10 Trace Elements Excluding Iron—Chromium and Zinc

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I. INTRODUCTION

The mounting public awareness of the increased risk of chronic disease associated with physical inactivity and nutritionally imbalanced diets is leading many
Americans to adopt healthful behaviors. Recommendations by public health organizations in the form of the Dietary Guidelines for Americans are available.\textsuperscript{7} Middle-aged (30–60 yr) adults are accepting the advice to boost participation in physical activity with the participation increasing, albeit modestly, from 55\% to more than 61\% in the past 5 years.\textsuperscript{2} Although considerable information exists about the health benefits of regular exercise in middle-aged adults,\textsuperscript{3} little information is available indicating the impact of micronutrients consumed in less than recommended amounts or large amounts on physiological function or performance during regular aerobic or resistance activities.

Chromium and zinc are two minerals that are limited in the diets of middle-aged adults. National nutritional surveys estimate that 20\% to 36\% of middle-aged men and women fail to consume the recommended intake of zinc.\textsuperscript{4} Similarly, chromium intakes are considered to be low because contemporary food processing depletes chromium.\textsuperscript{5}

Although the public press touts chromium for its supportive role in protein, carbohydrate, and lipid metabolism, the benefits of supplemental chromium in response to exercise training are controversial.\textsuperscript{6} Accumulating evidence supports the importance of adequate amounts of dietary zinc in promoting physiological function during exercise.\textsuperscript{7} An argument for supplementation of physically active people with chromium and zinc is based on findings of substantially increased urinary losses of these minerals after strenuous physical exercise.\textsuperscript{8} This chapter critically evaluates the roles of chromium and zinc in support of optimal physiological function in response to physical activity in middle-aged adults; it examines the effects of supplementation with chromium or zinc on various measures of performance and body composition in response to training; concludes with a consensus opinion on the value of chromium or zinc supplementation on exercise-related outcomes in middle-aged adults, and highlights recommendations for further research.

II. CHROMIUM

Chromium (Cr) exists in nature in many oxidation states ranging from Cr\textsuperscript{2-} to Cr\textsuperscript{6+}; the predominant forms are Cr\textsuperscript{3+} (trivalent) and Cr\textsuperscript{6+} (hexavalent). Trivalent chromium is nutritionally active and found in food, whereas hexavalent chromium is a toxic form that is produced during industrial processes.\textsuperscript{9} Chromium is a putatively essential mineral that can play a role in carbohydrate and lipid metabolism;\textsuperscript{5} it potentiates insulin binding to insulin-sensitive cells and facilitates gene expression.\textsuperscript{6,10}

A. CHROMIUM HOMEOSTASIS

1. Dietary Chromium

Chromium is widely distributed in the food supply but most foods contain only very small amounts (1–2 \( \mu \)g per serving). Good sources of chromium include whole-grain products, some fruits (grapes and bananas) and vegetables (broccoli and potatoes), meat (beef), and some spices (garlic and basil).\textsuperscript{11} In contrast, foods high in simple sugars, such as sucrose and fructose, are low in chromium content.\textsuperscript{12} Estimation of
dietary chromium intake is problematic because of the high variability in reported chromium content of foods due to agricultural and processing practices.\(^9\)

The lack of reliable data on the chromium content of foods and the paucity of controlled feeding studies in human contribute to the lack of a Recommended Dietary Allowance for chromium.\(^{13}\) However, an Adequate Intake, which indicates the amount that healthy people typically consume, for chromium has been established at 35 µg and 25 µg for men and women, respectively.\(^{13}\)

2. Absorption

Absorption of chromium from the intestines is low, with estimates ranging from 0.4% to 2.5% of the amount ingested, with the remainder excreted in feces.\(^{14-17}\) Food components, such as vitamin C in fruits and vegetables and niacin in meats, poultry, fish, and grain products enhance the absorption of chromium.\(^8\) Absorbed chromium is stored in the liver, spleen, soft tissues, and bone.\(^{19}\) However, diets high in simple sugars (more than 35% of energy intake) increase urinary excretion of chromium.\(^{12}\)

Inorganic (chloride) and organic (nicotinate, picolinate, and a histidine complex) compounds of trivalent chromium are available. However, the predominant chemical form promoted to enhance biological function, including performance enhancement and weight reduction is chromium picolinate because of its increased bioavailability compared with other trivalent chromium compounds.\(^{20,21}\)

