Effect of Exercise (Running) on Serum Glucose, Insulin, Glucagon, and Chromium Excretion

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SUMMARY

Chromium is involved in normal glucose metabolism. To test whether chromium is also associated with the exercise-induced increases in glucose utilization, urinary chromium excretion, serum glucose, insulin, and glucagon of nine male runners (23–46 yr) were evaluated. Blood samples were taken prior to, immediately following, and 2 h after a strenuous 6-mile run. Urine samples were also taken at these times, and total daily urine collections were made the day of the run and the following day. Mean serum glucose for all runners immediately after running was 185 ± 19 mg/dl compared with 90 ± 1 mg/dl (mean ± SE) prior to running. Mean serum glucagon immediately after running was significantly elevated compared with that observed prior to or 2 h after running; serum insulin levels were not altered significantly. Mean urinary chromium concentration was increased nearly five-fold 2 h after running; similar results were obtained when chromium concentration was expressed per mg of creatinine. Total daily urinary Cr excretion was approximately two times higher the day of running compared with the following nonrun day. Daily urinary excretion of sodium, potassium, and calcium were measured to determine if exercise had a general nonspecific effect on renal function; daily urinary excretion of these was not changed by exercise. These data demonstrate that accompanying the exercise-induced changes associated with increased glucose utilization, there is a significant increase in chromium excretion. DIABETES *31*:212–216, March 1982.

Glucose uptake by exercising muscles is increased 7- to 20-fold above basal levels, depending on the intensity and duration of the exercise.[1] To meet this increased need for glucose, hepatic glucose production is increased three- to five-fold[1,2] and plasma levels of glucagon,[3,4] growth hormone,[5,6] catecholamines,[4,7] and cortisol[8] are increased and serum insulin is decreased.[9]

Chromium is also involved in glucose metabolism; therefore processes that increase glucose utilization may also affect Cr mobilization and/or excretion.[10] To test this postulate, the chromium excretion, and related hormone and metabolite levels of nine trained runners, prior to and following a strenuous 6-mile run, were measured.

MATERIALS AND METHODS

Experimental subjects: Nine male runners ranging in age from 23 to 46 yr were selected (Table 1). All runners appeared healthy and were taking no medications, except subject number 3, who was taking Isoniazid. Subjects were asked to run a 6-mile course at or near their maximal capacity. The study was approved by the Human Nutrition Study Committee, United States Department of Agriculture. All subjects were informed of the purpose of the run and signed an informed consent form; the results were presented and are available to the participants. Subjects were examined by a physician prior to the run with special attention given to cardiovascular problems but none was detected. Subjects were asked to fast from midnight until 2 h after running; no foods or drinks, other than water and black coffee, were permitted until the 2-h postrun blood and urine samples were collected. Running commenced at 10:00 a.m. and all subjects were able to eat their normal respective lunches at approximately 12:45 p.m., following the 2-h sampling period.

Analytical determinations. Creatinine was determined by method of Jaffe.[11] Immunoreactive insulin and glucagon were determined using RIA kits (Cambridge Nuclear, Billerica, Massachusetts); glucose was determined using a CentrifiChem System 500 (Union Carbide, Rye, New York). Chromium was determined by method of additions on nonashed urine samples (25 μl) with a Perkin Elmer 5000 and a HGA-500 furnace with pyrolytic coated tubes. Furnace conditions for direct analysis of Cr in urine were the following: first drying, 100°C, ramp, 15 s, hold, 20 s, internal argon

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TABLE 1
General information about participants

Runner no.	Age	Height (in)	Weight (lbs)	Miles/day	Miles/wk	Time (min/mile)	Training time (mo)
1	33	66	130	6	36	6.5	>24
2	45	71	153	3-6	20-30	9	8
3	24	70	155	3-6	20-30	10	2
4	39	73	170	5	33	8	>24
5	26	72	160	10	70	7	>24
6	36	72	165	6.5	45	7.5	>24
7	35	67	145	3-6	9	10	1
8	23	77	235	4-5	25	8.5	1
9	46	70	175	5	18	8	2

drying flow, 300 ml/min; second drying, 130°C, ramp, 10 s, hold, 20 s, internal argon flow, 300 ml/min; ash, 1200°C, ramp, 15 s, hold, 60 s, internal argon flow, 300 ml/min; atomize, 2700°C, ramp, 0 s, hold 4 s, internal argon flow, 50 ml/min; clean out, 2700°C, ramp, 1 s, hold, 4 s, internal argon flow, 300 ml/min.

