



Variance in the Acute Inflammatory Response to Prolonged Cycling Is Linked to Exercise Intensity

Authors

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Abstract

This study investigated the influence of age, body composition, physical fitness, training volume and intensity, and underlying systemic inflammation on exercise-induced inflammation and innate immune function in a heterogeneous group of cyclists. Subjects included 31 male cyclists (mean – standard deviation, age 38.8 – 10.6 years, body fat 17.8% – 5.6%, VO₂max 55.8 – 8.4 mL kg⁻¹ min⁻¹) who cycled for 1.75 h at 60% wattmax followed by a 10-km time trial (18.3 – 0.3 min). Blood samples were collected pre-, post-, and 1-h-postexercise, and analyzed for WBCs, 9 cytokines [interleukin (IL)-6, tumor necrosis factor- α , granulocyte-macrophage colony-stimulating factor, interferon- γ , IL-1b, IL-2, IL-8, IL-10, and IL-12p70], and granulocyte and monocyte phagocytosis (GR-PHAG and MO-PHAG) and oxidative burst activity (GR-OBA and MO-OBA). Exercise-induced changes varied widely, with significant increases measured for 8 of 9 cytokines, GR-PHAG (mean change 99%) (95% confidence limits, 69%, 128%) and MO-PHAG (43%) (28%, 58%), and WBC (160%) (133%, 187%), and decreases for GR-OBA (- 30%) (- 43%, - 16%) and MO-OBA (- 23%) (- 36%, - 10%). Correlation and stepwise regression analysis revealed that changes in these variables were not related to age, body fat percentage, VO₂max, training volume, or pre-exercise C-reactive protein. Performance measures, specifically the average heart rate and rating of perceived exertion, were correlated with changes in several variables, including IL-8 ($r = 0.68$ and 0.67 , respectively, $P < 0.001$) and IL-6 ($r = 0.51$, $P = 0.004$, and $r = 0.46$, $P = 0.011$, respectively). In summary, variance in exercise-induced inflammation and innate immunity in male cyclists in response to 2 h of endurance exercise is best explained by exercise intensity.

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This study investigated the influence of age, body composition, physical fitness, training volume and intensity, and underlying systemic inflammation on exercise-induced inflammation and innate immune function in a heterogeneous group of cyclists. Subjects included 31 male cyclists (mean–standard deviation, age 38.8–10.6 years, body fat 17.8%–5.6%, VO_{2max} 55.8–8.4 mL kg⁻¹ min⁻¹) who cycled for 1.75 h at 60% $watts_{max}$ followed by a 10-km time trial (18.3–0.3 min). Blood samples were collected pre-, post-, and 1-h-postexercise, and analyzed for WBCs, 9 cytokines [interleukin (IL)-6, tumor necrosis factor- α , granulocyte-macrophage colony-stimulating factor, interferon- γ , IL-1b, IL-2, IL-8, IL-10, and IL-12p70], and granulocyte and monocyte phagocytosis (GR-PHAG and MO-PHAG) and oxidative burst activity (GR-OBA and MO-OBA). Exercise-induced changes varied widely, with significant increases measured for 8 of 9 cytokines, GR-PHAG (mean change 99%) (95% confidence limits, 69%, 128%) and MO-PHAG (43%) (28%, 58%), and WBC (160%) (133%, 187%), and decreases for GR-OBA (-30%) (-43%, -16%) and MO-OBA (-23%) (-36%, -10%). Correlation and stepwise regression analysis revealed that changes in these variables were not related to age, body fat percentage, VO_{2max} , training volume, or pre-exercise C-reactive protein. Performance measures, specifically the average heart rate and rating of perceived exertion, were correlated with changes in several variables, including IL-8 ($r=0.68$ and 0.67 , respectively, $P<0.001$) and IL-6 ($r=0.51$, $P=0.004$, and $r=0.46$, $P=0.011$, respectively). In summary, variance in exercise-induced inflammation and innate immunity in male cyclists in response to 2 h of endurance exercise is best explained by exercise intensity.

