Integrative and Natural Therapies for Disordered Eating

OAND Conference  |  November 21-23, 2014
10:45 to 12:15pm

James Greenblatt, MD
Chief Medical Officer, Walden Behavioral Care
Is This a Struggle for Control?

You don’t see what I see!
Cultural attitudes toward thinness have relevance to the psychopathology of eating disorders, but they are unlikely to be sufficient to account for the pathogenesis of these disorders.

versus

Social ritual of dieting for a cultural ideal of body type

Intense fear of food and weight gain that does not diminish as weight loss progresses
“The factors that may contribute to the onset of anorexia nervosa may be unrelated to the physiological dynamics that sustain the illness and cause such emotional turmoil for patients and their families.”

14th century:
Catherine of Siena practiced an extreme form of fasting and eventually died of starvation
Difficulties in Treating Patients with Eating Disorders

- Greater than 30% of patients with AN become chronically ill over 10 years
- Mortality rates: 10% at 10 years, 20% at 20 years!
- Highest risk for suicide among all psychiatric illnesses
- Highest number of hospital days of any psychiatric illness

No Advances in the Biological Treatment of Anorexia Nervosa in 50 years
Pathological Fear
“What differentiates the majority of young people who naturally register anxious distress over weight as puberty unfolds from the unfortunate few who inexplicable succumb to a fear of weight that is irrational, unrelenting and disabling?”

Those with anorexia may have inherited factors that lead to the “‘overexpression’ of fear-based learning…, a far greater than normal acquisition of conditioned fear to weight, progressing rapidly thereafter to absolute, unrelenting morbid dread necessitating food avoidance.”

Chronic Obsessional Anxiety/ Pathological Fear

- Starve
- Excessive exercise
- Alcohol
- Starve
- More exercise
- Prescription drugs
- Recreational drugs
- Starve
- More drugs
Difficulty in Treating Patients with Eating Disorders

1. Who Wants Help?

2. No Consistent Treatment Model

3. No Clear Scientific or Medical Solution

4. Comorbidity

5. Malnutrition
Eating Disorders are characterized by severe weight loss from self-starvation yet signs or symptoms of vitamin and mineral deficiencies are rarely studied or integrated into treatment.
Polypharmacy Highway

“Dr. Cymbalta”
“Dr. Prozac”
“Dr. Seroquel”
Standard of Care - Medication

There is no FDA Approved Medication for Anorexia Nervosa

Yet, the majority of patients treated with psychotropics

60% may be on SSRIs

Polypharmacy is the Norm
Depression is **NOT** a Prozac deficiency
Polypharmacy Highway

40% Relapsed within 15 weeks

20% Incapacitated or committed suicide

66% Residual symptoms
$200 Billion Lost to Current Treatment Model

Placebo Rates Comparable to Antidepressants
“This study failed to demonstrate any benefit from fluoxetine in the treatment of patients with Anorexia Nervosa following weight restoration. Future efforts should focus on developing new models to understand the persistence of this illness and on exploring new psychological and pharmacological treatment approaches.”

“In conclusion, our results challenge the efficacy of SSRI medication in the treatment of eating disorder psychopathology as well as depressive and obsessive-compulsive comorbidity in adolescent AN. Clinicians should be chary in prescribing SSRI in adolescent AN unless randomized controlled trials have proofed the benefit of these drugs.”

1Walsh BT et al. JAMA. 2006;295:2605-2612.
Antidepressants, ED and Suicide

- 7 y/o with OCD
  Prozac 10 mg – Aggressive thoughts of self-harm attempted suffocation

- 16 y/o 100% IBW with ED and depression
  No history of suicidal ideation
  - Cymbalta SI within 1 week

- 14 y/o 90% IBW with history of ED
  No history of suicidal ideation
  - Prozac SI within 2 weeks
Antidepressants and the Risk of Suicidal Behaviors

