Orthomolecular Treatment for Eating Disorders
James Greenblatt, MD

Orthomolecular Treatments for Eating Disorders

Memory Lane

“You are not going to prescribe vitamins, are you?”

EATING DISORDERS

• Anorexia Nervosa (AN)
• Bulimia Nervosa (BN)
• Eating Disorder Not Otherwise Specified (ED NOS)
• Binge Eating Disorder (BED)
  40% comorbidity with obesity
• Night Eating Syndrome (NES)
  just emerging as a significant problem

147/165 ED patients dx with EDNOS.

The majority of patients with Eating Disorders are given a diagnosis without specified criteria

Anorexia Nervosa

• 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 FDA approved medications

No Advances in the Biological Treatment of Anorexia Nervosa in 50 years

• 6000 patients
• 265 died during 30 year follow up
• Most frequent cause of death suicide (37%)
• Average age at death was 34
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Standard of Care

There is no FDA Approved Medication for Anorexia Nervosa

Yet, the majority of patients treated with psychotropics

60% may be on SSRIs

A retrospective study of SSRI treatment in adolescent Anorexia nervosa: insufficient evidence for efficacy


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.


Compared with placebo, olanzapine resulted in a greater rate of increase in weight, earlier achievement of target body mass index, and a greater rate of decrease in obsessive symptoms.

“A baby just needs to be loved”

The American Journal of Psychiatry

A Brazilian model who was “too fat”

5’ 8” and 112 pounds

One of the top models in her country, Uruguay

Collapsed and died following a walk on the runway during Uruguay’s Fashion Week in 2006

LUISEL RAMOS: 1984-2006
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Misplaced Blame

Cultural attitudes toward thinness have relevance to the psycho-pathology of eating disorders, but they are unlikely to be sufficient to account for the pathogenesis of these disorders.

Social Ritual of Dieting for a Cultural ideal of body type

Vs

Intense fear of food and weight gain that does not diminish as weight loss progresses

Standard of Care

Anorexia Nervosa is a poorly understood disorder of unclear etiology associated with high morbidity and high mortality for which conventional therapies have limited efficacy.

Therapeutic Reframe

Reintroduce a biological orthomolecular framework to the understanding, treatment and prevention of Anorexia Nervosa

The Brain

- 100 billion neurons
- 2000+ connections to other neurons
- 20,000 inputs from other neurons
- 250+ neurotransmitters
- 2 % of the body weight

20-25% of total body metabolism

A majority of young women diet at some point in time yet only a small fraction develop eating disorders.

Why?
Eating Disorders and Genetics

- Genetics have clearly been shown to be associated with increasing or decreasing risks for Eating Disorders.

Twin Studies

- 52 – 57% variance in eating pathology in 17 year old twins.
- No genetic factors in weight preoccupation and eating pathology in 11 year old twins.

The Genetics of Eating Disorders

- Activation of the heritability of eating pathology is mediated by changes in puberty.

Puberty and Onset of Anorexia Nervosa

- “I don’t know what went wrong. My childhood memories are full of vacations and family time. There was a lot of love and laughter. It was perfection. Something must have been lacking that no one was aware of. Maybe it was puberty.”
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Epigenesis

- Changes that influence development without altering the genetics
  - Nutrition
  - Sensory experiences
  - Learning
  - Stress
  - Social Interactions

Genetics as a Biological liability
Not Destiny

The Theory

Nutritional Deficiencies during puberty may effect expression of genetic material in the onset and/or maintenance of Anorexia Nervosa

Adolescent Development – Myelination

- Increasing the speed the neurons can signal by adding a fat/protein 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

Pruning

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

- Fat stores increase to 17% of body mass in women
- Brain development integrates emotional processing and cognition
- During puberty, adolescents gain:
  - 20% of their adult height
  - 45-50% of peak bone mineral
  - 50% of their adult weight and skeletal mass

Puberty and Zinc

During puberty, the recommended daily allowance for zinc increases from 8mg to 15mg

Puberty → rapid period of growth
vulnerability to Zinc deficiency

Zinc

- Similarities between symptoms of Zinc deficiency and Anorexia Nervosa:
  - Loss of weight
  - Loss of appetite
  - Alterations in taste
  - Amenorrhea (females)
  - Impotence (males)
  - Nausea
  - Skin lesions
  - Depression

