Vitamin deficiencies and requirements in bariatric surgery

Thomas Bøhmer and Erlend T Aasheim

Ernæringslaboratoriet,
Oslo University Hospital, Aker
Biliopancreatic diversion (N=2241) operated through 21 years år (Scopinaro):

- Weight reduction 75% of overweight
- 100% normalisation of blood sugar and cholesterol
- Bone demineralization increasing up to 4 y.
- Calcium and vit D supplementation needed
- Neurological complications can be prevented by B-vitamins
- 3% proteinloss, change the length of the bypass

Økning av antall operative inngrep for overvekt

Total
RYGP; gastrisk bypass,
AGB justerbar gastric binding,
BPD/DS; biliopancreatic diversion with duodenal switch.
Gastric bypass

85%

gastric pouch
≈ 25 ml

Duodenal switch

15%

laparoscopic surgery

sleeve created along 30-32 F tube

alimentary limb
150 cm  200 cm

biliopancreatic limb
50 cm  variable

common channel
variable  100 cm

Figures by Ole-Jacob Berge

Aasheim et al. Tidsskr Nor Laegeforen 2007; 127: 38-42
Causes for nutrient deficiencies after bariatric surgery

**Altered anatomy**
- Bypass of uptake site
- Biliary/pancreatic function
- Intrinsic factor (B12)
- Altered pH
- Intestinal transit speed
- Vomiting, diarrhea

**Low intake**
- Diet (meat intolerance)
- Not taking supplements
- Anorexia

**Interaction of factors**
- Zinc deficiency (vitamin A)
- Stomal ulcer, regained menses (iron)

Odstrcil, Elizabeth A. Am J Clin Nutr 2010;92:704
# Medical consequences of vitamin deficiencies.

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Deficiency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>*B1-tiamin-PP</td>
<td>Wernicke, dry beriberi, polyneuropathy</td>
<td>Transketolase, Bacterial overgrowth, tiamin. B-vit., Mg++</td>
</tr>
<tr>
<td>B2-riboflavin</td>
<td>Cheilosis, dermatitis,</td>
<td>blood measure</td>
</tr>
<tr>
<td>B6 pyridoxal-5-fo</td>
<td>Cheilos, seizures,</td>
<td>Homocysteinemi, serum assay</td>
</tr>
<tr>
<td>*Folate</td>
<td>Anemia, diarrhoea, MCV</td>
<td>Homocysteinemi, bakt. overgrowth</td>
</tr>
<tr>
<td>B12 cobalamin</td>
<td>Anemia, neurological</td>
<td>Homocysteinemi, MCV</td>
</tr>
<tr>
<td>*C-ascorbic acid</td>
<td>Scurvy, depression, arthritis</td>
<td>Peroxidative protection, 250 mg/d ?</td>
</tr>
<tr>
<td>*A-vit, retinol</td>
<td>Night blindness, zeroptalmia</td>
<td>Transport depends on Zn</td>
</tr>
<tr>
<td>*25-OH vit D</td>
<td>Reduced bone-muscle strength, Ca-upptake</td>
<td>To be evaluated over prolonged time</td>
</tr>
<tr>
<td>E-tocopherol/Lip.</td>
<td>Ataxia, peroxidative protection</td>
<td>Keeps lipid membranes reduced</td>
</tr>
<tr>
<td>K-vitamin</td>
<td>Bleeding</td>
<td></td>
</tr>
</tbody>
</table>
## Vitamin assays

