Vitamins, Minerals, & Neuromusculoskeletal Health

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Objectives

By the end of the presentation, the learner should be able to:

• List the most common vitamins and minerals involved in neuromusculoskeletal health
• Recall signs, symptoms, and associated factors related to deficiencies or excesses of the most common vitamins and minerals involved in neuromusculoskeletal health
• Appropriately order and interpret diagnostic tests for the most common vitamins and minerals involved in neuromusculoskeletal health
• Develop an appropriate treatment plan for patients with deficiencies or excesses of the most common vitamins and minerals involved in neuromusculoskeletal health

Common Vitamins & Minerals Involved in Neuromusculoskeletal Health

Magnesium
“Vitamin” D
Calcium
Vitamin E
Vitamin C
Vitamin B12
Factors Affecting Vitamin & Mineral Absorption

- Reduced intake:
  - Malnutrition (either quantitative or qualitative)
  - Total parenteral nutrition
- Excessive intake:
  - Intentional:
    - Mega dose supplementation
  - Unintentional:
    - Poly supplementation
    - Food or beverage additive
- Malabsorption
  - Chronic bowel disease - e.g., Celiac, Crohn’s disease & ulcerative colitis
  - Bariatric surgery or short bowel syndrome
  - Chronic cholestasis or pancreatitis
  - Cystic fibrosis
  - Simultaneous medication or supplementation consumption

Magnesium

- Mineral
- Cofactor for 300+ enzymatic reactions
- Primary role in nerve transmission, neuromuscular conduction, muscular contraction/relaxation
- Most magnesium is stored in the bones and intracellularly
- Only 1% of total body magnesium is in the plasma
- Magnesium blood level is tightly regulated by the body
Magnesium Deficiency

- ~60% of US adults do not consume the recommended dietary intake for magnesium
- Hypomagnesemia: (7% US population)
- Can lead to:
  - Hypokalemia
  - Hypocalcemia
  - Neuromuscular excitability
  - Osteoporosis
  - DM II
  - HTN
  - Dysthyrhythmias
  - Mitral Valve Prolapse
  - CAD
  - Dyslipidemia

Assessing Magnesium Status

- Magnesium, serum level:
  - Tightly regulated by the body
  - Does NOT reflect total body magnesium levels
- Erythrocyte magnesium
  - May be a better indicator of magnesium status
- Magnesium loading/tolerance test, urine
  - “Gold standard” for adults
  - Good indicator of hypomagnesemia
  - Cumbersome

When I see a patient that has...

- Hyperalgesia
- Hypertonicity

  - I ask...
    1. Are you taking magnesium?
    2. Do you have diarrhea?
    3. Has a doctor ever said you have kidney problems?

  - If the answer to all 3 questions is “No”, I recommend oral magnesium supplementation.
**Oral Magnesium Supplementation**

For non-pregnant adults with decent kidney function:
- Start at 250mg or less
  - Increase by 1 pill every 3 days until GI symptoms occur (ex. loose stool, bloating)-> then decrease by 1 pill & stay at that dose.
  - Continue on this dosage as tolerated for at least a couple months to a couple years.
- Max dose= 1,000mg/day
- Caution in patients with severe kidney disease or chronic diarrhea. May ask pregnant patients to check with OB or don’t have them increase the dose.

**How to Get More Magnesium into the Body When Patient Can’t Tolerate PO Supplementation?**

1. Try Slow-Mag or Magnesium Glycinate PO
2. Magnesium-rich foods PO
3. Epsom salt soaks or topical magnesium oils/gels
4. IV magnesium

**Tolerable Magnesium Supplementation Upper Intake Levels for the Non-Magnesium-Deficient Patient**

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Pregnant</th>
<th>Lactating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 12 months</td>
<td>None established</td>
<td>None established</td>
<td>None established</td>
<td>None established</td>
</tr>
<tr>
<td>1–3 years</td>
<td>65 mg</td>
<td>65 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4–8 years</td>
<td>110 mg</td>
<td>110 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9–18 years</td>
<td>350 mg</td>
<td>350 mg</td>
<td>350 mg</td>
<td>350 mg</td>
</tr>
<tr>
<td>19+ years</td>
<td>350 mg</td>
<td>350 mg</td>
<td>350 mg</td>
<td>350 mg</td>
</tr>
</tbody>
</table>

