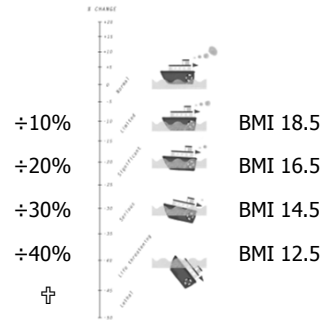


- ❑ Adaptation and re-feeding
- ❑ Hypokalemia
- ❑ Bone complications

**René Klinkby Støving**  
Odense University Hospital  
Denmark



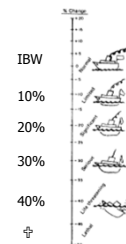
*Willmore DW, The Metabolic Management of the critically ill, Plenum Medical Book Company 1977*

Hunger strike  
Belfast 1981: 30 IRA prisoners

10 died 46 – 73 days  
Mean weight loss 40% (BMI 12.5)

To the limit of extreme malnutrition

Jacob Frølich M.D., Camilla Viola Buskbjerg Palm M.D., Rene K. Støving M.D., Ph.D.



*Nutrition 2016*

**65% BMI 7.8**



JOURNAL OF  
ADOLESCENT  
HEALTH  
www.jahonline.org

Editorial  
Refeeding Hospitalized Adolescents With Anorexia Nervosa: Is "Start Low, Advance Slow" Urban Legend or Evidence Based?

*Katzman, J Adolesc Health 2012*

### Why do Individuals with Anorexia Die? A Case of Sudden Death

"Too much, too soon"

Cardiogenic shock caused by a left midventricular obstruction during refeeding in a patient with anorexia nervosa

Acute respiratory failure due to refeeding syndrome and hypophosphatemia induced by hypocaloric enteral nutrition

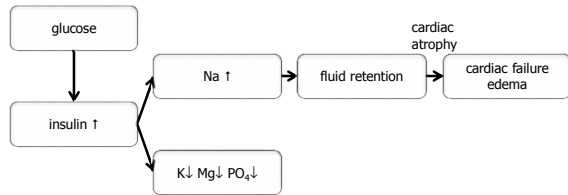
Central Pontine Myelinolysis as a Complication of Refeeding Syndrome in a Patient With Anorexia Nervosa

**Acute Edema/Cutaneous Distention Syndrome Associated With Refeeding in a Patient With Anorexia Nervosa**

Cardiac Arrest and Delirium: Presentations of the Refeeding Syndrome in Severely Malnourished Anorexia Nervosa

Severe acute liver damage in anorexia nervosa

refeeding syndrome: pathophysiology

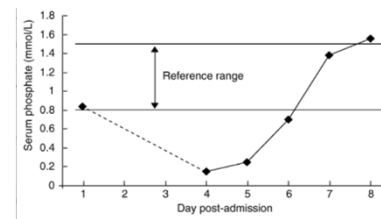
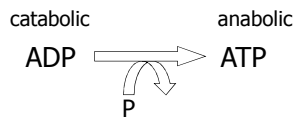


Kwashiorkor: an unexpected complication to anorexia nervosa

Camilla Viola Buskbjerg Palm,<sup>1</sup> Jacob Stampe Frølich,<sup>1</sup> Lena Sønder Snogdal,<sup>2</sup> René Klinkby Støving<sup>1</sup> *BMJ Case Rep 2016*