Introduction

Prolonged and intensive exercise can cause acute, transient physiologic stress, elevations in stress hormones, inflammation, oxidative stress, immune dysfunction, and disturbances in host pathogen defense (Nieman 1997, 2000). Heavy exercise workloads are associated with elevations in a variety of cytokines, including interleukin (IL)-6, IL-10, IL-8, IL-1ra, granulocyte colony-stimulating factor (G-CSF), monocyte chemoattractant protein 1, macrophage inflammatory protein 1 beta, tumor necrosis factor- α (TNF- α), and macrophage migration inhibitory factor (Nieman and others 2001; Nieman 2009). Cells from the innate immune system are particularly affected, with a transient postexercise increase in granulocyte phagocytosis, and decreases in granulocyte oxidative burst activity and natural killer cell lytic activity (Nieman and others 1998).

Blood levels of inflammation-related biomarkers vary widely in individuals after intensive and prolonged exercise.

For example, change in plasma IL-6, IL-8, and IL-10 levels varied widely [coefficient of variations (CV) of 1.23, 1.12, and 1.20, respectively] in athletes competing in the 42.2 km Charlotte Marathon Race and the 160-km Western States Endurance Run (Nieman and others 2001; Nieman 2009). Predictors of this variance in post-exercise inflammation have not yet been determined. In the community, chronic or systemic inflammation is strongly related to age, body mass index, body composition, exercise frequency, and physical fitness status (Beavers and others 2010). Individuals engaging in endurance exercise vary widely in age, body composition, training workloads, and fitness levels, and whether or not variance in post-exercise inflammation and innate immune function is related to these demographic, training, and fitness factors has not yet been investigated. Additionally, although unstudied, variance in pre-exercise inflammation measures may predict the extent of exercise-induced inflammation. In other words, an individual with high baseline C-reactive protein (CRP) may experience an exaggerated

inflammatory response to heavy exertion compared to those with low CRP.

The purpose of this study was to investigate the influence of age, body composition, physical fitness, training habits, systemic inflammation, and metabolic demands on exercise-induced inflammation and innate immune function in a heterogeneous group of trained cyclists. We hypothesized that each of these factors would have a significant influence on the degree of inflammation experienced by cyclists following an intensive and prolonged bout of cycling.

Materials and Methods

Subjects

Thirty-one male cyclists who trained for and competed in road or mountain bike races were recruited from the Charlotte, NC, area via mass advertisement. Inclusion criteria included a capability of cycling 75 km in a laboratory setting, and a willingness to stay weight stable and avoid the use of large-dose vitamin/mineral supplements (more than 100% of recommended dietary allowances), herbs, and medications known to affect inflammation and immune function for 1 month before the laboratory cycling session. Written informed consent was obtained from each subject, and the experimental procedures were approved by the institutional review board of Appalachian State University.

Research design

Before the study, subjects came to the Human Performance Laboratory for orientation and baseline testing. Demographic and training histories were acquired with questionnaires. Maximal power, oxygen consumption, ventilation, and heart rate were measured during a graded exercise test (25 watt increase every 2 min, starting at 150 watts) with the Cosmed Quark CPET metabolic cart (Rome, Italy) and the Lode cycle ergometer (Lode Excaliber Sport, Lode B.V., Groningen, Netherlands). Body composition was measured with the Bod Pod body composition analyzer (Life Measurement, Concord, CA). Subjects were instructed to stay weight stable and avoid all medications and supplements known to influence inflammation and immune function for 1 month after baseline testing.

One month after baseline testing, subjects returned to the Human Performance Laboratory at 2:45 p.m. for the cycling test session. The last meal was at 12:00 noon, and consisted of a standardized liquid meal (Boost Plus; Mead Johnson Nutritional, Evansville, IN) at an energy level of 10 kcal/kg⁻¹ (41.9 kJ/kg⁻¹) body mass. Subjects provided blood samples, and then cycled from approximately 3:00 to 5:00 p.m., with additional blood samples collected immediately postexercise, and then again 1-h post-exercise.

