INE | INSTITUTE OF NUTRITIONAL ENDOCRINOLOGY

Micronutrients: Chromium

Dr. Ritamarie Loscalzo

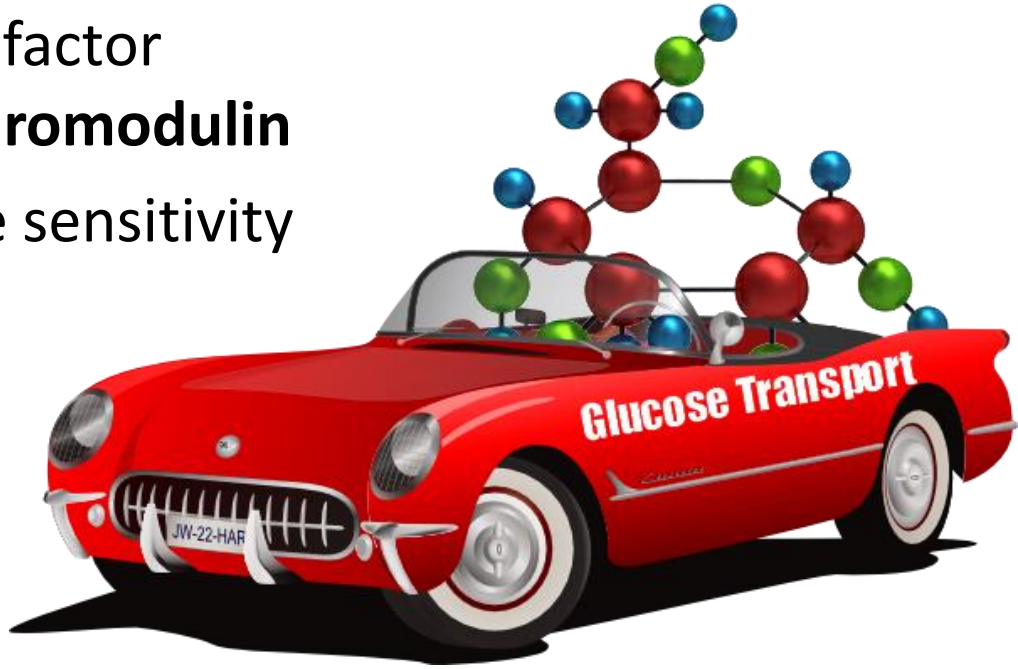
Medical Disclaimer: The information in this presentation is not intended to replace a one-on-one relationship with a qualified health care professional and is not intended as medical advice. It is intended as a sharing of knowledge and information from the research and experience of Dr. Ritamarie Loscalzo, drritamarie.com, and the experts who have contributed. We encourage you to make your own health care decisions based upon your research and in partnership with a qualified health care professional.

Chromium General Info

- ✓ Chromium (Cr_0) is a ubiquitous trace metal
- ✓ It was first discovered in 1797
- ✓ The predominant chromium form in the body is **trivalent chromium (Cr_3+),** which plays a role in normal insulin function
- ✓ Trivalent chromium (Cr_3+) is the **most stable oxidation state of chromium**
- ✓ Forms relatively inert complexes with proteins and nucleic acids
- ✓ Hexavalent chromium (Cr_6+) is another common and stable form
- ✓ Hexavalent chromium **is highly toxic** and is classified as a human carcinogen when inhaled
  - ➢ Derived from trivalent chromium by heating at alkaline pH and used for industrial purposes
  - ➢ readily reduced to trivalent chromium in the acidic environment of the stomach which limits the absorption of hexavalent chromium

