

# The Nutritional Relationships of Chromium

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In 1959 a physiological role for chromium was determined. It is known that chromium is a constituent of the glucose tolerance factor (GTF) and is synergistic with insulin in promoting cellular glucose uptake. Chromium deficiency produces an increase in the requirement for insulin. Chromium facilitates insulin at intracellular sites including the ribosomes, and is known to stimulate some enzymes *in vitro*. Chromium is important for the structure and metabolism of nucleic acids.<sup>1 2 3</sup>

## Body Content and Requirements

The total body content of chromium in the adult is estimated at 5 to 6 milligrams. Animal studies have shown that chromium concentrations are high in the spleen, testes, epididymis, and bone marrow. Tissue chromium levels are highest at birth and decline with age. The daily requirement for chromium based upon urinary excretion studies has been estimated at 1 microgram per day. Dietary requirements range from 30 to 200 micrograms in order to compensate for its poor absorption.<sup>4</sup>

In the plasma, chromium is transported by its attachment to transferrin. Hexavalent chromium is better absorbed than the trivalent form.<sup>5</sup>

## Assessment of Chromium Status — Serum

A reliable range for serum chromium is lacking.<sup>6</sup> At this time, serum determination is not a good indicator of body status since the serum is not in equilibrium with tissue stores.<sup>7</sup> Studies report that serum and urinary chromium are not affected significantly by chromium supplementation.<sup>8 9</sup>

## Tissue Mineral Analysis

Tissue mineral analysis (TMA) of human hair is a good method of assessing chromium status. TMA is known to relate to body stores better than either serum or

urine.<sup>10</sup> Doisy and co-workers reported that both the liver and hair levels of chromium in diabetics were decreased proportionately.<sup>11</sup> The chromium content found in the hair is apparently related to and reflective of chromium nutritional status.<sup>12</sup> An increase in TMA chromium levels have been reported in patients receiving chromium supplementation.<sup>13</sup> Thus TMA is a useful tool for evaluating chromium nutrition and tissue storage, particularly since biological GTF is significantly active in hair follicles.<sup>14</sup>

## Conditions Associated with Chromium Deficiency

A number of physiological and disease conditions are related to chromium status and have shown a correlate with TMA chromium levels.

### Diabetes

Hambidge, et al, reported that children with juvenile diabetes as a group had lower hair chromium levels than found in a normal control group.<sup>15</sup> In adult diabetics the TMA chromium levels were found low only in female patients.<sup>16</sup> Some studies have reported conflicting results of TMA chromium levels and suggest its usefulness for determining the chromium status of groups rather than individuals. However, this may only be due to interpretive differences of TMA results. The interpretive and therapeutic usefulness of TMA on individuals will be discussed later.

### Peripheral Neuropathy

A case of peripheral neuropathy was reported in a patient on long term TPN. The patient developed glucose intolerance, weight loss, and other metabolic disturbances that did not respond to increased insulin. After chromium supplementation, her metabolic dysfunctions improved along with improvement in glucose tolerance and peripheral neuropathy. Insulin requirements were also reduced.<sup>17</sup>

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### Cardiovascular Heart Disease (CHD)

Experimental animal studies have revealed that chromium may be associated with the development of atherosclerosis.<sup>18</sup> Chromium deficiency has been noted with hypercholesterolemia,<sup>20</sup> aortic plaques, and corneal opacity.<sup>21</sup> Schroeder, et al, found chromium levels in the aorta of subjects who died of CHD to be lower than in those who died of accidental causes.<sup>22</sup> Chromium supplementation has resulted in improved cholesterol levels and an increase in high density lipoproteins (HDL). Stout presented evidence that insulin itself may be related to the pathogenesis of atherosclerosis.<sup>23</sup> Studies have shown a close relationship between insulin levels and cardiovascular disease. Serum insulin has been found to be elevated in myocardial infarct patients as well as those who have atherosclerosis, cerebral vascular disease, and peripheral vascular disease. Stout further emphasized that "although diabetes is often regarded as a disease of insulin deficiency, insulin concentrations are commonly above normal in non-insulin-dependent diabetics who are obese, as well as in patients using insulin." Insulin in high concentrations is known to stimulate cholesterol synthesis in smooth muscle and lipid synthesis in the arterial wall. Low insulin levels have the opposite effect. Other endocrine factors are probably involved as well and will be discussed later.

