostate-specific antigen.[30] The fundamental idea behind the concept of reference values is that they come from subjects who are relevant control subjects for the patients under study.[20] Standard reference ranges, like those in use at our institution, usually are derived from healthy individuals, usually volunteers from the general population.[16] None of the participants in our study experienced an adverse medical event; nevertheless, a number of the laboratory parameters for these runners were outside the standard reference ranges. This indicates that the use of the general population as a reference might not be appropriate for marathon runners being evaluated for medical conditions, especially after competition. It may be desirable to establish specific expected ranges for populations such as marathon runners. The minimum number of reference subjects necessary to establish a reference range recommended in the literature ranges from 30 to 700.[31] The smallest number of subjects required to estimate a 95% confidence interval by nonparametric methods is 39. Our study, therefore, might not unequivocally establish reference ranges for basic laboratory parameters for marathon runners. However, our data provide information about trends in laboratory values in marathon runners that physicians will find extremely useful in the "routine" treatment of such patients. Further studies with larger samples and with samples obtained at multiple time points during and after exercise will be needed to confirm that the reference ranges derived from our sample, which were influenced by time of sampling, environmental conditions, fluid replacement, and methodological limitations, can be applied to the general population of all marathon runners. Until such studies are completed, our data provide a useful compilation of basic laboratory parameters in marathon runners for evaluation of clinical problems.

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