Biochemical Individuality - Why We Must Incorporate Laboratory Diagnostics

Presented by: Dr. Ron Grabowski
Houston, Texas
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Correlating Nutritional Deficiencies with Specific Pathologies

- Nutrient Deficiencies
  - Cardiology
    - Bariatrics
  - Neurology
    - Endocrinology
  - Musculoskeletal
    - Oncology
Thinking Outside the Box
Nutrition and Neurology
Clinical Manifestations of Vitamin B\textsubscript{12} Deficiency

- **Hematologic**
  - Megaloblastic anemia
  - Pancytopenia (leukopenia, thrombocytopenia)

- **Neurologic**
  - Paresthesia's
  - Peripheral neuropathy
  - Combined systems disease (demyelination of dorsal columns and corticospinal tract)

- **Psychiatric**
  - Irritability, personality change
  - Mild memory impairment, dementia
  - Depression
  - Psychosis

- **Cardiovascular**
  - Possible increased risk of myocardial infarction and stroke. (AAFP – 2003)
Serum Vitamin B12

- Approximately 50 percent of patients with subclinical disease have normal serum $B_{12}$ levels. (AAFP – 2003)
Nutritional Neuropathies

- Optimal functioning of the central and peripheral nervous system is dependent on a constant supply of appropriate nutrients.

- Neurologic signs occur late in malnutrition. (Neurol Clin (2007))
Nutritional Deficiencies and Peripheral Neuropathies

- Thiamin
- Riboflavin
- Niacin
- Pyridoxine
- Pantothenic acid
- Vitamin B12
- CoQ10

- Serine
- Copper
- Vitamin E
- Biotin
- Alpha Lipoic acid
- Acetyl L-Carnitine
Statins and CoQ10

- CoQ10-lowering effect of statins and its compensation by administration of CoQ10 was described approximately 15 y ago and since then has been confirmed in numerous studies of animals and humans. *(AJCN (1/2000))*

- Long-term statin treatment may be associated with chronic peripheral neuropathy. *(Eur J Clin Pharmacol. 1999 Jan;54(11):835-8.)*

- **Adverse reactions**—myalgia; myopathies; rhabdomyolysis; gastrointestinal symptoms, including hepatic injury; and the initiation or accelerated progression of cataracts and neoplasia—could be a direct or indirect consequence of the CoQ10-deficiency state associated with statin treatment. *(AJCN (1/2000))*
Mirror images are not always what they appear to be!
What is wrong with these patients?

**Multiple Sclerosis**
- Optic neuritis
- Demyelination
- Peripheral neuropathy
- Myopathy
- Spastic gait
- Sensory ataxia
- Fatigue
- MRI changes

**Copper Deficiency**
- Optic neuritis
- Demyelination
- Peripheral neuropathy
- Myopathy
- Spastic gait
- Sensory ataxia
- Fatigue
- MRI changes

Migraine Pathogenesis

Trigeminal ganglion

A trigger activates trigeminovascular fibers

5-HT_{1B/D}

Release of CGRP and SP

Neurogenic inflammation

Trigeminal nucleus caudalis

5-HT_{1F}

Pain

Cortex

Thalamus

Bianchi et al
Mitochondrial Hypothesis of Migraine Headaches

• Sangiorgi et al. – 1994
  ➢ Defect of reduced NADH, citrate synthase and Cytochrome–C-oxidase platelet activities.

• Okada et al – 1998
  ➢ Increase in lactic and pyruvic acid levels.

• Sarkela – 2001
  ➢ NO radicals can be produced in this structure.
Magnesium and Migraines

- Current evidence suggests that up to 50% of migraine patients have lowered levels of ionized magnesium during acute attacks.
- Inhibit platelet aggregation.
- Serotonin receptors are altered.
- Nitric oxide synthesis and release are affected by magnesium status.
- Reduce the inflammatory eicosanoids.
Coenzyme Q10

• **Mitochondrial Relationship**
  - Proton-electron translocation in mitochondria.
  - Protects mitochondria from oxidation.
  - Plays a role in permeability transition of the inner mitochondrial membrane.
  - Lowers serum lactate and pyruvate levels.
  - > 50% reduction post 3 months
    - Dosage 150 mg/day
Riboflavin

- FMN and FAD
  - Electron transport chain
  - Synergistic with NAD and NADP
- Amitriptyline
  - Increases the renal excretion of riboflavin.
  (Pinto & Rivlin-1987)
Vitamin B12

• Exerts a scavenging action against nitric oxide (NO).
  ➢ NO has been shown to inhibit respiratory chain by binding to complex I & III, and cytochrome c oxidase.

