Counseling on
Drug-Induced Nutrient Depletions

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author of
a) Drug-Induced Nutrient Depletion Handbook
b) The Nutritional Cost of Drugs

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Ross Pelton has not disclosed any financial or
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Goals & Objectives
• Be a better health educator and a more
effective healthcare professional
• Win/Win: Improve patient’s health outcomes
• Be more financially successful
Increased Sales (200 Rxs/day)

- Oral Contraceptives: 5 Rxs/day
- Statins: 6 Rxs/day
- Antibiotics: 15 Rxs/day
- Metformin: 5 Rxs/day
- GERD/acid suppressing drugs: 6 Rxs/day
- Acetaminophen pain meds: 15 Rxs/day
- TOTAL: 52 Rxs/day

52 Rxs/day x 24 days/month x $20/sale
$24,960 per month or $299,520/year

Drug-Induced Nutrient Depletions

- Female Hormones: FA, B6, B1, B2, B3, B12, C, E, Mg, Se, Zn, tyrosine, CoQ10, DHEA, GSH
- Anticonvulsants: D, K, FA, Ca
- Anti-diabetic Drugs: CoQ10, B12
- Anti-hypertensives: B6, CoQ10, Ca, Mg, K, Zn,
- Anti-inflammatory: Ca, K, Zn, Fe, B6, C, D, FA, K
- Cholesterol-lowering: CoQ10
- Beta-blockers: CoQ10, melatonin
- Phenothiazines/Tricyclics: B2, CoQ10
- SSRIs/SNRIs/NDRIs/TCA: Serotonin, 5-HTP, tyrosine, p-alanine
- Benzodiazepines: Melatonin
- Acid-blocking medications: B12, FA, C, D, Ca, Mg, Fe, Zn, protein
- Antibiotics: B-vitamins, vitamin K, Amino acids
- Pain meds/acetaminophen: Glutathione

Drug Side Effects

- New Rx: nausea, vomiting, rash, etc.
- Drug-induced nutrient depletions: gradual onset; often overlooked
- Oral contraceptives (B12, FA, Mg, CoQ10)
Oral Contraceptives

Oral contraceptives deplete more nutrients than any other class of commonly prescribed drugs.

Female Hormone Medications

Oral contraceptives: deplete B1, B2, B3, B6, B12, C, CoQ10, Mg, Se, Zn, tyrosine, DHEA, GSH

Estrogen replacement therapy (ERT & HRT): deplete B6, Mg, CoQ10

Nutritional Effects of Oral Contraceptive Use: A Review

- Enovid introduced in May 1960
- “After 2 decades of use, concern about the nutritional status of women consuming OC prompted this review: OC shown to depress levels of vitamins B2, B6, B12, C, folic acid, Zn.”

J. L. Webb, Nutritional Effects of Oral Contraceptive Use: A Review

Folate Depletion with Oral Contraceptive Use

Folate deficiency problems:
• Birth defects
• Cervical dysplasia
• ↑ Homocysteine = ↑ cardiovascular disease risk
• Anemia: weakness, low energy
• Depression
• ↑ breast and colorectal cancer

Drugs That Deplete Folic Acid

• Oral Contraceptives
• Anti-convulsants for epilepsy
• Antibiotics
• Metformin/Glucophage for diabetes
• Potassium-sparing diuretics: Dyazide, triamterene
• Anti-inflammatory drugs; steroids, NSAIDS (Motrin/ibuprofen, etc)
• All acid-suppressing/GERD drugs: Tagamet, Zantac, Pepcid, Prilosec, Prevacid
• Chemotherapy

Vitamin B-6 Depletion with Oral Contraceptive Use

• Reduced synthesis of serotonin and melatonin; elevated homocysteine/plaque
• Symptoms: depression, anxiety, decreased libido, impaired glucose tolerance
• Therapy: 40 mg B6/day restores biochemical values and relieves clinical symptoms

Oral Contraceptives
B6 & Depression

• 30 women using OCs for 2-5 years (none with depression)
10 of 30 (1/3) developed depression.

• In 9 of 12 clinical trials: depression occurs in 16-56% of women using oral contraceptives.

