New Findings in Nutritional Gastroenterology

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Talk Outline

- Does nutritional support improve outcome from critical illness?
- Can we lengthen short bowel, medically?
- The human microbiome: change your diet, change your cancer risk?
Does nutritional support improve outcome from critical illness?
Mortality is Higher with Malnutrition
Galanos et al. CCM 1997

3002 patients from 5 centers followed for 6 months

BMI is a predictor of survival in the ICU

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>62.0 ± 15.5</td>
</tr>
<tr>
<td>Number of comorbid conditions</td>
<td>2.1 ± 1.66</td>
</tr>
<tr>
<td>Number of prior admissions</td>
<td>1.2 ± 0.5</td>
</tr>
<tr>
<td>Acute Physiology Score (day 3)</td>
<td>41.1 ± 18.9</td>
</tr>
<tr>
<td>TISS (day 3)</td>
<td>28.1 ± 15.3</td>
</tr>
<tr>
<td>Body mass index</td>
<td>24.7 ± 7.2</td>
</tr>
<tr>
<td>Weight loss prior to admission (lbs)</td>
<td>17.2 ± 17.5</td>
</tr>
<tr>
<td>Albumin (day 3)</td>
<td>3.2 ± 0.7</td>
</tr>
<tr>
<td>Gender (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>57.0</td>
</tr>
<tr>
<td>Married (%)</td>
<td>52.5</td>
</tr>
<tr>
<td>Race (%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>79.3</td>
</tr>
<tr>
<td>Weight loss prior to admission (%)</td>
<td>58.9</td>
</tr>
<tr>
<td>Dead within 180 days (%)</td>
<td>48.0</td>
</tr>
<tr>
<td>Surrogate responses (%)</td>
<td>55.0</td>
</tr>
<tr>
<td>Cognitively impaired (%)</td>
<td>5.0</td>
</tr>
<tr>
<td>ARF/MOSF (%)</td>
<td>42.9</td>
</tr>
<tr>
<td>COPD/CHF/cirrhosis (%)</td>
<td>34.4</td>
</tr>
<tr>
<td>Cancer (%)</td>
<td>16.9</td>
</tr>
<tr>
<td>Coma (%)</td>
<td>5.7</td>
</tr>
<tr>
<td>BMI &gt;85th percentile (%)</td>
<td>9.0</td>
</tr>
<tr>
<td>BMI ≤15th percentile (%)</td>
<td>24.6</td>
</tr>
<tr>
<td>BMI 15–85th percentile (%)</td>
<td>36.2</td>
</tr>
<tr>
<td>BMI missing (%)</td>
<td>30.2</td>
</tr>
</tbody>
</table>

TISS, Modified Therapeutic Intervention Scoring System; ARF/MOSF, acute respiratory failure/multiple organ system failure; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; BMI, body mass index.

\(^a\)BMI categories as per the National Health and Nutrition Examination Follow-up Study (NHEFS)\(^2\) by gender and age group.
How soon should we start?

- Body stores: designed to support recovery without eating
- In health, you need to loose >40% of body weight before you die
- In severe illness, catabolism increases the rate of loss of protein stores: 2 weeks in average ICU pts, 11 days in necrotizing pancreatitis
- The importance of maintaining gut function

**BOTTOM LINE:** NUTRITION SUPPORT IS NEVER AN EMERGENCY, UNLESS BMI <15
Nutritional Support Literature is Full of Observational, Uncontrolled Trials

- People believe in the inherent powers of feeding
- No robust RCTs have been conducted comparing interventional feeding to no feeding in the ICU
- Uncontrolled trials suggested that energy deficit in the first week led to worse survival, fueling the belief that early feeding improved survival
Feeding Early: 20% dextrose, TPN Day 3 plus enteral to meet requirements

Feeding Late: 5% dextrose plus EN (PN after 7 days)
Results

Late feeders:
- less ICU infections p<0.008
- less cholestasis – p<0.001
- less ventilation – p<0.006
- less cost – p=0.04
Results

Late feeders:
less ICU infections p<0.008
less cholestasis – p<0.001
less ventilation – p<0.006
less cost – p=0.04
Adequate enteral protein intake is inversely associated with 60-d mortality in critically ill children: a multicenter, prospective, cohort study

Nilesh M Mehta,² ⁵* Lori J Bechard,⁴ ⁵ David Zurakowski,³ ⁵ ⁶ Christopher P Duggan,⁴ ⁵ and Daren K Heyland⁶