• Homocysteine
  ➢ Homocysteic acid
    • Excitotoxin
Homocysteic Acid

- Endogenous agonist of N-methyl-D-aspartate (NMDA) receptors.
- Play a role in the initiation, propagation, and duration of cortical spreading depression.
- Effect trigeminovascular system
- Sensitize the dura mater and cerebral arteries.
Depression

- Major depressive disorder is very common, with a lifetime prevalence of 17% and a rate almost twice as high in women as in men.

- Treatment Success:
  - Between 19% and 34% of depressed patients still do not respond to acute antidepressant treatment.
  - 29–46% may fail to achieve and sustain a full remission.
  - Between 15% and 50% will have a recurrence of depression despite continuous antidepressant treatment.
Depression & B-Vitamins

- Low blood folate and cobalamin (vitamin B-12) concentrations have been found in patients with major depression in a number of studies.

  Psychosomatics 1980
  J Affect Disord 1990
  Psychiatr Prax 1995
  Acta Psychiatr Scand 1989

- Low blood folate concentrations have been associated with a poor response to antidepressant treatment, and in some studies there has been an inverse correlation between blood folate concentrations and the severity of depression.
  - Psychiatry Res 1994
  - Am J Psychiatry 1997
Tinnitus and B12

- Observations suggest a relationship between vitamin B12 deficiency and dysfunction of the auditory pathway.
- Patients with tinnitus and NIHL exhibited vitamin B12 deficiency in 47% of cases (blood levels \( \leq 250 \text{ pg/mL} \)).

(Am J Otolaryngol. 1993)
B-Vitamins and Homocysteine

Recent data suggest that homocysteine (Hcy), folate, vitamin B6 and vitamin B12 affect bone metabolism, bone quality and fracture risk in humans.

Clin Chem Lab Med. 2005
Methylation Pathway

- Methionine
- SAM
- MTase
- SAH
- SAHH
- Homocysteine
- Cystathionine
- Cysteine
- Glutathione
- THF
- BHMT
- Vitamin B-12
- Betaine
- Choline
- Vitamin B-6
- CBS
- ADA
- AK
- AMP
- Methylation of DNA, RNA, Protein, Membrane Phospholipid, Creatine
- Protein synthesis
- 5-CH₃THF
- MS
- mTHF
Osteoporosis

Have you considered all of the Nutrients?

Calcium
Vitamin D
Magnesium
Zinc
Vitamin K
Skeleton Integrity

- Calcium, phosphorus, magnesium and zinc are the primary bone-forming minerals.

- At birth an infant contains approximately 20–30 g calcium, 16 g phosphorus, 750 mg magnesium and 50 mg zinc, of which approximately 98%, 80%, 60% and 30%, respectively, are in the skeleton.

Magnesium and Osteoporosis

- On average, >60% of US men and women aged 20 y consume less than the dietary reference intake (DRI) for magnesium. (National Academy Press, 1997.)

- Serum magnesium is generally considered an unreliable indicator of magnesium nutritional status. (J Clin Chem Biochem 1980;18:257-70.)

- Conditions bone mineral crystal stability, largely by substitution of magnesium for calcium in surface positions of hydroxyapatite lattice.
Calcium & Magnesium

Magnesium and Calcium deficiency in humans:

- Arrhythmia
- Osteoporosis
- Migraine headaches
- Myocardial infarction

J Nutrition (9/2006)
Zinc and Osteoporosis

- Collagen synthesis and mineralization of bone.
- Synthesis of alkaline phosphatase.
- Augments the anabolic effect of insulin-like growth factor I on osteoblasts.

J Nutr (1982)
Peptides (1995)
Vitamin K

- Nutritional vitamin K intake decreases substantially with age (Jie et al. 1995).

- Two vitamin K-dependent proteins not involved in hemostasis are osteocalcin or bone Gla protein (BGP) and matrix Gla protein (MGP).