3. Factors Mediating Body Chromium

In addition to diet, other factors may contribute to depletion of chromium content of the body. Physiological states such as pregnancy and lactation increase chromium losses.\(^{22}\) Acute strenuous exercise, infection, and physical trauma markedly increase chromium losses, principally in the urine, and can lead to chromium deficiency, especially when chromium intakes are low.\(^{22,23}\) Aging also may reduce chromium in the body, as shown by decreased concentrations of chromium in the blood, hair, and sweat of older compared with younger adults.\(^{13}\)

4. Assessment of Chromium Nutritional Status

Accurate and sensitive biochemical indicators of human chromium nutriture are lacking. Plasma or serum chromium concentrations do not reflect tissue chromium levels.\(^{20,21}\) Serum chromium responds to chromium supplementation,\(^{23,24}\) but does not correlate with functional biomarkers of chromium action \textit{in vivo} such as serum glucose or insulin in the fasting state or after glucose load.\(^{25}\) Similarly, urinary chromium concentration and output are responsive to chromium supplementation but are inadequate indicators of chromium status because they fail to correlate with glucose, insulin, or lipid concentrations.\(^{25}\) Thus, assessment of chromium nutritional status remains elusive.

B. Chromium as an Ergogenic Aid in Middle-Aged Adults

Findings of marked increases in fat-free mass and concomitant decreases in fat in livestock supplemented with chromium picolinate (≥200 µg chromium) provided an incentive to determine the ergogenic effects and body composition changes of young adults during physical training.\(^9\) Although preliminary findings in young
adults suggested that chromium picolinate supplementation combined with physical training resulted in a gain in fat-free mass and loss of fat, subsequent studies did not confirm these initial results. Differences in physical training modes, doses of chromium picolinate, failure to assess dietary chromium intake, methods of assessment of outcomes, and initial fitness levels of the subjects may have contributed to the inconsistent results.

Studies in middle-aged and older adults, in whom impairments of glucose and insulin metabolism might be more prevalent than in younger and healthier adults, also have examined the effects of chromium picolinate supplementation. The goals of these studies were to ascertain whether supplemental chromium with or without regular physical activity affects body composition, physical performance, and some aspects of metabolism.

1. Chromium Supplementation and Body Composition

Excess body weight is associated with increased circulating insulin concentrations that are directly related to body fat content. The proposed link between trivalent chromium and facilitation of insulin action motivated investigators to determine the effects of supplemental chromium on weight loss and maintenance with an emphasis on reduction of body fat and preservation of lean body mass in a variety of experimental plans. In the studies with older adults, the amount of supplemental chromium far exceeded the dose of 200 μg/d used in the studies with young adults. The investigators apparently reasoned that weight loss increased chromium needs to ameliorate any deficits in insulin utilization associated with excess adipose tissue.

Studies to determine the effects of supplemental chromium on weight loss have yielded contradictory results. Forty-four obese middle-aged women were matched by body mass index then randomized to receive either 400 μg chromium as chromium picolinate daily or placebo for 12 wk. All women participated in an exercise component of the weight loss program, including 30 min of resistance training and 30 min of moderate-intensity walking daily, 2 d/wk. Only 20 women supplemented with chromium and 17 women receiving placebo completed the study. Neither body composition, determined by using underwater weighing, nor sum of the circumferences of the waist and hips, were affected by chromium supplementation compared with placebo. Plasma chromium concentration and urinary chromium excretion increased significantly only in the women supplemented with chromium. Muscular strength increased significantly regardless of treatment.

Two additional studies failed to provide reasonable evidence of a beneficial effect of chromium during weight loss. One hundred fifty-four obese middle-aged adults participated in a randomized, double-blind, placebo-controlled trial to determine the effects of chromium picolinate supplements on the composition of weight loss. Volunteers received 200 or 400 μg of chromium daily or placebo for 72 d. Supplemental chromium was provided in a proprietary drink containing protein and carbohydrate. Volunteers were asked to consume at least two servings daily, but there was no control of the volume of the drink, and hence chromium intake, consumed by a subject. No instruction regarding dietary practices or physical activity was provided to the participants. Body composition was determined by using underwater weighing before and after treatment. Compared with the placebo group,
significant decreases in body weight, fat weight, and body fatness were found for the chromium supplementation groups with no differential effect of chromium dose on these variables. Treatment did not significantly affect lean body mass. These findings are problematic because of the use of a body composition improvement index that accounts for fat loss (positive effect) and reduction of lean body mass (negative effect) that occurred during the trial. The investigators concluded that chromium supplementation facilitated significantly more positive changes in body composition compared with the results from the placebo. No effect of chromium level (200 vs. 400 μg/d) was found on the body composition improvement index.