Other conditions associated with human chromium deficiency include impaired growth, negative nitrogen balance, and decreased respiratory quotient.<sup>24</sup>

### Factors Contributing to CR Deficiency — Dietary

The chromium content of foods is markedly reduced by processing and refining. Losses are as high as 90 percent in some foods. Earlier studies that compared autopsied tissue in the U.S. with those of other countries found that the average tissue chromium content was 2 to 12 times higher than those of the U.S.<sup>25</sup> <sup>26</sup> However, TMA studies of over two thousand Europeans at Trace Elements, Inc. over the past two years do not show a major difference in TMA levels. This is perhaps due to a similarity developing in higher intake of

refined carbohydrates by Europeans. High glucose or sucrose intake results in chromium losses.<sup>27</sup> Mertz stated that animal protein is the best source of available chromium, and that insufficient protein intake would be expected to lead to a low chromium status,<sup>28</sup> a condition observed in malnourished children. Spices are also substantially high in chromium.

### Hormonal Factors Contributing to Chromium Deficiency — Insulin

Like glucose, insulin also contributes to chromium deficiency. Insulin injection is known to increase chromium excretion.<sup>25</sup> Since many patients with adult onset diabetes have excessive insulin production,<sup>30</sup> chromium deficiency would be expected in this group. Since both insulin and glucose increase the excretion of chromium, it is important to consider the effects of food consumption on serum insulin and glucose levels. Studies of the effects of different foods on serum glucose and insulin response (termed the glycemic index (GI) ) have revealed surprising results. Foods are categorized as percent (%) of GI. The higher the GI%, the higher the insulin and glucose response. As an example, glucose is listed as 100%. High GI foods include carrots 92%; parsnips 98%; honey 87%; cornflakes 80%; and white potato, 70%. Low GI foods include lentils, 29%; and peanuts 13%.<sup>31</sup> <sup>32</sup> <sup>33</sup> Consumption of foods with a high GI may make chromium replacement difficult.

### Estrogen

Chromium stores often become depleted during pregnancy.<sup>34</sup> Pregnancy produces a diabetogenic state characterized by insulin resistance.<sup>35</sup> This results in excessive endogenous insulin secretion,<sup>36</sup> thereby contributing to chromium excretion or transfer to the fetus. It is likely that excess estrogen contributes to the hyperinsulinism during pregnancy. Insulin levels are found to be highest in the last trimester. Estrogen therapy also contributes to the same metabolic effect of increased insulin production,<sup>37</sup> <sup>38</sup> either directly or indirectly.<sup>39</sup>

### Thyroid

The thyroid hormone and insulin are

mutually competitive.<sup>40 41 42 43</sup> Thyroid activity may directly or indirectly affect chromium status. Low thyroid function may allow increased insulin secretion resulting in chromium loss, or increased insulin production may suppress thyroid function or expression. At this time the thyroid-insulin relationship remains speculative. However a prevalence of thyroid failure occurring in diabetics has been reported.<sup>44</sup>

**Hyper-Parathyroidism (HPTH)**

HPTH may contribute to chromium deficiency due to hyperinsulinism. HPTH has been associated with hyperinsulinism due to tumours of the pancreatic islets, pituitary, or other organs. Symptoms of HPTH are not unlike those of diabetes.<sup>45</sup>

**Stress**

Physiological or emotional stress is known to affect chromium status. The stress of infections increases chromium excretion. Patients suffering from myocardial infarction commonly develop hyperglycemia and glucose intolerance without an exogenous glucose load. It has been proposed that the cardiac event can itself produce diabetes.<sup>46</sup> Emotional instability of insulin dependent diabetic patients (those with anxiety, depression, and other psychiatric symptoms), results in poor glucose control compared to diabetic patients without psychiatric symptoms.<sup>47</sup>

Obviously emotional changes trigger hormonal responses. In clinical practice one often sees prediabetic patients who develop manifestations of glucose intolerance following stressful or traumatic events. These patients may become emotionally stressed following an auto accident, for example. Their insulin and glucose levels may develop severe swings, resulting in instability and thus poor response to therapy. This type of trauma results in the syndrome termed post traumatic dysinsulinism. It is not uncommon for predisposed individuals to develop diabetes following this type of stress episode.

