Perinatal gastroenterology, microbiology, nutrition

Dept. Human Nutrition, University of Copenhagen

Winter School 2008-09:

Gastrointestinal tract in development of allergy and obesity
Pre- and probiotics - in early LIFE!

1) What is state-of-the-art within the field in question?
2) What are the hypotheses?
3) Which results have been achieved?
4) What are the most important areas to focus on?
5) What is the best way to use the results for prevention of allergy and/or obesity?

Winter School 2008-09:

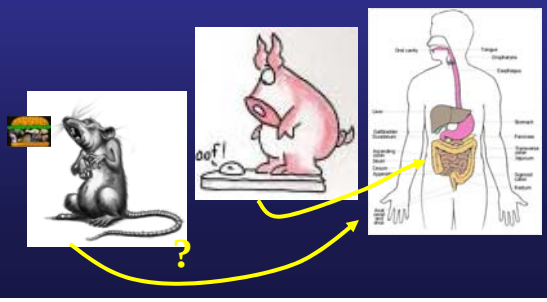
Gastrointestinal tract in development of allergy and obesity
Pre- and probiotics?

1) What is state-of-the-art within the field in question?
• Intense studies on time/dose/strains. A deep soup!
2) What are the hypotheses?
• That pre- and probiotics will positively affect gut flora
3) Which results have been achieved?
• A great pile of highly diverse, mainly clinical, results
4) What are the most important areas to focus on?
• The biological mechanisms of pre- and probiotic action
5) What is the best way to use the results for prevention of allergy and/or obesity?
• Make more combined cell, animal and human studies

Main conclusions from early LIFE work:

1) Initial colonization in at birth plays a major role for gut health (Gastroenterology, 2006)
2) Gut colonization depends on birth mode (caesarean/vaginal) (Am.J.Physiol. 2008)
3) Antibiotics at weaning greatly alters gut colonization/immunity (Br. J. Nutr. 2007)
4) Enteral versus parenteral nutrition greatly affects colonization (Am. J. Physiol. 2009)
5) Immunomodulatory diets affect immunity and colonization (J. Nutr., Gastroenterology 2009, submitted)
6) Milk lactose is a pre-biotic, nutritional fermentation is crucial (Am. J. Physiol. to be submitted)
7) Probiotics decrease inflammation via mucosal protection (J. Nutr., 2008)
8) Probiotics may be harmful for hypersensitive subjects (J. Ped. Gastr. Nutr., 2008)

Animal models in pre – and probiotic research?



What is a good model for gut-nutrition-microflora?

1) Similarity in key nutrition-relevant organs/tissues?
(gastrointestinal tract, liver, metabolism.....)

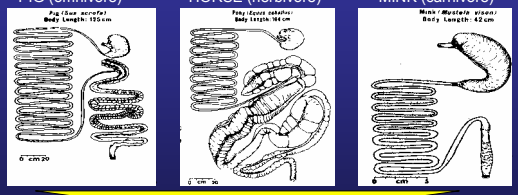
2) Similarity in natural dietary habits?
(herbivore, omnivore, carnivore, meal pattern, seasonal changes....)

3) Spontaneous nutrion-related diseases
(e.g. type-2, CHD, obesity, allergy, malabsorption, atherosclerosis...?)

4) Life cycle development & body composition
(maturity at birth, life span, nutritional transitions.....)

Gut anatomy - a key factor for species-specific nutrition & gut microflora

PIG (omnivore) | HORSE (herbivore) | MINK (carnivore)



Similar tissue/cell metabolism

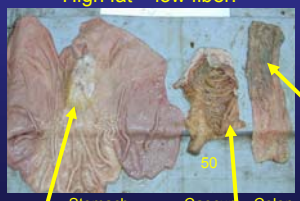
Nutrition/mrobiota-related gut disease:

DP Burkitt (1975):

Big fæces → Small hospitals

Small faeces → Big hospitals

High fat – low fiber:



Low fat – high fiber:

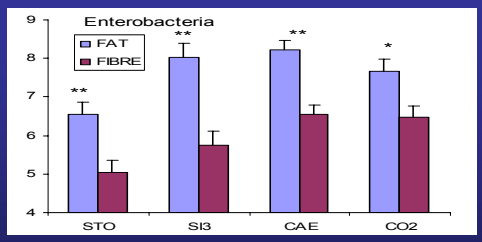
Stomach | Caecum | Colon

Stomach: Keratinization and mild erosive damage (early ulcer)

Caecum: Red/brown/yellow inflamed mucosal surface

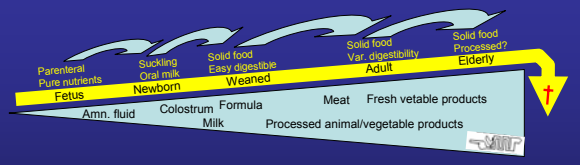
Colon: Sticky food material with much epithelial contact

Nutrition-induced gut microflora change?