<table>
<thead>
<tr>
<th>vitamin</th>
<th>tissue</th>
<th>analyte</th>
<th>method</th>
<th>manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>serum</td>
<td>retinol</td>
<td>HPLC</td>
<td>Bio-Rad</td>
</tr>
<tr>
<td>B1</td>
<td>blood</td>
<td>thiamin pyrophosphate</td>
<td>HPLC</td>
<td>In-house</td>
</tr>
<tr>
<td>B2</td>
<td>blood</td>
<td>flavin mononucleotide</td>
<td>HPLC</td>
<td>Chromsystems</td>
</tr>
<tr>
<td>B6</td>
<td>serum</td>
<td>pyridoxal-5’-phosphate</td>
<td>HPLC</td>
<td>Chromsystems</td>
</tr>
<tr>
<td>Folate</td>
<td>serum</td>
<td>folic acid</td>
<td>multianalyser</td>
<td>Boehringer</td>
</tr>
<tr>
<td>B12</td>
<td>serum</td>
<td>cobalamine</td>
<td>multianalyser</td>
<td>Boehringer</td>
</tr>
<tr>
<td>C</td>
<td>serum</td>
<td>ascorbic acid</td>
<td>micromethod</td>
<td>Zannoni</td>
</tr>
<tr>
<td>D</td>
<td>serum</td>
<td>25-hydroxyvitamin D</td>
<td>RIA</td>
<td>DiaSorin</td>
</tr>
<tr>
<td>E</td>
<td>serum</td>
<td>(\alpha)-tocopherol</td>
<td>HPLC</td>
<td>Bio-Rad</td>
</tr>
</tbody>
</table>
Surgery for Obesity

Colquitt JL et al. Cochrane Database Syst Rev 2009;CD 003641

Bariatric surgery: lack of rigorous studies

In a meta-analysis on bariatric surgery

< 5 % of studies were randomized controlled
< 2 % were high-quality

Which operation is best suited for the individual patient?
Aim of our studies in the obese patients:

1. Are vitamin reductions and deficiencies present before surgery?
2. Will surgery induce vitamin deficiencies?
3. Can these deficiencies be overcome and how?
Percentage of obese patients with inadequate vitamin status.

<table>
<thead>
<tr>
<th></th>
<th>Patients number</th>
<th>B1-tiamin</th>
<th>B12</th>
<th>C- ascorbic acid</th>
<th>D,25 OH-vit D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ernst B. 2009</td>
<td>&gt;89</td>
<td>0</td>
<td>18</td>
<td>-</td>
<td>25</td>
</tr>
<tr>
<td>Coupaye M. 2009</td>
<td>49</td>
<td>25</td>
<td>10</td>
<td>47</td>
<td>16</td>
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<tr>
<td>Flancbaum L. 2006</td>
<td>141</td>
<td>29</td>
<td>0</td>
<td>-</td>
<td>68</td>
</tr>
<tr>
<td>Madan AK. 2006</td>
<td>100</td>
<td>-</td>
<td>13</td>
<td>-</td>
<td>40</td>
</tr>
</tbody>
</table>
## Clinical status

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Obese</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 58</td>
<td>n = 110</td>
<td></td>
</tr>
<tr>
<td>BMI kg/m²</td>
<td>24 ± 3</td>
<td>45 ± 6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age years</td>
<td>39 ± 11</td>
<td>39 ± 10</td>
<td></td>
</tr>
<tr>
<td>Female sex %</td>
<td>52</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>Diabetes %</td>
<td>0</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Alcohol intake g/day</td>
<td>5.0 ± 5.6</td>
<td>1.4 ± 3.2</td>
<td>0.001</td>
</tr>
</tbody>
</table>

CRP, Hemoglobin, Triacylglycerols...

Significantly higher in patients than in controls

Vitamin status in morbidly obese patients (n = 110)

Vitamin B-6, C, D and E: low levels in 10 – 40% of patients
A, B-1, B-2, folate and B-12: normal levels in > 95%

Aasheim et al
Am J Clin Nutr 2008; 87: 362-9
Objective

Gastric bypass or duodenal switch
Compare changes in weight and vitamin status
until 1 year after operation of superobese.

