Medical Complications of Eating Disorders

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University of Colorado
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ACUTE: the story

• Philip S. Mehler, MD, CEDS, FAED
• Team
• Wonderful patients & cases
• Growth & finance
• Research
Low Prealbumin is a Significant Predictor of Medical Complications in Severe Anorexia Nervosa

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ABSTRACT
Objective: Prealbumin levels have been proven to correlate with hospital length of stay, wound healing, infection rates, and mortality in adults hospitalized for medical or surgical purposes, or those who have chronic illnesses. Little is known about the utility of prealbumin in predicting medical complications in patients with eating disorders, particularly admission prealbumin levels had a three-fold increased risk of refeeding hypophosphatemia and a twofold increase in hypoglycemia compared with patients who had a normal admission prealbumin, independent of admission BMI. Discussion: A low serum prealbumin level appeared concurrent with other complications.

Hematological abnormalities in severe anorexia nervosa

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Factors influencing hematological abnormalities in severe anorexia nervosa

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Who are ACUTE patients?

- 17-65 years old (average 29)
- 10% men
- Average BMI on admission 12.5 kg/m²
- Wide variety of pre-admission function
- Average length of stay around 2 weeks
- From all over the country
Falling through the cracks

Too medically sick for me…

too mentally ill for you
Anorexia nervosa

- **Genetic** predisposition in personality & temperament “loads the gun”
- **Environment**, with hyper-focus on dieting, weight loss, and thinness, “pulls the trigger”
Objectives: Teach...

• The medical complications of severe caloric restriction and underweight
• The medical complications of severe purging
• Evidence based (and sometimes expert opinion based) best practices of care
Format: Discuss...

- Cases
- Pathophysiology
- Best practices to manage/fix
- What we say to our patients
- Literature/evidence
What is definitive stabilization?

• Use best medical evidence to provide safe, sensible, supported multidisciplinary care until patients meet our discharge criteria:
  – 2000-3000 kcal (oral) a day/sufficient to be gaining 1 kg lean weight weekly
  – Labs normal or normalizing
  – Completed refeeding syndrome and no longer on electrolyte repletion
  – Bowels working, minimal edema
  – Physically strong enough to transfer to mental health setting
Mortality risk

- In a 200 patient study in Sweden, standardized mortality ratios (SMR) were 45 x for lowest BMI ever <10.5 kg/m2, 33% of patients with BMI <11.5 kg/m2 died, no increased mortality in BN. ²
- 6000 patient: 6x mortality generally, 30% of deaths from suicide, age 34 years old. Alcohol abuse strong predictor of death. ³
- In hospital mortality Japanese study, average admission BMI 13 kg/m2, was 0.7%, most deaths under BMI 11 kg/m2 ⁴

Medical complications

• In AN-R
  – Organ dysfunction due to under-weight and malnutrition
  – High risk for refeeding syndrome

• In purging (AN or BN)
  – Type of purging used, frequency, and duration
  – Detox can be complicated too
What’s the medical evidence?
The good news:

Nearly all medical complications can resolve with consistent nutrition and full weight restoration.
Disease Spectrum

Ideal Body Weight (IBW)
Women: 5 feet = 100 lbs
Plus 5 lbs/inch
Men: 5 feet = 106 lbs
Plus 6 lbs/inch

BMI
≈ 12
EDM CENTER FOR EATING DISORDERS
ACUTE Center for Eating Disorders

Medical Insurance Benefit

Behavioral Health Insurance Benefit
IP/Residential TX
Outpatient Treatment

Anorexia Nervosa is diagnosed at 85% IBW or BMI 17.5
Case: AN-R

- A 23 year old started an intensive workout and diet program with her sorority sisters...only she couldn’t stop
- Over two years, weight 74 lb, 5’5”, 60% IBW, BMI 12.5 kg/m2
- Insists on outpatient care the whole time
- Has good energy and works full-time
- Labs are “fine”...just some increase in her liver tests and a low white blood cell count
- Finally team and family insist on admission to a program
Case: AN-R