Women & Depression

Many more women are depressed than men

• A literature review spanning 33 years from 1966-1999 reported that depression occurs twice as often in women than in men

• A study sponsored by the World Health Organization (WHO) reported that depressive disorders occur from 1.5 to 3 times more frequently in women than men

Vitamin B-6 / pyridoxine

• Vitamin B-6 is required for the conversion of 5-HTP to serotonin

• Drugs that deplete B-6: birth control pills, hormone replacement therapy, loop diuretics (Lasix/furosemide), corticosteroids (prednisone)
Oral Contraceptives Deplete Tyrosine

- Precursor for synthesis of dopamine & norepinephrine
- Dopamine/norepinephrine neurotransmitter pathways are critical for overall mental & emotional health


Nutrient Precursors / Cofactors Required for Neurotransmitter Synthesis

<table>
<thead>
<tr>
<th>Serotonin Pathway</th>
<th>Dopamine Norepinephrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>Folic Acid</td>
</tr>
<tr>
<td>Calcium</td>
<td>Iron</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>Vitamin B-6</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Vitamin B-6</td>
</tr>
<tr>
<td>Vitamin B-6</td>
<td>Magnesium</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Vitamin C</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Copper</td>
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<tr>
<td>Zinc</td>
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</tbody>
</table>

Drug-Induced Nutrient Depletions & Depression

Neurotransmitter Precursors / Cofactors

- Female Hormones: FA, B6, B1, B2, B3, B12, C, E, Mg, birth control pills & HRT, Se, Zn, Co Q10, DHEA, tyrosine
- Anticonvulsants: D, K, FA, Ca
- Anti-diabetic Drugs: CoQ10, B12
- Anti-hypertensives: B6, CoQ10, Ca, Mg, K, Zn,
- Anti-inflammatory: Ca, K, Zn, Fe, B6, C, D, FA, K
- Cholesterol-lowering: CoQ10
- Beta-blockers: CoQ10, melatonin
- Phenothiazines/Tricyclics: B2, CoQ10
- Benzodiazepines: Melatonin
- Anti-acid/GERD meds: B12, FA, D, Ca, Fe, Zn, protein
- Antibiotics: B-vitamins, vitamin K
- Chemotherapy: Destroys GI/most nutrients depleted
OCs: Weakened Immune System

Key antioxidants depleted by oral contraceptives

- Vitamin C
- Vitamin E
- Selenium
- Zinc
- Coenzyme Q10
- Glutathione

Estrogen Replacement Therapy

ERT or HRT

- Vitamin B6
- Magnesium

Increased Need for Magnesium with the Use of Combined Oestrogen and Calcium for Osteoporosis Treatment

- “Prophylactic treatment of postmenopausal osteoporosis with oestrogen and calcium, often in combination, disregards the likelihood that an excess of each agent may increase magnesium requirements and decrease magnesium levels.”

- Low Mg = increase in thromboembolic cardio & cerebrovascular events.

Seelig, MS. Increased need for magnesium with the use of combined oestrogen and calcium for osteoporosis treatment. Magnesium Research 3(3) (Sept 1990) : 197-215.
Magnesium Deficiency: Pathophysiologic and Clinical Review

• If magnesium is depleted, bone stores contribute magnesium to the extra cellular fluid

• “The serum magnesium can be normal in the presence of intracellular magnesium depletion; the occurrence of a low serum level usually indicates significant magnesium deficiency.”


Blood Pressure Meds

<table>
<thead>
<tr>
<th>Hydralazine</th>
<th>B6, CoQ10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loop</td>
<td>Ca, Mg, K, Zn, B1, B6, C</td>
</tr>
<tr>
<td>Thiazides</td>
<td>Mg, K, Zn, CoQ10</td>
</tr>
<tr>
<td>Potassium-sparing</td>
<td>Ca, Zn, FA</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>CoQ10, melatonin</td>
</tr>
<tr>
<td>Clonidine/Methyldopa</td>
<td>CoQ10</td>
</tr>
<tr>
<td>ACE</td>
<td>Zn</td>
</tr>
<tr>
<td>Chlorthalidone</td>
<td>Zn</td>
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</table>

Loop Diuretics & Thiazide Diuretics: Magnesium depletion & Heart Attacks

• Low magnesium ↑ risk of sudden cardiac death

• Only 1% of magnesium is in blood


CoQ10

- Propranolol: Decrease CoQ10-succinoxidase and CoQ10-NADH-oxidase
- Metoprolol, HCTZ, hydralazine and clonidine inhibit CoQ10-NADH-oxidase
- Methyldopa: weak succinoxidase inhibitor


Cholesterol Lowering Drugs

<table>
<thead>
<tr>
<th>HMG-CoA Reductase Inhibitors “Statins”:</th>
<th>deplete Coenzyme Q10</th>
</tr>
</thead>
<tbody>
<tr>
<td>The “fibrates”:</td>
<td>depletes B12, E, Cu, Zn</td>
</tr>
<tr>
<td>Gemfibrozil:</td>
<td>depletes CoQ10, E</td>
</tr>
<tr>
<td>Bile Acid sequest:</td>
<td>depletes A, D, E, K, B12, Ca, Mg, P, Zn, Fe, Folic Acid, beta-carotene, fat</td>
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</tbody>
</table>

Statins: How They Work

- Statins inhibit an enzyme named HMG-CoA reductase (3-hydroxy-3-methyl-glutaryl-coenzyme A reductase)
- This prevents/reduces synthesis of cholesterol in the liver
- Blocking HMG-CoA reductase also blocks synthesis of CoQ10
Coenzyme Q10