Collection of urine and blood samples. Subjects were asked to collect urine from midnight the day of the run until the run in plastic-lined 24-h urine containers, (Scientific Products, McGaw Park, Illinois). Subjects voided immediately prior to running, within 5 min of completing the run and 2 h after the run; all other collections were at the convenience of the subjects. Immediately following and 2 h after the run, urine was collected in Falcon polypropylene 8-oz specimen containers; urine from 2 h after the run until 12 midnight was collected in 24-h urine specimen containers. A 24-h urine sample was then collected beginning at midnight. Blood was drawn using a Minicath-21 infusion set (Deseret Co., Sandy, Utah) and 25 ml Sarstedt Safety-Monovette (W. Sarstedt, Inc., Princeton, New Jersey). Immediately following running, subjects ran to the blood drawing area and a sample was taken immediately; no delay was encountered in drawing blood from any of the runners. Statistical analyses were performed using repeated measure analysis of variance and Duncan's Multiple Range Test (SAS Institute Inc., Cary, North Carolina).

RESULTS

Serum glucose of all the runners tested was increased following a strenuous 6-mile run (Table 2). Subject number 9 who had been training for only 2 mo had serum glucose immediately after the run of greater than 200 mg/dl as did subjects 1 and 5, who were very well-trained runners that had completed several marathons. Other runners with similar serum glucose values immediately after running 6 miles displayed varying degrees of general physical conditioning and training times. Serum glucose values of all runners 2 h after the run were similar to those values observed prior to running (Table 2). The runners tested did not have histories of glucose intolerance; sugar was not detected in the urine of any of the runners.

The elevated serum glucose levels were not accompanied by elevated insulin levels. Except for subject number 5, there was little or no difference in the insulin levels prior to, immediately following, and 2 h after running 6 miles (Table 2).

Serum glucagon levels were elevated significantly immediately after running but also returned to prerun values within 2 h of running (Table 2). While no apparent correlation between insulin and glucagon was observed, increases in glucagon did accompany increases in glucose.

TABLE 2
Effect of running 6 miles on serum glucose, insulin, and glucagon

Subject no.		Glucose (mg/dl)	Insulin (μU/ml)	Glucagon (ng/ml)
1	A	87	5	0.38
	B	300	7	0.71
	C	75	6	0.48
2	A	86	4	0.54
	B	117	7	0.53
	C	80	5	0.48
3	A	89	12	0.43
	B	134	10	0.61
	C	77	6	0.48
4	A	97	7	0.40
	B	157	5	0.62
	C	80	6	0.48
5	A	85	7	0.58
	B	236	23	0.68
	C	69	5	0.48
6	A	93	5	0.46
	B	170	6	0.48
	C	77	5	0.58
7	A	93	12	0.43
	B	170	10	0.62
	C	83	6	0.43
8	A	89	10	0.45
	B	169	12	0.54
	C	71	9	0.46
9	A	94	2	0.46
	B	212	8	0.45
	C	84	5	0.40
Mean ± SE	A	90 ± 1*	7.1 ± 1.2	0.46 ± 0.02*
	B	185 ± 19	9.6 ± 1.8	0.58 ± 0.03
	C	77 ± 2*	5.9 ± 0.4	0.47 ± 0.02*

Samples designated as A, B, and C refer to blood samples taken prior to running 6 miles, immediately following, and 2 h after the run, respectively.