Max adult dose= 1,000mg po/day
History Clues Patient Could Benefit from Magnesium Supplementation

- Chronic pain
- Tight muscles
- Proton-pump inhibitor
- Diuretic
- Hypokalemia
- Hypocalcemia
- Osteoporosis
- Diabetes II or insulin resistance
- HTN
- Chronic inflammatory disorder
- Bariatric surgery or short bowel
- Heavy alcohol consumption
- Elderly
- Idiopathic Mitral Valve Prolapse
- Fibromyalgia
- Restless leg syndrome

Ow! It’s too tight!!

It needs more magnesium!

Calcium

- Mineral
- Most common signal transmitter
- >99% in skeleton
- Calcium blood level is tightly regulated by the body
- Extracellular concentrations also tightly regulated
Calcium Deficiency

- Most adolescents, elderly, & female adults do not consume the recommended daily intake
- Whole body calcium deficient more likely with:
  - Low calcium consumption
  - Low Vitamin D
  - High dietary sodium consumption
- Chronic whole body deficiency ultimately leads to osteoporosis
- Hypocalcemia is usually secondary to endocrine disorders or renal disease
- Whole body calcium excess: rare
  - Causes: excessive Calcium or Vitamin D intake
  - Signs/symptoms: weakness, fatigue, lethargy, confusion, anorexia, N/V, constipation, excessive thirst, frequent urination

Assessing Whole-body Calcium Status

- Serum Calcium levels
  - Do not reflect total body status
- Bone density testing for osteopenia or osteoporosis evaluation

Calcium Supplementation

- Usually a good idea
- Most people's diets do not contain recommended daily intake
- Should be taken divided dosed throughout day
- Should be taken with food
- Different recommended daily intakes for different age groups and genders
Increased table salt consumption pushes the calcium out into the urine

“Vitamin” D

- Vitamin D deficiency:
  - Signs/symptoms: myopathy (50%) with weakness, muscle wasting, myalgia, delayed relaxation; carpopedal spasms; bone pain; & osteomalacia or rickets; serum Ca++ may be normal or low
  - Bariatric patients need ~5-7 times as much Vit D supplementation than those with a fully-functioning GI tract
- Hypervitaminosis D: rare
  - Signs/symptoms: same as hypercalcemia—weakness being the predominate muscular symptom

Vitamin E

- Fat-soluble antioxidant
- α-tocopherol seems to be only type of vitamin E used in the body
- Counteracts lipid peroxidation of cell membranes
- Requires Vitamin C to reduce it back to its useful form
- Increased oxidative stress increases requirement for Vitamin E
Vitamin E Deficiency

• ONLY 8% of US men & 2% of US women consume the RDI of vitamin E
• Deficiency causes:
  – Progressive peripheral sensory neuropathy
  – Hemolysis
  – Weakness
• Severe deficiency is rare (fat malabsorption or genetic disorder) and can cause ataxia
• Excess:
  – Increased tendency to bleed, myalgias & proximal weakness

Assessing Vitamin E Status

• Vitamin E, serum level (12-14 hours fasting)
  • Significant deficiency: <3.0 mg/L
  • Significant excess: >40 mg/L

Vitamin E Supplementation

• For 2yo and older, supplement if serum Vit E is <4 mg/L
• Ester forms prevent oxidation of vitamin E in the bottle & are readily hydrolyzed into α-tocopherol in the body
• Needs to be taken with a fatty meal
Upper Tolerable Levels for Vitamin E Supplementation