Co Q10: 2 main functions
- a) lipid soluble antioxidant
- b) required for mitochondrial energy production

New Theory of Aging: Professor Anthony Linanne
Mitochondrial DNA (mDNA) damage


Mortensen: Dose-related CoQ10 Decline
- CoQ10, an essential mitochondrial redox-component; endogenous antioxidant packaged into LDL and VLDL fractions of cholesterol; and it is an important protector against atherosclerosis
- 45 hypercholesterolemic patients DB, 18 weeks; lovastatin (20-80 mg/d); pravastatin (10-40 mg/d)
- Significant dose-related decline in serum CoQ10
  - Pravastatin: 1.27 to 1.02 mmol/l = - 19.7%
  - Lovastatin: 1.18 to 0.84 mmol/l = - 28.8%
Ghirlanda: HMG-CoA RI Lower CoQ10

- DB PC trial: 2 groups of 5 healthy subjects and 30 hypercholesterolemic patients
- Pravastatin or simvastatin 20mg/day x 1 mo.
- Results: in both healthy and hypercholesterolemic patients there was a 40% reduction in total cholesterol and a corresponding 40% reduction in CoQ10

Coenzyme Q10: Clinical Benefits with Biochemical Correlates Suggesting a Scientific Breakthrough in the Management of Chronic Heart Failure

- Patients with myocardial failure have lower CoQ10 and CoQ10 deficiency increases with increasing symptoms
- CoQ10 100mg/day: 69% cardiomyopathy and 43% ischaemic heart disease good clinical response
- “Results suggest that CoQ10 is a novel and effective breakthrough in heart failure therapy & no side effects”


Statins: Cardiovascular Side Effects

Low levels of CoQ10:

- Weakens the heart muscle


- Increase in congestive heart failure

Treatment of Essential Hypertension with Co Q10

- 109 patients: 80% of patients of diagnosis over 9.2 years
- Average dose = 225 mg/day added to their existing antihypertensive medications
- 51% of patients were able to completely discontinue from 1 to 3 medications within the first 6 months (average time 4.4 months)


Cardiovascular Drugs That Deplete Coenzyme Q10

1. Statins
2. Thiazide diuretics (HCTZ)
3. Hydralazine vasodilators
4. Adrenergic agonists (clonidine, methyldopa)
5. Beta-blockers (propranolol, atenolol, etc... over 20)

Other drugs depleting CoQ10: OCs, HRT, Sulfonylureas & Biguanides, Tricyclic antidepressants (Elavil + others), Major tranquilizers (Thorazine, Haldol, + others)

Dose: 200-400 mg/day/largest meal/fat for enhanced absorption

Anticonvulsants

Barbiturates: Vitamins D, K, FA, Biotin, Ca
Dilantin: Vit.D, K, FA, B12, B1, Biotin, Ca
Tegretol: Vitamin D, FA, Biotin
Mysoline: Vitamins D, K, FA, Biotin, Ca
Depakane: FA, Carnitine, Cu, Se, Zn
Anticonvulsants
Folate & Pregnancy

- Serum & red cell folate: 50 non-pregnant and 46 pregnant epileptic women (49 pregnancies)
- All women: serum and red cell folate inversely related to plasma levels of Phenobarb and Dilantin
- 10 abnormal (20.4%): 4 spontaneous abortions (8.2%) and 6 congenital malformations (12.2%)
- Folate significantly lower in abnormal outcomes


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Anti-diabetic Drugs

Sulfonylureas:
CoQ10

Biguanides:
CoQ10, B1, B12, FA

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Malabsorption of Vitamin B12 and Intrinsic Factor Secretion during Biguanide Therapy

- 46 diabetic patients: 30% had malabsorption of vitamin B12
- Withdrawal normalized absorption in only half of those with malabsorption
- Biguanides can induce malabsorption by 2 different mechanisms:
  a) one is temporary and unrelated to intrinsic factor
  b) the other causes permanent ↓ in intrinsic factor secretion
- Recommend sublingual methylcobalamin or IM injections

Psychotherapeutic Drugs

<table>
<thead>
<tr>
<th>Class</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenothiazines</td>
<td>deplete B2, CoQ10, melatonin</td>
</tr>
<tr>
<td>Tricyclics</td>
<td>deplete B2 &amp; CoQ10</td>
</tr>
<tr>
<td>Phelizine (MAOI)</td>
<td>deplete vitamin B6</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>deplete CoQ10, vit. E, melatonin</td>
</tr>
<tr>
<td>Lithium</td>
<td>deplete inositol</td>
</tr>
<tr>
<td>SSRIs</td>
<td>deplete sodium, melatonin, tryptophan</td>
</tr>
<tr>
<td>SNRIs, NDRIs, NRIs</td>
<td>Rs deplete amino acid precursors</td>
</tr>
</tbody>
</table>