Study design
Randomised controlled trial
Stratified for: age < 35 y,
BMI < 55
hospital

Oslo and Sahlgrenska University Hospitals

Patients (n = 60)
Inclusion criteria
BMI 50-60 kg/m²
age 20-50 years

Exclusion criteria
previous bariatric surgery
drug abuse, severe psychiatric illness
### Randomized study of laparoscopic bypass versus laparoscopic duodenal switch for superobesity

<table>
<thead>
<tr>
<th></th>
<th>gastric bypass</th>
<th>duodenal switch</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 31</td>
<td>n = 29</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>162 ±24</td>
<td>162 ±20</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>55 ±3</td>
<td>55 ±4</td>
</tr>
<tr>
<td>Age (years)</td>
<td>35 ±7</td>
<td>36 ±5</td>
</tr>
<tr>
<td>Women (%)</td>
<td>74</td>
<td>66</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>32</td>
<td>31</td>
</tr>
</tbody>
</table>
Follow-up

Supplements daily to all patients
- multivitamin 1 pill (≈ RDA intake)
- iron 100 mg
- vitamin \(D_3\) 800 IE
- calcium carbonate 1000 mg
- ursodeoxycholic acid 250 mg x 2 for 6 months

Gastric bypass patients only
- vitamin B12 1 mg i.m. every 3 months (Norway), or 1 mg p.o. daily (Sweden)

Clinical visits
- before surgery and 2, 6, and 12 months after surgery
Management of low vitamin levels after surgery

We aimed to observe "spontaneous" changes in vitamin status.

Therefore, we set the intervention cut-off below the lower reference limit:

- **Predefined cut-off:**
  - Reference interval: **no top-up supplement**
  - Low level: **top-up supplement**
  - Clinical symptoms
Top-up supplements were given

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Female controls</th>
<th>Lower limit before suppl.</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-1, (nmol/L)</td>
<td>99 ±19</td>
<td>55</td>
</tr>
<tr>
<td>B-6, (nmol/L)</td>
<td>46 ±24</td>
<td>11</td>
</tr>
<tr>
<td>Vit A, (umol/L)</td>
<td>1.9±0.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Vit 25-OH D, (nmol/L)</td>
<td>54 ±22</td>
<td>37</td>
</tr>
<tr>
<td>Vit E, (mmol/mmol*)</td>
<td>5.0±0.7</td>
<td>2.2</td>
</tr>
</tbody>
</table>

Top supplements were possibly discontinued after 4-6 w.

*Vit E/(cholesterol+triacylglycerols)

Water soluble vitamins mean (SE)

**Vitamin B-1**

- Duodenal switch
- Gastric bypass

2-factor repeated-measures ANOVA:
* $P < 0.05$ for change after surgery
† $P < 0.05$ for time × procedure interaction

**Vitamin B-2**

Normal range
Water soluble vitamins

mean (SE)

![Graphs showing changes in vitamin B-6 and vitamin C levels](image)

- **Vitamin B-6**: Mean levels increase over time, with a significant change after surgery.
- **Vitamin C**: Mean levels also increase, with a significant time × procedure interaction.

- **Duodenal switch**: Solid line and dots.
- **Gastric bypass**: Dashed line and triangles.

**Data**: Baseline, 2, 6, 12 months

**Statistical Tests**: 2-factor repeated-measures ANOVA,
* \( P < 0.05 \) for change after surgery
† \( P < 0.05 \) for time × procedure interaction

**Normal Range**: Baseline 20 – 60 µmol/L

---

**Notes**: Water soluble vitamins include vitamin B-6 and vitamin C.
Water soluble vitamins median (IQR)

- **folic acid**
  - Baseline: 10
  - 2 months: 15
  - 6 months: 20
  - 12 months: 25

- **vitamin B-12**
  - Baseline: 500
  - 2 months: 550
  - 6 months: 600
  - 12 months: 650

2-factor repeated-measures ANOVA:

- * P < 0.05 for change after surgery
- † P < 0.05 for time × procedure interaction
Concentrations of 25-OH vit D and PTH before and after operation mean ± SD

25-OH-vitamin D † *

PTH

2-factor repeated-measures ANOVA:
* $P < 0.05$ for change after surgery
† $P < 0.05$ for time × procedure interaction

Dietary supplement use %

- **multivitamins**
  - Baseline: Gastric bypass 10, Duodenal switch 80
  - 2 months: Gastric bypass 70, Duodenal switch 100
  - 6 months: Gastric bypass 80, Duodenal switch 60
  - 12 months: Gastric bypass 50, Duodenal switch 50