* Values in the same column not sharing a common superscript (*) are significantly different from each other at $P < 0.05$.

TABLE 3
Effect of running 6 miles on urinary Cr concentration

Subject no.	Cr Concentration (ppb) Prerun	Cr Concentration (ppb) 2 h postrun	Postrun/prerun
1	0.29	1.45	5.0
2	0.06	0.20	3.3
3	0.10	0.86	8.6
4	0.36	1.95	5.4
5	0.10	0.79	7.9
6	0.06	0.09	1.5
7	0.18	0.64	3.6
8	0.16	0.37	2.3
9	0.04	0.18	4.5
Mean ± SE	0.15 ± 0.03*	0.72 ± 0.21*	4.7 ± 0.8
Range	(0.04–0.36)	(0.09–1.95)	(1.5–8.6)

* Significantly different from each other at $P < 0.05$.

TABLE 5
Effect of running 6 miles on urinary Cr excretion per hour

Subject no.	Urinary excretion (ng/h) Rest day	Urinary excretion (ng/h) 2 h after run	Run/rest
1	7.5	51.0	6.8
2	7.5	4.0	0.5
3	1.3	32.5	25.0
4	9.6	88.0	9.2
5	8.3	51.5	6.2
6	4.6	7.0	1.5
7	5.8	8.0	1.4
8	7.5	27.0	3.6
9	<4.6	12.5	>2.7
Mean ± SE	6.3 ± 0.8*	31.3 ± 9.3*	6.3 ± 2.5

* Significantly different from each other at $P < 0.05$.

Absorbed chromium is excreted primarily in the urine and only small amounts are lost in hair, perspiration, and bile;[12,13] therefore urinary Cr is a good indicator of total Cr excretion. The urinary Cr concentration 2 h after running was higher for all runners; the ratio of the 2-h-postrun to the prerun values ranged from 1.5 to 8.6 with a mean ratio of 4.7 (Table 3). Chromium excreted immediately after the run was minimal, accounting for 2% or less of the total daily excretion. Changes in urine volume were minimized by expressing Cr excretion as the ratio of urinary Cr concentration to urinary creatinine concentration;[14] running also increased this ratio (Table 4). When urinary Cr was expressed as ng of Cr excreted per h, there was also a significant difference in the Cr excreted in the 2 h following the run compared with the Cr excreted per hour on the rest day (Table 5). Cr excreted per hour in the 10 h prior to running, Cr excreted in the remaining 14 h of the first day of collection excluding the 2 h immediately after running, and that excreted per hour on the rest day were not significantly different.

Total daily urinary excretion of chromium is shown in Table 6; approximately 2 times as much Cr was lost in the urine on the day of the run as that on the following nonrun day. Completeness of urine collection for 24-h samples was monitored by determination of 24-h creatinine excretions. Daily urinary creatinine excretion for nine runners on a rest day was 1672 ± 422 mg (mean ± SD) compared with 2075 ± 420 mg on the run day. Total urinary Cr excretion reported here for the rest day following running was very similar to that observed for normal free living subjects.[15] Running 6 miles significantly increased daily urinary excretion of Cr with an approximate doubling for all subjects (Table 6).

TABLE 4
Effect of running 6 miles on Cr/creatinine ratio in urine

Subject no.	Prerun Cr/creatinine ratio (ng Cr/mg creatinine)	2-h postrun Cr/creatinine ratio (ng Cr/mg creatinine)	Postrun/prerun
1	0.16	0.67	4.2
2	0.09	0.06	0.7
3	0.05	0.27	5.4
4	0.16	0.86	5.4
5	0.11	0.71	6.5
6	0.05	0.12	2.4
7	0.07	0.13	1.9
8	0.08	0.26	3.2
9	0.04	0.14	3.5
Mean ± SE	0.09 ± 0.02*	0.36 ± 0.10*	3.7 ± 0.62
Range	(0.04–0.16)	(0.06–0.86)	(0.7–6.5)

* Significantly different from each other at $P < 0.05$.

