

## ***Effects of Exercise and Alkalosis on Serum Insulin-Like Growth Factor I and IGF-Binding Protein-3***

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### **Catalog Data**

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**Mots-clés:** *hormones, stress physique, effort anaérobie, équilibre acido-basique, pH*

### **Abstract/Résumé**

*This investigation examines the effects of orally induced alkalosis on serum IGF-I and IGFBP3 concentrations in response to an acute 90-s bout of high intensity cycle exercise. Ten healthy, active men, ages  $24.60 \pm 4.90$  years, participated in a randomized, double-blind, counterbalanced trial order with a cross-over design. Subjects ingested an experimental bicarbonate solution or a placebo solution. Blood was sampled at baseline; pre-exercise; and 0, 5, 10, and 30 min postexercise. The pH between groups for pre-exercise and*

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*postexercise time points differed significantly ( $p \leq .05$ ) in the experimental condition (from  $7.42 \pm 0.01$  to  $7.35 \pm 0.02$ ) versus the placebo condition (from  $7.36 \pm 0.01$  to  $7.25 \pm 0.03$ ). Increases in IGF-1 over resting conditions occurred with placebo conditions at 5 and 10 min postexercise and in the experimental condition at 5 min postexercise. Concentrations of IGFBP3 were elevated above baseline at IP in both experimental and placebo conditions.*

*Le but de l'étude est d'analyser les effets de l'alcalose induite par voie buccale sur les concentrations sériques de IGF-1 et de IGFBP-3 au cours d'un effort intense sur vélo d'une durée de 90 s. Dix sujets normaux en bonne santé ( $24,6 \pm 4,9$  ans) sont répartis aléatoirement selon un schéma d'expériences croisées à double insu. Les sujets ingurgitent soit une solution de bicarbonate soit une solution placebo. Des échantillons sanguins sont prélevés pour établir le niveau de base, les concentrations pré-exercice et post-exercice (0, 5, 10 et 30 min). Les valeurs de pH sont, à tout moment, significativement plus élevées dans le groupe expérimental que dans le groupe placebo ( $p < 0,05$ ) ; avec l'effort, les valeurs du groupe expérimental passent de  $7,42 \pm 0,01$  avant l'effort à  $7,35 \pm 0,02$  après l'effort et celles du groupe placebo, de  $7,36 \pm 0,01$  à  $7,25 \pm 0,03$ . L'accroissement des concentrations de IGF-1 au delà des valeurs de repos s'est réalisé 5 et 10 min après l'effort dans la condition placebo et 5 min après l'effort dans la condition expérimentale. Immédiatement après la fin de l'effort, les concentrations de IGFBP3 sont au-dessus des valeurs de base dans les deux conditions expérimentales. D'après ces observations, l'alcalose induite par voie buccale n'affecte pas les ajustements des IFG à l'effort de haute intensité.*

## Introduction

It has been shown that exercise at or above the lactate threshold (LT) has a dramatic effect on the acid-base status of the circulating blood (Donovan and Brooks, 1983; Heigenhauser and Jones, 1991). Exercise has been demonstrated to increase the circulatory activity of the IGF system (Bang et al., 1990; Cappon et al., 1994; Felsing et al., 1992; Hornum et al., 1997; Schwarz et al., 1996). However, high intensity cycle and treadmill exercise (at or over the LT) has been shown to stimulate the entire IGF system to a greater extent than lower intensity exercise (Bang et al., 1990; Cappon et al., 1994; Schwarz et al., 1996). Schwarz et al. (1996) specifically demonstrated this by showing that high intensity exercise (at LT) stimulated larger magnitudes of increases in blood concentrations of IGF-I, IGF-II, IGFBP-3, and IGFBP-3 proteolytic activity than did low intensity exercise (below LT).