- Osteocalcin is a low-molecular-weight protein (49-50 residues, depending upon species) containing three Gla residues that give the protein its mineral-binding properties. (Price 1988)
Vitamin K and Fractures

- Patients with hip fractures or spinal compression fractures were reported to have very low concentrations of circulating phylloquinone (Hart et al. 1984, Hart et al. 1985, Hodges et al. 1993) and menaquinone (Hodges et al. 1993).

- It has been shown that vitamin K supplementation increases the serum markers for bone formation (including osteocalcin and bone alkaline phosphatase) and may reduce urinary calcium and hydroxyproline excretion (Knapen et al. 1989, Knapen et al. 1993, Plantalech et al. 1990).
Case #1

- 51 year old female
- CC: Myalgia and Osteopenia
- Past Medical Hx:
  - Ulcerative colitis
  - Cervical degenerative discopathy
  - Polymyalgia rheumatica
  - Anemia
- Lab results (12/2006)
  - Asparagine, Carnitine, Vitamin D and Calcium
  - Marginal values: Vitamin B12, Oleic acid, Serine
  - Spectrox: 79.4
Case Study #2

- 53 year old male
- Initial visit: May 17, 2006
- Previous diagnosis: Plantar fascitis
  - History: Burning feet bilaterally x7 years
  - Surgery: Calcaneal spurs removed seven years ago.
  - Examination: Negative for plantar fasciitis and Tarsal tunnel syndrome
- Medications: Nortriptyline – 25mg/bedtime, Tylenol arthritic pain – 1 tablet every 4 hours.
- Supplementation with 1000mg pantothenic acid and within 4 weeks burning sensation was resolved. Dosage is presently 500mg/day
- Burning feet syndrome
Case Study #3

• 20 year old female
• Initial visit: January 2, 2008
• Chief Complaint: Migraine headaches and chronic sinusitis
  ➢ History: PMS, three to four sinus infections per year, migraines for the past four to five years, depression and anxiety.
  ➢ Surgery: Fractured fifth digit of right hand.
  ➢ Examination: Cheilosis, dry skin. Neurological and orthopedic examination were WNL.
• Medications: Yaz (OCA) and OTC analgesics and anti-inflammatories
• Lab Results: Vitamin B12, Pantothenate and Vitamin D.
  ➢ Marginal Values: Riboflavin, folate, choline, serine, CoQ10 and vitamin E
Case Study #4

- 52 year old male
- CC: Pemphigus vulgaris (Dx: 5/2004)
- History: Diabetes mellitus II
- Medications: Metformin, Actos and Prednisone – 80 mg
- 9/2004
  - Riboflavin, Vitamin B12, Pantothenate, oleic acid, biotin, glutamine, glucose/insulin interaction, Spectrox – 23.9
  - Tests unable to be determined
  - CoQ10, Vitamin D, Carnitine, Vitamin E, Selenium, N-Acetyl cysteine, Glutathione, Alpha lipoic acid
Pemphigus vulgaris
Nephrolithiasis

- Patient #1 (8/2005)
  - 35 year old female
  - Medical History:
    - Nephrolithiasis (x4)
    - Migraine headaches
    - Fatigue
    - Hypothyroidism
  - Lab results
    - Deficiencies: B2, Mg and CoQ10

- Patient #2 (11/2008)
  - 43 year old female
  - Medical History:
    - Nephrolithiasis (x5)
    - Migraine headaches
    - Fatigue
  - Lab results
    - Deficiencies: Mg and Zinc
Case Study #5

• 14 year old female
• CC: Multiple stress fractures
• PM Hx: GERD, Anxiety and Eczema
• Lab results (3/02/2011)
  ➢ Vitamin B12
  ➢ **Marginal:** B2, B6, Vitamin D3
Case Study #6

- Patient: 37 year-old female
- Dx: Osteopenia with bilateral patellar fracture post running.
- PM Hx: Migraine H/A, Premature graying, muscle spasms.
- Lab Diagnostics:
  - Vitamin B12
  - Pantothenate
  - Homocysteine: 14 (< 11.0 umoles/L)
  - **Marginal value**: Vitamin B6
Case Study #7

- 56 year old female
- CC: Anxiety, Tinnitus, Fatigue
- PM Hx: Migraine and tension headaches, GERD, Depression
- Medication: Clonazepam
- Lab results (2/25/2011)
  - Vitamin B12, Folate
  - Marginal: Vitamin D, Zinc and CoQ10
Questions and Answers