- 159,810 users of 4 antidepressant drugs

- Risk of nonfatal suicidal behavior is increased in the first month after starting antidepressants, especially during the first 1-9 days

- Nonfatal suicidal behavior is 4X more likely to occur within ≤10 days and almost 3X more likely to occur within 10-29 days after receiving a first antidepressant prescription than in more than 90 days after the first prescription

Study tracked medical records of 162,625 U.S. residents, ages 10 to 64, who were diagnosed with depression and prescribed SSRI between 1998 and 2010

More than half of antidepressants in that period were prescribed by practitioners not specialized in mental health

Among patients 24 and younger, those who started treatment with a higher-than-usual dose of SSRI were more than twice as likely to harm themselves intentionally than those whose treatment began at the customary dose and increased slowly.

Anorexia and Suicide


Researchers ‘Astonished’ By Anorexia Death Rates

Anorexia nervosa is a very dangerous illness, not just over the short term but over the long term as well. Patients with this disorder need continuing, diligent follow-up care.

- 6000 patients followed during inpatient treatment
- 265 died during 30 year follow up
- Most frequent cause of death suicide (37%)
- Average age at death was 34
Antidepressants are the mainstay of treatment for bulimia nervosa (BN).

Only a minority of patients met full remission criteria.

Fluoxetine is the only FDA approved drug for Bulimia Nervosa (BN).

Most found 50% reductions in binging and purging behavior.

Dosage was effective at 60 mg/day; no difference from placebo at 20 mg/day.

No FDA approved medications for Anorexia, EDNOS, or Binge Eating Disorder.
At least 250 are known

Neurotransmitter levels affect every facet of a biological system

Release of these chemicals causes electrical impulses throughout the brain resulting in thoughts, feelings, & behavior
How is Serotonin Made?

L-tryptophan → TPH → 5-HTP → AADC → Serotonin

+ Folate (5-MTHF)
+ Vitamin B6 (P5P) + Zinc

Serotonin Supports:
• Positive mood
• Relaxation and calming
• Moderate occasional stress
• Healthy eating behavior

Melatonin
Increasing Tryptophan in Diet → Increases Serotonin in the brain

Decreasing Tryptophan in Diet → Decreases Serotonin in the brain

In any normal diet animal based or vegetarian tryptophan is the least plentiful of all 20 amino acids (9:1)
Tryptophan Depletion Studies

• Tryptophan depletion has a mood-lowering effect in subgroups of depressed patients, patients with seasonal affective disorder, and vulnerable healthy subjects.

• Tryptophan depletion studies are conducted in animals and humans.

Why not Tryptophan Repletion Studies?

Symptomatic Relapse in Bulimia Nervosa Following Acute Tryptophan Depletion

- Tryptophan-free amino acid mixture administered to 10 clinically recovered, medication-free females with a history of bulimia

- 12 healthy controls with no history of psychiatric disorder

- 7 hours following administration of amino acid mixture
  - Compared with healthy controls subjects with a history of bulimia had significant
    - Increases in ratings of body image concern
    - Subjective loss of control of eating following the tryptophan-free mixture

How is Dopamine made?

Phenylalanine → Tyrosine

TH → L-Dopa

AADC → Dopamine

Dopamine Supports:
- Alertness
- Cognitive function
- Positive mood
- Sense of reward

Dopamine + Folate (5-MTHF)

Dopamine + Vitamin B6 (P5P) + Zinc

Norepinephrine

DH → Dopamine

Copper
Marsha ate the “perfect” diet

- Low levels of all essential amino acids
- Recommendations:
  - AA Custom Formula
  - Digestive Enzyme with HCl
- Two weeks – significant improvement
- 4 weeks – “back to herself”

Bruce ate fish daily
The Importance of Gastric Acid

Amino acid availability for neurotransmitter synthesis is dependent upon digestive enzymes and their activation by hydrochloric acid in the stomach.

HCl: TRIGGERS ENTIRE DIGESTIVE CASCADE

Neurotransmitter synthesis
Why Are Amino Acid Levels So Low?