²Critical Care Medicine, Department of Anesthesiology, Perioperative and Pain Medicine, ³Department of Anesthesiology, Perioperative and Pain Medicine, and ⁴Center for Nutrition, Division of Gastroenterology, Hepatology and Nutrition, Boston Children’s Hospital, Boston, MA; ⁵Harvard Medical School, Boston, MA; and ⁶Kingston General Hospital, Kingston, Canada

In a prospective, multicenter, cohort study that included 59 pediatric intensive care units from 15 countries, 1245 consecutive children (age: 1 mo to 18 y) who were mechanically ventilated for >48 h were enrolled. The adequacy of enteral protein intake was measured, and the association with 60-d mortality was assessed.

The adequacy of enteral protein intake was significantly associated with 60-d mortality. Conclusions: Delivery of >60% of the prescribed protein intake is associated with lower odds of mortality in mechanically ventilated children.
Multicenter, randomized, controlled trial involving 1440 critically ill children to investigate whether withholding parenteral nutrition for 1 week (i.e., providing late parenteral nutrition) in the pediatric intensive care unit (ICU) is clinically superior to providing early parenteral nutrition.

Results: In the late PN group

- Mortality similar
- Less bloodstream infections
- Shorter ICU stay
- Higher likelihood of an earlier live discharge from the ICU at any time
- Shorter duration of mechanical ventilatory support
- Less dialysis
- Shorter duration of hospital stay
- Lower plasma LFTs and CRP
Initial Trophic vs Full Enteral Feeding in Patients With Acute Lung Injury

The EDEN Randomized Trial

context

The amount of enteral nutrition patients with acute lung injury need is unknown.

objective

To determine if initial lower-volume trophic enteral feeding would increase ventilator-free days and decrease gastrointestinal intolerances compared with initial full enteral feeding.

Figure 1. Enrollment, Randomization, and Follow-up

7968 Patients screened

6968 Excluded
1158 Chronic lung disease
1069 Unable to provide consent
778 Outside acute lung injury time window
775 Outside mechanical ventilation time window
710 Fatal underlying disease
631 Severe liver disease
503 Moribund
356 Refractory shock
288 Physician refusal
245 Intracranial hemorrhage
221 Total parenteral nutrition
214 Not committed to full support
182 Refused consent
152 Severe neuromuscular disease
144 Severe malnutrition
1218 Other

1000 Randomized

508 Randomized to receive trophic enteral feeding
508 Received trophic enteral feeding as randomized

492 Randomized to receive full enteral feeding
492 Received full enteral feeding as randomized

0 Lost to follow-up
1 Lost to follow-up (day 96)

508 Included in primary analysis
492 Included in primary analysis
with full feeding. There were no differences in infectious complications between the groups. Despite receiving more prokinetic agents, the full-feeding group experienced more vomiting (2.2% vs 1.7% of patient feeding days; \(P = .05\)), elevated gastric residual volumes (4.9% vs 2.2% of feeding days; \(P < .001\)), and constipation (3.1% vs 2.1% of feeding days; \(P = .003\)). Mean plasma glucose values and average hourly insulin administration were both higher in the full-feeding group over the first 6 days.
A Randomized Trial of Glutamine and Antioxidants in Critically Ill Patients

Daren Heyland, M.D., John Muscedere, M.D., Paul E. Wischmeyer, M.D., Deborah Cook, M.D., Gwynne Jones, M.D., Martin Albert, M.D., Gunnar Elke, M.D., Mette M. Berger, M.D., Ph.D., and Andrew G. Day, M.Sc., for the Canadian Critical Care Trials Group

1223 critically ill, ventilated ICU pts with MOF
2x2 factorial design to glutamine (30g/d), antioxidants (Se, Zn, b carotene, vit E, vit c), both or placebo
Start <24h
Primary Outcome 28d mortality
Glutamine Associated With Increased Mortality