Antidepressants Deplete Amino Acids

GERD & Acid-Suppressing Drugs

<table>
<thead>
<tr>
<th>Class</th>
<th>Deficiencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-2 Receptor Antagonists</td>
<td>B12, folic acid, vit. D, Ca, Fe, Zn (protein)</td>
</tr>
<tr>
<td>Proton Pump Inhibitors</td>
<td>B12, C, Ca, Mg, Fe, Zn, (protein)</td>
</tr>
</tbody>
</table>
Acid Suppressing/GERD Drug Depletions


Anti-inflammatory Drugs

Corticosteroids: Vit A, C, D, B6, B12, FA, Ca, Cr, Mg, K, Se, Zn
Sulfasalazine: Folic acid
Indomethacin: Folic acid, iron
Colchicine: Vit B12, Ca, Na, K, P, B-carotene
NSAIDS: Folic acid, melatonin, microbiome
Salicylates: Vit C, FA, B5, Ca, Fe, Na, K

The Microbiome: New Frontier In Medicine & Healthcare

- Common rice plant *Oryza sativa* has 45,000 genes
- Over 99% of your DNA is bacterial
Microbiome-Disrupting Drugs

- Antibiotics
- Proton Pump Inhibitors
- H2 Blockers
- NSAIDs
- Corticosteroids
- Chemotherapy Drugs
- Estrogen-containing meds (OCs & HRT)

Microbiome-Disrupting Drugs
Dysbiosis
Nutrient Depletions

- Probiotics produce B-vitamins, vitamin K, & aromatic amino acids (tryptophan, tyrosine, & phenylalanine)
- Beneficial bacteria produce proteases, lipases, lactase that aid in digestion of food & absorption of nutrients
- Dysbiosis causes inflammation which further disrupts digestion and absorption of nutrients

DNA Gene Sequencing Technologies
Human Microbiome Project
The New Frontier in Medicine

- 2007-2012 ($115M; 200 scientists/80 institutions)
- Our 100 trillion bacteria: not passive passengers; they are active participants directing & controlling much of our life

May 2016
Funded with $521 million
$121 million from US gov.
$400 million from private institutions

The Discordant Identical Twin Study

Can Yogurt Cure depression?
Psychology Today/April 2014

The Psychobiotic Revolution
The Gut-Brain Connection

How gut bacteria control & influence moods, emotions & state of mind

Postbiotics: Microbiome Revolution
Diversity & Balance

• Probiotics: multi-strain
• Prebiotics: Feeding your probiotics
• Postbiotic Metabolites:
  Short-chain fatty acids (SCFAs)
  B-Vits, vit. K & amino acids
  Anti-microbial peptides (AMPs)
  H2O2, antioxidants, fulvic acid, immune system, cell signaling

Chemotherapy Drugs

• Most nutrients are depleted
• Beneficial bacteria are killed
• Cytotoxic drugs can cause:
  – damage to gastric & GI mucosa/maabsorption
  – inflamed GI tract/painful, decreased appetite
  – nausea and vomiting
  – dysbiosis
Glutathione Depletion (IDEAL)
I = Immune system regulation
DE = Detoxification
A = Antioxidant
L = *Lactobacillus fermentum* ME-3

Acetaminophen & Glutathione Depletion
1) Depletes glutathione and cysteine in kidneys
   - 34%/young, - 58%/mature, - 64% old
   24-hr recovery 95%/young, 98% mature, 56% old

2) Depletes glutathione & catalase in liver; GSH 83% lower in 60 min.; increase in H₂O₂ & hydroperoxides, which causes cell/tissue injury

Acetaminophen & Liver Failure

*DO YOU KNOW?*
**Acetaminophen overdose is the leading cause of liver failure in the U.S.**

Nearly half of overdoses are unintentional.

Check the medication's label and do not exceed 4,000 mg of acetaminophen daily, or less if you drink alcohol.
Keystone Strains

Sub-dominant Strains
Of Probiotic Bacteria
With Large Biological Effects

*Lactobacillus fermentum* ME-3
A Glutathione-Producing Probiotic

- Isolated 1995 from GI track/healthy 1-year old child
- Boosts glutathione via 3 mechanisms
- Glutathione/Master Antioxidant & Master Detox Agent
- Produces MnSOD & increases paraoxonase activity
- Human clinical trials: 49% increase in GSH/GSSG and 26% increase in total antioxidant activity

Boosting Glutathione Levels
Glutathione: BioMarker of Aging

Glutathione is not effective orally
Glutathione nutritional precursors
NAC, lipoic acid, selenium, milk thistle
Liposomal delivery system (better)
*Lactobacillus fermentum* ME-3 (exceptional)
Questions & Discussion