Nutritional Pearls in IBD
(Needs, Primary Treatment, Maintain in Remission)

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Université Paris Sud
Pre test
Question 1

- Enteral nutrition as an induction therapy:

  1. Is the treatment of choice in children and teens

  2. Elemental is more efficient than polymeric

  3. Can be prescribed in patients with fistula and abscess

  4. Improves symptoms but not endoscopy
Question 2

- Enteral nutrition in CD

1. Should be hypercaloric and hyperproteic

2. Should be prescribed in patients with severe UC and toxic megacolon

3. Trace elements and vitamins should be added to the diet

4. Contra-indicated in patients with intestinal obstruction
Epidemiology
Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies

Ng, et al. Lancet 2018; 390:2769
Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies

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Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies

Ng, et al. Lancet 2018; 390:2769
Incidence of IBD and abdominal tuberculosis in immigrants from Bangladesh living in London (UK) (Am J Gastro 2004;99:1749)

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>UC</td>
<td>2.4</td>
<td>8.2</td>
<td>2.1 (0.9-3.9)</td>
</tr>
<tr>
<td>CD</td>
<td>2.3</td>
<td>7.3</td>
<td>2.5 (1.2-4.6)</td>
</tr>
</tbody>
</table>
Environmental factors suspected to have a role in IBD

- Perinatal infections
- Intestinal infections
- Listeria
- Mycobacteria
- Pseudomonas Fluorescens
- Adherent-invasive E Coli
- Yersinia
- Viruses (Norovirus)

- Smoking
- Appendectomy
- Hygiene
- Sunshine exposure
- Antibiotics, oral contraceptives NSAIDs, ipilimumab, ildelalisib
- No breast feeding
- **Diet**
  - Pollution
  - Stress
IBD: is it in the diet?
What is diet?

- **Food**
  - meat- fish- eggs
  - sugar
  - fat
  - dairy products
  - cereals – legumes
  - fruits - vegetables

- **Nutrients**
  - Macronutrients: Protein, Lipids, Carbohydrates
  - Micronutrients: Minerals, vitamins and trace elements
But also:

- Food patterns
- Additives, pollutants, heavy metals
- Cooking and conservation
- Snacking
-et.c…
Diet

IBD
Diet

IBD
EPIC database
diet and disease

- Nested case-control studies
  Incident validated cases of IBD matched with 4 controls
  n=360 000, 10 centres, 7 countries (Germany, Denmark, France, Italy, Netherlands, UK, Sweden)

- N=500 000 healthy volunteers, 23 centres in 10 countries
- Follow up by validated questionnaires validated since 1990: lifestyle, diet

E3N: A cohort study

Non Cases N = 67504

Prevalent IBD
N = 117

Incident IBD
N = 77

End of follow up

Am J Gastroenterol 2010; 105:2195–2201
Data on diet in E3N cohort

- Semi quantitative food frequency questionnaire (1993)

→ Estimated consumption in 208 food items/beverages (g/j)
+ Calculation of the corresponding energy and nutrient intakes

Validation: Lucas et al. 1995 (Livret); Van Liere et al. 1997 (Questionnaire)
### Associations between nutrients and IBD in large scale prospective studies

<table>
<thead>
<tr>
<th></th>
<th>IBD in EPIC</th>
<th>Nurse study</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Protein</td>
<td>CD in women</td>
<td>NA</td>
</tr>
<tr>
<td>Sugar</td>
<td>None</td>
<td>NA</td>
</tr>
<tr>
<td><strong>High n-6 (red meat, margarine, cooking oils)/Low n-3 Fatty acids</strong></td>
<td>UC</td>
<td>UC</td>
</tr>
<tr>
<td>Fiber (fruits, vegetables)</td>
<td>NA</td>
<td>CD</td>
</tr>
<tr>
<td>Vitamine D</td>
<td>CD (sunshine exposure)</td>
<td>CD (predicted level)</td>
</tr>
</tbody>
</table>