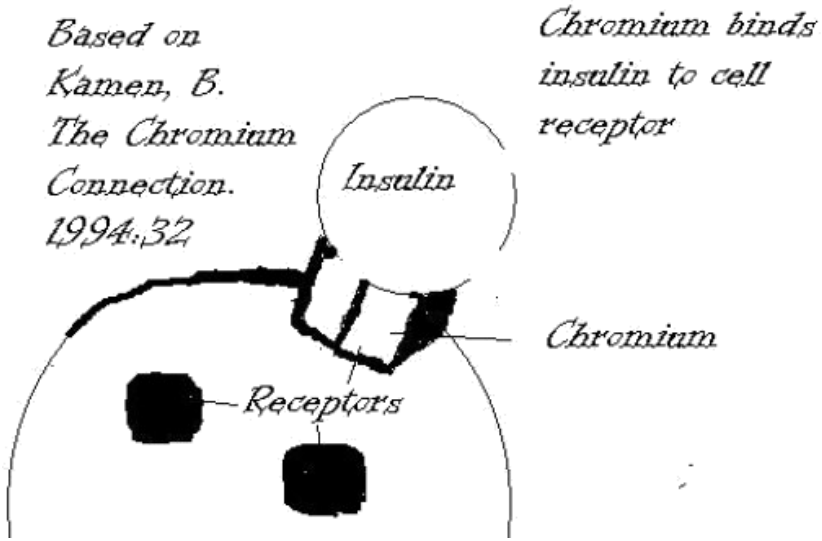
Functions of Chromium

- ✓ **Enhances the effects of insulin** on target tissues
- ✓ Stimulates fatty acid and cholesterol synthesis
- ✓ Involved in carbohydrate, fat, and protein metabolism
- ✓ Inorganic chromium does not potentiate insulin action and must be **converted to an organic biologically active** form
- ✓ Trivalent chromium is the cofactor for an oligopeptide called **chromodulin**
- ✓ **Chromodulin** improve tissue sensitivity to insulin and facilitates glucose transport into cells



Chromium and Insulin Sensitivity

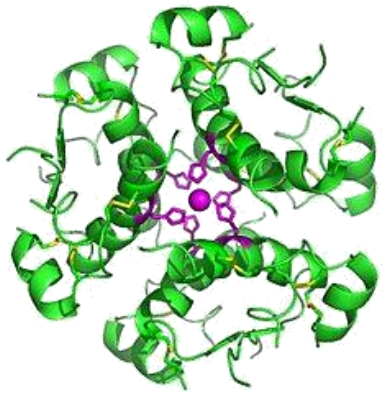
- ✓ Binding of insulin to insulin receptor stimulates movement of chromium into the cell
  - ➢ Chromium binds to **apochromodulin**, a form of chromodulin that lacks chromium
  - ➢ Chromodulin binds to the insulin receptor and upregulates insulin signaling molecules
  - ➢ This increases the translocation of **glucose transporters (GLUT-4)** into the cell membrane
- ✓ Chromium **inhibits the activity of protein tyrosine phosphatase-1B (PTP-1B)** and other negative regulators of insulin signaling
- ✓ Chromium improves insulin sensitivity under insulin-resistant conditions
- ✓ Chromium reduces insulin clearance and enhances insulin signaling by inhibiting the proteolysis of insulin
- ✓ Chromium **reduces oxidative stress and inflammation** known to contribute to insulin resistance