In a second study, 122 obese middle-aged adults were randomized to receive a capsule containing either 400 μg of chromium (chromium picolinate) daily or placebo and participate in an exercise program for 90 d.\textsuperscript{29} Subjects self-reported daily caloric intake and energy expenditure to fitness instructors. Although body fat, assessed with dual x-ray absorptiometry, decreased in both groups, the loss of fat was significantly greater in adults supplemented with chromium. Both treatment groups had non-significant loss of lean body weight. The investigators further adjusted the body composition data by calculating additional changes in fat weight on the basis that 3500 kcal energy expenditure reflected a 1 lb loss of body fat. After controlling for self-reported differences in energy intake and output, the subjects supplemented with chromium, as compared with the placebo group, lost significantly more weight (7.8 vs. 1.8 kg) and fat weight (7.7 vs. 1.5 kg) without loss of lean body mass.

Interpretation of the data from these studies\textsuperscript{28,29} is confounded by some key concerns. Use of the body composition improvement index from self-reported energy expenditure rather than actual assessments of body composition is suspicious. Also, the lack of control and estimation of chromium intake and assessment of energy intake and expenditure restrict the interpretation of the findings. Similarly, calculation of loss of fat based on 3500-kcal energy expenditure associated with physical activity fails to acknowledge homeostatic adaptation in energy metabolism and produces uncertain conclusions. Therefore, conclusions from these results should be viewed with caution.

A double-blind, placebo-controlled pilot study evaluated the effects of trivalent chromium-bound niacin on weight loss and its composition in obese women.\textsuperscript{30} Twenty African-American women were randomized to two groups that received either a total of 600 μg of chromium daily or placebo in a repeated measures, crossover designed trial. One group began with 200 μg/d of chromium supplementation administered three times daily (total supplemental chromium 600 μg/d) for 2 months, then a 1 month washout, followed by 2 months of placebo. Concurrently, the other group received placebo first then the chromium supplement. In the group treated with placebo first, body fat weight, assessed with bioelectrical impedance, decreased significantly more and lean body weight decreased significantly less with the chromium-bound niacin compared with placebo. In contrast, the group supplemented first with chromium lost significantly more fat weight and less lean body weight during the placebo compared with chromium supplementation. These findings suggest that although chromium-bound niacin had beneficial effects on fat loss and preservation of lean body weight when provided initially, placebo also was effective for weight loss. Because
the rate of initial weight loss was independent of chromium supplementation. One can conclude that the effects were the result of a sequence effect.

Chromium also has been used in conjunction with other dietary components to augment weight loss. Thirty-three obese women who completed a 2-wk very low-calorie diet were randomized to receive a supplement containing chromium picolinate (200 μg), fiber (20 g), carbohydrate (50 g), and caffeine (100 mg), or placebo for 16 months. The amount and course of the weight regain was similar between the groups with no differences in change in body composition by treatment. These results indicate that chromium, as a component of a multifactor supplement, was not useful in maintaining weight loss in weight-reduced adults.

The effect of different chromium-containing organic compounds has been evaluated in conjunction with exercise training in obese middle-aged adults. Grant et al. studied 43 obese women who participated in a cross-training exercise program including step aerobics, cycling, and resistance training for 9 wk. They were randomly assigned to one of four treatment groups: chromium picolinate without exercise, exercise training supplemented with chromium picolinate, exercise training with placebo, and exercise training with chromium nicotinate. Chromium supplements, each containing 200 μg, were consumed as two capsules daily for a total chromium intake of 400 μg/d. Body weight increased significantly only in the nonexercising women supplemented with chromium picolinate. Thus, chromium picolinate supplementation was not effective in reducing body weight, positively affecting body composition assessed by using underwater weighing, nor on fasting glucose or insulin concentrations. However, in response to an oral glucose tolerance test, the area under the insulin curve was significantly reduced only in the women treated with chromium nicotinate and exercise. These findings suggest that chromium as nicotinate, not picolinate, may be beneficial in risk factor modification in obese adults.

Attempts to demonstrate the benefit of chromium on weight maintenance have not been successful. Twenty-one obese patients who successfully completed an 8-wk very low-calorie diet were supplemented with 200 μg of chromium daily either as chromium picolinate or chromium-enhanced yeast daily, or placebo for an 18-wk weight maintenance period. Although body weight and body fatness, estimated from skinfold thicknesses, were not influenced by treatment, lean body mass significantly increased in the group supplemented with chromium picolinate compared with the other treatments. This finding suggests that chromium picolinate, but not chromium-enhanced yeast, promotes muscle retention, and may enhance muscle accretion during weight maintenance after weight loss.