Food patterns and risk of IBD in the EPIC cohort (Racine et al. IBD 2015, in press)

• A priori: Mediterranean food score $1-2(0>9)$
  – Favorable: vegetables, legumes, fruits, cereals, fish and seafood
  – Unfavorable: meat, dairy products, ratio monounsaturated/saturated fat, alcohol

• A posteriori: food patterns by PCA in controls based upon 25 food groups $^3$

Mediterranean food score and IBD risk
(Racine IBD 2015, in press)

<table>
<thead>
<tr>
<th>Mediterranean score (0-9)</th>
<th>UC (n=256)</th>
<th>CD (n=117)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>Ref.</td>
<td>Ref.</td>
</tr>
<tr>
<td>3</td>
<td>1,19 (0,77-1,82)</td>
<td>0,95 (0,51-1,74)</td>
</tr>
<tr>
<td>4</td>
<td>1,45 (0,94-2,23)</td>
<td>1,26 (0,70-2,25)</td>
</tr>
<tr>
<td>5-6</td>
<td>1,19 (0,78-1,81)</td>
<td>0,61 (0,30-,1,24)</td>
</tr>
<tr>
<td>7-9</td>
<td>0,79 (0,48-1,32)</td>
<td>0,90 (0,45-1,77)</td>
</tr>
<tr>
<td>P trend</td>
<td>0,41</td>
<td>0,67</td>
</tr>
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Conditional logistic regression (matched upon age, sex, centre and inclusion date)
IRR adjusted upon energy intake, BMI and smoking
## Sugar and soda pattern and UC risk

*(Racine IBD 2015, in press)*

<table>
<thead>
<tr>
<th>Pattern «sweets and soda»</th>
<th>UC (n=256)</th>
<th>UC≥ 2 years (n=196)</th>
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<tbody>
<tr>
<td>Quintile 1</td>
<td>Ref.</td>
<td>Ref.</td>
</tr>
<tr>
<td>Quintile 2</td>
<td>0.75 (0.47-1.15)</td>
<td>1.00 (0.58-1.73)</td>
</tr>
<tr>
<td>Quintile 3</td>
<td>0.87 (0.55-1.36)</td>
<td>1.10 (0.65-1.85)</td>
</tr>
<tr>
<td>Quintile 4</td>
<td>1.06 (0.67-1.66)</td>
<td>1.24 (0.72-2.12)</td>
</tr>
<tr>
<td>Quintile 5</td>
<td>1.31 (0.85-2.02)</td>
<td>1.68 (1.00-2.84)</td>
</tr>
<tr>
<td><strong>P trend</strong></td>
<td>0.05</td>
<td>0.02</td>
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Conditional logistic regression (matched upon age, sex, centre and inclusion date)
IRR adjusted upon energy intake, BMI and smoking
**Interaction between vegetables and sugar/soda pattern**

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<th>Pattern «sweets and sodas»</th>
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<td>Vegetables &lt;median</td>
</tr>
<tr>
<td>Quintile 1</td>
<td>Ref.</td>
</tr>
<tr>
<td>Quintile 5</td>
<td>11,70 (3,65-37,51)</td>
</tr>
<tr>
<td>P heterogeneity</td>
<td>&lt;0,0001</td>
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Conditional logistic regression (matched upon age, sex, centre and inclusion date)
IRR adjusted upon energy intake, BMI and smoking
Interaction between vegetables and sugar/soda pattern

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Higher risk of UC in persons who eat a lot of sweets and sodas and a few vegetables

Conditional logistic regression (matched upon age, sex, centre and inclusion date)
IRR adjusted upon energy intake, BMI and smoking
Confounding factor

Diet

IBD
Experimental data
Western diet induces dysbiosis with increased *E. coli* in CEABAC10 mice, alters host barrier function favouring AIEC colonisation

Margarita Martinez-Medina,1,2,3 Jérémy Denizot,1,2 Nicolas Dreux,1,2 Frédéric Robin,1,2,4 Elisabeth Billard,1,2,5 Richard Bonnet,1,2,4 Arlette Darfeuille-Michaud,1,2,4,5 Nicolas Barnich1,2,5