1. Low protein intake / Vegetarianism

2. Insufficient HCl and Digestive Enzymes

3. Antacid Use

4. Stress
Augmentation strategies for antidepressant medications

- Optimal supply of Amino Acid precursors to major neurotransmitters
- 5-HTP, Tryptophan, Phenylalanine Tyrosine
- Digestive Enzymes with HCL
NO FATS?
Essential Fatty Acids Are Involved in Neurotransmission

Synthesis
Degradation
Release
Re-uptake
Binding

60% dry weight of the brain

60% FAT
Essential Fatty Acids are Associated with Depression in Adolescents with EDs


- 217 adolescents (209 girls, 8 boys) with ED were analyzed for fatty acids (FA)

- Low omega-3 status is related to depression in adolescents with indication that specific nutritional deficiencies influence the expression of psychopathology in ED

- Plasma polyunsaturated fatty acid levels measured in 33 medication-free depressed subjects monitored for suicide attempt over a 2-year period

- Seven subjects attempted suicide on follow-up

- A lower docosahexaenoic acid percentage of total plasma polyunsaturated fatty acids and a higher omega-6/omega-3 ratio predicted suicide attempt
Omega-3 and Suicide Attempt

- 100 suicide-attempt cases and another 100 control patients injured by accidents
- Low n-3 fatty acid levels in tissues were a risk factor of suicide attempt

Omega-3s and Suicide in the Military


- Study of 800 U.S. servicemen and women who committed suicide between 2002 and 2008 (compared to 800 who didn’t)

- Personnel with medical records showing low blood levels of DHA were 62% more likely to have been suicide victims than those with the highest levels

- **Study found that U.S. service personnel generally have low levels of DHA in their blood**
42 patients (40.5 y/o) with dietary intake of Omega 3 <3 gms/day

- DBPC 1.8 gms EPA .4gms DHA Omega 3 supplements or placebo BID x 8 weeks

- Celexa 20-40mg

Higher proportion of patients achieved full remission in Omega 3 group versus the placebo group; 44% vs. 18%
Omega-3s May Have Ability to Delay or Prevent Psychosis

- Study participants: 81 adolescents or young adults with subthreshold psychosis
- Supplementation: 1.2 g omega-3 fatty acids or placebo daily for 12 weeks

- **After 40 weeks:**
  - 5% (2 out of 41 individuals) in omega-3 group developed psychosis
  - 28% (11 of 40 individuals) in placebo group developed psychosis

Case study involving a 15 year old female with anorexia was given three months of EPA\(^2\):
- Within weeks, there was a gradual improvement in diet, weight, and mood

AN patients received 1g EPA/ day for 3 months\(^1\):
- 43% recovered
- 57% showed improved symptoms in:
  - Weight gain
  - Reversal of growth retardation
  - Improvement in mood
  - Improvement in general functioning

Not a Quick Fix

It takes at least 10 weeks for cerebral membranes’ highly unsaturated fatty acid levels to recover following chronic deficiency.

“By modifying natural fats, we have altered the basic building blocks of the human brain – weakening cerebral architecture. And, like unstable buildings that come apart in an earthquake or storm, poorly structured human brains are failing to cope with the mounting stress of modern life.”
The Majority of Young Women Diet

Why do so few develop eating disorders?
Genetics and Anorexia Nervosa

- Family history of Anorexia is a risk factor for Anorexia

- First degree relatives of individuals with AN are 10X more likely to have AN than relatives of unaffected individuals

- When a family member has AN, there is also an increased risk for having any eating disorder, not just AN

- First-degree relatives of individuals with BN have approx. a 12-fold greater lifetime risk of having AN than relatives of unaffected individuals
Changes that influence development without altering the genetics