Subjects first cycled for 1.75 h using their own bicycle on CompuTrainer Pro Model 8001 trainers (RacerMate, Seattle, WA) with the exercise load set at 60% w_{max}, and heart rate and rating of perceived exertion (RPE) recorded every 30 min and workload monitored using the CompuTrainer MultiRider software system (version 3.0; RacerMate, Seattle, WA). Immediately following, subjects engaged in a 10-km time trial, cycling as fast as possible while workload, heart rate, and RPE were recorded every 5 min. During the cycling bout, subjects drank water ad libitum, and no other beverage or food were consumed. RPE was determined using the Borg

15-point rating (6–20) of perceived exertion scale (Utter and others 2009).

During orientation, a dietitian instructed the subjects to follow a diet moderate in carbohydrate (using a food list) during the 3-day period before the cycling test session. Subjects recorded food intake in a 3-day food record before each of the test sessions, with the dietary record analyzed using a computerized dietary assessment program for energy and macronutrient content (Food Processor; ESHA Research, Salem, OR).

Complete blood count, leukocyte subset counts, CRP, and creatine phosphokinase

Routine complete blood counts were performed by our clinical hematology laboratory using a Coulter Ac.TTM 5Diff Hematology Analyzer (Beckman Coulter, Inc., Miami, FL) and provided leukocyte subset counts, and hemoglobin and hematocrit for the determination of plasma volume change using the method of Dill and Costill (1974). Creatine phosphokinase (CPK) and high-sensitivity CRP were measured using an LX-20 clinical analyzer (Beckman Coulter Electronics, Brea, CA).

Granulocyte and monocyte phagocytosis and oxidative burst activity

Granulocyte and monocyte phagocytosis and oxidative burst activity were measured as originally described by Szejda and others (1984), and adapted by our research group (Nieman and others 1998). Phagocytosis was measured through the uptake of fluorescein isothiocyanate (FITC)-labeled bacteria. Oxidative burst was measured through the oxidation of non-fluorescent-hydro-ethidine (HE) to fluorescent ethidium bromide in cells stimulated with unlabeled bacteria, and provides a quantitative assay of H₂O₂-dependent oxidative product formation generated by the cell's oxidative metabolic burst (Szejda and others 1984). Unlabeled and FITC-labeled bacteria (*Staphylococcus aureus*; Molecular Probes, Eugene, OR) were suspended in phosphate-buffered saline (PBS) to working concentrations of 133,333 particles/mL. For each sample, 100 mL of blood were dispensed into 2 polypropylene tubes. To 1 tube, 10 mL of HE working solution (10 mg HE/mL; Molecular Probes) was added and the tubes incubated at 37°C for 15 min, and then cooled at 4°C for 12 min. Using a bacteria to phagocyte (neutrophils and monocytes) ratio of 8:1, unlabeled bacteria were added to the HE-loaded tubes and FITC-labeled bacteria were added to the second tube in the set. Both tubes were incubated at 37°C for 20 min and placed in an ice water bath, and 100 mL of quench solution was added to allow suppression of surface-bound FITC bacteria fluorescence. Cells were washed twice with cold PBS and re-suspended in 50 mL cold fetal bovine serum. Samples were processed on a Q-Prep™ Workstation (Beckman Coulter, Inc.) and analysis was performed within 18 h of blood collection using a Beckman Coulter FC-500 flow cytometer. After gating on the granulocyte and monocyte populations using forward scatter and side scatter, the mean fluorescence intensity (MFI; x-mean) and percent positive cells for FITC (FL1) and oxidized HE (FL2) were determined.

Plasma cytokines

Total plasma concentrations of 9 inflammatory cytokines [IL-6, TNF- α , granulocyte-macrophage colony-stimulating

factor (GM-CSF), interferon gamma (IFN-g), IL-1b, IL-2, IL-8, IL-10, and IL-12p70] were determined using an electrochemiluminescence-based solid-phase sandwich immunoassay (Meso Scale Discovery, Gaithersburg, MD). All samples and provided standards were analyzed in duplicate, and the intra-assay CV ranged from 1.7% to 7.5%, and the inter-assay CV 2.4%–9.6%, for all cytokines measured. The minimum detectable concentration of IL-6 was 0.27 pg/mL, TNF- α 0.50 pg/mL, GM-CSF 0.20 pg/mL, IFN-g 0.53 pg/mL, IL-1b 0.36 pg/mL, IL-2 0.35 pg/mL, IL-8 0.09 pg/mL, IL-10 0.21 pg/mL, and IL-12p70 1.4 pg/mL. Pre- and post-exercise samples for the cytokines were analyzed on the same assay plate to decrease inter-kit assay variability.