ascites  
ulcers  
hypoalbuminemia

keep an eye on the phosphate fluctuation

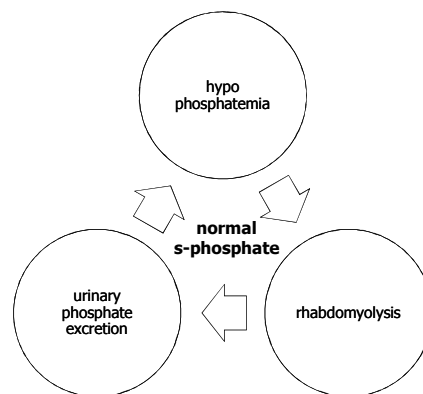


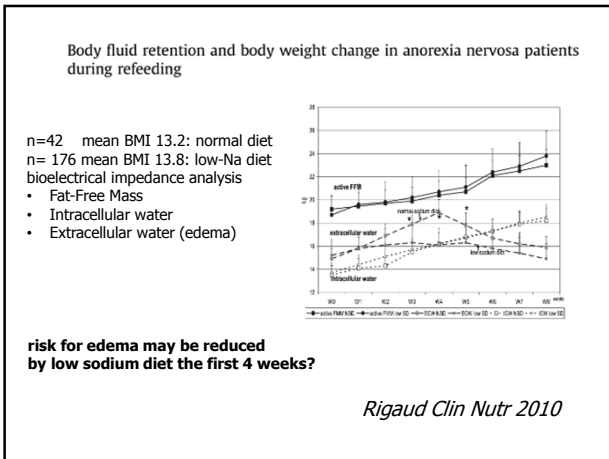
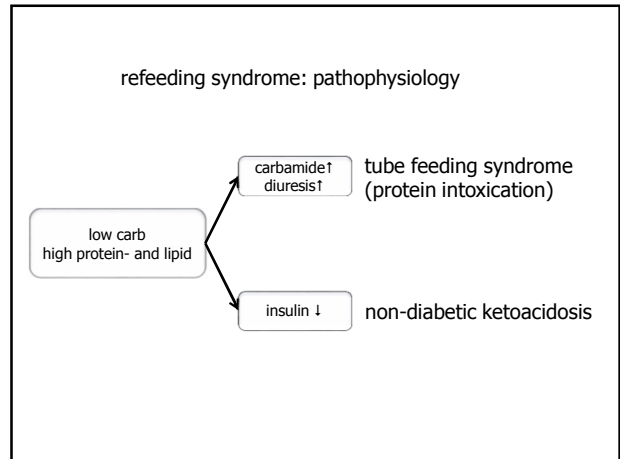
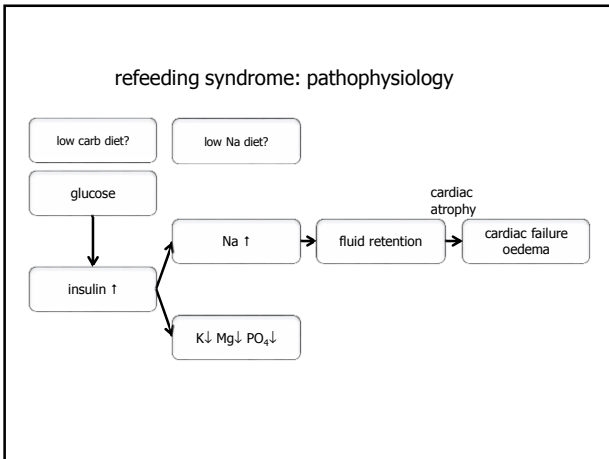
Fung, MJA 2005

Hypophosphataemia (s-phosphate < 0.5 mmol/l)

Clinical manifestations

- Hematologic: hemolysis, thrombocytopenia
- CNS: convulsions, delirium, coma
- Cardiac: cardiac failure, arrhythmias
- Muscles: rhabdomyolysis → phosphate ↑  
→ renal failure  
→ respiratory failure





initial energy level	(Kcal/kg/day)
World Health Organization	40
AMERICAN PSYCHIATRIC ASSOCIATION Member Oriented, Science Based, Patient Focused.	30
Royal College of Physicians MARSIPAN	20
NHS National Institute for Health and Clinical Excellence	10

guidelines: initial energy level

BW 30 kg:

NHS  
National Institute for Health and Clinical Excellence

10 Kcal/kg

Royal College of Physicians  
MARSIPAN

20 Kcal/kg

risky

ELSEVIER  
Clinical Nutrition  
journal homepage: <http://www.elsevier.com/locate/cinu>

Original article  
Prognosis in 41 severely malnourished anorexia nervosa patients