Dietary-fat-induced taurocholic acid promotes pathobiont expansion and colitis in IL10−/− mice

Suzanne Devkota1, Yunwei Wang1, Mark W. Musch1, Vanessa Leone1, Hannah Fehlner-Peach1, Anuradha Nadimpalli1, Dionysios A. Antonopoulos2, Bana Jabri1 & Eugene B. Chang1

Diagram showing the relationship between diet, host, and gut microbes:
- **Diet**: Milk-derived saturated fat
- **Host**: ↑ Taurocholic acid
- **Gut microbes**: Growth of *Bilophila wadsworthia*

Flowchart illustrates:
- Wild-type mouse to Healthy gut
- Genetically susceptible mouse to Inflamed gut
Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome

Benoit Chassaing¹, Omry Koren², Julia K. Goodrich³, Angela C. Poole³, Shanthi Srinivasan⁴, Ruth E. Ley³ & Andrew T. Gewirtz¹

CMC: carboxymethylcellulose. P80: Polysorbate 80
• **Emulsifiers** increase intestinal permeability and depletes mucus in mice
• **Emulsifiers** increase intestinal permeability and depletes mucus in mice

Emulsifiers, ubiquitous in processed foods disturb host-microbiota interactions, resulting in low-grade inflammation. They might have promoted the increase in IBD.
Skepticism is the beginning of faith

Oscar Wilde
Modulen
IBD

Nutritional Management of Crohn's Disease

Nutritionally complete and balanced
Adaptable caloric density up to 1.5 kcal/ml
Neutral flavour for flexible use

Net Weight 400 g
Clinical data
Enteral nutritional therapy for induction of remission in Crohn’s disease (Narula, Cochrane Database Syst Rev 2018 Apr 1;4:CD000542)

• No difference between polymeric and
  – elemental
  – semi elemental,
  – low fat

• Higher remission rates with very low fat (<3g/d) and very low LCT diets
Enteral nutritional (EN) therapy for induction of remission in Crohn’s disease *(Narula, Cochrane Database Syst Rev 2018 Apr 1;4:CD000542)*

- EN vs corticosteroids

- Meta-analysis of 8 trials: 50% (111/223) remission with EN vs 72% (133/186) with steroids (RR 0.77, 95% CI 0.58-1.03)
  - Adults: 45% (87/194) vs 73% (116/158) (RR 0.65; 0.52-0.82)
  - Children: 83% (24/29) vs 61% (17/28) (RR 1.35; 0.92 to 1.97; significant in per protocol analysis)
Randomized controlled trial of enteral nutrition vs steroids in children with Crohn’s

Figure 3. Crohn’s Disease Endoscopic Index of Severity scores in the 2 groups of patients at baseline and at the follow-up evaluation (10 weeks after the beginning of therapy). *P < .001 vs CS group. **P < .001 vs baseline. Horizontal bars indicate mean value. □, Polymeric group; ■, CS group.
When prescribe enteral nutrition in Crohn disease?

- Children and teenagers
- Malnutrition
- Perioperative
- Complicated CD: fistula and abscess
- Short bowel syndrome (parenteral)
Enteral nutrition for maintenance of remission in Crohn’s disease

- Elemental vs polymeric: 58% (11/19) relapsed with elemental vs 57% (8/14) with polymeric diet (NS). More withdrawals in the elemental group.

- Elemental vs free diet: 35% (9/26) relapsed with elemental (half of energy intake) vs 64% (16/25) with free diet (RR 0.54, 95% CI 0.30 to 0.99).

- Elemental vs 6 MP: 38% (12/32) relapse with elemental vs 23% (7/30) with 6-MP group (NS).