On further questioning:
- Early satiety, bloated, “so full”
- Dry eyes, “muffled” hearing
- Occasionally coughs with liquids, pneumonia 1 mo ago
- Episodes of feeling sweaty and lightheaded
- No menstrual period for 3 years; walks to keep bones strong

She struggles with any sense she’s ill
- Discounts words of concern and over-values statements of normalcy/praise
Case: AN-R

Admitting data:

- EKG with sinus bradycardia at 36
- BP 70/35
- WBC 2.1 K/μL
- 93 K/μL
- Electrolytes normal
- Albumin normal, prealbumin 13 mg/dL (>20 nl)
- LFTs in the 400s U/L
- Vit D-OH of 16 ng/ml (> 30 goal)
- INR of 1.36
AN-R

Refeeding syndrome
• Gastroparesis
• Osteoporosis
• Low cell counts
• Hepatitis
• Hypoglycemia
• Vital sign abnormalities
• Cardiac abnormalities
• Dysphagia
• Lagophthalmos/autophonia
Refeeding syndrome

Potentially deadly syndrome that occurs when a starved person begins to take in nutrition.
Refeeding syndrome

National Institute for Clinical Excellence (NICE) Guidelines for Management of Refeeding Syndrome:

**Patients at risk for refeeding syndrome**

<table>
<thead>
<tr>
<th>One or more of the following: -OR-</th>
<th>Two or more of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>· BMI &lt; 16 kg/m²</td>
<td>· BMI &lt; 18.5 kg/m²</td>
</tr>
<tr>
<td>· Unintentional weight loss of &gt;15% in the previous 3-6 months</td>
<td>· Unintentional weight loss of &gt;10% in the previous 3-6 months</td>
</tr>
<tr>
<td>· Little or no nutritional intake for &gt;10 days</td>
<td>· Little or no nutritional intake for &gt; 5 days</td>
</tr>
<tr>
<td>· Low levels of potassium, phosphorus, or magnesium before refeeding</td>
<td>· History of alcohol abuse or drugs including insulin, chemotherapy, antacids, or diuretics</td>
</tr>
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</table>
Refeeding syndrome

Phosphorous

Metabolism of food pulls phosphorous into cells, used for energy building blocks

Food (carbohydrates) consumed

Low serum phosphorous
Refeeding syndrome

- Low phosphorous can be dangerous...or deadly
- Full-blown refeeding syndrome
  - Respiratory failure
  - Red and white blood cell dysfunction
  - Muscle breakdown
  - Seizures
  - Congestive heart failure
  - Cardiac arrest
- Refeeding hypophosphatemia can be caught and corrected before complications
Refeeding syndrome

- **Edema (fluid retention)**
  - In AN-R and –BP during early refeeding
  - Insulin effect on the kidney causes salt and water retention
  - Goes away naturally within a week or two
  - Set expectations!
Refeeding syndrome

- Close monitoring prevents full-blown syndrome
  - Start calories around 1400-2000/day, low salt, <40% kcals from carbohydrates
    - Important Australian contributions at the leading edge
  - Intensive dietician input and support
  - Advance by 400 kcal every 3 days, checking phosphorus levels daily in week 1, replete <3 mg/dL
  - Encourage leg elevation, compression stockings

Whitelaw M, Gilbertson H, Lam PY, Sawyer SM. Does aggressive refeeding in hospitalized adolescents with anorexia nervosa result in increased hypophosphatemia? J Adolesc Health 2010;46:577-582

Kohn MR, Madden S, Clarke SD. Refeeding in anorexia nervosa: increased safety and efficiency through understanding the pathophysiology of protein calorie malnutrition. Curr Opin Pediatr 2011;23:390-394
Prealbumin

- 47% of patients had low prealbumin at admission
- 11% of patients had low albumin ("albumin paradox")
- Majority had normalized by dc on average 14 days later
- Predicts:
  - 3x risk refeeding hypophosphatemia
  - 2x risk hypoglycemia, both independent of admission BMI.
  - After correction for weight, low albumin predicted > 4x increase in incidence refeeding edema, but did not predict hypophosphatemia or hypoglycemia.
Gastroparesis