**Specialized medical unit in Dijon:**

- BMI < 11 (n=41 out of 484)
- Day 2 – 10 according to NICE
- † 1
- Myocardial infarction: 2
- Heart rate 10 (pacemaker): 1

Rigaud, Clin Nutr 2012

### ***start low advance slow***

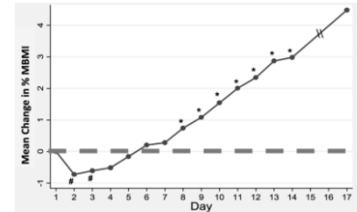
#### **Under-feeding syndrome**

- Further drop in body weight.
- Masked by re-hydration, edema, constipation

### **Under-feeding syndrome**

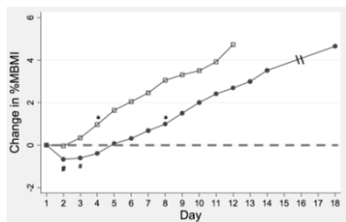
A Prospective Examination of Weight Gain in Hospitalized Adolescents With Anorexia Nervosa on a Recommended Refeeding Protocol

- n=34
- %MBMI 80±12



*Garber, J Adolesc Health 2012*

Higher Calorie Diets Increase Rate of Weight Gain and Shorten Hospital Stay in Hospitalized Adolescents With Anorexia Nervosa



High caloric start  
Low caloric start

n= 56 MBMI 79% ± 1.5

*Garber, J Adolesc Health 2013*

## **Wanted!**

RCT multicenter: high risk patients BMI<12

- Low carb vs normal carb
- Low Na vs normal Na
- Low energy vs full energy

Primary outcome: survival

Secondary outcome: hypophosphatemia

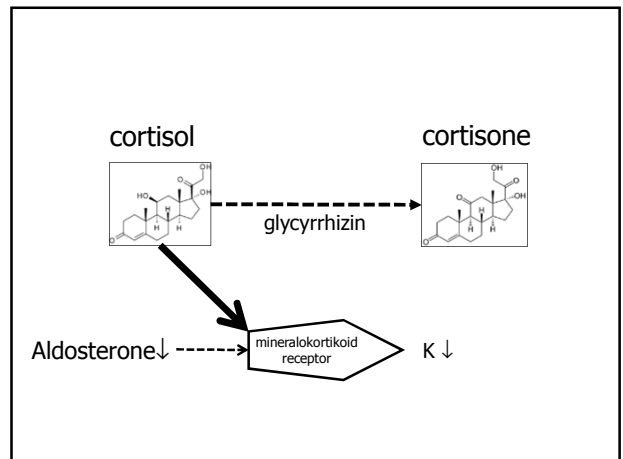
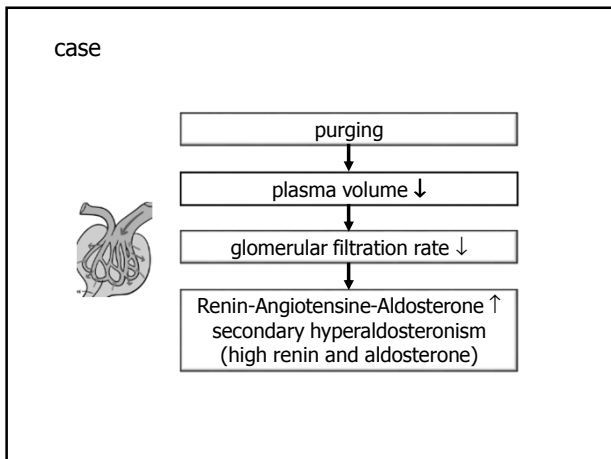
## **Purging**