- Polymeric vs mesalamine: 42% (18/43) relapse with polymeric vs 55% (22/40) with mesalamine (NS).
Enteral nutrition for maintenance of remission in Crohn’s disease

- Elemental vs polymeric: 58% (11/19) relapsed with elemental vs 57% (8/14) with polymeric diet (NS). More withdrawals in the elemental group

The efficacy and safety of enteral nutrition in quiescent CD is uncertain

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- Polymeric vs mesalamine: 42% (18/43) relapse with polymeric vs 55% (22/40) with mesalamine (NS)
Dietary intervention as induction therapy (16 weeks) in CD
(Limketkai BN, Cochrane Database Syst Rev. 2019)

- 18 RCTs, 1878 participants, endpoint: clinical remission

- Low microparticle diet: 23/52 vs 13/51 (NS)

- Symptoms-guided diet: 16/32 vs 0/19 (RR=20; 95%CI: 1.27-315.40). Follow up unclear

- Low calcium diet: 16/43 in clinical remission vs 12/40 (NS).
Dietary intervention as maintenance therapy (16 weeks) in CD
(Limketkai BN, Cochrane Database Syst Rev. 2019)

• Low refined carbohydrate diet: 176/264 relapsed vs 193/303 (NS)

• Symptoms-guided diet: 24/50 relapsed vs 40/48 (RR=0.53; 95%CI: 0.28-1.01)

• Low red and processed meat: 63/96 relapsed vs 75/118 at 48 weeks (NS)

• Alberta anti inflammatory diet; Carrageenan-free; Milk-free: NS
Crohn’s Disease Exclusion Diet is Equally Effective but Better Tolerated than Exclusive Enteral Nutrition for Induction of Remission in Mild to Moderate Active Paediatric Crohn’s Disease: A Prospective Randomized Controlled Trial


¹.Dalhousie University, Halifax, Canada, 2.University of Alberta, Edmonton Canada, 3.Schneider Hospital Israel, 4.Wolfson Medical Center Holon, 5.Meyer Hospital Haifa, Kaplan Hospital Rehovot, 6.Tel Aviv Medical Center, Tel Aviv, 7.HaEmek hospital Afula, French Hospital Nazareth, 9. Poriah hospital, Tiberias, 10. Hadassah Hospital, Jerusalem, 11.Tel Aviv University, 12. Mount Saint Vincent University, Halifax 13.Shaarey Zedek Hospital, Jerusalem
Week 6 Primary and Secondary Endpoints

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Tolerance</th>
<th>Good compliance</th>
<th>Response</th>
<th>Remission PCDAI≤10</th>
<th>Remission PCDAI≤7.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDED</td>
<td>97.5</td>
<td>82.5</td>
<td>85</td>
<td>80</td>
<td>75</td>
</tr>
<tr>
<td>EEN</td>
<td>73.7</td>
<td>76.5</td>
<td>85.3</td>
<td>73.5</td>
<td>58.8</td>
</tr>
</tbody>
</table>

p-values:
- Tolerance: p=0.002
- Good compliance: p=0.52
- Response: p=0.36
- Remission PCDAI≤10: p=0.51
- Remission PCDAI≤7.5: p=0.14
Sustained remission week 12

- PCDAI≤10: 70.00%
- PCDAI<10: 65.00%

CDED: EEN

P<0.01
Median Calprotectin over 12 weeks

CDED+PEN

Calpro Wk 0
Calpro Wk 6

P = 0.001
P = 0.002

P = 0.01
P = 0.026
In summary

• Epidemiological and experimental data suggest that western diet is associated with intestinal inflammation
• Enteral nutrition is an efficient induction treatment in CD
• CDED might maintain remission in CD
Post test
Question 1

- Enteral nutrition as an induction therapy:

1. Is the treatment of choice in children and teens
2. Elemental is more efficient than polymeric
3. Can be prescribed in patients with fistula and abscess
4. Improves symptoms but not endoscopy
Question 2

- Enteral nutrition in CD

1. Should be hypercaloric and hyperproteic

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3. Trace elements and vitamins should be added to the diet

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Merci de votre attention