Differences in experimental designs, including the dose and chemical form of chromium and lack of assessment of energy intake, complicate any interpretation of these findings. A recent study, however, has overcome many of these limitations and provides a clearer view of the effects of chromium supplementation on body weight and composition. Eighty-three middle-aged women were matched by body mass index and randomized in a double-blind study to receive one of three treatment groups; chromium picolinate (200 μg), picolinic acid in an amount equivalent to the dose in the matched chromium picolinate, and placebo. After assessment of individual energy needs, the women consumed only food and beverages provided for 12 wk. The study tested the hypothesis that supplemental chromium promotes weight
loss and selective loss of fat and gain of lean body mass when energy intake was constant. Body weight was maintained within 2% of admission values. Body composition, determined at admission and 12 wk by using dual x-ray absorptiometry, did not change significantly. Another outcome measure was frequency of increases in food (energy) intake needed to maintain body weight. Daily caloric intervention (increases) were needed statistically more in the placebo (48%) than in the chromium picolinate (20%) and picolinic acid (15%) groups. Thus, under conditions of constant energy intake, supplemental chromium (200 μg) affected neither body weight nor composition.

2. Compositional and Functional Effects in Older Adults
Advancing age has been associated with significant decreases in muscle mass and impairments in ambulatory function as well as decreased insulin sensitivity. Because of its putative role in anabolism as a potentiator of insulin action, chromium supplementation independently and in conjunction with weight training has been hypothesized to increase muscle mass in the elderly.

Nineteen middle-aged and older healthy men and women were randomly assigned in a double-blind study and received either 1000 μg chromium as chromium picolinate or placebo for 8 wk. Serum chromium concentrations increased significantly with supplementation. Body composition and insulin sensitivity were unchanged in both groups. Thus, chromium picolinate neither changed body composition nor improved insulin sensitivity in healthy older men and women.

The interaction of supplemental chromium and resistance training on body composition and strength gain has been determined. Eighteen healthy middle-aged men were randomly assigned (double-blind) to groups that consumed either 924 μg chromium as chromium picolinate or placebo daily for 13 wk while participating in a supervised resistance training program. For 5-d sequences during each 3-wk testing period, the men consumed controlled diets designed to maintain constant chromium intake (~60 and ~100 μg chromium daily in a 2-d rotating menu). Lean body mass, muscle mass, and rates of strength gain increased independently of chromium supplementation.

A similar study was conducted in middle-aged women. Seventeen sedentary women were randomized to groups that received either 924 μg chromium as chromium picolinate or placebo daily for 13 wk and participated in a supervised resistance training program. Resistance training significantly increased muscle strength of the muscle groups trained; these responses were not affected by chromium picolinate supplementation. Fat-free mass and body fatness were not changed by resistance training in the weight-stable women regardless of chromium supplementation.

3. Conundrum of Chromium
Lack of evidence describing the importance of supplemental chromium in promoting changes in body weight and composition raises question about the biological role of chromium on energy balance. If trivalent chromium potentiates insulin action, it should stimulate anabolism. Thus, chromium should up-regulate protein synthesis and promote gain of muscle and lean body mass when energy balance is neutral or positive. However, the mechanism by which supplemental chromium is hypothesized to promote weight loss while decreasing fat and concomitantly increasing muscle or
fat-free mass\textsuperscript{39} is unknown and contradicts the anabolic function of chromium as a facilitator of insulin action. Thus, acceptance of the findings of decreased body weight and selective fat loss with supplemental chromium should be viewed guardedly until appropriately designed human trials have been undertaken and the results critically reviewed.

\section{ZINC}

Zinc is a transition element that forms stable complexes with side chains of proteins and nucleotides with a specific affinity for thiol and hydroxy groups and ligands containing nitrogen.\textsuperscript{40} The zinc ion acts as a good electron acceptor, but does not participate in direct oxidation-reduction reactions. These characteristics explain the diverse biological functions of zinc in the regulation of body metabolism, which is bolstered by the requirement for zinc in more than 200 enzymes in various species.\textsuperscript{41}

Zinc has several recognized functions in zinc-metalloenzymes including catalytic, structural, and regulatory roles.\textsuperscript{42} Catalytic function specifies that zinc participates directly in facilitating the action of the enzyme. If the zinc is removed by chelates or other agents, the enzyme becomes inactive. Carbonic anhydrase is an enzyme in which zinc plays a catalytic role.\textsuperscript{43}