Statistical analysis

Data are expressed as mean – standard deviation (SD) and were analyzed across time within each variable using paired *t*-tests contrasting pre-exercise levels with immediate post-exercise and 1-h post-exercise levels. Variance in pre-to-post-exercise was expressed as CV by dividing the SD of change by the mean change. Significance was set after Bonferroni adjustment at $P \leq 0.025$. Pearson correlation coefficients were calculated between variables listed in Table 1 and the change from pre-exercise to immediately post-exercise for variables in Table 2. After determining that the average RPE and percent heart rate attained during the entire 2.1-h cycling bout were related to change in several inflammation measures, stepwise regression was used to test this relationship with age, percent body fat, VO_{2max} , and CRP (baseline inflammation) listed as potential predictive variables for the stepwise regression model.

Results

Subject characteristics and performance measures

Subject characteristics (N=31) and performance measures for the 2.1-h cycling bout (1.75-h pre-load and 10-km time trial combined) are summarized in Table 1. The cyclists

Table 1. Subject Characteristics and Cycling Performance Measures During the 2.1-h Cycling Bout (N=31)

Variable, subject characteristics	Mean – SD
Age (years)	38.8 – 10.6
Height (m)	1.79 – 0.11
Weight (kg)	79.0 – 10.0
Body fat (%)	17.8 – 5.6
Maximal power (watts)	360 – 45
Maximal oxygen consumption, VO_{2max} (mL $kg^{-1} min^{-1}$)	55.8 – 8.4
Maximal ventilation, VE_{max} (L min^{-1})	159 – 20
Maximal heart rate, HR_{max} (beats min^{-1})	180 – 13
<i>Performance measures, 2.1-h cycling</i>	<i>Mean – SD % Maximal</i>
Power output (watts)	222 – 30 61.6% – 1.1%
Heart rate (beats min^{-1})	146 – 18 81.2% – 6.1%
Rating of perceived exertion	13.3 – 1.1
10-km time trial (min)	18.3 – 1.7

SD, standard deviation.

Table 2. Plasma Cytokine Measures Pre-exercise, Immediately Postexercise (2.1h Cycling), and 1-h Postexercise in Cyclists (N=31) (Mean – Standard Deviation)

Variable	Pre-Exercise	Postexercise	1-h Postexercise
TNF- α (pg/mL)	6.07 – 1.4	7.98 – 1.95*	7.63 – 1.78*
IL-6 (pg/mL)	1.57 – 1.7	11.4 – 7.3*	7.84 – 4.23*
IL-2 (pg/mL)	1.11 – 1.1	1.59 – 1.22*	1.22 – 0.72
IL-12-p70 (pg/mL)	3.38 – 5.5	3.74 – 6.01	3.24 – 5.57
IL-8 (pg/mL)	3.31 – 1.2	9.16 – 3.62*	8.93 – 4.01*
IL-10 (pg/mL)	2.94 – 1.7	12.2 – 13.9*	16.3 – 14.5*
GM-CSF (pg/mL)	1.34 – 1.4	1.49 – 0.84*	1.47 – 0.67
IFN-g (pg/mL)	1.74 – 1.4	1.98 – 1.45*	1.84 – 1.17
IL-1b (pg/mL)	0.33 – 0.33	0.42 – 0.33*	0.44 – 0.33*

* $P < 0.025$ relative to pre-exercise.