Increased urinary excretion of Cr was not a nonspecific effect on renal function since the daily excretion of sodium, potassium, and calcium remained essentially constant with a run/rest ratio of 1.06, 1.12, and 0.96, respectively.

DISCUSSION

The stimulatory effect of exercise on glucose uptake by skeletal muscles has been known since 1886[16] and has been documented on numerous occasions. Costill et al.[17] reported a slight increase in serum glucose of 6 mg/dl after 30 min of exercise and no further increases during the rest period; Naveri et al.[18] reported a 71% increase in blood glucose following strenuous intermittent running. Galbo et al.[7] did not detect any significant increase in blood glucose at the point of exhaustion or 30 min postexhaustion; glucose levels were slightly below initial levels as has been reported

TABLE 6
Effect of running 6 miles on 24-h urinary excretion of Cr

Subject no.	Cr Excretion (μg/day) Run	Cr Excretion (μg/day) Rest	Run/rest
1	0.38	0.18	2.1
2	0.11	0.18	0.6
3	0.15	0.03	5.0
4	0.62	0.23	2.7
5	0.57	0.20	2.9
6	0.14	0.11	1.3
7	0.15	0.14	1.1
8	0.29	0.18	1.6
9	0.11	<0.11	>1.0
Mean ± SE	0.30 ± 0.07*	0.16 ± 0.02*	2.1 ± 0.52
Range	(0.11–0.62)	(<0.11–0.23)	(>1.0–2.9)

* Significantly different from each other at $P < 0.05$).

by others.[19–22] Blood glucose levels of trained runners were not altered significantly immediately following a 42-km marathon but were elevated following a 10,000-meter run.[23] However, others have reported significant elevations of blood glucose following running in a marathon.[24] Richards et al.[25] reported a wide range of blood sugar levels of runners immediately following completion of a marathon and also in those unable to complete the run.

In our study the serum glucose immediately after the run was elevated dramatically, often reaching 200 mg/dl, and was 300 mg/dl in one subject. Elevated levels of glucose immediately after running appear to be a normal response and are not related to impaired glucose tolerance. For example, subject number 1, who had serum glucose of 300 mg/dl after running, displayed glucose and insulin values similar to his fasting levels 90 min after an oral glucose tolerance load of 1 g glucose/kg body weight. The consequences of such dramatic increases in blood glucose of runners unable to utilize glucose efficiently requires further study. For example, the effects of increases in blood glucose to 200–300 mg/dl due to exercise, in individuals with impaired glucose homeostasis need to be ascertained. In patients with decompensated diabetes mellitus, 5–30 min after only 5-min exercise on a bicycle ergometer, blood sugar levels remained elevated.[26] Individuals prone to glucose intolerance may need to take additional precautions when exercising strenuously.

Elevated levels of glucose were not accompanied by elevated insulin (Table 2). This represents another dramatic example that following exercise, other endogenous mechanisms, in addition to blood glucose concentration, regulate circulating plasma immunoreactive insulin (IRI).

Glucagon levels are also dependent on the intensity and duration of exercise. During graded exercise, a 35% increase was reported and 3 times the normal values were reported after prolonged exercise.[7] The runners in our study displayed a significant increase in serum glucagon which is within the expected values based on the duration and intensity of the exercise.