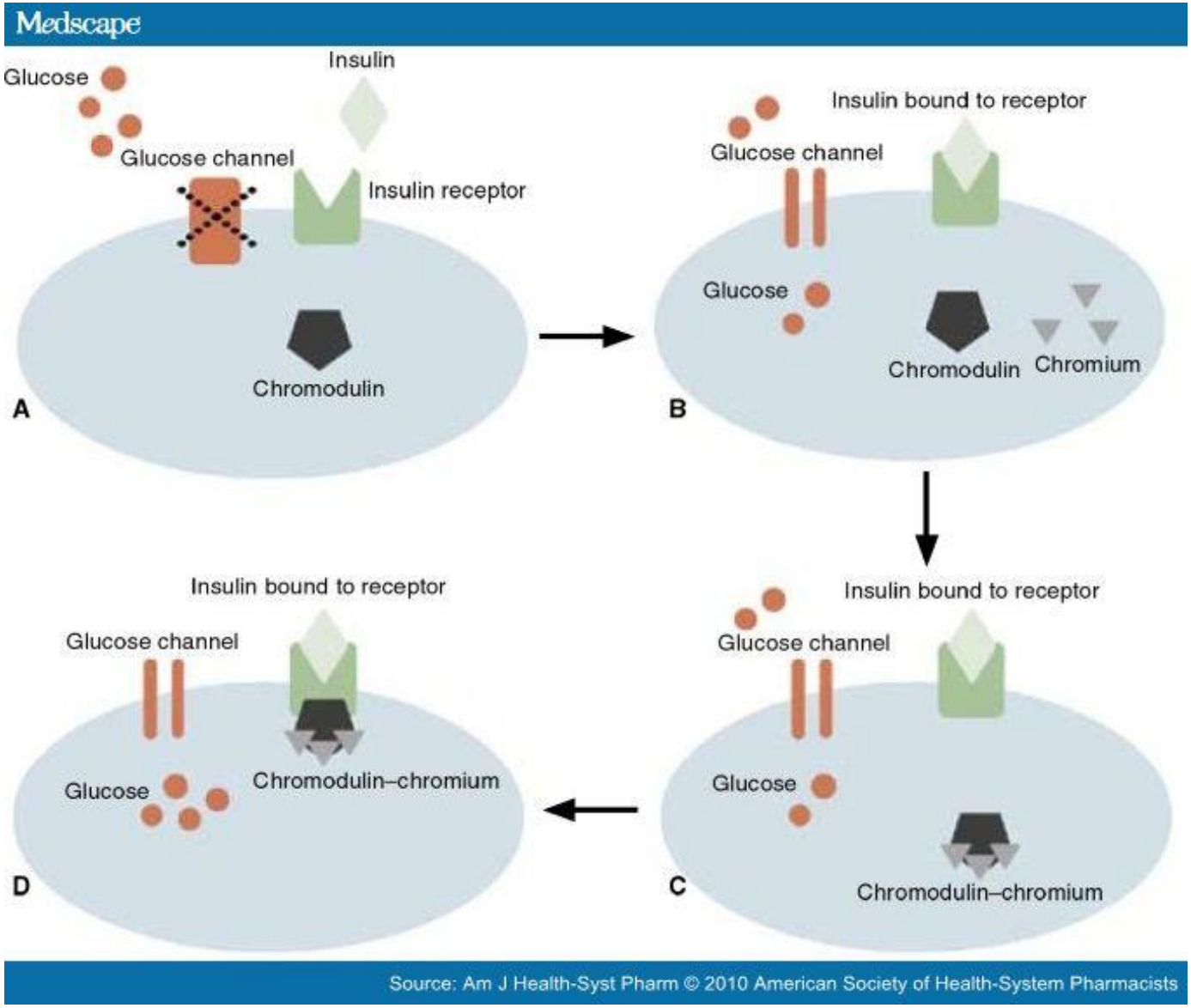
Chromium And Insulin Signaling

- ✓ Oligopeptide low-molecular-weight chromium-binding substance (LMWCr) tightly binds four chromic ions
- ✓ Binds to the tyrosine kinase active site of the insulin receptor
- ✓ Chromium is readily transferred from transferrin to apoLMWCr at near neutral pH
- ✓ Release of chromium is related to a mechanism by which Cr_3 may generate hydroxyl radicals in cells
- ✓ Trivalent chromium might be the cofactor of a low-molecular-weight chromium-binding substance, LMWCr or chromodulin
- ✓ Chromodulin believed to **enhance the cascade of signaling events** induced by the binding of insulin to extracellular α-subunit of the insulin receptor (IR)
- ✓ Upon insulin binding, the tyrosine kinase domain of the intracellular β-subunit of the IR becomes activated
  - ➢ Causes the **phosphorylation of tyrosine residues** in the β-subunit itself
  - ➢ Insulin receptor activation triggers a series of rapid phosphorylation reactions
  - ➢ Activates many downstream effectors
  - ➢ Results in an increase in glucose uptake and storage