Table 3. Clinical Outcomes in All 1218 Study Patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Glutamine</th>
<th>No Glutamine</th>
<th>P Value</th>
<th>Antioxidants</th>
<th>No Antioxidants</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death — no. of patients/total no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At day 28</td>
<td>198/611 (32.4)</td>
<td>165/607 (27.2)</td>
<td>0.05※</td>
<td>190/617 (30.8)</td>
<td>173/601 (28.8)</td>
<td>0.48</td>
</tr>
<tr>
<td>At day 14</td>
<td>157/611 (25.7)</td>
<td>129/607 (21.3)</td>
<td>0.07</td>
<td>154/617 (25.0)</td>
<td>132/601 (22.0)</td>
<td>0.23</td>
</tr>
<tr>
<td>In hospital</td>
<td>227/611 (37.2)</td>
<td>188/607 (31.0)</td>
<td>0.02</td>
<td>216/617 (35.0)</td>
<td>199/601 (33.1)</td>
<td>0.51</td>
</tr>
<tr>
<td>At 6 mo†</td>
<td>259 (43.7)</td>
<td>218 (37.2)</td>
<td>0.02</td>
<td>242 (40.4)</td>
<td>235 (40.6)</td>
<td>0.87</td>
</tr>
</tbody>
</table>
Nutrients provide not only the fuel for human cells but also the engine, the chassis, and the body of the car. Consequently, the feed must contain a balanced mixture of all these components and not an excess or deficiency of specific nutrients that might support fuel or structural needs.
Body Stores

- Water and electrolytes: days
- Water soluble vitamins: weeks
- Carbohydrate: days
- Fat soluble vitamins: months
- Fat: there is approximately 75,000 Kcals stored as fat, a quantity that would provide energy needs for approximately 6 weeks
- Protein: ??
Estimation of how long body protein stores will last without feeding

In Health
1. Suppose initial wt = 70 kg, Ht 1.7 m, BMI 24:
then muscle mass = 30 kg (~43% of body wt)
2. Suppose all the loss of protein is from muscle. This is a conservative assumption, but probably not far from what really happens
3. Suppose danger point is BMI = 15. Wt would then be 43.4 kg. If muscle mass is the same proportion of body wt, it would then be 18.6 kg; therefore loss of muscle = 11.4 kg
4. If muscle contains 20% protein, loss of protein = 2.28 kg
5. Calculated initial protein loss 91g/d, estimated final loss 30g/d, average 61g/d
8. From 4 and 5 above, this would take 2280/61 = 37 days

In severe necrotizing pancreatitis
1. Suppose initial wt = 70 kg, Ht 1.7 m, BMI 24:
then muscle mass = 30 kg (~43% of body wt)
2. Suppose all the loss of protein is from muscle. This is a conservative assumption, but probably not far from what really happens
3. Suppose danger point is BMI = 15. Wt would then be 43 kg. If muscle mass is the same proportion of body wt, it would then be 18.6 kg; therefore loss of muscle = 11.4 kg
4. If muscle contains 20% protein, loss of protein = 2.28 kg
5. Calculated protein loss in necrotizing pancreatitis 207g/d
8. From 4 and 5 above, this would take 2280/207 = 11 days

after Waterlow JC 2007
Who needs Nutritional Support?
Guidelines
Variables: Stores and Sickness

O'Keefe
2015
2388 patients with unplanned admission to ICU randomized to EN or PN
Start within 36h continued for up to 5 days
92% ‘no malnutrition’
Primary outcome: mortality at 30 days
Primary outcome: Mortality 33% vs 34%
TPN and Enteral Feeding both have their own specific indications and should not be applied interchangeably:

- If the gut is functional, **enteral feeding** should be used.
- If the gut cannot be used for *extended* periods of time, **TPN** should be used.
- If the patient is marasmic (BMI <15) and where enteral feeding results in diarrhea/malabsorption, short term supplemental **TPN plus enteral (or oral) feeding** is needed to break the vicious cycle.
Summary

- We have the tools to feed any patient in hospital
- Enteral feeding is safer and more effective than parenteral nutrition
- Both EN and PN have complications and must not be given unless benefits exceed risks
- Use body stores: There is no urgency for full EN or PN, unless BMI <15kg/m²
- Maintenance of gut function may reduce long term complications
Can we lengthen short bowel, medically?
Glucagon-like Peptide-2 (GLP-2)

- Principally secreted from terminal ileum and colon (L-cells)
- Slows gastric emptying
- Reduces gastric secretion
- Increases mucosal blood flow
- Stimulates growth of small and large intestine
- Increases epithelial proliferation
- Inhibits apoptosis

Teduglutide:
Recombinant Analogue of GLP-2

Phase 1 and 2 human studies:
- Increases villus height, crypt depth, plasma citrulline\(^2,3\)
- Increases fluid, energy, and electrolyte absorption in SBS patients\(^2,3\)