In a prior study using the same exercise protocol as in the current study, Gordon et al. (1994) demonstrated that with the 90-s maximal exercise bout, the postexercise growth hormone (GH) responses were most related to the concentration of hydrogen ions. In addition, orally induced alkalosis reduced the magnitude of the GH responses to the exercise stress. However, studies have shown that the responses of IGF-I are independent of the endogenous GH responses (Bang et al., 1990; Bereket et al., 1996; Cappon et al., 1994; Ewton and Florini, 1995; Hermansen and Osnes, 1972; Kraemer et al., 1992; Kraemer et al., 1995; Zanconato et al., 1994). The response of postexercise concentrations of serum IGF-I and IGFBP-3 to orally induced alkalosis following such high intensity exercise (i.e., 90-s bout of maximal exercise) remains unknown. However, if the more dramatic exercise-induced (at or above LT) increases of IGF-I and IGFBP-3 observed postexercise in prior studies are due to the increased acidity of the circulating blood, then an

experimentally induced (i.e., oral bicarbonate solution ingestion) reduction of this normal acidity would be hypothesized to also reduce the serum concentrations of IGF-I and IGFBP-3 following high intensity exercise stress. Therefore, the purpose of this investigation was to examine the effects of orally induced alkalosis on serum IGF-I and IGFBP3 concentrations in response to an acute 90-s bout of maximal intensity cycle exercise.

## Methods

### SUBJECTS

Ten healthy, normally active men ages 18–35 years gave their written informed consent to participate in this investigation after having the risks of the experiment explained to them. All subjects were medically screened by a physician prior to participation. None of the subjects used tobacco products, had a history of endocrine disorders, or were on any medications or hormonal supplements at the time of the study that might confound the results of this investigation. The mean physical characteristics of the subjects were (a) age (yr)  $24.6 \pm 4.9$ , (b) height (cm)  $176.8 \pm 4.6$ , (c) weight (kg)  $77.9 \pm 8.4$ , (d) body fat (%)  $11.4 \pm 4.9$ , and (e) fat-free mass (kg)  $68.8 \pm 6.0$ . Age and body composition indicate that these subjects were considered to be young, lean individuals. Body density was estimated using a seven-site skinfold method described by Jackson and Pollock (1978).

### EXPERIMENTAL TREATMENT

A randomized, double-blind, counterbalanced experiment with cross-over design was employed. Each subject performed two experimental trials separated by one week. During each trial, the subjects ingested either an experimental or a placebo solution. Per kilogram of body weight, the experimental solution consisted of 5 ml decaffeinated tea, 0.3 g  $\text{NaHCO}_3$  and 0.02 g dextrose/saccharin sweetener. The placebo solution consisted of exactly the same amount of tea and sweetener but substituted 0.04 g  $\text{NaCl} \cdot \text{kg bw}^{-1}$  for the  $\text{NaHCO}_3$  to approximate the salty taste of the bicarbonate solution. Thus, subjects ingested a total of approximately 400 ml of experimental or placebo solution during each of the two trials.

### EXPERIMENTAL TIMELINE

Both experimental trials were conducted at the same time of the day for each subject between 0800 and 1400 hr to reduce the influence of diurnal variation. Subjects arrived for testing after an overnight fast and had not consumed caffeine for 12 hr prior to the test. Furthermore, subjects were not allowed to consume alcohol or perform strenuous activity for 24 hr prior to testing.

Subjects were seated in a chair, and a 20-gauge Teflon cannula was positioned in a superficial antecubital vein. The cannula was kept patent with a continuous flow of isotonic saline (approximately  $45 \text{ ml} \cdot \text{hr}^{-1}$ ). The subject remained quiet for 15 min in a seated position before baseline blood samples were obtained. After baseline blood samples were drawn, immediate ingestion of either the experimental or placebo solution occurred. Thereafter, an absorption/equilibration period of 75 min ensued while the subject rested comfortably in a seated position.

A pre-exercise (PreEX) blood sample was drawn at the 2-hr mark of the absorption/equilibration period. The test consisted of the positioning of the subject on a Monark Ergometer, Model 818E (Monark AB, Varberg, Sweden), a full review of instructions, and a warm-up session and test administration of 3.5 min. Blood samples were obtained immediately postexercise (IP, 0 min—within the first minute after cessation of the 90-s cycle exercise test during the cool-down period) as well as intervals of 5, 10, and 30 min postexercise (5P, 10P, 30P). Heart rate was monitored throughout the test using a Model 8799 Uniq Heart Watch (Computer Instruments Co., Hempstead, NY). Also, perceived exertion rating (RPE) was requested immediately postexercise to account for potential influences of psychological stressors on the hormonal response to the test. The RPE was used to describe the overall bodily perception of exertion and utilized a Borg 10-point category-ratio scale with magnitude estimation (Noble et al., 1983).