- Loss of normal stomach peristalsis (movement)
  - Nearly universal in severe underweight
  - Causes early fullness, nausea, bloating, gassiness
  - Rarely is a nuclear med emptying study needed in this population

Can cause acute gastric dilatation
Acute gastric dilatation
Gastroparesis

Worsens
- High fiber diets
- Long time underweight

Helps
- Smaller meals
- Liquids/semi-solids
- Low fiber
- Kcal dense
Gastroparesis

• Prescription options
  – Metoclopramide 2.5 mg 30 min before meals
  – Erythromycin ethinylsuccinate 200-400 mg another option
  – Limited time
  – Review risks and benefits
SMA Syndrome

- With dramatic weight loss/very low weight, 3rd portion of duodenum gets trapped between aorta and superior mesenteric artery
- Loss of physiologic fat pad
SMA Syndrome

- Causes mechanical obstruction of proximal (near stomach) small intestine
- Can cause acute gastric dilatation
SMA Syndrome

• Little in the literature
• Diagnose by upper GI series (barium swallow with small bowel follow-through or CT scan
• We have seen many cases and many different pre-ACUTE treatment attempts

Adson DE. Mitchell JE. Trenkner SW. The superior mesenteric artery syndrome and acute gastric dilatation in eating disorders: a report of two cases and a review of the literature. IJED 1997;21:103-114
SMA Syndrome

• Our recommendations (clinical expertise)
  – If incomplete obstruction (no gastric dilatation, partial but not total narrowing of duodenum), liquid only diet under careful medical monitoring
  – After some degree of weight restoration, it will resolve
  – Placement of surgical jejunostomy tube as last resort (poorly tolerated)
Pancytopenia

• **Gelatinous Marrow Transformation**
  – Replacement of cell-producing marrow with an acellular “goo” due to starvation
  – All cell lines may be affected
  – Source of inappropriate workup
Pancytopenia

• Abnormalities of 1-3 cell lines common
  – 53 ACUTE patients, nadir BMI 12.4 kg/m2, 90% women, mean age 28
  – 83% with anemia
  – 79% with leukopenia
  – 30% with neutropenia
    • Most resolved by hospital dc
  – 25% with thrombocytopenia
  – 35% with thrombocytosis, half developing in-hospital

Pancytopenia

- Leukopenia/neutropenia (<4.5 K/µL, ANC <1K/µL)
  - For unclear reasons, no evidence of increased infections in these patients
  - We don’t follow “neutropenic precautions” in patients with an absolute neutrophil count (ANC) <1.0 for this reason
  - Nutrition is the solution to bone marrow dysfunction, not stimulation factors
  - Recommend the flu shot in season
Panctyopenia

- **Anemia (hematocrit <37%)**
  - Very common
  - 3/53 patients were iron deficient and anemic
  - Zero incidence of anemia of chronic dz, B12, or folate deficiency
  - Generally don’t transfuse unless hematocrit is <21%, or if serious symptoms/active bleeding
  - Comes up on its own with nutrition
Vital signs

- Vital signs abnormalities highly prevalent
  - Adaptive, compensatory responses to malnutrition, “hibernation mode”
    - Hypotension
    - Hypothermia
    - Bradycardia at rest (vagal tone)
    - Tachycardia with movement
      - Deconditioning, not orthostasis
      - Helps distinguish between “athletic” and “starved” heart
Cardiac dysrhythmias

• Previous hypothesis: prolonged QT leads to death

• Newer hypotheses:
  – Not the QT (watch out for psych meds though!)
  – Variable blocks, junctional bradycardia, junctional tachycardia, HR variability, QT dispersion...
Junctional Bradycardia

Exercise Electrocardiography Extinguishes Persistent Junctional Rhythm in a Patient with Severe Anorexia Nervosa