Randomised placebo-controlled trial of teduglutide in reducing parenteral nutrition and/or intravenous fluid requirements in patients with short bowel syndrome

P B Jeppesen,¹ R Gilroy,² M Pertkiewicz,³ J P Allard,⁴ B Messing,⁵ S J O’Keefe⁶

<table>
<thead>
<tr>
<th>Optimize PN</th>
<th>Stable PN Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 0 days</td>
<td>4 weeks</td>
</tr>
<tr>
<td></td>
<td>Teduglutide, 0.05 mg/kg/d (n = 32)</td>
</tr>
<tr>
<td></td>
<td>Teduglutide, 0.10 mg/kg/d (n = 32)</td>
</tr>
<tr>
<td></td>
<td>Placebo (n = 16)</td>
</tr>
</tbody>
</table>

26 centers screened 139 patients to randomize 84 patients
## Primary Endpoint Result

### ITT Population

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 16)</th>
<th>Low Dose (n = 35)</th>
<th>High Dose (n = 32)</th>
<th>Total (n = 83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonresponder</td>
<td>15 (93.8%)</td>
<td>19 (54.3%)</td>
<td>24 (75.0%)</td>
<td>43 (64.2%)</td>
</tr>
<tr>
<td>Responder</td>
<td>1 (6.3%)</td>
<td>16 (45.7%)</td>
<td>8 (25.0%)</td>
<td>24 (35.8%)</td>
</tr>
<tr>
<td>Difference from placebo for % Responders</td>
<td>39.46%</td>
<td>18.75%</td>
<td>29.5%</td>
<td></td>
</tr>
<tr>
<td>95% CI for difference</td>
<td>(12.77%, 57.66%)</td>
<td>(–9.28%, 38.20%)</td>
<td>(5.2%, 42.6%)</td>
<td></td>
</tr>
<tr>
<td>(P)-value for Difference</td>
<td>0.01</td>
<td>0.14</td>
<td>0.04</td>
<td></td>
</tr>
</tbody>
</table>

Before

3 months

6 months

1 month after
Last Visit: 6 Months
Teduglutide Reduces Need for Parenteral Support Among Patients With Short Bowel Syndrome With Intestinal Failure

PALLE B. JEPPSENE,* MAREK PERTKIEWICZ,† BERNARD MESSING,* KISHORE IYER,§ DOUGLAS L. SEIDNER,* STEPHEN J. D. O’KEEFE,* ALASTAIR FORBES,** HARTMUT HEINZE,†† and BO JOELSSON§§

*Department of Medical Gastroenterology, Rigshospitalet, Copenhagen, Denmark; †Department of General Surgery and Clinical Nutrition, Warsaw, Poland; ‡Hospital Beaujon Service de Gastroenterologie et Assistance Nutritive, Clichy, France; §Mount Sinai Medical Center, New York, New York; †Vanderbilt University Medical Center, Nashville, Tennessee; *University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; **University College London, London, UK; ††Nycomed, a Takeda Company, Nycomed GmbH, Konstanz, Germany; and §§NPS Pharmaceuticals, Bedminster, New Jersey

See Covering the Cover synopsis on page 1403; see editorial on page 1416.

Keywords: Clinical Trial; Glucagon-Like Peptide 2; Gastrointestinal Disorder; Therapy.

Watch this article’s video abstract and others at http://tiny.cc/j026c.

In this multinational, multicenter, randomized, double-blind, placebo-controlled, parallel-group, 2-stage, phase 3 study (Figure 1), patients were recruited from 27 sites in 10 countries across Europe and North America. Stage 1 consisted of a screen-
RESULTS:
Primary Efficacy Endpoint – Responder Rate

Statistical Test, Cochran-Mantel-Haenszel

\[ P = .002 \]

Teduglutide (n = 43):
63% (n = 27)

Placebo (n = 43):
30%

Overall Conclusions

- Both GH and GLP-2 analogues have the potential to enhance ‘adaptation’ in the remnant intestine of patients with massive intestinal loss and intestinal failure dependent on lifelong IVs and PN
- GLP-2 analogues have the advantage that they are gut-specific
- Concern about long-term cancer risk due to enhancement of mucosal proliferation, potential exacerbation of obstructive and biliary complications in SB-IF patients
- Careful post-marketing follow-up studies indicated
Change Your Diet, Change Your Cancer Risk
African-African American Studies