In a structural role, zinc atoms are required to stabilize the tertiary structures of the enzyme protein and to maintain the integrity of the complex enzyme molecules, but it does not impact enzyme activity. Zinc plays a structural role in the enzymes superoxide dismutase and protein kinase \textit{c}.\textsuperscript{41}

The importance of zinc in biological systems is reflected by the various functions and activities on which zinc exerts a regulatory role.\textsuperscript{10} Zinc is needed for macronutrient metabolism, and is required for nucleic acid and protein metabolism and, hence, cell differentiation and replication. Similarly, zinc is vital for glucose utilization, the secretion of insulin, and lipid metabolism. Zinc is also required for the production, storage, and secretion of individual hormones including growth and thyroid hormones, gonadotrophins and sex hormones, prolactin, and corticosteroids. Zinc status regulates the effectiveness of the interaction of some hormones at receptor sites and end-organ responsiveness.

Integrated biological systems also require zinc for optimal function. Adequate zinc intake is necessary for proper taste perception, reproduction, immuno-competence, skin integrity, wound healing, skeletal development, brain development, behavior, vision, and gastrointestinal function in humans.\textsuperscript{13} Zinc, therefore, is a nutrient that regulates many physiological and psychological functions and is required in adequate amounts to promote human health and well-being.

\section{Zinc in the Human Body}

Zinc is an intracellular cation that is present in all organs, tissues, fluids, and secretions of the body. It is associated with all organelles of the cell but only 60\% to 80\% of cellular zinc is localized in the cytosol; the remainder is bound to membranes, which may be important in defining the effects of zinc deficiency on cellular function. The concentration of zinc in extracellular fluids is very low, with plasma zinc
concentration only 65 nmol/L. If the body plasma concentration is 45 mL/kg body weight, then a 70-kg man has about 3 L of plasma, which contains 3 mg of zinc, or about 0.1% of the body zinc content.

The zinc concentration in various organs and tissues of the body is variable. Although the concentration of zinc in skeletal muscle is not large, the substantial mass of skeletal muscle makes it the principal reservoir of zinc in the body. Bone and skeletal muscle account for almost 90% of the body zinc content.

The zinc concentration of muscles varies with their metabolic functions. The highest zinc concentrations are found in skeletal muscles that are highly oxidative, with a large proportion of slow-twitch fibers. Rat soleus muscle, composed of 63% slow-twitch fibers, contains about 300 μg zinc per gram dry weight. Conversely, the extensor digitorum longus, which is primarily a fast-twitch glycolytic muscle, has only 100 μg of zinc per gram dry weight. Dietary restriction of zinc generally does not significantly reduce the zinc concentration in skeletal muscles, except for small decreases (~5%) in the soleus. The size and number of various types of muscle fibers, however, may be reduced and their relative distribution altered in a muscle, with a characteristic decrease of the slow-twitch oxidative and an increase in the fast-twitch glycolytic fibers. Thus, skeletal muscle, at least on a tissue level, is relatively unresponsive to changes in dietary zinc.

Because the concentration of zinc in bone is quite large relative to other body tissues and organs, and the amount of bone is substantial, the skeleton is the major depot of zinc. Restricted zinc intake adversely affects zinc concentration of bone, particularly in young, growing animals and to a lesser extent in older animals. Bone zinc concentration is more responsive to dietary zinc level than other tissues, and it may better reflect the gradual decline in overall zinc status of the body compared with plasma zinc concentration, even in older animals.

B. ZINC HOMEOSTASIS

1. Absorption

The amount of zinc in the body represents a dynamic balance between the zinc intake and losses. Zinc is absorbed throughout the gastrointestinal tract, with highest rate of absorption in the jejunum and duodenum and only negligible amounts absorbed in the stomach and the large intestine. After a meal, the quantities of zinc in the intestines is the sum of zinc from food and beverages, and the zinc-containing endogenous secretions from the pancreas, gall bladder, and stomach that aid in digestion and cellular zinc flux into the gut. Post-prandially, the amount of zinc in the lumen of the small intestine exceeds the quantity of zinc ingested because of endogenous secretions.