- **vitamin D and calcium**
  - Baseline: Gastric bypass 5, Duodenal switch 10
  - 2 months: Gastric bypass 20, Duodenal switch 80
  - 6 months: Gastric bypass 60, Duodenal switch 70
  - 12 months: Gastric bypass 80, Duodenal switch 90

- **iron**
  - Baseline: Gastric bypass 20, Duodenal switch 80
  - 2 months: Gastric bypass 80, Duodenal switch 20
  - 6 months: Gastric bypass 60, Duodenal switch 60
  - 12 months: Gastric bypass 40, Duodenal switch 40

- **top-up supplement**
  - Baseline: Gastric bypass 0, Duodenal switch 0
  - 2 months: Gastric bypass 10, Duodenal switch 50
  - 6 months: Gastric bypass 30, Duodenal switch 70
  - 12 months: Gastric bypass 50, Duodenal switch 90
Explanation for increased vitamin concentrations after surgery

1. Use of supplements

2. Less inflammation

![Bar chart showing the use of multivitamins over time](chart1.png)

![Graph showing c-reactive protein levels](chart2.png)
Vitamin A deficiency: malabsorptive surgery

3% night blindness after BPD
Fetal injuries: retinal defects, microphthalmia

Scopinaro, Surg Obes Relat Dis 2005

Aasheim, Am J Clin Nutr 2009; E-pub 13 May
Aasheim, Surg Obes Relat Dis 2008; 4: 685-6
Wernicke encephalopathy

Incidence 1 in 500?

- 90% persistent vomiting
- 50% intestinal obstruction
- 18% iv glucose
- 2% alcoholism

Wernicke occurred within 6 months of obesity surgery in 94%

**Suggested postoperative supplementation***

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Our use‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin mineral (RDA)</td>
<td>100-200 %</td>
</tr>
<tr>
<td>Cobalamin (B12)</td>
<td>1000 ug/m.</td>
</tr>
<tr>
<td>(i.m)</td>
<td>1000 ug/ i.m.every 3 m.</td>
</tr>
<tr>
<td>(oral)</td>
<td>350 -500 ug/d</td>
</tr>
<tr>
<td>Folate</td>
<td>&lt; 1000 mg/d</td>
</tr>
<tr>
<td>Additional elemental calcium</td>
<td>0.4 mg</td>
</tr>
<tr>
<td>citrate (RYGB)</td>
<td>carbonate</td>
</tr>
<tr>
<td></td>
<td>RYGB 1500-2000 mg/d</td>
</tr>
<tr>
<td></td>
<td>BPD/DS 1800-2400 mg/d</td>
</tr>
<tr>
<td>Iron</td>
<td>18-27 mg/d</td>
</tr>
<tr>
<td>Vit A</td>
<td>10 000 IU</td>
</tr>
<tr>
<td>Vit D</td>
<td>Vit D2 2000 IU</td>
</tr>
<tr>
<td>Vit K</td>
<td>300 ug</td>
</tr>
<tr>
<td>Ursodeoxycholic acid</td>
<td>250 mg x 2 for 6 months</td>
</tr>
</tbody>
</table>

Clinical visits before surgery, and 2, 6, 12 months after, yearly.

‡Aasheim et al. Am J Clin Nutr 2009;90:15-22
Proportion of patients (%) with low biomarker concentrations* of vitamins 1 year after operation

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>Gastric pass (n=31)</th>
<th>Duodenal switch(n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1-Hb(pmole/gHb)</td>
<td>0</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>B-2 (nmol/L)</td>
<td>3</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>B-6 (nmol/L)</td>
<td>16</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Folic acid (nmol/L)</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>B-12 (pmol/L)</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>C (mmol/L)</td>
<td>73</td>
<td>23</td>
<td>20</td>
</tr>
<tr>
<td>A (umol/L)</td>
<td>7</td>
<td>7</td>
<td>48</td>
</tr>
<tr>
<td>D (nmol/L)</td>
<td>33</td>
<td>26</td>
<td>33</td>
</tr>
<tr>
<td>E/Lipids (umol/mmol)</td>
<td>27</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

* Defined as below lower value for reference group
Proportion of patients (%) with low biomarker concentrations* of vitamins 5 years after operation GBP (449) and DS (42)