- vomiting
- laxatives
- diuretics

### case

Worried family in Western Jutland: 27 y daughter

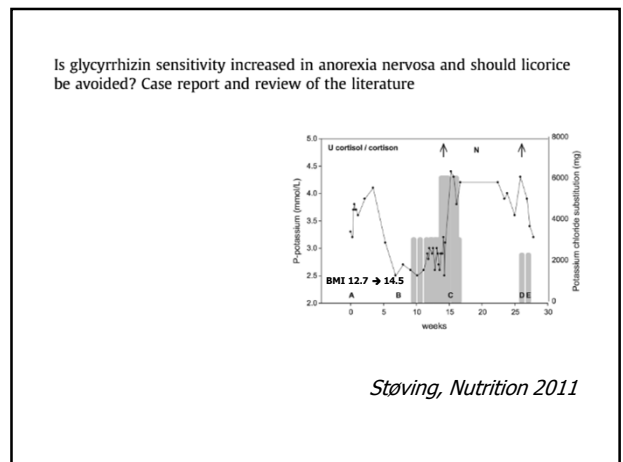
- Admitted to the Nutrition Unit.
- Weight loss 30%/6 months: BMI 12.7
- +6 kg/6 weeks
- Transferred to Psychiatric Unit
- Severe hypokalemia: substitution 6000 mg KCl



case

**renin and aldosterone**

- Purging: Elevated
- Licorice: Suppressed

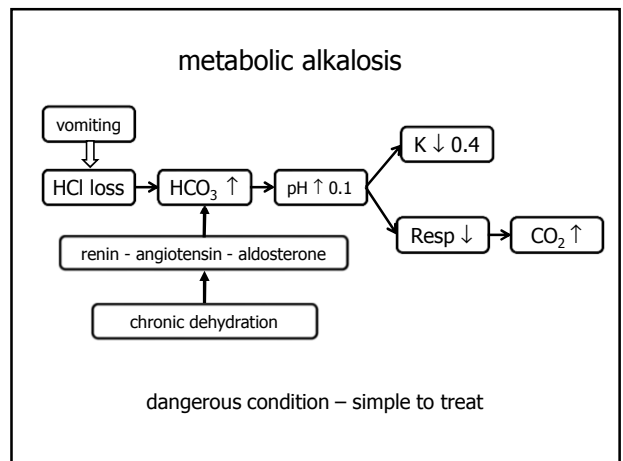


potassium mixture with licorice

**Indholdsstoffer**  
Kaliumchlorid

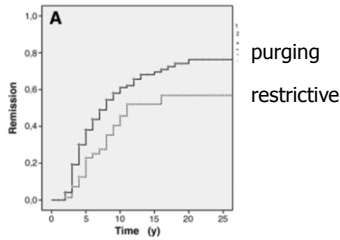
**Hjælpestoffer**  
Konservering: Methylparahydroxybenzoesyre (E218)  
Propylparahydroxybenzoesyre (E216)  
Smag: Asin  
Lubrid: Andre  
Ethanol

**Firma**



Purging behavior in anorexia nervosa and eating disorder not otherwise specified:  
A retrospective cohort study

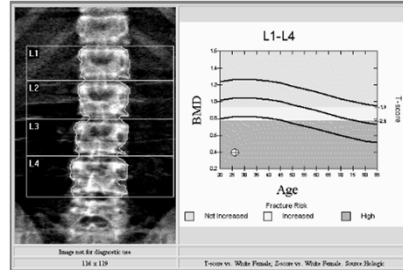
- n=339 AN  
10 y remission rates
- restrictive 55%
  - purging 40%



Støving, Psych Res 2012

no fractures  
normal Vitamine D

## Osteoporosis?



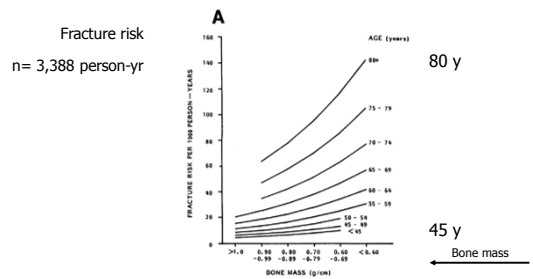
areal Bone Mineral Density (BMD) g/cm<sup>2</sup>

what is osteoporosis?