TNF- α , tumor necrosis factor-alpha; IL, interleukin; IFN-g, interferon-g; GM-CSF, granulocyte-macrophage colony-stimulating factor.

ranged widely in age, body composition, and cardiorespiratory fitness levels. Subjects had been engaged in training and racing for 8.1 – 6.7 years (mean – SD), averaged 267 – 109 km/week in training, and were registered in cycling race categories ranging from the professional level down to class

5. During the 1.75-h cycling bout and ending 10-km time trial (18.3 – 1.7 min), subjects cycled at 60% and 74% – 12% of $watts_{max}$, respectively, for a 2.1-h average of 62% – 1% $watts_{max}$. This workload resulted in a heart rate response of 81% – 6% maximal heart rate (% HR_{max}), but this ranged widely from 68% to 93%. The RPE (6–20 scale) rose from 12.1 – 1.1 at a power output of 216 – 27 watts during the first 30 min of cycling to 19.0 – 1.1 at the end of the 10-km time trial and a power output of 355 – 115 watts. The average RPE for the entire 2.1-h cycling bout ranged from 11.5 to 15.4. Heart rate and average RPE were positively correlated as exercise intensity measures ($r = 0.59$, $P = 0.001$ for average heart rate, and $r = 0.50$, $P = 0.005$ for % HR_{max}). Weight loss averaged 1.2 – 0.6 kg immediately after the cycling bout, with a plasma volume decrease of 2.1% – 0.1%. CPK increased slightly from 200 – 121 to 228 – 145 immediately postexercise ($P < 0.001$). Three-day food records before the exercise trial showed that energy intake was 2,639 – 640 kcal/day (11.1 – 2.8 MJ/day) with carbohydrate representing 55.6% – 8.4%, protein 17.3% – 3.9%, and fat 27.1% – 7.2% of total energy.

Cytokine and innate immune measures

Tables 2 and 3 summarize exercise-induced increases in plasma levels for 8 of 9 cytokines, total blood leukocytes, and granulocyte and monocyte phagocytosis, and decreases measured 1-h post-exercise for granulocyte and monocyte oxidative burst activity. The changes immediately after exercise for these variables varied widely. For example, CVs for pre-to-post-exercise changes in plasma IL-6, IL-8, and IL-10 were 0.77, 0.58, and 1.51, respectively. CVs for granulocyte phagocytosis and total blood leukocytes were 0.81 and 0.47, respectively.

Correlation and regression statistics

Correlation coefficients were analyzed for age, VO_{2max} , and training volume (Table 1), and the pre-to-post-exercise

Table 3. Innate Immune and Leukocyte Subset Count Measures Pre-Exercise, Immediately Post-exercise (2.1 h Cycling), and 1-h Post-exercise in Cyclists ($N=31$) (Mean – Standard Deviation)

Variable	Pre-Exercise	Post-exercise	1-h Post-exercise
Granulocyte phagocytosis (MFI)	144–74	243–101*	224–82*
Monocyte phagocytosis (MFI)	88.4–41.8	131–55*	154–59*
Granulocyte oxidative burst activity (MFI)	18.2–1.3	18.6–1.0	11.7–5.0*
Monocyte oxidative burst activity (MFI)	11.4–0.6	13.1–0.6*	8.53–3.90*
Total blood leukocyte count (10^9L^{-1})	6.28–0.31	15.9–1.0*	13.6–4.5*
Blood neutrophil count (10^9L^{-1})	3.66–0.24	11.4–0.8*	11.1–3.9*
Blood lymphocyte count (10^9L^{-1})	1.85–0.09	3.14–0.18*	1.44–0.45*
Blood monocyte count (10^9L^{-1})	0.49–0.03	0.99–0.08*	0.70–0.28*

* $P<0.025$ relative to pre-exercise.
MFI, mean fluorescence intensity.

change in variables listed in Table 2, and none were found to be significant.

Pre-exercise measures of chronic inflammation (CRP, plasma cytokines, and the total blood leukocyte count) varied widely. For example, CVs for serum CRP, plasma IL-6, and total blood leukocyte counts were 0.92, 0.75, and 0.28, respectively. Pre-exercise serum CRP was positively correlated with percent body fat in these cyclists ($r=0.66$, $P<0.001$). However, pre-exercise measures of chronic inflammation were not significantly correlated with exercise-induced changes in Table 2 variables.