#### EXERCISE TEST

The exercise test consisted of a 2-min warm-up period where the subject pedaled in a free-wheel fashion solely against the intrinsic frictional resistance of the ergometer at a rate of 60 rpm. Exercise intensity during this period of time was considered negligible because no external opposing force was applied. At the end of the warm-up period, the subject proceeded directly to the exercise test. The subject accelerated to his maximum possible pedaling rate over the course of 3–5 s at which point an opposing force was applied to initiate the test. The exercise test consisted of a maximal effort for 90 s against an opposing force of 0.49 N (0.05 kg) per kg of body weight. The subjects were instructed not to pace themselves. Flywheel revolutions were monitored during the test via IBM Personal System 2, Model 55 SX. Peak power (W), mean power (W), percent decline of power, and total work were calculated using an IBM PC2 computer by recording flywheel revolution utilizing the SMI Power 1.02 program (Sports Medicine Industries, St. Cloud, MN). The cool-down period lasted 2.5 min with the subject continuing to pedal in the absence of an opposing force at 60 rpm. Similar to the warm-up period, the intensity and work were considered negligible. This period was necessary to reduce the faintness experienced after the exertion and to facilitate the subject's recovery. While remaining seated, the IP and 5P blood samples were taken. After the 5 min collection, subjects were seated in a chair for the remaining sample collections.

#### BLOOD COLLECTION PROCEDURES

A three-way stopcock assembly into two separate syringes was utilized. A plastic syringe was used for collection of samples for IGF-I, IGFBP3, lactate, hematocrit, and hemoglobin analyses. Blood samples for lactate, hematocrit, and hemoglobin analyses were immediately transferred to a prechilled (4 °C) heparinized glass tube, mixed gently, and placed in a ice bath. Hematocrit was determined in triplicate using a standard microcapillary technique. Hemoglobin samples were aliquoted and stored for future analysis. The frozen blood was stored no longer than 2 months at -88 °C and only thawed once for analysis. The blood gas sample was

anaerobically obtained directly from the stopcock using an internally pretreated glass syringe. The pretreatment consisted of a light heparin sodium solution (1000 USP units/ml). The glass syringe was then immediately immersed in an ice bath and analyzed 3 hr after being obtained. Preliminary testing indicated a 6-hr stability of less than 0.07 for pH.

#### BIOCHEMICAL ANALYSES

Serum human total IGF-I and IGFBP3 were determined in duplicate by an immunoradiometric assay (IRMA; Diagnostic System Laboratories Inc., Webster, TX) utilizing an LKB model 1272 clinigamma counter with on-line data reduction capabilities (Pharmacia LKB Nuclear, Inc., Gaithersburg, MD). The sensitivity of the IGF-I IRMA assay as determined by the dilution method was  $7 \text{ ng} \cdot \text{ml}^{-1}$ . The antibodies displayed no detectable cross-reactivity with IGF-2 or insulin. The test included a simple extraction step in which IGF-I was separated from BP-3. The extraction solution contained hydrochloric acid extraction medium. The intra- and interassay variance were 7.4% and 6.6% for IGF-I and BP-3, respectively.

Lactate concentration was immediately analyzed from the remaining heparinized whole blood sample. Whole blood lactate concentrations were determined in duplicate by enzymatic-amperometric method using a YSI 1500 Sport Lactate Analyzer (Yellow Springs Instrument Co., Inc., Yellow Springs, OH). Hemoglobin was analyzed in duplicate colorimetrically by the cyanmethemoglobin method (Sigma Chemical Co., St. Louis, MO). Hematocrit was determined in triplicate via standard microcapillary technique. Plasma volume shifts were determined via equations from Dill and Costill (1974). Duplicate blood gas measurements were accomplished using a Corning 168 pH Blood Gas System (Corning Medical, Corning Glass Works, Medfield, MA). Blood hydrogen ion concentration was calculated from blood pH. Quality control samples run throughout the experiment demonstrated a reproducibility for pH and blood gas measurements to within .05% for pH.