- Africans rarely get colon polyps or cancer <5:100,000

- African Americans have the highest prevalence of colon cancer in the USA: >65:100,000

Epidemiology of Colon Cancer

<table>
<thead>
<tr>
<th>Increase Risk</th>
<th>Decrease Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red meat</td>
<td>Fiber</td>
</tr>
<tr>
<td>Animal fat</td>
<td>Vegetable</td>
</tr>
<tr>
<td>Processed meats</td>
<td>Calcium</td>
</tr>
<tr>
<td>Obesity</td>
<td>Fish oils</td>
</tr>
<tr>
<td>Inactivity</td>
<td>Antioxidants, selenium</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Folic acid</td>
</tr>
<tr>
<td>Cigarettes</td>
<td>Postmenopausal hormones</td>
</tr>
</tbody>
</table>

Colon cancer rates per country

Approximately 90% of GI cancers are due to differences in diet

Colon Cancer is a Westernized Disease

- It takes 1 generation to change

Le Marchand. Journal of the National Cancer Institute Monographs No. 26, 1999
The African Diet

- First recognized by Dennis Burkitt to be associated with a low incidence of non-infective colonic diseases, and particularly with colon cancer
- The traditional diet was rich in complex carbohydrates from grains, beans, and wild green vegetables and fruits, and low in meat and fat
- Fiber content was >50g/d

Burkitt, D.P., Epidemiology of cancer of the colon and rectum. Cancer. 1971
The Hadza’s average daily fiber intake is 75 to 100 grams, seven times the U.S. average, mostly from pulp and seeds of baobab fruits.
Samp and Beans, Mandela’s Favorite
Baseline African-American
The Western Diet

Grilled or fried meat
Fat
Carbohydrate
Alcohol
Preservatives
Fruit and vegies??
Fiber????????????
1. Colon cancer risk is determined by the effects of dietary residues on the microbiota, who produce metabolites that are either beneficial or harmful to the colonic mucosa.

2. The high risk of colon cancer in western populations is due to a lack of high fiber foods.
The Microbiota

- A living, vibrant mass of organisms within our body
- Metabolic rates similar to those of the liver
- Totally dependent on what we eat
- Synthesis and secretion of a wide range of bioactive molecules
- Intimate proximity to the gut epithelium
- In health, highly mutualistic, antineoplastic
- In disease, antagonistic, potentially carcinogenic
Diet and Colon Cancer


**Inflammatory and Carcinogenic**
- Ammonia: barrier function, mucus, mucosal permeability proliferation
- Branch chain fatty acids: inflammatory
- Aromatic amino acids: phenolics, indoles, p-cresol, N-nitrosoamines
- Hydrogen sulfide: inflammatory, DNA damage, genotoxic

**Cell metabolism:** energy supply
**Genetic-Epigenetic regulation:** histone deacetylase inhibition, miRNA, down-regulation of canonical Wnt-signaling
**Anti-proliferative:** p53, p21 activation, reduced cell cycling, apoptosis
**Immunomodulatory and anti-inflammatory:** GPR43, GPR109α activation, Treg activation of Foxp3 and IL-10 expression, NF-κB suppression
**Mucosal health and defence:** mucin synthesis, tight junctions, trefoil factors, antimicrobial peptides, heat shock proteins, transglutamase, β-glucuronidase activity
**Microbiota homeostasis:** phenolics, antioxidants

**FOOD**
- LIVER PANCREAS
- DIGESTION
- ABSORPTION

**BODY**
- mono di-saccharides, amino acids, fatty acids, vitamins, minerals, water, bile acids

**INDIGESTIBLE RESIDUES**
- BILE ACIDS
- PROTEIN
- FIBER, PLANT CELL WALLS, GLYCANS

**Deconjugation**
- 2β bile acids
- NH₃, phenolics, aromatics, H₂S, choline

**Degradation, Synthesis, Fermentation**
- Phytochemicals: phenolics, antioxidants
- Vitamins: folate, biotin, niacin, B12

**Short chain fatty acids:** Butyrate, acetate, propionate, CH₄

**CANCER RISK**
Humphreys et al. conducted randomized controlled cross-over study in healthy volunteers given either a high red meat diet (300g/d) or a high red meat diet plus resistant starch supplement for 4 weeks.

The high red meat diet increased rectal mucosal oncogenic miRNA (miR17–92 cluster) expression and cell proliferation, in association with a decrease in miR17–92 target gene transcript levels.