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Fig. 1. Arrows demonstrate P waves of restored sinus rhythm, which are initiated rapidly (0:01 mins) with exercise, and then disappear again during the recovery phase despite a resting heart rate of 98 bpm.
Osteoporosis

- The one potentially irreversible complication
  - Onset of bone loss is rapid (2.5%/year) and severe
  - By the end of the second decade, more than 90% of peak bone mass has been achieved in healthy woman: in adolescent-onset AN this never occurs
  - Highly prevalent

Mehler PS, Cleary BS, Gaudiani JL. Osteoporosis in anorexia nervosa. Eat Disord 2011;19:194-202
# Osteoporosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Value</th>
<th>Adolescents</th>
<th>Adult women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal density</td>
<td>Z score &gt; -1.0</td>
<td>50%</td>
<td>90%</td>
</tr>
<tr>
<td>Osteopenia</td>
<td>Z score -1.0 to -2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Z score &lt; -2.5</td>
<td>25%</td>
<td>38%</td>
</tr>
</tbody>
</table>

Osteoporosis

Postmenopausal  Anorexia Nervosa

Net  Net
Osteoporosis

- **Gold standard: weight restoration**
  - Until resumption of menstrual cycle in women
  - 2010 Spanish study compared BMD improvement in AN patients restoring weight (20% mean increase in weight) with those who did not gain weight
    - At 2 years, gainers had improved bone density 2 to 5%
    - Non-gainers had lost 1% to 4% bone density

Osteoporosis

• Calcium and Vitamin D
  – Keep Vitamin D-OH levels above 20-30 ng/UL
  – Don’t give while in refeeding phase, as calcium binds dietary phosphorus
Osteoporosis

• Estrogen
  – Virtually all RCTs conclude...just say no to estrogen
  – Use obscures the benefits of natural menstrual cycle resumption (and precipitates monthly blood loss)
Osteoporosis: Exercise

• Doesn’t exercise help bone density?
• While underweight: exercise worsens bone density
• Once restored: even intense exercise helps bone density

What we tell our patients:

• *Serious exercise is a privilege of recovery.*
Osteoporosis

• Bisphosphonates
  – Effective in improving bone mineral density in AN:
    • Harvard RCT in 2011 studied 77 women, mean age 27, mean BMI 18 kg/m2, mean Z score around -1.5
    • At 1 year, improvements in BMD 3%, lateral spine BMD 4%, and hip BMD 2%

Osteoporosis: bisphosphonates

- **Women of child bearing age**
  - Stays in system a long time, crosses the placenta, animal harm
  - Limited human studies look reasonably safe in carefully selected population
    - Greek meta-analysis of 78 patients in literature \(^1\)
    - Serbian 12 year follow-up case \(^2\)

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\(^1\)Stathopoulos IP et al. The use of bisphosphonates in women prior to or during pregnancy and lactation. Hormones 2011;10(4):280-91

Osteoporosis

• High risk athletes
  – Athletes tend to have higher BMD (by 5-15%) vs. age-matched controls
  – Thus a z-score < 1.0 in an athlete requires evaluation!
Osteoporosis

• Men
  – Men typically have 1/3 the rate of osteoporotic hip and vertebral fracture rates of women
  – Men with AN had greater loss of bone than women even though men typically had shorter duration of their disorder
  – Men may fracture at higher bone density level than women

Hepatitis

- Liver function tests (LFTs) are often elevated in severe AN
  - Starvation mediated:
    - Autophagy on biopsy, recovers with refeeding. More common. *Often worsens for 1st week of refeeding.*
  - Refeeding mediated:
    - Steatohepatitis, recovers with slowed refeeding

How to tell which etiology?
Hepatitis

- If starvation mediated:
  - LFTs may continue to rise days into refeeding
  - Ultrasounds will show normal size, not enlarging liver
    Push forward with refeeding

- If refeeding mediated:
  - Ultrasounds will show enlarging, steatotic ("fatty") liver
    Reduce rate of refeeding for a few days
Hypoglycemia