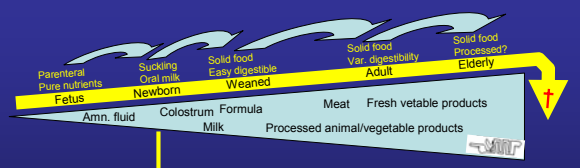


- Microbiology (more pathogens, sub-optimal fermentation)
- Patology/histology (inflammation, histology OK)
- Organ anatomy (smaller stomach, colon)
- Gene expression (reduc. ClCa-1 mRNA, 90 others OK)
- Mucosa physiology (OK digestive enzymes)

Developmental Nutrition & Microbiology



Developmental Nutrition & Microbiology



Preterm birth + milk + flora → NEC

- Probiotic diet?
- Prebiotic diet?
- Birth colonization?
- Immunosuppresives?
- Immunostimulants?
- Milk bioactives?

Problems of nutritional transition at birth:

Parenteral nutrition | **Enteral nutrition**

Birth

MIKROFLORA

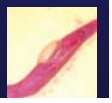
Child

Pig

Child | Pig

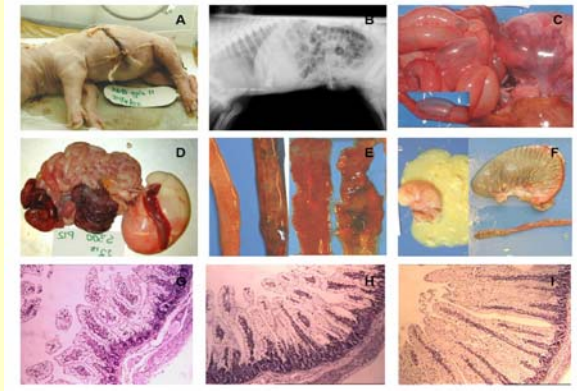
Gastroenterology, 130, 2006

Child

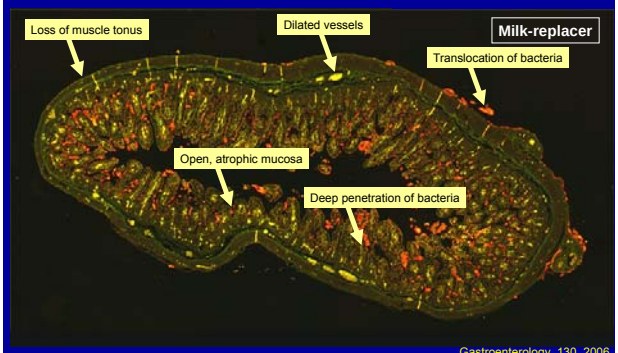


Pig

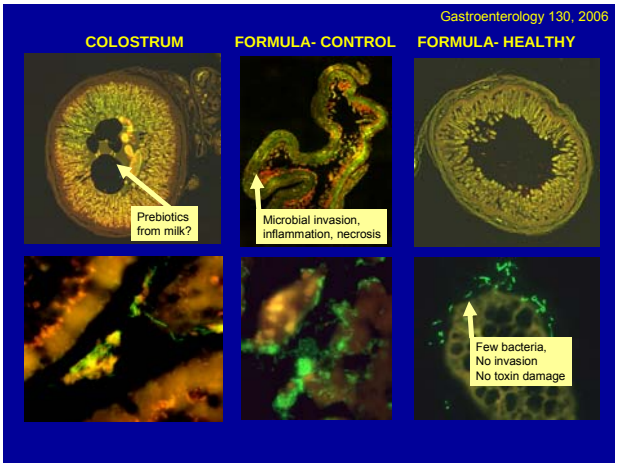
Necrotising enterocolitis in preterms



Milk og microflora in preterms:

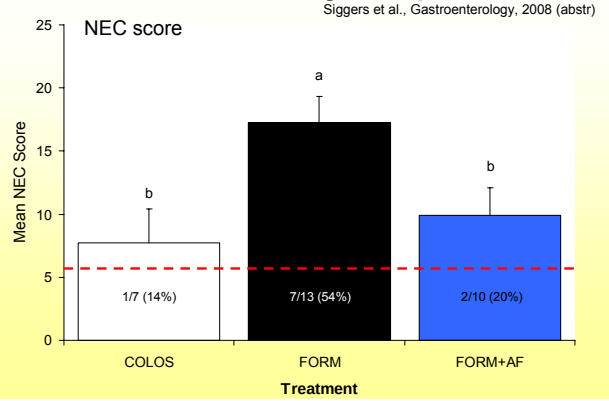


Gastroenterology, 130, 2006
Am.J.Physiol. 289, 2005
J. Nutr. 135, 2005

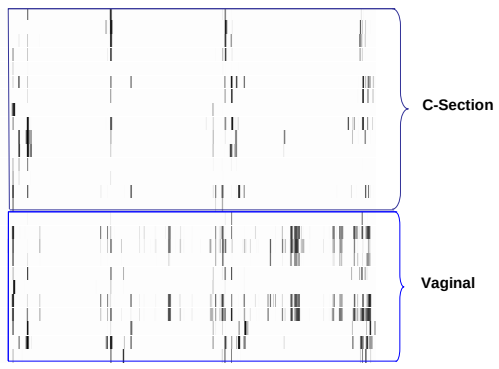


Amniotic fluid feeding after preterm birth

Siggers et al., Gastroenterology, 2008 (abstr)

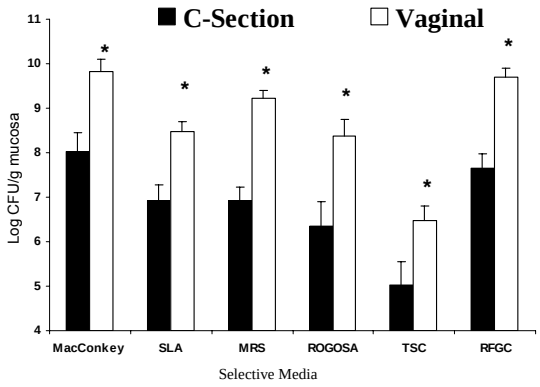


T-RFLP Bacterial Identification

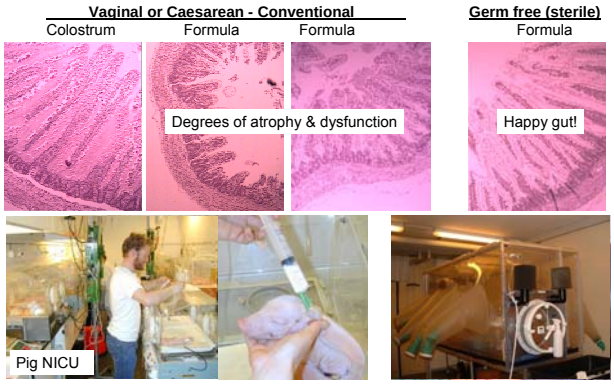


Vaginal Delivery = Significant Increase in Bacterial Diversity

Microbial load in colonic mucosa of preterm pigs



Is gut microflora crucial?

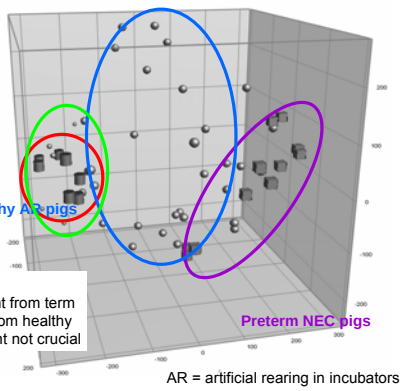


Am. J. Physiol. 294, 2008

Gastroenterology 130, 2006

Diet, prematurity & gut microbiology

PCA(Principal Component Analysis) of gut microbiology in newborn pigs



CONCLUSIONS:
- Preterm different from term
- NEC different from healthy
- Diet/environment not crucial

(Cilieborg et al., unpublished)

AR = artificial rearing in incubators

Bifidobacterium animalis
Lactobacillus acidophilus
Lactobacillus casei
Lactobacillus pentosus
Lactobacillus plantarum

10^{10}/d during TPN/formula

NEC score ↓
Structure ↑
Function ↑
Fermentation ↓
Clostridium ↓
Commensals ↑

UNIVERSITY OF COPENHAGEN — FACULTY OF LIFE SCIENCES

Department of Human Nutrition

Conclusions:

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