http://www.drritamarie.com/go/PubMed10766445

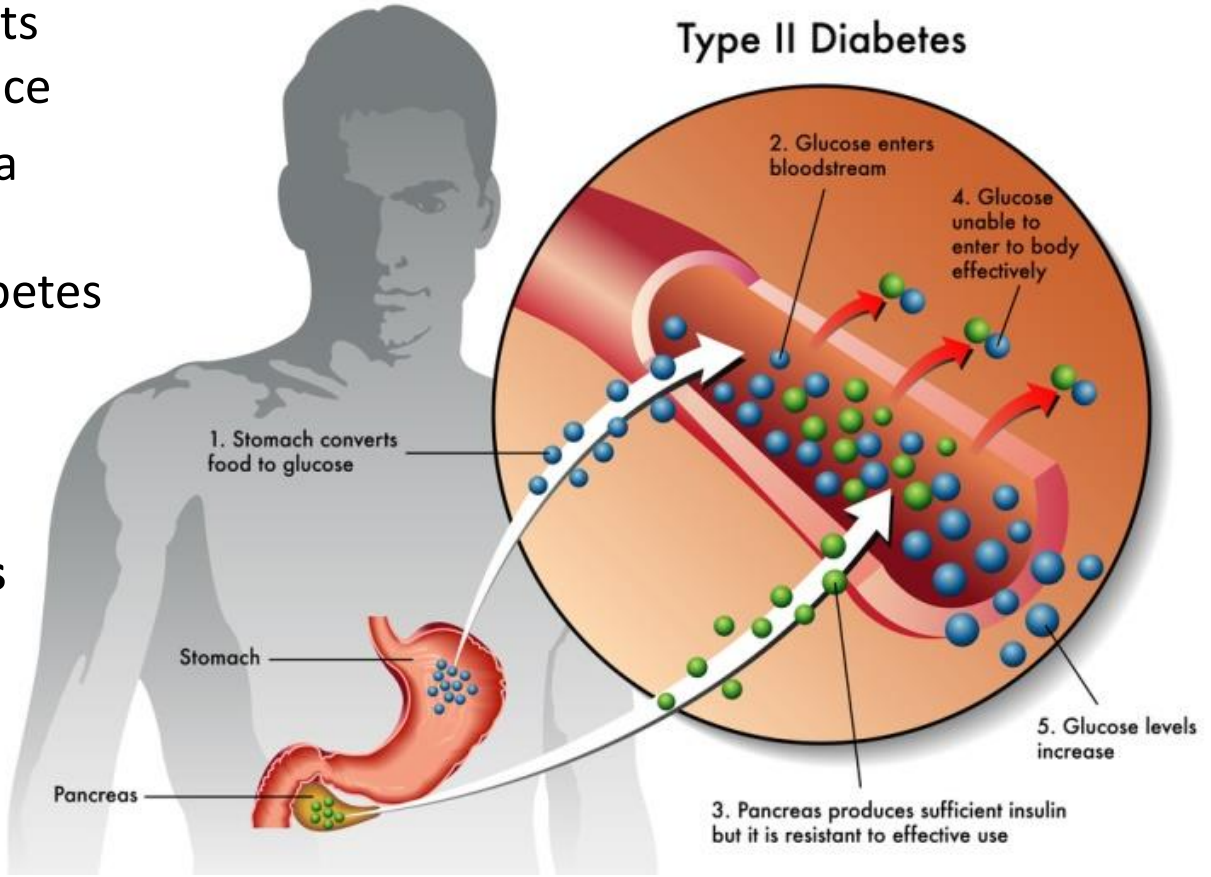


Chromium: Effects on Insulin Receptors



Chromium Deficiency

- ✓ **Long-term intravenous feeding** (parenteral nutrition) without supplemental chromium
  - ➢ Abnormal glucose utilization and increased insulin requirements
  - ➢ Improved with chromium supplementation
- ✓ **Chromium deficiency** results in impaired glucose tolerance
- ✓ **Chromium insufficiency** is a contributing factor to the development of type 2 diabetes
- ✓ **<u>Urinary chromium loss</u>** is increased by endurance exercise
- ✓ Resistive exercise **increases chromium absorption**



Chromium and Cardiovascular Disease

- ✓ Impaired glucose tolerance and type 2 diabetes are associated with adverse changes in lipid profiles and increased risk of cardiovascular disease
- ✓ Chromium leads to
  - ➢ Reductions in serum total cholesterol, LDL-cholesterol, and triglyceride levels
  - ➢ Increases in HDL-cholesterol levels