#### STATISTICAL ANALYSES

Two-way analysis of variance with repeated measures was employed for the physiological data, and one-way analysis of variance with repeated measures was employed for analysis of the performance data. Statistical power was determined to be 0.80 for the sample size used at the 0.05 alpha level (nQuery Advisor® software, Statistical Solutions, Saugus, MA). Subsequent pairwise comparisons were made using Tukey's post-hoc tests. Significance in this investigation was set at  $p \leq .05$ .

## Results

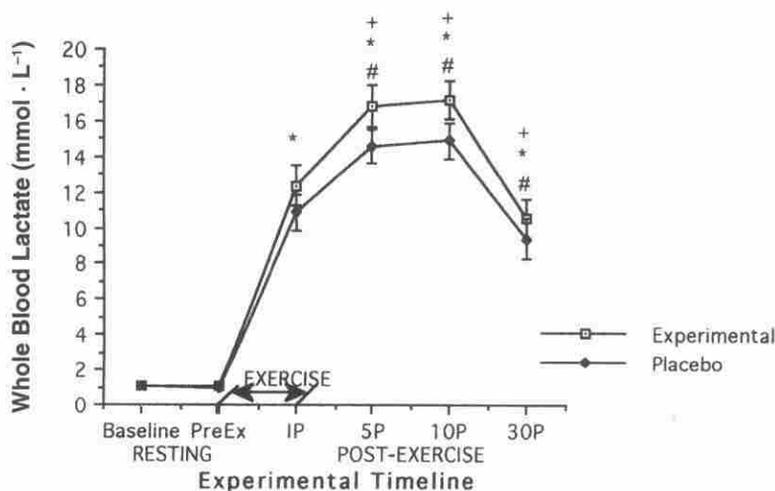
The performance parameters of mean and peak power, total work, and power decline are presented in Table 1. There were no significant differences between the experimental and placebo conditions in any of the absolute or relative (body weight normalization) parameters measured. There were no significant differences in the experimental or placebo conditions for plasma volume changes, which were as

follows: *Experimental treatment*, pre-ex =  $-1.17 \pm 1.20$ , IP =  $-17.64 \pm 1.18$ , 5P =  $-17.40 \pm 1.32$ , 10P =  $-15.06 \pm 1.11$ , 30P =  $-4.91 \pm 1.07$ ; *Placebo*, pre-ex =  $-1.40 \pm 1.16$ , IP =  $-17.05 \pm 1.39$ , 5P =  $-18.41 \pm 1.28$ , 10P =  $-15.48 \pm 1.25$ , 30P =  $-5.13 \pm 1.67$ . Whole blood lactate concentrations between experimental and placebo conditions during exercise are illustrated in Figure 1. Baseline values between the two groups are virtually identical. There were no significant differences between con-

**Table 1** Selected Performance Variables From the Exercise Test

Variables	Conditions	
	Alkalosis	Control
Mean Power (W)	324 ± 14	325 ± 14
Mean Power (W · kg <sup>-1</sup> )	4.15 ± 0.06	4.18 ± 0.09
Peak Power (W)	669 ± 24	670 ± 21
Peak Power (W · kg <sup>-1</sup> )	8.58 ± 0.14	8.61 ± 0.15
Total Work (J)	29,121 ± 1,248	29,278 ± 1,260
Total Work (J · kg <sup>-1</sup> )	374 ± 6	376 ± 8
Power decline (%)	69.1 ± 1.2	68.5 ± 1.7

*Note:* Values are means ± SE of 10 subjects in alkalotic and control conditions.