WHO:

1. Low energy fracture in the spine or femur
2. BMD  $T < -2.5 \text{ SD}$   
***postmenopausal women***

Bone mass - Fracture risk: strongly age dependent



Hui, J Clin Invest 1988

adapted to chronic semi starvation

- mechanical load ↓
  - bone marrow fat ↑
  - auto cannibalism:
    - cortisol ↑
    - IGF-1 ↓
    - estrogen ↓
    - leptin ↓
- reversible BMD↓

completely different from normal nutritional state

Young patients with anorexia nervosa:  
Osteoporosis **cannot** be defined solely by BMD

$Z < \div 2.5$ : "below expected range for age"



### The Role of Body Weight on Bone in Anorexia Nervosa: A HR-pQCT Study

Jacob Frølich<sup>1,2,4</sup> · Stinus Hansen<sup>2</sup> · Laura Al-Dakheel Winkler<sup>1,2</sup> · Andreas K. Andresen<sup>3</sup> · Anne Pernille Hermann<sup>2</sup> · René K. Støving<sup>1,2</sup>

High Resolution peripheral Quantitative CT (HR-pQCT)

- n=25 AN women
- age 20-40 y
- controls age- and height matched

*Calcif Tissue Int 2017*

### The Role of Body Weight on Bone in Anorexia Nervosa: A HR-pQCT Study

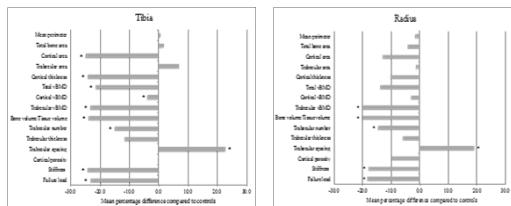
Jacob Frølich<sup>1,2,4</sup> · Stinus Hansen<sup>2</sup> · Laura Al-Dakheel Winkler<sup>1,2</sup> · Andreas K. Andresen<sup>3</sup> · Anne Pernille Hermann<sup>2</sup> · René K. Støving<sup>1,2</sup>

- cortical bone ↓
- trabecular bone ↑
- bone marrow fat ↑

### The Role of Body Weight on Bone in Anorexia Nervosa: A HR-pQCT Study

Jacob Frølich<sup>1,2,4</sup> · Stinus Hansen<sup>2</sup> · Laura Al-Dakheel Winkler<sup>1,2</sup> · Andreas K. Andresen<sup>3</sup> · Anne Pernille Hermann<sup>2</sup> · René K. Støving<sup>1,2</sup>

weight bearing vs non-weight bearing bones



*Calcif Tissue Int 2017*

### Fractures in Patients with Anorexia Nervosa, Bulimia Nervosa, and Other Eating Disorders—A Nationwide Register Study

Peter Vestergaard,<sup>1\*</sup> Charlotte Emborg,<sup>2</sup> René K. Støving,<sup>3</sup> Claus Hagen,<sup>3</sup> Leif Mosekilde,<sup>1</sup> and Kim Brixen<sup>3</sup>

1977 - 1998  
AN n = 2149 (24,555 person years)

*IJED 2002*

### Fractures in anorexia nervosa

Relative risk: high  
Absolute risk: strongly age-dependent

can fractures be prevented pharmacologically?

- Estrogen
- Bisphosphonate
- Parathyroid hormone (PTH)
- Denosumab (monoclonal antibody)

Effects of an Oral Contraceptive (Norgestimate/Ethinyl Estradiol) on Bone Mineral Density in Adolescent Females with Anorexia Nervosa: A Double-Blind, Placebo-Controlled Study

Gary R. Strokosch, M.D.<sup>a</sup>, Andrew J. Friedman, M.D.<sup>b</sup>, Shu-Chen Wu, Ph.D.<sup>c</sup>, and Marc Kamin, M.D.<sup>d,\*</sup>

- RCT n=112
- age 11 – 17 y
- mean BMI 17.7
- 13 cycles x 28 days
- Dropouts 21 + 13
- BMD (g/cm<sup>2</sup>) +0.021 vs +0.017 (NS)
- BMI +1.5 vs +1.1 (NS)