Zinc in the Central Nervous System

- Maintains protein structure
- Promotes enzymatic activity
- Maintains neurotransmitter activity
- Structural function in the hippocampus
- Practically all enzymatic reactions in the brain require Zinc.
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Zinc Supplementation in Anorexia Nervosa

<table>
<thead>
<tr>
<th>Study</th>
<th>Zinc Dose</th>
<th>Study Design</th>
<th>Outcome</th>
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<tbody>
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<td>50 mg/day</td>
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Physical Symptoms of AN and Zinc Deficiency

1. Decreased appetite and meat avoidance
2. Decreased taste and smell
3. Nausea and bloating during re-feeding
4. Insomnia and poor sleep habits
5. Depression
6. Attention difficulties

Decreased Taste and Smell

- Zinc deficiency alters taste and smell receptors.
- Taste is mediated through salivary zinc dependent enzyme.

**Zinc and Appetite**

- 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.

**Zinc and Digestive Enzymes**

- Zinc increases the activity of digestive enzymes in pancreatic tissue 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.

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<td>Protein</td>
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</tr>
<tr>
<td>Carboxypeptidase</td>
<td>Protein</td>
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<td>Lipase</td>
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<tr>
<td>Amylase</td>
<td>Polysaccharides</td>
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<tr>
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<tr>
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<td>Lactose</td>
<td>Yes</td>
</tr>
<tr>
<td>Papain</td>
<td>Protein</td>
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More than 100 enzymes, including all major gastrointestinal enzymes, are dependent on Zinc for proper functioning.

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Physical Symptoms of AN and Zinc Deficiency

**Anorexia Nervosa**
1. Decreased appetite and meat avoidance
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**Zinc Deficiency**
1. Decreased appetite and meat avoidance
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Adolescent Dietary Choices
- Low consumption of foods rich in bioavailable Iron and Zinc (red meat) and high consumption of foods rich in inhibitors of iron and zinc absorption – wheat (phytates), soda drinks (phosphorous).

Vegetarianism
- A large percentage of patients with Anorexia Nervosa are vegetarians.
- Distaste and dislike for animal products are common.
- Zinc is most easily obtained from animal products

“Fake Vegetarianism”
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### The Development of Anorexia Nervosa

![Diagram showing factors contributing to Anorexia Nervosa](image)

- **Genetic Vulnerability**
  - Stress
  - Puberty
  - Zinc Deficiency
  - Environmental Toxins

- **Excess Estrogen**
- **LBW**
- **Zinc Deficiency**
- **SAD**
- **Strenuous Physical Activity**

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### Zinc Status Before and After Zinc Supplementation of Eating Disorder Patients

Craig J. McClain, MD, FACN, Mary A. Stuart, PhD, RD, Beverly Vivian, RD, Marion McClain, MS, Ramesh Talwalker, PhD, Laurel Snelling, MS, and Laurie Humphries, MD

*Journal of the American College of Nutrition, Vol 11, No. 6, 694-700*

- **RDBPC Trial**
  - 33 ED patients (15 AN 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

### Zinc Intake Prior to Hospitalization

- AN and BN patients had decreased urinary Zinc vs placebo
- Urinary Zinc Status increased in all Zinc supplemented patients vs placebo
- All AN patients receiving placebo had decrease in Zinc at end of study even though consuming RDA for Zinc (significant decrease from admission)
- Increased anabolic demands for Zinc during refeeding
- AN patients receiving placebo gained less weight than Zinc supplemented AN patients

### 24 hour Urinary Zinc

![Graph showing Zinc Intake](image)

*Fig. 3. Twenty-four hour urinary zinc (Zn) values in anorexia nervosa patients before and after 4 weeks of therapy in an eating disorder unit. Urinary Zn rose significantly in supplemented patients (p < 0.01). Placebo patients’ Zn values decreased or remained unexpectedly low. Normal 24-hour urinary Zn was 200–700 µg.*
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Aggressive refeeding without supplementing with Zinc further aggravates zinc deficient state and impairs the recovery process.