Pruett[21] demonstrated that special diets in which the relative amounts of fat and carbohydrate were varied did not affect glucose and insulin response to exercise. Any change in the blood glucose found during exercise must be due to changes brought about by exercise and not due to the diets alone.[21] Similarly, in our study diet does not appear to be the causal factor in causing increased Cr excretion following exercise. Other than fasting prior to running, runners were asked not to alter their eating and drinking habits during the duration of the study period. Daily Cr excretion for eight of nine runners increased on a run day as opposed to a rest day, indicating that unless essentially all of the runners were altering their Cr intake substantially, approximate doubling of intake or ingestion of some unknown substance that doubles Cr excretion, the increase in Cr excretion was due to exercise and not changes in diet. In a previous study, we reported a daily urinary excretion of Cr for 17 male subjects of 0.18 ± 0.04 μg (mean ± S.E.).[15] In this study, we observed a nearly identical daily urinary excretion of 0.16 ± 0.02 μg for the nine male subjects on a day without exercise (Table 6). However, on the day of the run the mean urinary Cr excretion was almost double both of these values. We have also measured the daily variation in Cr excretion for individual subjects when there were no restrictions on keeping their respective diets constant; daily Cr excretion for the same individual subjects was usually within 25%. Further, Cr excretion (ng/h) in the 2 h following exercise during which no foods were eaten was also higher than any other period examined during the run and following rest day (Table 5). Changes due to exercise are much larger than those attributed to hourly or diurnal variation[14] and do not appear to be related to fluctuations in the dietary intakes of chromium.

The increases in urinary Cr concentration, chromium/creatinine ratio, ng of Cr exerted per hour, and 24-h excretion of Cr following exercise suggest an increased requirement but not necessarily increased intake (vide infra) of Cr for individuals who exercise routinely. Many sedentary Americans appear to be marginally Cr deficient;[10,13–15] therefore additional cumulative losses of Cr due to exercise may need to be replaced to prevent overt deficiency. This could be accomplished by increased dietary intake, which does not appear likely, since well-balanced diets may contain less than the recommended safe and adequate amount for Cr,[27] which is 50–200 μg, or through increased absorption and more efficient utilization of dietary Cr. Trace element absorption is often regulated by status of the animal;[28] this would be the most likely means to overcome the additional losses due to exercise. Increased Cr absorption has been reported in insulin-requiring diabetics.[29] Chromium absorption varies and is usually less than 1%, even if it doubled this would be difficult to detect.

Our data indicate that accompanying the exercise induced increases in glucose metabolism there is an increase in Cr excretion. Exercising individuals appear to compensate for increased Cr losses by an undetermined means.

REFERENCES

[1] Wahren, J., Felig, P., Ahlborg, G., and Jorfeldt, L.: Glucose metabolism during leg exercise in man. J. Clin. Invest. *50*:2715–25, 1971.

[2] Rowell, L. B., Masaro, E. J., and Spencer, M. J.: Splanchnic metabolism in exercising man. J. Appl. Physiol. *20*:1032–40, 1965.

[3] Felig, P. and Wahren, J.: Fuel homeostasis during exercise. N. Engl. J. Med. *293*:1078–84, 1975.

[4] Galbo, H., Richter, E. A., Hilsted, J., Holst, J. J., Christensen, N. J., and Henricksson, J.: Hormonal regulation during prolonged exercise. Ann. NY Acad. Sci. *301*:72–80, 1977.

[5] Hansen, A. P.: Serum growth hormone patterns in juvenile diabetes. Dan. Med. Bull. *19* (Suppl. 1): 1972.

[6] Roth, J., Glick, S. M., Yalow, R. S., and Berson, S. A.: Secretion of human growth hormone: physiologic and experimental modification. Metabolism *12*:577–79, 1963.

[7] Galbo, H., Holst, J. J., and Christensen, N. J.: Glucagon and plasma catecholamine response to graded and prolonged exercise in man. J. Appl. Physiol. *38*:70–76, 1975.

[8] Few, J. D.: Effect of exercise on the secretion and metabolism of cortisol in man. J. Endocrinol. *62*:341–53, 1974.

[9] Pruett, E. D. R.: Plasma insulin concentration during prolonged work at near maximal oxygen uptake. J. Appl. Physiol. *29*:155–58, 1970.

[10] Anderson, R. A.: Nutritional role of chromium. Sci. Total Environ. *17*:13–29, 1981.

[11] Bonsnes, R. W., and Taussky, H. H.: On the colorimetric determination of creatinine by the Jaffe reaction. J. Biol. Chem. *158*:581, 1945.