- Nutrition
- Sensory experiences
- Learning
- Stress
- Social interactions

Genetics as a Biological Liability

*Not Destiny*
Puberty moderates genetic influences on disordered eating

KELLY L. KLUMP*, PATRICK S. PERKINS², S. ALEXANDRA BURT¹, MATT McGUE³ AND WILLIAM G. IACONO³

¹ Department of Psychology, Michigan State University, East Lansing, MI, USA; ² Weill Medical College of Cornell University, New York, NY, USA; ³ Department of Psychology, University of Minnesota, Minneapolis, MN, USA

Activation of the heritability of eating pathology is mediated by changes in puberty
Neurodevelopmental Changes

**Pruning**
- Brain development depends on the loss of neurons
- Pruning refines the existing neural circuits in the brain based on environmental demands

**Myelination**
- Increasing the speed the neurons can signal by adding an insulating material to the neuron
50% of caloric intake of American children is obtained from **added** fat and sugar.

20-24% of calories for 2-19 year olds come from soft drinks!

<15% of school children consume recommended servings of fruit.

<20% of school children consume recommended servings of vegetables.
“I started my vegetarianism for health reasons, then it became a moral choice, and now it’s just to annoy people.”
“The factors that may contribute to the onset of anorexia nervosa may be unrelated to the physiological dynamics that sustain the illness and cause such emotional turmoil for patients and their families.”

VEGANS BEWARE
Zinc and Vegetarianism

- 45 pts with AN outpatient clinic, never hospitalized
- Plasma zinc all deficient
- 55% abstained from meat for more than one year before onset of AN (some up to 6 years)

“Fake Vegetarian”
Vegetarianism and Eating Disorders

- Women with a history of eating disorders are nearly four and a half times more likely to have been vegetarian at some point in their lives compared to women without eating disorders.

- Women with an eating disorder history compared to control group of women with no history of eating disorders:
  - more likely to have ever been vegetarian (52% vs 12%)
  - currently vegetarian (24% vs 6%)
  - motivated to be vegetarian for weight-loss reasons (42% vs 0%)

- Study suggests vegetarianism "can be a symptom of an eating disorder for some women"

<table>
<thead>
<tr>
<th>Anorexia Nervosa</th>
<th>Zinc Deficiency</th>
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<tbody>
<tr>
<td>1. Decreased appetite and meat avoidance</td>
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</tr>
<tr>
<td>2. Decreased taste and smell</td>
<td>2. Decreased taste and smell</td>
</tr>
<tr>
<td>3. Nausea and bloating during re-feeding</td>
<td>3. Nausea and bloating during re-feeding</td>
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<td>4. Insomnia and poor sleep habits</td>
<td>4. Insomnia and poor sleep habits</td>
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<tr>
<td>5. Depression</td>
<td>5. Depression</td>
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<tr>
<td>6. Attention difficulties</td>
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</table>
• Zinc deficiency alters taste and smell receptors.

• Taste is mediated through a salivary zinc dependent enzyme.
• **Cholecystokinin** is a neuropeptide secreted in the duodenum to decrease rate of gastric emptying and promote satiety
• After a meal, anorexic patients show a peak of plasma CCK levels that is twice as high as normal!

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**Zinc is required to metabolize CCK**

**Dynorphin and Neuropeptide Y cannot function properly to stimulate feeding behavior if deficient in zinc.**

Blanchard, RK and Cousins, RJ. *Journal of Nutrition*. 2000;130:1393S-1398S
Zinc and Digestive Enzymes

Zinc increases the activity of digestive enzymes in pancreatic tissues and the small intestines.

Zinc deficiency influences the activity of carbonic anhydrase (CA).