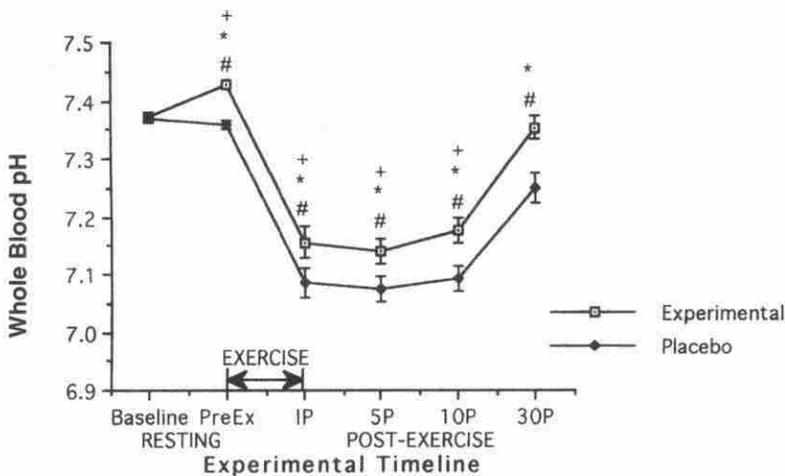
**Figure 1.** Comparison of whole blood lactate (mean ± SE) in experimental and placebo condition trials at rest and after 90 s of high intensity anaerobic exercise. #,  $p \leq .05$  between conditions at specified time points. \*,  $p \leq .05$  within placebo condition compared to resting conditions. +,  $p \leq .05$  within experimental condition compared to resting conditions.

ditions at baseline and pre-exercise. However, there was a significant difference at all postexercise time points between groups. Experimental values at 5P–30P were  $16.83 \pm 1.21$ ,  $17.16 \pm 1.10$ , and  $10.52 \pm 1.11$   $\text{mmol} \cdot \text{L}^{-1}$ , respectively. Placebo values for the aforementioned time points were  $14.57 \pm 0.95$ ,  $14.90 \pm 1.01$ , and  $9.39 \pm 1.09$   $\text{mmol} \cdot \text{L}^{-1}$ , respectively.

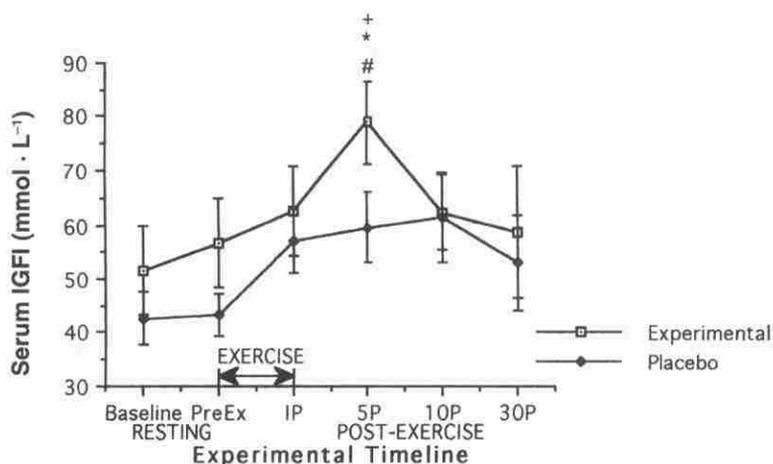
The pH levels in the blood between the placebo and supplemented groups are depicted in Figure 2. Between conditions there was no significant difference at baseline (experimental,  $7.37 \pm 0.008$ ; placebo,  $7.36 \pm 0.007$ ). However, pre-exercise and all postexercise time points differed significantly as the experimental condition (from  $7.42 \pm 0.008$  to  $7.35 \pm 0.020$ ) was higher than the placebo condition (from  $7.36 \pm 0.006$  to  $7.25 \pm 0.026$ ). Pre-exercise values were significantly higher in the experimental condition compared to resting conditions. Three postexercise values were significantly lower in both conditions than the resting conditions.

The IGF-I concentrations between experimental and placebo conditions during the experimental timeline are illustrated in Figure 3. The values observed in this study were higher at rest than typical averages (e.g.,  $30 \text{ nmol} \cdot \text{L}^{-1}$  a typical average). A significant difference between conditions was observed at 5 min postexercise (5P). The experimental condition exhibited a value of  $79.00 \pm 7.66$   $\text{nmol} \cdot \text{L}^{-1}$  and the placebo condition,  $59.55 \pm 6.54$   $\text{nmol} \cdot \text{L}^{-1}$ . The experimental condition at 5P ( $79.00 \pm 7.66$   $\text{nmol} \cdot \text{L}^{-1}$ ) was significantly higher than resting conditions. In the placebo condition both 5P and 10P were significantly higher resting conditions.