Chromium and Muscle Mass

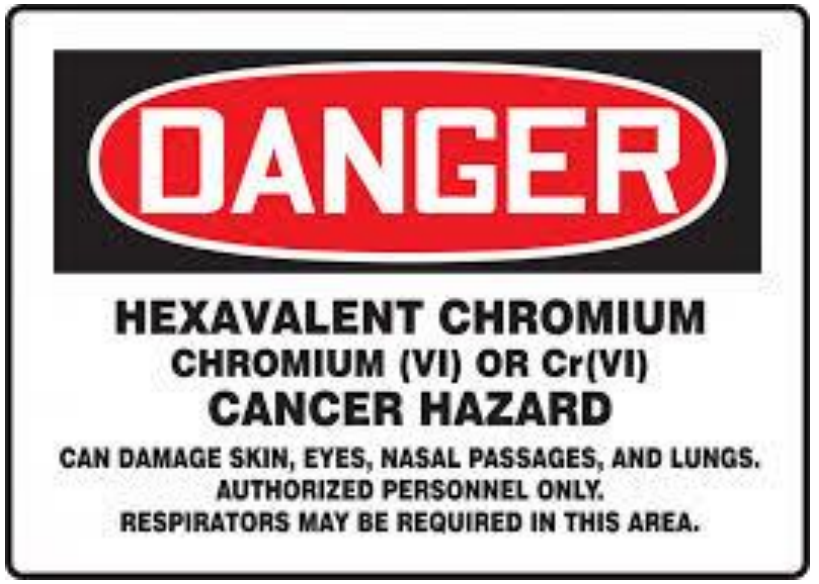
- ✓ Chromium supplementation increases lean body mass and decreases body fat due to the relationship between chromium and insulin action
- ✓ Insulin affects fat and protein metabolism
- ✓ Also regulates glucose metabolism

Chromium and Diabetes

- ✓ Chromium regulates insulin sensitivity and blood glucose levels
- ✓ Those with overt type 2 diabetes for over two years have **higher rates of urinary chromium loss** than healthy individuals
- ✓ Chromium supplementation with type 2 diabetics **reduced insulin concentrations and improved blood lipid profiles**
- ✓ Chromium supplementation beneficial in the treatment of type 2 diabetes
- ✓ Chromium either 200 mcg/day or 1,000 mcg/day is associated with **reduced insulin concentrations**
- ✓ Hemoglobin A1c (HbA1c) is also significantly reduced
- ✓ Chromium intake of at least 250 mcg/day for no less than three months significantly **reduces fasting glucose concentrations** in diabetics but has no effect on the levels of HbA1c
- ✓ **Greater doses of chromium needed to** observe beneficial effects of chromium supplementation
- ✓ Women with gestational diabetes supplemented with 4 mcg of chromium picolinate/kg for eight weeks had **decreased fasting blood glucose** and insulin concentrations compared to those who took a placebo

Chromium Toxicity

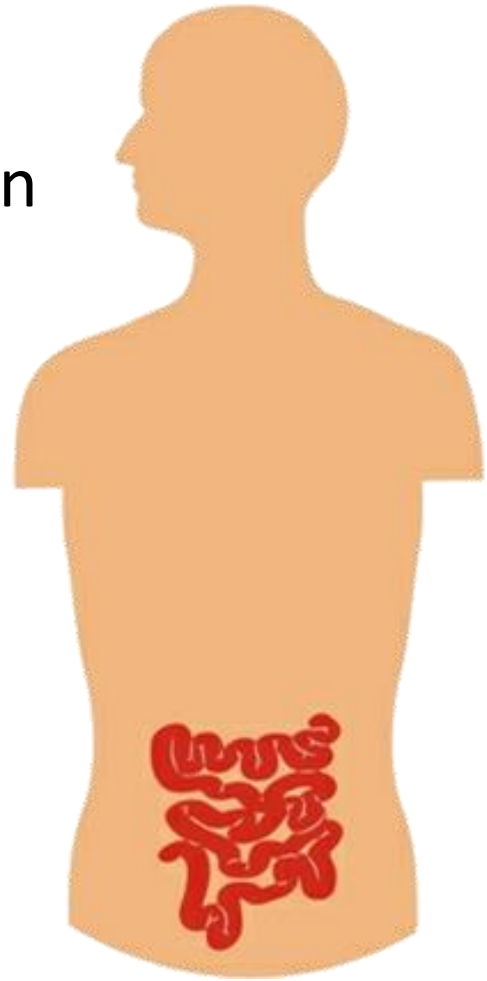
- ✓ **Hexavalent chromium** (Cr_6+) is a recognized carcinogen
- ✓ <u>Exposure to hexavalent chromium in dust</u>
  - ➢ Associated with an increased incidence of lung cancer
  - ➢ Known to cause inflammation of the skin (dermatitis)
- ✓ Little evidence that trivalent chromium (Cr_3+) is toxic to humans