CA is also used to form acid salts in the gastric mucosa. Zinc deficiency and therefore CA deficiency causes insufficient gastric acid production.
# Zinc Dependent Enzymes

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Digests</th>
</tr>
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<tbody>
<tr>
<td>Trypsin</td>
<td>Protein</td>
</tr>
<tr>
<td>Chymotrypsin</td>
<td>Protein</td>
</tr>
<tr>
<td>Elastase</td>
<td>Protein</td>
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<tr>
<td>Carboxypeptidase</td>
<td>Protein</td>
</tr>
<tr>
<td>Lipase</td>
<td>Fat</td>
</tr>
<tr>
<td>Amylase</td>
<td>Polysaccharides</td>
</tr>
<tr>
<td>Maltase</td>
<td>Maltose</td>
</tr>
<tr>
<td>Sucrase</td>
<td>Sucrose</td>
</tr>
<tr>
<td>Lactase</td>
<td>Lactose</td>
</tr>
<tr>
<td>Pepsin</td>
<td>Protein</td>
</tr>
</tbody>
</table>
Zinc and Depression

- 23 students with moderate and severe depression vs 23 healthy controls

- Both the daily zinc intake and serum zinc concentrations of MDD group were about two thirds of healthy index

Serum zinc levels are inversely correlated to depression scales

30 women were randomly assigned to two groups

- Group 1: 1 multivitamin daily for 10 wks
- Group 2: 1 multivitamin + 7 mg Zn daily for 10 wks

Women who took the multivitamin and zinc showed a significant reduction in anger-hostility and depressive symptoms

Women who only took the multivitamin did not
Effect of Zinc Supplementation on Antidepressant Therapy

- 12 week study with 14 patients

- In addition to standard therapy (TCAs and SSRIs):
  - 25 mg Zinc daily or placebo

- Zinc supplemented patients had significantly reduced HDRS and BDI scores compared to placebo group

Zinc supplementation augments efficacy of imipramine in treatment resistant patients

- 12 week study with 60 patients with unipolar depression

- In addition to imipramine (~140 mg/day):
  - 25 mg Zinc daily or placebo

- Zinc supplementation significantly reduced depression scores (CGI, BDI, HADRS and MADRS) in antidepressant treatment resistant patients

- No difference between placebo and zinc in non-resistant patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Dosage</th>
<th>Participants</th>
<th>Effects</th>
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</table>
| **Katz 1987**    | 220 mg/day Zinc sulfate | 14 patients with AN; 20 healthy-weight controls; ages 14-19 years-old; | Compared with placebo, zinc supplementation led to:  
• Significantly less depression and anxiety  
• Greater weight gain  
• Improved taste function  
• More rapid sexual development  
• Resolution of skin problems |
| **Sufai-Kutti 1990** | 45-90 mg/day Zinc sulfate | 20 AN patients ages 14-26 years old | • 17 patients increased their weight by more than 15%  
• 1 patient increased weight by 57% and another by 24%  
• No patients lost weight  
• Menstruation returned in 13 patients |
| **McClain 1992** | 75 mg/day Zinc acetate | 15 AN, 18 BN, 12 Control  
Age 14-36, mean 19.7 AN  
21.1 BN | • Urine and blood zinc levels increased in all patients receiving zinc supplements |
| **Lask 1993**    | 50 mg Zinc sulfate  | 26 hospitalized children  
9-14 years old | • Zinc deficiency was common.  
• Zinc levels in the blood rose whether patients received zinc supplements or not.  
• No significant difference was seen in weight gain between the zinc supplement and placebo groups  
• BUT only three of seven subjects receiving zinc completed the study and were included in the data analysis |
| **Birmingham 1994** | 100 mg Zinc gluconate | 35 patients with AN  
ages 15-30 years-old  
35 inpts, 16 Zinc, 19 placebo | • Patients receiving zinc had double the daily rate of weight gain as those who received a placebo |
Zinc Status Before and After Supplementation

• RDBPC Trial
  – 33 ED patients (15 AN and 18 BN)

• All patients admitted to Clinical research center (CRC) 3 days prior to admission to inpatient ED unit and 3 days following inpatient Treatment
  – AN – 4 wk inpatient stay
  – BN – 3 wk inpatient stay

McClain C.J., et. al., Journal of the American College of Nutrition, Vol. 11, No. 6, 694-700
Zinc Status After Treatment

24 hr Urinary Zinc

Zinc Supplementation

Placebo

Zinc (µg/dl)

Normal Range
Zinc in Depression: A Meta-Analysis

• Seventeen studies, measuring peripheral blood zinc concentrations in 1643 depressed and 804 control subjects, were included

  – Zinc concentrations were approximately -1.85 µmol/L lower in depressed subjects than control subjects

Depression is associated with a lower concentration of zinc in peripheral blood.