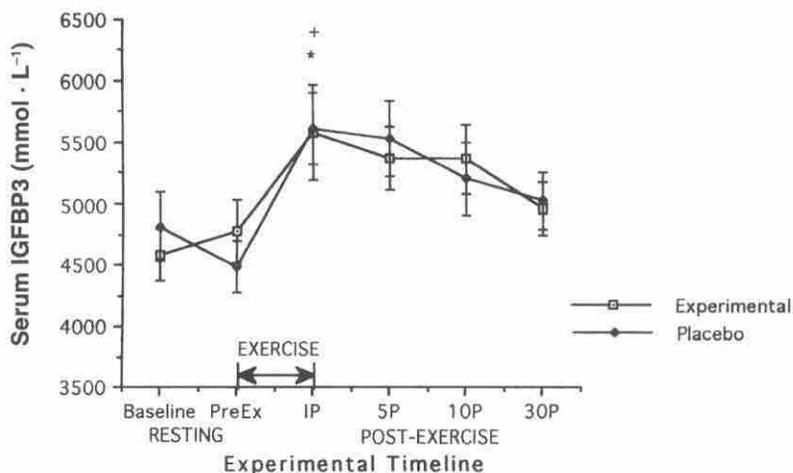
The IGFBP3 concentrations between experimental and placebo conditions during the experimental timeline are illustrated in Figure 4. Baseline concentrations were  $4587.0 \pm 216.3$   $\mu\text{g} \cdot \text{L}^{-1}$  for experimental and  $4811.6 \pm 281.0$   $\mu\text{g} \cdot \text{L}^{-1}$  for



**Figure 2.** Comparison of whole blood pH (mean  $\pm$  SE) in the experimental and placebo condition trials at rest and after 90 s of high intensity, anaerobic exercise. #,  $p \leq .05$  between conditions at specified time points. \*,  $p \leq .05$  in placebo condition compared to resting conditions. +,  $p \leq .05$  in experimental condition compared to resting conditions.



**Figure 3.** Comparison of serum total insulin-like growth factor I (mean  $\pm$  SE) in experimental and placebo condition trials at rest and after 90 s of high intensity anaerobic exercise. #,  $p < .05$  between conditions at specified time points. \*,  $p \leq .05$  in placebo condition compared to resting conditions. +,  $p \leq .05$  in experimental conditions compared to resting conditions (placebo only at 10P).



**Figure 4.** Comparison of serum total insulin-like growth factor I Binding Protein 3 (mean  $\pm$  SE) in experimental and placebo condition trials at rest and after 90 s of high intensity anaerobic exercise. \*,  $p \leq .05$  within placebo condition compared to resting conditions. +,  $p \leq .05$  within experimental condition compared to resting conditions.

placebo conditions. There were no significant differences between conditions at any time points. However, both experimental and placebo conditions demonstrated a significant increase in IGFIBP3 concentrations at time point immediate postexercise (ImPost) above resting conditions. The 0 IGFIBP3 value for the experimental condition was  $5582.6 \pm 388.96 \mu\text{g} \cdot \text{L}^{-1}$  and for the placebo condition was  $5607.9 \pm 290.53 \mu\text{g} \cdot \text{L}^{-1}$ .

## Discussion

The intensity of exercise above the LT has been shown to be important for the magnitude of increases in variables related to the IGF system (Schwarz et al., 1996). A dramatic increase in the acidity of the circulating blood results when such exercise is performed (Donovan and Brooks, 1983; Gordon et al., 1994). Therefore, it was hypothesized in this investigation that by reducing the physiological cue(s) of acidosis by orally induced alkalosis, a significant reduction in the serum concentrations of IGF-I and IGFBP-3 would be observed following an acute bout of high intensity exercise. This was the first study to experimentally manipulate the acid-base system after intense exercise to examine the IGF system. The primary finding in this investigation was that changing the magnitude of blood acidosis by using voluntary bicarbonate ingestion to induce alkalosis did not reduce the serum concentrations of IGF-1 and IGFBP-3 after volitional, maximal cycle exercise of 90 s. These findings argue against our hypothesis that increased acidosis per se with higher intensity exercise is the critical mechanism that mediates intensity dependent responses of the IGF-1 system (Bang et al., 1990; Cappon et al., 1994; Felsing et al., 1992; Hornum et al., 1997; Schwarz et al., 1996). In general, circulatory acidosis associated with high intensity exercise stress appears to have limited influence(s) on the potential mechanism(s) that mediate increases in circulating concentrations of IGF-1 and IGFBP-3 observed in this investigation. In addition, increases in the two treatment conditions cannot be explained by differential changes in the plasma volume shifts.