**Minerals**

Figure 1 shows the minerals that are antagonistic to chromium.<sup>48 49</sup> The solid lines indicate a direct antagonism either on a metabolic or absorptive level. The broken lines indicate an indirect antagonistic relationship. A patient with increased tissue retention of any one or combination of these essential and toxic elements can be expected to have increased chromium requirements. Depending upon the individual, supplementation of these trace elements, individually or in combination, can contribute to chromium losses or decreased absorption.

Minerals that are considered synergistic to chromium include:

- |           |            |
|-----------|------------|
| Magnesium | Manganese  |
| Zinc      | Iron       |
| Potassium | Phosphorus |

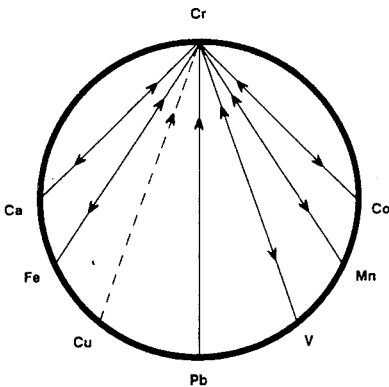


Figure 1.

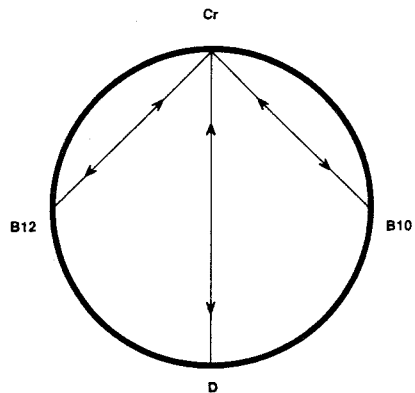


Figure 2.

**NOTE:** Some minerals may appear as both synergistic and antagonistic — a common phenomena among trace elements. In physiological quantities a mineral can be synergistic, but at pharmacological or toxic levels it becomes antagonistic.

Many of the synergistic nutrients are frequently found to be deficient in diabetic patients.<sup>50</sup> A nutritional deficiency of these trace elements can also contribute to chromium deficiency.

### Vitamins

Figure 2 represents the vitamins that are considered antagonistic to chromium. Chronic high intake can contribute to chromium deficiency and/or increased requirements.

A deficiency of the synergistic vitamins may also lead to poor chromium status in some individuals. The following list of vitamins are considered synergistic to chromium.<sup>51</sup>

Thiamin (B <sub>1</sub> )	Vitamin E
Riboflavin (B <sub>2</sub> )	Vitamin A
Pyridoxine (B <sub>6</sub> )	Niacin (B <sub>3</sub> )

### Assessing Chromium Status and Therapy From TMA Patterns of Individuals

Presently there are conflicting views on the essentiality of chromium in human nutrition, due to the variation in clinical and biochemical response of diabetic patients to chromium supplementation.<sup>52</sup> There is also uncertainty surrounding the use of TMA in evaluating chromium status and therapy in individuals. Much of this confusion can be cleared up in light of the many factors that can affect chromium status and function. It is important to note that diabetes is not a singularly caused disease but a series of related metabolic, endocrine,<sup>53</sup> and nutritional<sup>54</sup> disorders that lead to poor glucose control and abnormal insulin production or action.

The ideal TMA chromium level established at TEI is 0.08 Mg%. However, indications of functional chromium requirements should not be based upon the TMA chromium level alone, but in relation to other nutritional factors known to affect chromium status, with serological glucose and insulin tests as an adjunct.

TMA results have revealed patterns asso-

ciated with the different types of diabetes. In review of the prevalence of these different types 85-90% of patients have the less severe adult-onset form, or Type II. Type I (juvenile-onset) affects approximately 10-15%. A true type I diabetic condition is characterized by a lack of insulin production or secretion from the pancreas. The islets may be atrophied or completely destroyed. On the other hand, insulin production in type II diabetes in many cases is actually normal or higher than normal.<sup>55</sup> As mentioned previously, both glucose and insulin increases chromium excretion; therefore, chromium deficiency would be expected in both groups. Response to chromium supplementation may vary considerably between the two groups.