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Pregnancy</th>
<th>Lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3 years</td>
<td>200 mg</td>
<td>200 mg</td>
<td>(300 IU)</td>
<td>(300 IU)</td>
</tr>
<tr>
<td>4-8 years</td>
<td>300 mg</td>
<td>300 mg</td>
<td>(450 IU)</td>
<td>(450 IU)</td>
</tr>
<tr>
<td>9-13 years</td>
<td>600 mg</td>
<td>600 mg</td>
<td>(900 IU)</td>
<td>(900 IU)</td>
</tr>
<tr>
<td>14-18 years</td>
<td>800 mg</td>
<td>800 mg</td>
<td>800 mg</td>
<td>800 mg</td>
</tr>
<tr>
<td></td>
<td>(1,200 IU)</td>
<td>(1,200 IU)</td>
<td>(1,200 IU)</td>
<td>(1,200 IU)</td>
</tr>
<tr>
<td>19+ years</td>
<td>1,000 mg</td>
<td>1,000 mg</td>
<td>1,000 mg</td>
<td>1,000 mg</td>
</tr>
<tr>
<td></td>
<td>(1,500 IU)</td>
<td>(1,500 IU)</td>
<td>(1,500 IU)</td>
<td>(1,500 IU)</td>
</tr>
</tbody>
</table>

Earl, the Vitamin C-loving squirrel is nuts!

Vitamin C (Ascorbic Acid)

- Water soluble
- Potent reducing agent/antioxidant
- Essential for Vitamin E to be effective
- Required for collagen, carnitine & many neurotransmitters synthesis
- Half-life in humans: 14-40 days
Vitamin C Deficiency

- ~7% US; 14% of smokers
- ~20% US has marginal Vitamin C status
  - Myalgias, arthralgias & weakness
  - Lassitude
  - General malaise
  - Elevated histamine
  - Scurvy (severe vitamin C deficiency) is rare in US
    - All the above +
      - Hemorrhages
      - Gum deterioration
      - Impaired wound healing
      - Bone lesions
      - Lower extremity edema
      - Skin rash
  - Excess: excreted in urine & may promote the formation of oxalic acid & uric acid renal stones

Assessing Vitamin C Status

- Vitamin C, plasma (12-14 hours fasting)
- Ascorbic Acid degrades rapidly in extracted plasma, hence samples must be rapidly handled & preserved & frozen for reliable results

Vitamin C Supplementation

- Ascorbic acid is heat sensitive
- Ascorbic acid concentrations in supplements & foods affected by:
  - Packaging materials
  - Exposure to air
  - Storage & cooking temperatures
- Citrus fruits- retain most ascorbic acid when raw & not bruised or peeled
- Liquid vitamin C least stable
Patients that smoke need to consume more vitamin C.

Vitamin B12 (cobalamin)

- Water soluble
- Required for:
  - Proper red blood cell formation
  - Neurological function
  - DNA synthesis
- Naturally found in animal products, including fish, meat, poultry, eggs, milk, and milk products
- Not naturally present in plant foods, but fortified breakfast cereals are common
- Requires intrinsic factor for absorption

Vitamin B12 Deficiency

- Prevalence: 1.5-15% of US
- Signs/symptoms:
  - Megaloblastic anemia
  - Paresthesia and/or numbness in the hands, legs, or feet
  - Difficulty walking (problems with balance)
  - Glossitis
  - Constipation
  - Loss of appetite
  - Depression
  - Cognitive difficulties
  - Weakness
  - Fatigue
- Causes:
  - Pernicious anemia, inadequate intake, metformin, PPIs, malabsorption issues
Assessing Vitamin B12 Status

- Vitamin B12, serum
- Methylmalonic acid, serum level
  - Elevated with B12 deficiency
  - Highly specific for B12 metabolism, but also will be elevated with chronic renal insufficiency
- Intrinsic factor blocking antibody, serum
  - Positive with pernicious anemia

Vitamin B12 Supplementation

- GI absorption limited by the capacity of intrinsic factor
- Oral supplementation is ineffective for patients with pernicious anemia
- IM B12 injections or nasal spray/gel are required if GI absorption issue
- Sublingual preparations have not been shown to be better absorbed than tablets or lozenges