To date, the current theory for IGF-I secretion is that it does not follow a standard "endocrine" release in response to endogenous GH increases. Our prior work has shown that under identical conditions the postexercise GH concentrations are significantly reduced by orally induced alkalosis, causing a reduction in hydrogen ions (Gordon et al., 1994). The importance of this GH finding to this study resides in the fact that our current data on the IGF system further supports this lack of an acute endocrine regulatory link of GH to IGF-I and IGFIBP3 following an acute high intensity exercise stress. How such acute GH changes may affect IGF system over a longer period of recovery (e.g., 24–48 hr) remains unclear. However, a prior study by Kraemer et al. (1995) attempted to address this question using a heavy resistance exercise protocol that caused significant increases in serum GH, but no changes were observed in the serum IGF-I concentrations over a 24-hr period. This again demonstrated the lack of GH influence on the IGF system with acute exercise (Bang et al., 1990; Bereket et al., 1996; Cappon et al., 1994; Ewton and Florini, 1995; Hermansen and Osnes, 1972; Zanconato et al., 1994). Thus, the acute physiological cue(s) of the GH and the IGF system appear to be different.

The physiological cues for exercise-induced increases in serum IGF-I and IGFBP-3 may be sensitive to the lactate changes and not responsive to other aspects of the acid-base status in the blood (e.g., hydrogen ions). Alkalosis did not diminish the lactate responses to the exercise. In fact just the opposite occurred. The higher lactate response in the experimental treatment condition may have been the predominant physiological cue to the IGF system. While the exercise intensity was the same between conditions, this difference in blood lactate may be due to an increase in efflux of lactate from muscle cells during and after exercise (Gaitanos et al., 1991; Gordon et al., 1994; Heigenhauser and Jones, 1991). This efflux appears to be driven by increased activity of a carrier-mediated pH gradient-sensitive transport mechanism when the intracellular-extracellular lactate concentration increases (Gaitanos et al., 1991; Gordon et al., 1994; Heigenhauser and Jones, 1991). Elevation in blood pH by induced alkalosis generates a larger gradient (Gaitanos et al., 1991; Gordon et al., 1994; Heigenhauser and Jones, 1991). It may be that the IGF-1 and IGFBP-3 are more sensitive to the lactate anion concentrations than other measures of the acid base status, such as hydrogen ions, which are more related to postexercise GH concentrations (Gordon et al., 1994). Such data provides some insights into IGF and GH regulation with intense exercise. More specifically, there were adequate concentrations of lactate anions under both conditions, and, therefore, the IGF system demonstrated postexercise increases. Conversely, the induced alkalosis caused reduction in acidity of the circulating blood mediated by a reduction in hydrogen ions resulting in a diminished response in serum GH concentrations. The importance of this investigation resides in the fact that these data indicate that different variables within the acid-base status of the blood may differentially mediate IGF and GH responses to high intensity exercise.

In summary, the data from this investigation demonstrate that different from GH, the IGF system responses to an acute bout of maximal exercise are not attenuated by increasing the alkalosis of the blood. Such data gives some insights into the potential separation of GH and IGF system variables with exercise stress and physiological cues (e.g., lactate vs. hydrogen ions). Even though the physiological parameters of decreased pH and increased hydrogen ions were observed, the induced alkalosis from ingestion of bicarbonate did not eliminate an exercise response of the serum concentrations of IGF-1 or IGFBP3. The increased lactate responses under both experimental treatment conditions may help explain this effect as the exercise stress was maintained above the LT. Therefore, these data support the importance of the LT in predicting the magnitude of the IGF system response, and it appears to be a crucial variable in intensity-related findings of the IGF system responses. The direct mechanism(s) and interactions of the hydrogen ions and lactate anions with the GH and IGF system remain the next step in this line of investigation.

## References

- Bang, P., Brandt, J., Degerblad, M., Enberg, G., Kaijser, L., Thoren, M., and Hall, K. (1990). Exercise induced changes in insulin-like growth factor and their low molecular weight binding protein in healthy subjects and in patients with growth hormone deficiency. *Eur. J. Clin. Invest.* 20: 285-292.