[12] Hopkins, L. L., Jr.: Distribution in the rat of physiological amounts of injected Cr^{51} (III) with time. Am. J. Physiol. *209*:731–35, 1965.

[13] Doisy, R. J., Streeten, D. H. P., Souma, M. L., Kalafer, M. E., Rekant, S. L., and Dalakos, T. G.: Metabolism of chromium^{51} in human subjects. *In* Newer Trace Elements in Nutrition. Mertz, W., and Cornatzer, W. E., Eds. New York, Marcel Dekker, 1971, Chapt. 8.

[14] Gurson, C. T., and Saner, G.: Urinary chromium excretion, diurnal changes and relationship to creatinine excretion in healthy and sick individuals of different ages. Am. J. Clin. Nutr. *31*:1162–66, 1978.

[15] Anderson, R. A., Polanksy, M. M., Bryden, N. A., Roginski, E. E.,

Glinsmann, W. H., Patterson, K. Y., and Veillon, C.: Chromium supplementation of free-living subjects: effect on urinary Cr excretion. Fed. Proc. *40*:885, 1981.

[16] Cheuveau, M. A., and Kaufman, M.: C. R. Acad. Sci. Ser. D 104, pp. 1126-32, 1886.

[17] Costill, D. L., Bennet, A., Branam, G., and Eddy, D.: Glucose ingestion at rest and during prolonged exercise. J. Appl. Physiol. *34*:764-69, 1973.

[18] Naveri, H., Rehunen, S., Kuoppasalmi, K., Tulikoura, I., and Harkonen, M: Muscle metabolism during and after strenuous intermittent running. Scand. J. Clin. Lab. Invest. *38*:329-36, 1978.

[19] Boje, O.: Der blutzucker wahrend und nach korperlicher. Arbeit. Scand. Arch. Physiol. Suppl. *10*:1-48, 1936.

[20] Christensen, E. H., and Hansen, O.: Arbeitsfahigkeit und ernahrung. Scand. Arch. Physiol. *81*:160-77, 1939.

[21] Pruett, E. D. R.: Glucose and insulin during prolonged work stress in men living on different diets. J. Appl. Physiol. *28*:199-208, 1970.

[22] Koivisto, V., Soman, V., Nadel, E., Tamborlane, W. V., and Felig, P.: Exercise and insulin: insulin binding, insulin mobilization, and counterregulatory hormone secretion. Fed. Proc. *39*:1481-86, 1980.

[23] Lavine, R. L., Lowenthal, D. T., Gellman, M. D., Kline, S., Recant, L. R., and Rose, L. I.: The effect of long distance running on plasma immunoreactive glucagon levels. Eur. J. Appl. Physiol. *43*:41-44, 1980.

[24] Maron, M. B., Horwath, S. M., and Wilkerson, J. E.: Acute blood biochemical alterations in response to marathon running. Eur. J. Appl. Physiol. *15*:173-81, 1975.

[25] Richards, D., Richards, R., Schofield, P. J., and Ross, V.: Biochemical and haematological changes in Sydney's the Sun City-to-Surf for runners. Med. J. Aust. *3*:449-53, 1979.

[26] Povolotskaya, G. M., and Svyatelik, G. V.: Effect of physical stress on some carbohydrate and fat metabolism indexes in diabetes mellitus. Endokrinologuja *8*:71-74, 1978..

[27] Kumpulainen, J. T., Wolf, W. R., Veillon, C., and Mertz, W.: Determination of chromium in selected United States Diets. J. Agric. Food Chem. *27*:490-99, 1979.

[28] Underwood, E. J.: Trace Elements in Human and Animal Nutrition. 4th Edit. New York, Academic Press, 1977.

[29] Doisy, R. J., Streeten, D. H. P., Freiberg, J. M., and Schneider, A. J.: Chromium metabolism in man and biochemical effects. *In* Trace Element Metabolism in Human Health and Disease. Prasad, A. S., Ed. New York, Academic Press, 1976, pp. 79-104.