Could the refeeding process of hospitals and residentialss perpetuate the chronicity of this disorder?

Walden Research

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<th>Av weight lbs/ Day</th>
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<tr>
<td>SSRI</td>
<td>0.31</td>
</tr>
<tr>
<td>Zinc</td>
<td>0.43</td>
</tr>
<tr>
<td>Zinc and B Vitamins</td>
<td>0.53</td>
</tr>
<tr>
<td>Atypical, Zinc and B Vitamins</td>
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The Facts

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.

Questions Answered by Zinc Deficiency Hypothesis

- Why AN appears in more affluent, industrialized countries
- Why AN has been increasing and was rare until the end of the 20th Century
- Why AN is predominant in girls and starts mostly in adolescents
- Why certain “subgroups” of adolescent females are more at risk.

Primary Prevention Model for Anorexia Nervosa

Primary Prevention Measures Suggested by the Zinc Hypothesis

- Dietary Changes consistent with nutrient dense whole foods
- Zinc levels should be monitored throughout childhood and adolescents
- Meat avoidance and changes in dietary habits should act as a warning sign
- Pubertal girls should be discouraged from dieting
- Stress and high demands should not be placed on “at-risk” “sensitive” girls and they should be helped by building self-esteem and self-confidence early

Zinc Supplementation in AN

“Oral supplementation with zinc is inexpensive and free of significant side effects. However, while treatment guidelines from Canada and Australia/New Zealand recommend routine use of zinc supplementation in AN, the American Psychiatric Association Guidelines, the American Dietetic Association Position Statement and the National Institute for Health and Clinical Excellence Guidelines from Great Britain have not.”

Birmingham & Gritzner, Eat Weight Disord 2006
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Essential Fatty Acids are involved in Neurotransmission

- Synthesis
- Degradation
- Release
- Re-uptake
- Binding

- At least 25% of the brain’s white matter consists of phospholipids derived from essential fatty acids.
- 60% dry weight of the brain is fat.

A pilot open case series of Ethyl-EPA supplementation in the treatment of anorexia nervosa
Agnes K. Aynon,* Amer Azzaz, David F Horrobin

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

Essential Fatty Acids and Zinc

There is substantial evidence to suggest that Anorexia nervosa is due to a combined deficiency of zinc and EFAs. Understanding of the roles of zinc and EFAs in these various clinical situations is likely to lead to improved therapy.


The Development of Anorexia Nervosa

Genetic Vulnerability
- Temperament
- Eating Disorder
- Puberty

Zinc Deficiency

EFA Deficiency

B Vitamin Deficiency – B₁

Malnourished Minds

Anorexia Nervosa

Change in brain chemistry
- Decreased melatonin
- Nausea
- Bloating GI discomfort

Zinc Deficiency

Depression
- Attention difficulties
- Decreased appetite
- Meat avoidance
- Amenorrhoea
- Decreased taste
- Inhibition of EFA metabolism
- Changes in opioid receptors
- Vulnerability to stress
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Anorexia Nervosa is a disorder of complex etiology which genetic, biological, psychological, sociocultural factors significantly contribute to susceptibility.

No single factor has been shown to be either necessary or sufficient to express the disorder.

Risk Factors for Anorexia Nervosa:
- Perinatal stress + LBW
- Genetics
- Temperament
- Early Puberty
- Dieting
- Standard American Diet
- Comorbid Psychiatric Disorders: OCD, Anxiety, Depression

Although risk factors may not all be reversible, environmental and nutritional modulators are.

It is not always simple

“I started taking the liquid zinc and after three days I had an appetite… I felt hungry… I was scared… I stopped the zinc.”

Summary
- Cellular DNA contains a limited amount of information so all developmental effects can not be regarded as controlled by genes
- Nutritional influences throughout the life span can effect expression of genetic material
- Zinc deficiency may trigger onset of AN
- Prevention of AN is possible with better understanding of risk factors and triggers in those genetically vulnerable
Prevention as the Goal

- Aggressive treatment is crucial as these disorders affect children and young adolescents when they are most vulnerable, quickly destroying their foundation for psychological development and setting the foundation for permanent health consequences.

Thank You