- Potentially deadly
  - Glucoses < 60 mg/dL are low
  - In underweight, result from depletion of gluconeogenic building blocks
  - Liver tests > 3 x normal predict hypoglycemia
  - Tx: IVF vs. NG feeds, then adequate kcal intake
Lagophthalmos

• Failure of eyelids to close fully due to enophthalmos
• Causes dry, irritated eyes
• Can lead to corneal scarring
• Use tears (preservative free), ointment and eye taping nightly
• Resolves rapidly with hydration, modest weight restoration

Dysphagia

• Occurs in AN due to weak swallowing muscles, +/- concurrent reflux disease
• May lead to aspiration pneumonia
• Likely more common than thought

Dysphagia

• Treatment
  – Depending on degree of severity:
  – Speech-language pathologist evaluation, modified barium swallow to assess, exercises, and aspiration precautions. NG tube rarely, briefly
  – No straws
Elevated INR

- **International Normalized Ratio (INR)**
  - Measures clotting tendency of blood
  - Normal level is around 1
  - Vitamin K dependent
  - Often elevated (= more prone to bleed) in patients on admission
    - Vitamin K deficiency or malabsorption?

Case: Purging

- A 31 year old woman
  - 7 years as a normal-weight bulimic
  - Last three years restricted more and converted to AN-BP
  - Never been in treatment
  - Restricts to 500 kcal/day, exercises daily, purges for 4 hours every night (vomiting), uses 20 laxatives daily
  - Weight now 63 lbs at 5’1”, 60% IBW
  - Three ED visits in last month, 12 lbs up in 8 hours
Superficial peril of longterm vomiting
Case: Purging

- Sodium 123, potassium 1.9, bicarb 42, BUN 31 and Cr is 1.1
Purging (AN or BN)

- Properly managing volume depletion (dehydration)
- Avoiding volume overload
- The potassium problem & other electrolytes
- Constipation and the perils of laxatives
- Acute sialadenosis
Purging

• Medically unstable due to abnormal electrolytes
  – Low sodium, low potassium, high bicarbonate

• Also unstable due to risks of detox off of purging
  – Potential for severe rebound edema (swelling), severe constipation, sialadenosis: symptoms can be triggering, compel pt to leave treatment, or can be deadly
Dehydration and edema

- Preventing edema in those who purge
  - With or without IV fluids
Pseudo-Bartter Syndrome

- Secondary hyperaldosteronism
- Responsible for swelling after purging cessation
- Resolves after 2 weeks of hydrated state
- Causes urinary K loss

Pseudo-Bartter Syndrome

- Key points to treat
  1. Stop purging
  2. **Slowly** give IV fluid (no faster than 50 ml/hr)
  3. (Or follow low sodium diet and 2-3 liters fluid a day), feet up
  4. Treat the hormone over-production until body downregulates
Pseudo-Bartter Syndrome

To prevent edema from Pseudo-Bartter Syndrome

Spironolactone

Aldosterone
Perils of stimulant use

• Constipation universal in severe underweight
  – Slowed GI transit
• High fiber worsens at low weights
Constipation

• Manage expectantly
  – Set expectations for normal range of bowel function
  – Polyethylene glycol, no stimulants
  – Intestine works best at K of 4.5 or so
X-ray promise
Cathartic Colon Syndrome

A.K.A “Why we don’t taper stimulant laxatives...we STOP them”
Electrolytes

- **Low sodium** (135-143 mmol/L normal)
  - Volume depletion
  - Insufficient free water excretion
    - Overdrinking fluids (> 15+ L over a day)
    - Undereating relative to normal fluid intake
      = “low solute, poor free water excretion”
  - SIADH
    - Meds
  - Can cause seizure
  - Over-rapid correction also dangerous
Electrolytes: management

• Low sodium
  – Slowly!
    • Central pontine myelinolysis (CPM) risk
  – If volume depletion, normal saline at 50 cc per hour, frequently checking serum sodium
  – For those not dehydrated, restrict fluids to 2 liters total daily, check regularly...as calories increase, fluid can too
With thanks as ever to Dr. Mehler and the ACUTE team