### TMA Indications of Chromium Requirements

The antagonistic minerals (figure 1) and the synergistic minerals to chromium should be evaluated in conjunction with TMA chromium levels. An elevation above the ideal of the antagonistic minerals would indicate increased chromium requirements. Synergistic minerals below the ideal TMA level may also indicate increased requirements. The ideal levels established at TEI are:

Calcium	42 Mg%	Phosphorus	16 Mg%
Potassium	10 Mg%	Iron	2.8 Mg%
Copper	2.5 Mg%	Manganese	0.15 Mg%
Zinc	20 Mg%	Lead	<0.5 Mg%
Magnesium	6 Mg%		

The significant ratio that should be considered with chromium is calcium to magnesium. The TEI ideal calcium/magnesium ratio is 7.1:1.

TMA chromium levels in type II diabetic patients are usually found below the ideal. Frequently the calcium/magnesium ratio is disturbed. An elevated calcium/magnesium ratio (greater than 15:1) may be used as an indicator of insulin production. The mechanism of the disturbed calcium/magnesium relationship is based upon the mediation of insulin secretion by calcium.<sup>56-57</sup> TMA calcium levels usually exceed the ideal in patients with a type II condition, and indicate other endocrine influences that occur concomitantly with type II diabetes. Any factor that contributes to increased calcium absorption or

retention can be considered a chromium antagonist, resulting in increased insulin secretion due to decreased tissue sensitivity.

### Vitamin D

Vitamin D is considered a chromium antagonist due to its multiple effects. Vitamin D activity is similar to parathyroid activity, which increases serum vitamin D<sub>3</sub> metabolites,<sup>58</sup> thereby increasing calcium absorption and retention. This results in a relative magnesium deficiency.<sup>59</sup> Since vitamin D enhances the synthesis of insulin, and insulin enhances the synthesis of vitamin D,<sup>60 61</sup> we can readily see that PTH, vitamin D, calcium, and insulin can individually or collectively contribute to chromium deficiency, especially in type II diabetic conditions. Together these related factors produce a vicious cycle, resulting in chromium depletion and thereby increasing insulin production in order to compensate for decreasing tissue insulin sensitivity. These combined factors can result in elevated TMA calcium levels and calcium/magnesium ratios.

### Copper

Copper is considered an indirect chromium antagonist due to its close relationship with estrogen and diabetogenic effects.<sup>62</sup> It is well known that serum copper increases during pregnancy, estrogen therapy, and oral contraceptive use. Plasma insulin elevates during pregnancy along with estrogen<sup>63</sup> and in conjunction with estrogen therapy.<sup>64</sup> This again leads to the cycle of insulin enhanced vitamin D synthesis, which enhances parathyroid activity and increases intestinal calcium absorption, and renal reabsorption. This relationship contributes to decreased insulin sensitivity as a result of induced chromium deficiency. Copper toxicity can eventually lead to adult-onset diabetes.

These interrelated factors can also be involved in the incidence of arteriosclerosis found in diabetic patients.

Type I diabetic patients may or may not show markedly low TMA chromium levels, and may not respond as remarkably to chromium supplementation. Type I patients do, however, show extremely low tissue zinc levels (usually below 50% of the ideal) along with low TMA calcium and

magnesium levels. A zinc deficiency results in the inability to store insulin adequately. Poor insulin production is due to increased catabolic glandular activity.<sup>65</sup> Increased requirements for the synergistic nutrients to calcium and particularly zinc<sup>66</sup> would be expected to be increased in type I diabetics, since increased adrenal and thyroid activity increases calcium and magnesium excretion from the body,<sup>67 68</sup> as well as copper.<sup>69</sup> The increase in catabolic glandular activity would also decrease vitamin D metabolism<sup>70</sup> and lower insulin production and PTH activity.<sup>71 72 73</sup> Elevated blood glucose contributes to chromium loss in type I diabetes, which is due to increased gluconeogenesis precipitated by excessive catabolic glandular activity.

### Conclusion

In summary, TMA can be useful for determining chromium status in individuals when evaluated with its other synergistic and antagonistic co-factors. The calcium to magnesium ratio is as important as the evaluation of the chromium level alone and can be used as an indicator of functional chromium deficiency, regardless of the chromium level itself.

It has been found that the GTF activity of chromium consists of the combination of chromium with glycine, glutamic acid, cysteine, and niacin. Chromium supplementation may produce little response without these co-factors. Presently this combination is provided by Trace Nutrients, professional products.

**Footnote** — The TMA results (mineral levels and ratios) discussed in this article are based upon atomic absorption spectrophotometric analysis and laboratory procedures utilized by Trace Elements, Inc., and may not apply as well to different laboratory techniques and preparatory procedures.

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