During digestion, secreted enzymes release zinc from food and endogenously secreted proteins. The free zinc can form coordination complexes with various exogenous and endogenous ligands, such as amino acids, organic acids, and phosphates. The amino acids histidine and cysteine have a high affinity for zinc, and are very efficiently absorbed, more so than zinc sulfate. Other compounds such as iron
and phytate, found in the intestine after a meal, can compete with zinc for mucosal binding sites or form insoluble complexes that inhibit zinc absorption.49 After a meal, zinc absorption follows the concentration gradient from the intestinal lumen to mucosal cells. Kinetic measurements indicate that the mucosal cell affinity for zinc uptake has a wide range, with highest rate under conditions of low zinc intake, which suggests an up-regulation of zinc transport when consumption is less than meets physiological needs.49 Zinc uptake in the small intestine has saturable or active transport and passive components. Albumin is the major protein in the blood to transport zinc from the intestines to the liver. Evidence of an effect of acute or chronic physical activity on zinc absorption and homeostasis is not available.

Functional evidence reveals that at least 24 specific transporters are responsible for either zinc influx or efflux in mammalian cells. These transporters are designated as two gene families: the ZnT proteins and the Zip family.50 ZnT transporters reduce intracellular zinc availability by promoting zinc efflux from cells, whereas Zip transporters increase intracellular zinc availability by promoting extracellular uptake of zinc. Evidence shows that human ZnT and ZIP genes exhibit either up-regulation or down-regulation in response to zinc intake and probably contribute to homeostatic control.51 Information about the actions of these transporters in muscle or other tissues in response to physical activity is lacking.

The total body content of zinc is controlled partially by the regulation of the efficiency of intestinal absorption of zinc. Numerous studies in animals and humans have reported an inverse relationship between zinc intake and absorption.52-54 Thus, the regulation of zinc absorption by the mucosal cell provides a general control of total body zinc.

2. Excretion

Control of zinc excretion in feces represents another regulatory mechanism for maintenance of body zinc. Secretion of pancreatic zinc-containing enzymes, mucosal cell loss into the gut, and transepithelial flux of zinc from the serosal to mucosal direction into the gastrointestinal tract is the major route of zinc excretion.54 In normal dietary circumstances, the feces are the major route of zinc excretion. In healthy humans with an average zinc intake of 10 to 14 mg/d, more than 90% of dietary zinc is excreted in the feces.52,55 Some of the zinc in the feces is from endogenous secretions. Studies indicate that 2.5 to 5 mg of zinc is secreted into the duodenum after a meal.59 Much of the zinc secreted into the lumen of the gut is absorbed and returned to the body. The amount of zinc secreted into the gut varies with the zinc content of the meal. Endogenous zinc excretion in feces is directly related to dietary zinc intake. In humans, endogenous fecal zinc losses may range from 1 mg/d with very low zinc intakes (~1 mg/d) to 3 to 5 mg/d with usual zinc intakes (7 to 15 mg/d).13,56 In contrast to intestinal absorption, endogenous fecal zinc excretion represents a sensitive control to balance zinc retention to metabolic needs.

Other routes of zinc excretion are present in humans. Less than 1 mg of zinc is excreted daily in the urine and is refractory to change with a wide range of zinc intake (4 to 25 mg/d).54 Urinary zinc originates from the ultra-filterable portion of plasma zinc and represents a fraction of previously absorbed dietary zinc. Conditions that increase muscle breakdown (e.g., starvation or trauma) can raise urinary zinc
excretion rates. Other losses of zinc include semen (1 mg/ejaculate), menses (0.1–0.5 mg per menstrual period), and parturition (100 mg/fetus and 100 mg/placenta).\textsuperscript{40} Surface losses, which include sloughing of the skin, sweat, and hair, contribute up to 1 mg of zinc loss daily. A marked change in zinc intake results in parallel changes in surface zinc loss.\textsuperscript{56} Surface losses at rest range from 0.3–0.4 to 0.4–0.5 and 0.7–0.8 mg with intakes of 3–4, 8–9 and 33–34 mg/d, respectively.\textsuperscript{57}

Exercise in warm and hot environments increases zinc losses in sweat. Initial reports showed a mean zinc loss of 13.7 mg/d that decreased to 2.4 mg/d with acclimatization.\textsuperscript{58} Other data confirm a reduction in sweat zinc concentrations either with repeated bouts of moderate physical activity in the heat or repeated collections during prolonged exposure.\textsuperscript{59}  62 Using the mean zinc concentration after acclimation, zinc losses in sweat during physical activity are estimated to be 3 to 4 mg/d.