- ✓ The toxicity from oral intakes is considered to be low
  - ➢ Ingested chromium is poorly absorbed
  - ➢ Most absorbed chromium is rapidly excreted in the urine
- ✓ Because no adverse effects have been convincingly associated with excess intake of trivalent chromium from food or supplements, **the Food and Nutrition Board (FNB) of the Institute of Medicine did not set a tolerable upper intake level (UL)** for chromium

Chromium Absorption

- ✓ Small intestine, mainly in jejunum
- ✓ Absorbed via active transport and diffusion



Chromium Transport and Storage

- ✓ Transferrin (competes with iron)
- ✓ Albumin
- ✓ Stored in
  - ➢ Kidney
  - ➢ Liver
  - ➢ Pancreas
  - ➢ Muscle
  - ➢ Heart
  - ➢ Bone

Influences on Chromium

Decreases

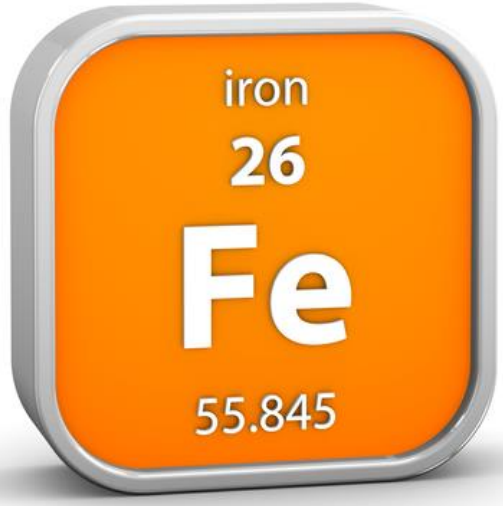
- ✓ Simple carbohydrates (sucrose, fructose, glucose)
- ✓ Phytates
- ✓ Zinc supplements
- ✓ Horsetail
- ✓ Corticosteroids
- ✓ Antacids, H2 blockers, proton pump inhibitors
- ✓ Vitamin B3 (niacin)
- ✓ Beta blockers (propranolol)
- ✓ Insulin
- ✓ NSAIDs

Increases

- ✓ Vitamin C
- ✓ Methionine
- ✓ Histidine

Chromium Iron Interactions

- ✓ Chromium competes for one of the binding sites on the iron transport protein, **transferrin**
- ✓ Iron overload in hereditary hemochromatosis may interfere with chromium transport by competing for transferrin binding
- ✓ Decreased chromium transport might contribute to the pathogenesis of diabetes mellitus in patients with hereditary hemochromatosis



Chromium - Vitamin C Interactions

- ✓ Chromium uptake is enhanced when given at the same time as vitamin C
- ✓ In a study of three women, administration of 100 mg of vitamin C together with 1 mg of chromium resulted in higher plasma levels of chromium than 1 mg of chromium without vitamin C

Cause of Chromium Deficiency

- ✓ Deficient soil
- ✓ Processed foods
- ✓ Fluoride in water
- ✓ Food antagonists: sugar, phytates
- ✓ Excess nutrient antagonists: iron, zinc
- ✓ Drugs

Impact of Chromium Deficiency

- ✓ Diabetes
- ✓ Metabolic syndrome
- ✓ Insulin resistance
- ✓ Blood sugar swings
- ✓ Anxiety
- ✓ Fatigue
- ✓ Muscle weakness
- ✓ Mood swings

Chromium Excess

- ✓ Daily doses of **up to 1,000 mcg** of chromium for several months have been found to be safe
- ✓ Little evidence to support concerns that trivalent chromium, especially chromium picolinate, may increase DNA damage
  - ➢ A study in 10 women taking 400 mcg/day of chromium picolinate found no evidence of increased oxidative damage to DNA
  - ➢ **Isolated reports** of serious adverse reactions to chromium picolinate
  - ➢ Kidney failure was reported five months after a six-week course of 600 mcg/day of chromium in the form of chromium picolinate
  - ➢ Kidney failure and impaired liver function reported after 1,200-2,400 mcg/day of chromium picolinate for four to five months
  - ➢ A 24-year old healthy male reportedly developed reversible, acute renal failure after taking chromium picolinate containing supplements for two weeks
- ✓ Individuals with **pre-existing kidney or liver disease** may be at increased risk of adverse effects and should limit supplemental chromium intake

http://www.drritamarie.com/go/ChomiumSafety

Assessing Status of Chromium

- ✓Blood testing not accurate
- ✓Hair test
- ✓White blood cell - Spectracell
- ✓Functional tests and physical exam
- ✓Glucose tolerance test