The Development of Anorexia Nervosa

Genetic Vulnerability

- Temperament
- Eating Disorder

- Stress
- Excess Estrogen
- Zinc Deficiency
- Environmental Toxins
- LBW

- Puberty

- SAD
- Strenuous Physical Activity

- Lasting recovery for body and mind
The Development of Anorexia Nervosa

- Depression
- Attention difficulties
- Decreased appetite
- Meat avoidance
- Amenorrhea
- Inhibition of EFA metabolism
- Decreased taste
- Changes in opioid receptors
- Vulnerability to stress
- Decreased pancreatic enzymes
- Decreased melatonin
- Nausea
- Bloating GI discomfort

Zinc Deficiency

Malnourished Minds

Anorexia Nervosa
Zinc Deficiency

As reported in the 1967 issue of *Mother Earth: Journal of the Soil Association*

- The orange trees in a grove failed to bear any fruit
- Nailed several “For Sale” signs on the trees
- In the following season, flowers and fruit appeared on every tree that bore a “For Sale” sign

The trees had been suffering from a zinc deficiency. The nails that held the signs in place were coated with zinc. Trees absorbed the mineral and restored to health
“ I started taking the liquid zinc and after three days I had an appetite...

I felt hungry...

I was scared...

I stopped the zinc.”
Augmentation Strategies for Antidepressant Medications

- Adequate Supply of Amino Acids
- Optimal EFA and Omega-3
- Optimal Folate
- Optimize Zinc Levels
- Check Vitamin B\textsubscript{12} Levels
- Check Vitamin D Levels

If you don’t test, how do you know?
Temperament and Personality Contribute to the Development of an Eating Disorder

Bulimia – Binge Eating Disorder – Obesity

Driving force is not that we are choosing to binge, rather our bodies are unable to regulate appetite and asking us to eat more.

A diverse range of physiologically generated food addictions
Neurobiological Mechanisms of Addiction

Phase 1: Binge/Intoxication
Phase 2: Withdrawal/negative effect
Phase 3: Preoccupation/cravings

“Dopamine made me do it”
Neural Correlates of Food Addiction

- Examination of the neural correlates of addictive-like eating behavior
- Forty-eight healthy young women ranging from lean to obese recruited for a healthy weight maintenance trial
- **Elevated activation in reward circuitry in response to food cues and reduced activation of inhibitory regions in response to food intake**

*Arch Gen Psychiatry. 2011;68(8):808-816.*
Primary Prevention Measures Suggested by the Malnutrition Hypothesis

- Dietary changes consistent with nutrient dense whole foods

- Zinc, folate and essential fatty acid levels should be monitored throughout childhood and adolescence

- Meat avoidance and changes in dietary habits should act as a warning sign

- Pubertal girls should be discouraged from dieting
The Tomato Effect

Rejection of Highly Efficacious Therapies

James S. Goodwin, MD, Jean M. Goodwin, MD, MPH

JAMA May 11, 1984 Vol. 251, No. 18
Tomato Effect

• When an efficacious treatment for a certain disease is ignored or rejected because it does not “make sense” in light of accepted theories of disease

• Americans would not eat tomatoes for over 200 years even though they were eaten since the 16th century in Europe
  – 1820: a public tasting without consequences

**Assassination Attempt with a Tomato?**
Thank You

James Greenblatt, MD  
Chief Medical Officer  
Walden Behavioral Care  
Waltham, MA

For more information, please visit:  
http://www.waldenbehavioralcare.com/dr-james-greenblatt/