The elimination of absorbed zinc from the human body has been described with a two-component model with an initial or rapid phase that has a half-life of 12.5 d and a slower turnover phase of about 300 d.\textsuperscript{40} The initial phase represents liver uptake of circulating zinc and its quick release into the circulation. The slower turnover rate reflects the different rates of turnover in various organs, excluding the liver. The most rapid rates of zinc uptake and turnover occur in the pancreas, liver, kidney, and spleen, with slower rates in erythrocytes and muscle. Zinc turnover is slowest in bone and the central nervous system.

Manipulation of dietary zinc impacts zinc turnover. In rats, dietary zinc restrictions promote loss of zinc from bone but not soft tissues and organs. The turnover of the slow zinc pool in adult humans is increased by ingestion of pharmacologic amounts (100 mg) of zinc. An exchangeable zinc pool in humans is decreased in size when zinc intake is severely reduced, which may indicate the amount of zinc available to tissues and provide a biomarker of zinc status. The exchangeable zinc pool includes plasma zinc and perhaps liver zinc.\textsuperscript{63}

3. Transport

Distribution of absorbed zinc to the extra-hepatic tissues occurs primarily in the plasma, which contains approximately 3 mg of zinc or about 0.1% of total body zinc. Zinc is partitioned among α₂-macroglobulin (40%), albumin (57%), and amino acids (3%) in plasma.\textsuperscript{40} Zinc is bound loosely to albumin and amino acids; these fractions are responsible for transport of zinc from the liver to tissues. The amino acid-bound zinc constitutes the ultra-filterable fraction that is filtered at the kidneys and excreted in the urine. Because the total amount of zinc present in tissue is far greater than the zinc in the plasma, relatively small changes in tissue zinc content, such as the liver, can have striking effects on the plasma zinc concentration.

4. Assessment of Zinc Status

Routine assessment of human zinc nutritional status is hampered by the lack of accepted blood biochemical indicators of tissue zinc content. The ease of collection and measurement of plasma zinc concentration is practical and appealing. Because zinc homeostatic control is effective, plasma zinc concentrations are maintained within a narrow range (12–18 μM or 8–12 μg/100 mL) despite a broad amount of
intake. Restriction of dietary zinc will significantly reduce plasma zinc concentration. Factors such as illness and consumption of food alter plasma zinc concentration and limit the usefulness of plasma zinc as a status indicator. Nevertheless, studies of physically active people have used plasma zinc to characterize zinc nutritional status. Promising biomarkers of zinc status include the expression of some genes associated with zinc metabolism, such as metallothionein, in formed cells in the circulation. This interesting approach has been used only in a few controlled studies and awaits broader applications.

B. Zinc as an Ergogenic Agent

Zinc supplements have been used by physically active adults to improve performance for competition and military actions. Analyses of usual dietary intakes reveal that zinc intakes can be low in some groups of athletes and soldiers during training.

Early evidence indicated an important role of zinc in skeletal muscle performance. Ex vivo studies of frog skeletal muscle found that zinc added to the media improved muscle strength by increasing tension without tetanus and prolonging the contraction and relaxation periods of the muscle twitch. The effects of supplemental zinc on muscle function were examined in adult male rats fed a chow diet and supplemented with modest amounts of zinc (2 or 4 mg/d) dissolved in water for 30 d. Rats supplemented with 4 mg zinc, as compared with 2 mg, performed significantly more work before fatigue. These findings should be viewed with caution because there is no evidence that the observed change in performance resulted from an improvement in zinc status or increased activity of zinc-dependent enzymes.

1. Zinc Status as an Indicator of Function

Findings from observational studies in humans link poor zinc status with impaired physiological function. Serum zinc concentrations of adolescent gymnasts were significantly decreased compared with nonathletic, age- and gender-matched controls; half of the athletes were characterized as subclinically zinc deficient. Serum zinc was significantly and positively correlated with adductor muscle strength in the gymnasts. Male professional soccer players with low compared with normal serum zinc concentrations had significantly decreased peak power output and increased blood lactate concentrations during peak cycle ergometer tests. These findings, although not definitive, provide evidence that zinc status, as indicated by serum zinc concentration, may be a predictor of physical performance.