Chromium Adequate Intake

Life stage	Chromium, µg/ day	
	Male	Female
Infants, months		
0 – 6	0.2	0.2
7 – 12	5.5	5.5
Children, years		
1 – 3	11	11
4 – 8	15	15
Adults, years		
9 – 13	25	21
14 – 18	35	24
19 –30	35	25
31 – 50	35	25

Food Sources of Chromium

- ✓ Brewer's yeast (GTF)
- ✓ Broccoli
- ✓ Oats
- ✓ Green beans
- ✓ Tomatoes
- ✓ Apples
- ✓ Romaine lettuce
- ✓ Black pepper
- ✓ Bananas
- ✓ Beef
- ✓ Turkey breast

Food Sources of Chromium

Food	Serving Size	Cals	Amount (mcg)	DRI/DV (%)
Broccoli	1 cup	54.6	18.55	53
Barley	0.33 cup	217.1	8.16	23
Oats	0.25 cup	151.7	5.38	15
Green Beans	1 cup	43.8	2.04	6
Tomatoes	1 cup	32.4	1.26	4
Romaine Lettuce	2 cups	16.0	1.25	4
Black Pepper	2 tsp	14.6	0.93	3

http://www.drritamarie.com/go/WHFoodsChromium

Herbs High In Chromium

- ✓Wild yam
- ✓Nettle
- ✓Catnip
- ✓Oat straw
- ✓Licorice
- ✓Horsetail
- ✓Yarrow
- ✓Red clover
- ✓Sarsaparilla

Chromium Supplementation

- ✓ Trivalent chromium in several forms
  - ➢ Chromium chloride
  - ➢ Chromium polynicotinate
  - ➢ Chromium picolinate
  - ➢ High-chromium yeast
- ✓ Doses range from 50 to 200 mcg of elemental chromium
- ✓ 19% of the US population uses chromium-containing supplements
- ✓ Highest proportion of users (29%) found in adults aged over 50 years
- ✓ Impaired glucose tolerance and type 2 diabetes – **Chromium polynicotinate or picolinate**

Chromium Drug Interactions

- ✓ Little is known about drug interactions with chromium in humans
- ✓ Large doses of calcium carbonate or magnesium hydroxide-containing antacids decreased chromium absorption in rats
- ✓ In contrast, non-steroidal anti-inflammatory drugs, aspirin, and indomethacin can increase chromium absorption in rats

http://www.drritamarie.com/go/DrugInteractionsChromium

Chromium References

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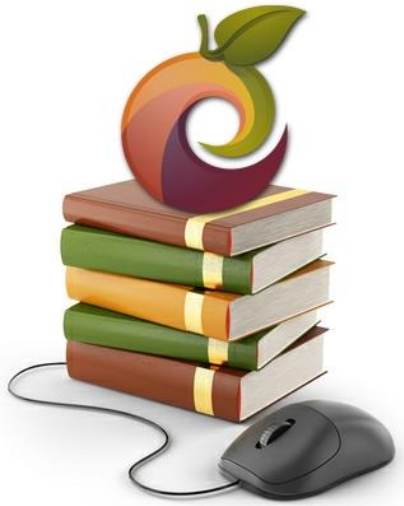
- ✓ *Modern Nutrition in Health and Disease*, 10th ed. – Shils, Shike, Ross, Caballero, and Cousins
- ✓ *Interrelations between Essential Metal Ions and Human Diseases* – Sigel, Sigel, and Sigel
- ✓ *PDR for Nutritional Supplements*. 2nd ed. – Hendler and Rorvik
- ✓ *Present Knowledge of Nutrition* – Erdman, Macdonald, and Zelssel
- ✓ WH Foods Website: http://www.drritamarie.com/go/WHFoodsChromium
- ✓ Linus Pauling Institute: http://www.drritamarie.com/go/LPIChromium



Chromium Research

- ✓ *http://www.drritamarie.com/go/PubMed10766445*
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