Performance measures, specifically the average RPE and %HR_{max} attained during the 2.1-h cycling bout, were significantly correlated with change in several variables listed in Table 2. Figure 1A and B shows the significant, positive relationship between the average %HR_{max} and RPE maintained during the cycling bout with the pre-to-post-exercise change in plasma IL-8 ($r=0.68$ and 0.67 , respectively, both $P<0.001$). Similar significant correlations were found for %HR_{max} and change in plasma IL-6 ($r=0.51$, $P=0.004$), TNF- α ($r=0.51$, $P=0.004$), granulocyte phagocytosis ($r=0.45$, $P=0.013$), monocyte phagocytosis ($r=0.38$, $P=0.038$), and the total blood leukocyte count ($r=0.38$, $P=0.040$). Exercise RPE was also related to change in plasma IL-6 ($r=0.46$, $P=0.011$) and TNF- α ($r=0.40$, $P=0.028$). Stepwise regression failed to demonstrate that age, percent body fat, VO_{2max}, and CRP (baseline inflammation) were significant predictor variables, and, consequently, none of these factors entered into the regression equation.

Discussion

The 1.75-h cycling bout at 60% watts_{max} combined with a 10-km cycling time trial induced significant inflammation in this heterogeneous group of trained cyclists, but the magnitude varied widely between subjects. We had hypothesized that unique subject characteristics such as age, body composition, cardiorespiratory fitness level, training volume, and systemic inflammation would predict the extent of post-exercise inflammation, but correlation and stepwise regression statistical analysis was non-supportive. In contrast, exercise-induced changes in plasma cytokine levels and granulocyte and monocyte phagocytosis were related to metabolic demand measures including the average RPE and %HR_{max} maintained during the 2.1-h cycling bout. Perceived exertion reflects the intensity of effort, strain, discomfort, and fatigue experienced by the subject during exercise, and is mediated

by central and peripheral physiologic indicators (Utter and others 2009). Heart rate and RPE measures during the 2.1-h cycling bout were positively correlated with each other and several inflammatory measures in this study.

The magnitude of increase in plasma levels of 8 of 9 cytokines, total blood leukocytes, and granulocyte and monocyte phagocytosis, and decrease in granulocyte and

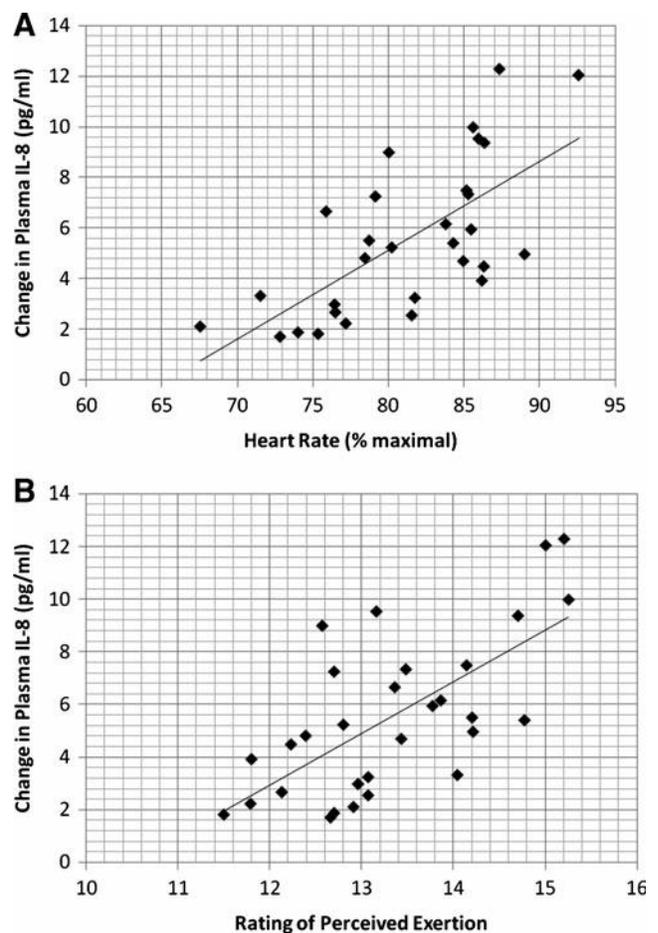


FIG. 1. (A, B) The average heart rate (%HR_{max}) and rating of perceived exertion maintained during the 2.1-h cycling bout were positively correlated with the pre-to-postexercise change in plasma IL-8 ($r=0.68$ and 0.67 , respectively, both $P<0.001$). IL-8, interleukin-8.