2. Zinc Supplementation and Performance in Middle-Aged Adults

Reports from controlled studies of the effects of zinc intake or supplementation on physiological function during exercise are limited. In a double-blind crossover study, middle-aged and older women received either 135 mg of zinc daily or placebo for 14-d periods with a 14-d washout period between treatments. Zinc supplementation significantly increased lower-body isokinetic strength and endurance with no effect on strength or endurance with placebo treatment. These findings suggest that zinc consumed at a pharmacological dose may enhance performance of muscles that are glycolytic in function by acting on lactate dehydrogenase, a zinc metallo-enzyme.
The effect of different levels of dietary zinc on muscle function was examined in more controlled studies. Men fed a formula-based diet containing low compared with adequate zinc content (1 vs. 12 mg/d) had significantly decreased serum zinc and zinc retention (e.g., diet minus losses in urine and feces); the reduced zinc status was associated with significant decreases in knee and shoulder extensor and flexor muscle strength. Also, men fed whole-food diets low in zinc (3–4 mg/d) that were consistent with zinc intakes of endurance athletes demonstrated significantly increased ventilation rates and decreased oxygen uptake, carbon dioxide output, and respiratory exchange ratio during prolonged submaximal cycle ergometer exercise. The low-zinc diet resulted in significantly decreased serum zinc concentration and decreased zinc retention. The activity of carbonic anhydrase, a zinc-dependent enzyme, in erythrocytes decreased significantly when the low-zinc diet was consumed. The attenuated oxygen uptake and carbon dioxide elimination, as well as the decreased respiratory exchange ratio, are consistent with previous findings in zinc-deprived men. Thus, subclinical zinc deficiency, evidenced by decreased concentrations of blood biochemical measures of zinc nutritional status and body zinc retention, adversely affects muscle strength and endurance and cardiorespiratory function.

IV. RESEARCH NEEDS

Secular trends indicate that the number of middle-aged adults will increase and many of them will have body weights in excess of the range proscribed for health. As these people adopt physical activity patterns to promote health, chromium and zinc will occupy increasingly important roles.

There is a burgeoning need to ascertain whether supplemental chromium has any beneficial effects on adults with impaired glucose, or on insulin metabolism in people with unhealthy body weight. Future studies must utilize combined dietary interventions, physical activity programs, and supplementation treatments that are properly designed to determine main and interactive effects of chromium supplementation and exercise on parameters of glucose utilization, insulin sensitivity, and body composition with appropriate technologies. An unresolved issue in the need to identify phenotypes that respond to chromium supplementation.

Future research should determine the amount of zinc required to optimize physical and mental function in middle-aged adults. Focused surveys of the relationships between traditional (intake and blood markers) and novel molecular markers of zinc nutritional status in parallel with objective measures of physical fitness (aerobic capacity and muscle strength and endurance) should be implemented. There also is a need to examine the effect of increasing physical activity patterns on the zinc needs of middle-aged and older adults. This work should include determination of the effects of different dietary levels of zinc (e.g., adequate intake, recommended dietary allowance, and supplemental levels) on zinc metabolism in adults undergoing different types of physical activity for health promotion such as endurance training for cardiovascular function and weight regulation and resistance training to combat sarcopenia. These investigations are needed to clearly determine whether current dietary recommendations for zinc are appropriate for the growing segment of the population that is aging and seeks to respond to current diet and physical activity guidelines for health maintenance.
V. CONCLUSIONS

Consensus for beneficial effects of chromium supplementation is conjectural because of inconsistent findings attributable to problems in experimental design. Many studies utilize samples of convenience and, thus, suffer from inadequate statistical power to test hypotheses. This limitation is significant because of the large within-subject variability in responses to supplementation and other interventions. There is a general lack of assessment of energy and chromium intakes before and during supplementation that limits interpretation of data on changes in body weight and composition. Determination of compliance regarding supplement consumption and adherence to training programs also is lacking in many studies. These concerns fuel the controversy surrounding the value of chromium supplementation as a weight loss aid. However, recent data from a randomized controlled trial in which energy intake was maintained throughout the study, showed no effect of supplemental chromium on weight and body composition change. This finding is the first evidence in support of the ruling of the U.S. Federal Trade Commission that there is no basis for claims that chromium as chromium picolinate promotes weight loss and fat loss in humans. There is consensus, however, that supplemental chromium has no ergogenic benefit on muscle strength gain during resistance training in adults.

Zinc has biological roles in protein, carbohydrate, and lipid metabolism and, hence, is needed for health and optimal performance. Experimental evidence describing the interaction of zinc intake and physical activity in middle-aged adults is limited and, thus, needed. Recent evidence indicates that restricted zinc intake reduces traditional zinc status indicators, impairs muscle strength and endurance, and impairs cardiorespiratory function of adults. Nascent biomarkers for assessment of human zinc status hold promise for studying interactions between zinc intake and physical activity.

REFERENCES


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Section IV

Minerals