B12 Recommended Dietary Allowance

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Pregnancy</th>
<th>Lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months*</td>
<td>0.4 mcg</td>
<td>0.4 mcg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7–12 months*</td>
<td>0.5 mcg</td>
<td>0.5 mcg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–3 years</td>
<td>0.9 mcg</td>
<td>0.9 mcg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4–8 years</td>
<td>1.2 mcg</td>
<td>1.2 mcg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9–13 years</td>
<td>1.8 mcg</td>
<td>1.8 mcg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14+ years</td>
<td>2.4 mcg</td>
<td>2.4 mcg</td>
<td>2.6 mcg</td>
<td>2.6 mcg</td>
</tr>
</tbody>
</table>

* Adequate Intake
My hands & feet hurt...

Hemochromatosis

- The most common genetic disease in Caucasians (1/200-500 people in the US)
- Increased iron can affect any organ
- Symptoms do not typically develop before 50 years old
- Early symptoms: arthralgias, myalgias, weakness, fatigue
- Classic tetrad: skin hyperpigmentation, diabetes, cirrhosis, & cardiac failure
- Bloodwork: TIBC & ferritin
- Treatment: therapeutic phlebotomy, decreased iron consumption, & less often iron chelation

Helpful Websites

- NIH- Office of Dietary Supplements: https://ods.od.nih.gov/
References I

- http://www.mayoclinic.org/patient-conditions/hemochromatosis/basics/definition/con-20023606
- http://www.merckmanuals.com/professional/nutritional_disorders/vitamin_deficiency_dependency_and_toxicity/vitamin_c.html

References II

- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3857120/
- http://www.hopkinslupus.org/lupus-info/lifestyle-additional-information/foods

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- http://bmp.oregonstate.edu/mic/vitamin/what-is-Vitamin-C
- https://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/
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- https://www.drugs.com/pro/nascobal.html
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- Foundations in Osteopathic Medicine, 2nd ed.
- Ferris's Clinical Advisor 2009
- [http://jp.physoc.org/content/588/21/4205.full](http://jp.physoc.org/content/588/21/4205.full)
- [http://sickle.bwh.harvard.edu/hemochromatosis.html](http://sickle.bwh.harvard.edu/hemochromatosis.html)
- [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4455825/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4455825/)
- Drawings by Loriel Catalane Bowers-Vernier

## Celiac Disease

- Autoimmune
- Genetically predisposed (1/3 of Americans have DQ2 or DQ8 genes)
- Onset at any age (triggers= major life events, emotional stress, pregnancy, surgery)
- About 1 in 133 Americans have
- Inflammation & damage to the lining of the small intestines
- Digestive problems are hallmark of disease (ex. bloating, pain, gas, diarrhea)- up to 40% of adults don't have these symptoms
- May also have:
  - Osteoporosis (50%)
  - Iron deficiency anemia (20%)
  - Dermatitis herpetiformis
  - Hypertension pain or cramps
  - Arthritis, iritis
  - Glycosuria and ketonuria
  - Memory & mood problems
  - Dental enamel defects or tooth discoloration (in children)
  - Antibodies:
    - Antitransglutaminase antibodies (tTGA)
    - Anti-endomysial antibodies (EA)
- Treatment: Do not ingest gluten (foods including wheat, rye, barley, and oats)
- [http://glutenfreedrugs.com/](http://glutenfreedrugs.com/)
- Wheat allergy (IgE) & wheat intolerance

## Nerve Problems

- **Hyperalgesia/allodynia:**
  - Magnesium deficiency
  - Vitamin E deficiency
- **Paresthesia/numbness:**
  - Vitamin E deficiency
  - B12 deficiency
Muscle Problems

• Hypertonicity/spasms:
  – Magnesium deficiency
  – Vitamin D deficiency
  – Potassium deficiency

• Myalgias:
  – Magnesium deficiency
  – Vitamin D deficiency
  – Vitamin C deficiency
  – Vitamin E excess (rare)

Nutrition deficiencies in the U.S. population

Vitamin E Recommended Daily Allowance
Neuromuscular symptoms of **hypertonicity** or **chronic pain** could be the only indication a person has that their whole-body magnesium stores are low.