- Bereket, A., Wilson, T.A., Kolasa, A.J., Fan, J., and Lang, C.H. (1996). Regulation of the insulin-like growth factor system by acute acidosis. **Endocrinol.** 137: 2238-2245.
- Cappon, J.P., Brasel, J.A., Mohan, S., and Cooper, D.M. (1994). Effect of brief exercise on circulating insulin-like growth factor I. **J. Appl. Physiol.** 76: 2490-2496.
- Dill, D.B., and Costill, D.L. (1974). Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. **J. Appl. Physiol.** 37: 247-248.
- Donovan, C.M., and Brooks, G.A. (1983). Endurance training affects lactate clearance, not lactate production. **Amer. J. Physiol.** 7: E83-E92.
- Ewton, D.Z., and Florini, J.R. (1995). Insulin-like growth factor binding proteins-4, -5, and -6 may play specialized roles during L6 myoblast proliferation and differentiation. **J. Endocrinol.** 144: 539-553.
- Felsing, N.E., Brasel, J., and Cooper, D.M. (1992). Effect of low- and high-intensity exercise on circulating growth hormone in men. **J. Clin. Endocrinol. Metab.** 75: 157-162.
- Gaitanos, G.C., Nevill, M.E., Brooks, S., and Williams, C. (1991). Repeated bouts of sprint running after induced alkalosis. **J. Sports Science** 9: 355-370.
- Gordon, S.E., Kraemer, W.J., Vos, N.H., Lynch, J.M., and Knuttgen, H.G. (1994). Effect of acid-base balance on the growth hormone response to acute high intensity cycle exercise. **J. Appl. Physiol.** 76: 821-829.
- Heigenhauser, G.J.F., and Jones, N.L. (1991). Bicarbonate loading. In: D.R. Lamb and M.H. Williams (Eds.), **Perspectives in Exercise Science and Sports Medicine. Ergogenics-Enhancement of Performance in Exercise and Sport**, p. 183-212. Carmel, IN: Brown.
- Hermansen, L., and Osnes, J. (1972). Blood and muscle pH after maximal exercise in man. **J. Appl. Physiol.** 32: 304-308.
- Hornum, M., Cooper, D.M., Brasel, J., Bueno, A., and Sietsema, K.E. (1997). Exercise-induced changes in circulating growth factors with cyclic variations in plasma estradiol in women. **J. Appl. Physiol.** 82: 1946-1951.
- Jackson, A.S., and Pollock, M.L. (1978). Generalized equations for predicting body density of men. **British J. Nutri.** 40: 497-504.
- Kraemer, W.J., Augilera, B.A., Terada, M., Newton, R.U., Lynch, J.M., Rosendaal, G., McBride, J.M., Gordon, S.E., and Häkkinen, K. (1995) Responses of insulin-like growth factor-I to endogenous increases in growth hormone after heavy-resistance exercise. **J. Appl. Physiol.** 79: 1310-1315.
- Kraemer, R.R., Kilgore, J.L., Kraemer, G.R., and Castracane, V.D. (1992). Growth hormone, IGF-I, and testosterone responses to resistive exercise. **Med. Sci. Sports Exerc.** 24: 1346-1352.
- Noble, B.J., Borg, G.A., Jacobs, I., Ceci, R., and Kaiser P. (1983) A category-ratio perceived exertion scale: Relationship to blood and muscle lactates and heart rate. **Med. Sci. Sports and Exerc.** 15: 523-528.
- Schwarz, A.J., Brasel, J., Hintz, R.L., Mohan, S., and Cooper, D.M. (1996). Acute effect of brief low- and high-intensity exercise on circulating insulin-like growth factor (IGF) I, II and IGF-binding protein-3 and its proteolysis in young healthy men. **J. Clin. Endocrinol. Metab.** 81: 3492-3497.
- Zanconato, S., Moromisato, D.Y., Moromisato, M.Y., Woods, J., Brasel, J., Leroith, D., Roberts C.T., Jr., and Cooper, D.T. (1994). Effect of training and growth hormone suppression on insulin-like growth factor I in young rats. **J. Appl. Physiol.** 76: 2204-2209.

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