monocyte oxidative burst activity measured in the cyclists participating in this study, is similar to what we have reported for runners and cyclists exercising for 2–3 h in other laboratory studies but below what endurance runners experience in marathon and ultramarathon race events (Nieman and others 2001, 2008, 2009; Nieman 2009; Utter and others 2009). To induce the largest inflammatory response, cyclists were restricted to water only during the exercise bout because carbohydrate intake attenuates the rise in cytokines and phagocytosis (Nieman 1997; Nieman and others 1998, 2001). The combined physiologic stress of prolonged and intensive exercise under carbohydrate-restricted conditions is associated with a large but variable increase in plasma cytokine levels. Low-intensity exercise, such as brisk walking, results in little or no increase in plasma cytokine levels (Nieman and others 2005b). The data from this study indicate that the largest change in plasma cytokine levels, and granulocyte and monocyte phagocytosis, occurred in athletes exercising at the highest intensities during the 2.1-h cycling bout. This relationship between exercise intensity and exercise-induced inflammation was measured in a group of cyclists varying widely in age, body composition, cardiorespiratory fitness level, training volume, and pre-exercise CRP, and none of these factors confounded this linkage.

Exercise-induced increases in cytokines are produced by multiple cell types both within and outside the immune system (Keller and others 2001; Frydelund-Larsen and others 2007; Nielsen and Pedersen 2008). Several laboratory studies indicate that IL-6, IL-8, IL-1b, and TNF- α mRNA content is increased within postexercise skeletal muscle biopsy samples, with the greatest fold increases measured for IL-6 and IL-8 mRNA (Nieman and others 2003). Laboratory studies also indicate that blood leukocytes may produce IL-8, IL-10, and IL-1ra during sustained exercise (Nieman and others 2006a). Primary signaling mechanisms for cytokine gene expression during exercise are poorly understood, but data suggest that nitric oxide production, leakage of endotoxins (lipopolysaccharide) from the intestines, elevation in catecholamines and cortisol, high core body temperature, muscle damage, oxidative stress, and glycogen deficiency are involved (Suzuki and others 1999; Nieman and others 2006b; Steensberg and others 2007). Each of these proposed mechanisms has some linkage with exercise intensity. We have previously associated endotoxemia from ibuprofen use and muscle damage (ie, elevated serum CPK) with elevated serum CRP and plasma cytokines in ultramarathoners competing in the 160-km Western States Endurance Run (Nieman and others 2005a, 2006b). In the current study, cyclists did not use ibuprofen for a month before the cycling test session, and muscle damage was low as supported by the small increase in serum CPK. Others have shown that exercise-induced muscle glycogen depletion increases skeletal muscle IL-6 production, and this is consistent with the preference for muscle glycogen as a fuel during high intensity exercise (Steensberg and others 2001; Keller and others 2001, 2005).

In conclusion, exercise intensity (both %HR_{max} and RPE) was the best predictor of the acute inflammatory response to 2.1 h exercise in a heterogeneous group of cyclists. Contrary to expectations, age, body composition, fitness level, training volume, and pre-exercise CRP were unrelated to the magnitude of exercise-induced changes in inflammatory mea-

sure. Thus, the degree of physiologic stress experienced by the cyclist during prolonged exercise is an important factor in predicting the acute inflammatory response. Data from larger groups are needed to confirm these findings and determine practical applications. For example, if high post-exercise inflammation is linked to increased risk of upper respiratory tract infection or other negative health outcomes in certain types of individuals (eg, diminished metabolic control in individuals with type 2 diabetes), exercise intensity thresholds may help improve the benefit-risk ratio from long-term training.

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Authors Disclosure Statement

No competing financial interests exist.

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