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Gastric bypass</th>
<th>Duodenal switch</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1-Hb (pmole/gHb)</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>B-2 (nmol/L)</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>B-6 (nmol/L)</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Folic acid (nmol/L)</td>
<td>0.7</td>
<td>0</td>
</tr>
<tr>
<td>B-12 (pmol/L)</td>
<td>2.0</td>
<td>18</td>
</tr>
<tr>
<td>C (mmol/L)</td>
<td>19</td>
<td>36</td>
</tr>
<tr>
<td>A (umol/L)</td>
<td>6.9</td>
<td>67</td>
</tr>
<tr>
<td>D (nmol/L)</td>
<td>18</td>
<td>25</td>
</tr>
<tr>
<td>E/Lipids (umol/mmol)</td>
<td>6.9</td>
<td>37</td>
</tr>
</tbody>
</table>

* Defined as below lower value for reference group

Eirik Aaseth Master thesis Oslo Universitet 2012
Our suggestion:

- Lifelong controle
- Gastric workup 2,6,12,24,36,48 (?)
- Hb, iron, TIBC, MCV, alb, CRP
- Nutritional analyses
  - B1,B6, Folate, B12, C,A,E,
  - 25(OH)- vit D, PTH, Ca++,Mg++
  - bone metabolism
  - zink
  - Urin Ca, Mg, creatinine (24 hours)
Conclusion:
Duodenal switch surgery will compared to gastric bypass cause:

• More pronounced weight reduction
• B1-deficiency more often the first month
• Vit A and D serum reductions 1, 5 years
• Hyperparathyreoidism, secondary more frequent
• Generally:
  – Vitamin conc. is reduced by inflammatory state
  – Reduced s-conc. # deficiency
• Patient compliance important to prevent deficiencies
• Two step operative procedure for suberobese (?)
Årsak til vekttap ved gastric bypass. malabsorbsjon, eller ?

14 måneder etter operasjon

Redusert matinntak 1418 ± 171 kcal

Malabsorbsjon 172 ± 60 kcal

Thank you

Aker Nutritional laboratory
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Jon Kristinsson
Carl Fredrik Schou
Ann Steen
S Hanvold

Kåre Birkeland

Sahlgrenska university hospital
Torsten Olbers
My Engstrøm
Sofia Bjørkman

Hospital of Vestfold
Jørnan Hjelmeseth
Rune Sandbu
Dag Hofsø
Malabsorptive procedures (BPD):
Checkup 1 month, every 3 months first year, every 6 months second year, annually thereafter

Lab tests are necessary to evaluate nutritional status and to adapt supplementation and drug treatment accordingly

Blood tests at 1, 4 and 12 months, thereafter annually:
liver function, complete blood cell count, vitamin B-12, 25-hydroxyvitamin D, PTH, bs-ALP, ferritin, kalsium, albumin, transferrin, creatinine, prothrombin time, urine

Lifelong daily vitamin and micronutrient supplementation (vitamins should be administered in a water-soluble form):
vitamin A, D, E and K; Ca citrate (total 2g/day)
**European guidelines: Gastric bypass**

**Lifelong follow-up after bariatric surgery**
Special care for potential nutritional deficiencies during rapid weight loss

**Gastric bypass:** Checkups after 1, 3, 6, 9, 12, 18, 24, 36, 48.. months

Prescribe **supplements** with vitamins and minerals

**Laboratory tests**
- Vitamin B-12, 25-hydroxyvitamin D, ferritin, calcium, PTH, albumin, magnesium, zinc (glucose, liver, kidney)

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**CLINICAL GUIDELINES**

Inter-disciplinary European guidelines on surgery of severe obesity

M Fried¹, V Hainer², A Basdevant³, H Buchwald⁴, M Deitel⁵, N Finer⁶, JWM Greve⁷, F Horber⁸, E Mathus-Vliegen⁹, N Scopinaro¹⁰, R Steffen¹¹, C Tsigos¹², R Weiner¹³ and K Widhalm¹⁴

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Int J Obesity 2007, p.569-77