Importantly, all these effects were negated by increasing butyrogenesis through fiber supplementation (40g of butyrylated high amylose maize starch per day, of which 60% is resistant).

*Humphreys et al Cancer Prevention Research Research 2015*
Diet, microbiota, and microbial metabolites in colon cancer risk in rural Africans and African Americans\textsuperscript{1–4}

Is it the Diet?

African-American Diet Exchange
Fat, fibre and cancer risk in African Americans and rural Africans

Stephen J.D. O’Keefe¹, Jia V. Li², Leo Lahti³,⁴, Junhai Ou¹, Franck Carbonero⁵,†, Khaled Mohammed¹, Joram M. Posma², James Kinross², Elaine Wahl¹, Elizabeth Ruder⁶, Kishore Vipperla¹, Vasudevan Naidoo⁷, Lungile Mtshali⁷, Sebastian Tims³, Philippe G.B. Puylaert³, James DeLany⁸, Alyssa Krasinskas⁹, Ann C. Benefiel⁵, Hatem O. Kaseb¹, Keith Newton⁷, Jeremy K. Nicholson², Willem M. de Vos³,⁴,¹⁰, H. Rex Gaskins⁵ & Erwin G. Zoetendal³
The Dietary Switch

<table>
<thead>
<tr>
<th></th>
<th>Fat</th>
<th>Fiber</th>
</tr>
</thead>
<tbody>
<tr>
<td>Native Africans g/d</td>
<td>145</td>
<td>7</td>
</tr>
<tr>
<td>African Americans g/d</td>
<td>41</td>
<td>55</td>
</tr>
</tbody>
</table>
Biomarkers of Colon Cancer Risk Changed Within 2 Weeks of Change to an African or Western Diet
High fiber feeding in Americans was associated with a shift from correlations between Bacteroides and potential butyrate-producing groups (Roseburia intestinalis et rel. and Clostridium symbiosum et rel.) towards stronger co-occurrence patterns including Firmicutes that are typically associated with complex carbohydrate fermentation.

Africans had stronger co-occurrence patterns between the genus-level taxa when consuming their usual high fiber diet, which included butyrate producers Eubacterium rectale et rel. and Clostridium symbiosum et rel., and bacteria associated with complex carbohydrate utilization, for example Oscillospira guillermondii et rel. Reduction in fiber consumption led to opposite associations.
Global Analysis: Metabolome

OPLS-DA scores plots of $^1$H NMR fecal spectra obtained from African Americans (AA) and native Africans (NA) during the home environment period (HE) and post dietary intervention (DI).
Integration of the enzymes of bacterial groups identified by the Human Intestinal Tract Chip (HITChip), host metabolic enzymes, and fecal and urinary metabolites by $^1$H NMR.)

Africans after

African-Americans after
The microbiota behaves as a community wherein intermicrobial interaction strives to produce a metabolic phenotype that supports colonic health and function.

It has a genetically determined need for food residues derived from a **healthy balanced diet**.

Provision of an **imbalanced diet** leads to disturbance in structure and function, with unopposed production of metabolites that can induce inflammation and proliferation which increase risk of neoplasia.
Conclusions

- From epidemiological studies, we know that westernization of the diet leads to an increase in colon cancer within one generation.
- Our results show that a change in diet composition produces immediate effects on the metabolic phenotype of the colonic contents associated with reciprocal mucosal biomarkers of cancer risk.
- Our results suggest that current guidelines for the consumption of fiber-rich foods are too low and increasing the fiber to >50g/d in African Americans, and indeed in all populations consuming a western diet, is likely to have an immediate effect on colon cancer risk.
- They warn against westernization of the African diet, where suppression of butyrogenesis may lead to the rapid progression of chronic colonic inflammation to cancer.
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  UKZN, Faye Brouard RD

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- Jeremy Nicholson, James Kinross, Jia Li

deVoss Lab: Microbiology, Wageningen University, The Netherlands
- Erwin Zoetendal, Leo Lahti

Gaskins Lab: University of Illinois at Urbana: Genomic Biology
- Rex Gaskins, Gerardo Nava, Franck Carbonera

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deVoss: The Spinoza Award of the Netherlands Organization for Scientific Research, the ERC Advanced Grant 250172 (Microbes Inside) of the European Research Council and the Academy of Finland (Grant 141140).