*J Adolesc Health 2006*

Effects of an Oral Contraceptive (Norgestimate/Ethinyl Estradiol) on Bone Mineral Density in Adolescent Females with Anorexia Nervosa: A Double-Blind, Placebo-Controlled Study

Gary R. Strokosch, M.D.<sup>a</sup>, Andrew J. Friedman, M.D.<sup>b</sup>, Shu-Chen Wu, Ph.D.<sup>c</sup>, and Marc Kamin, M.D.<sup>d,\*</sup>

**no evidence for oral contraceptives**

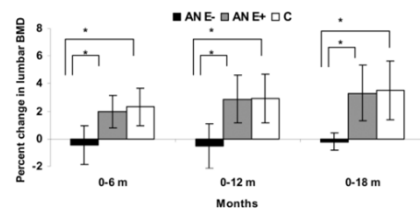
*J Adolesc Health 2006*

Physiologic Estrogen Replacement Increases Bone Density in Adolescent Girls with Anorexia Nervosa

- RCT n=110 AN + 40 C
- 18 months
- age 16.5±0.2 y
- BMI 17.4 ± 0.1 (% IBW 84.6 ± 0.6)

*Misra, JBMR 2011*

Physiologic Estrogen Replacement Increases Bone Density in Adolescent Girls with Anorexia Nervosa



*Misra, JBMR 2011*

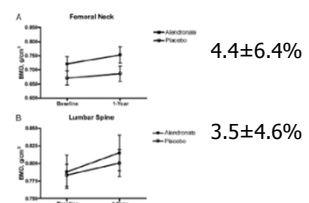
Physiologic Estrogen Replacement Increases Bone Density in Adolescent Girls with Anorexia Nervosa

**Transdermal estrogen replacement might be beneficial in adolescents with minor weight loss**

*Misra, JBMR 2011*

Alendronate for the Treatment of Osteopenia in Anorexia Nervosa: A Randomized, Double-Blind, Placebo-Controlled Trial

- n= 32, 12 months
- mean age 17 y
- BMI 16.3 ± 1.1

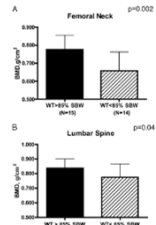


*Golden, JCEM 2005*



**Alendronate for the Treatment of Osteopenia in Anorexia Nervosa: A Randomized, Double-Blind, Placebo-Controlled Trial**

- treatment 1 y
- n= 32
- mean age 17 y
- BMI 16.3 ± 1.1



Strongest determinant: BW+8.7 kg +3.6 kg

Golden, JCEM 2005

**Alendronate for the Treatment of Osteopenia in Anorexia Nervosa: A Randomized, Double-Blind, Placebo-Controlled Trial**

**No evidence for bisphosphonates  
Strong evidence for weight gain**

Golden, JCEM 2005

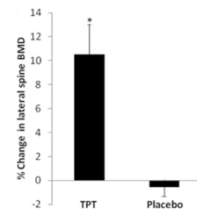
bisphosphonates concern

**unique pharmacokinetic:**

- stored in bone tissue for years
- released into the blood
- pass placenta

**Teriparatide Increases Bone Formation and Bone Mineral Density in Adult Women With Anorexia Nervosa**

n= 21  
6 months  
Age 47 ± 2  
BMI 17.1 ± 0.4



Fazeli, JCEM 2014

**Teriparatide Increases Bone Formation and Bone Mineral Density in Adult Women With Anorexia Nervosa**

**preliminary evidence for PTH in middle-aged women with mild underweight**

Fazeli, JCEM 2014

Case report:

**Use of Denosumab in a Patient with Chronic Anorexia Nervosa and Osteoporosis**

- 29 y, 17-year history, BMI 15
- heel bone fracture
- treated for 3 y
- well tolerated

Jamieson, JAMA 2016

**Aim not increase in BMD but fracture prevention.**

**So far, only one evidence based treatment:**

## Take Home Messages

- High risk patients:  
start low advance slow is *not* urban legend
- In hypokalemia: avoid licorice
- Osteoporosis cannot be diagnosed solely by DXA