Probiotics in Childhood Disease

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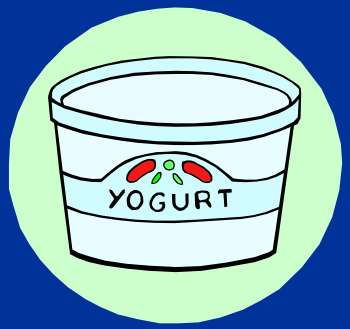


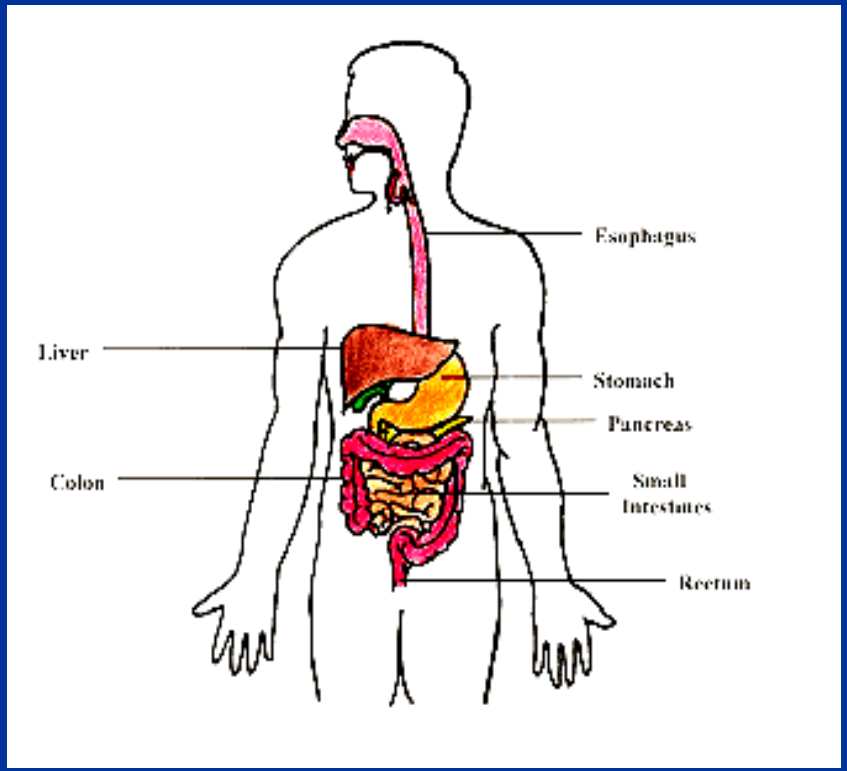
Outline

- Background
- Definitions
- Applications of Probiotics in Children
- Practical Issues
- Safety Concerns

History

- 1906 – Tissier noted that stool colonized with Bifidobacteria had a protective effect against diarrhea.
- 1908 – Metchnikoff noted Bulgarian peasants that lived longest consumed sour milk.

Colonization



- 10^{13} human cells in the body
- 10^{14} microbial cells in the body
- Diversity of cells and microbes

Early Colonization is Important

- GI tract is sterile at birth
- Colonized at birth

- Primes the GI tract immune system
- Differs:
  - breastfed vs. formula fed infants
  - caesarian section vs. vaginal delivery

Microflora

- Your bacterial flora is as unique as your fingerprint.

Prebiotics

- **Prebiotics:**
  - **“Non-digestible food ingredients (specific dietary fibres) that beneficially affect the host by selectively stimulating the growth and/or activity of one of more limited number of bacteria in the colon and thus improve host health” (Gibson & Roberfroid, 1995).**

Prebiotic Sources

psyllium

Chicory root

inulin

Probiotics: “Pro-life”

- “Live microorganisms (bacteria or yeast) which, once ingested in sufficient quantity, have functional and beneficial effects on the health of the host.” (FAO/WHO, 2001)

Bifidobacteria

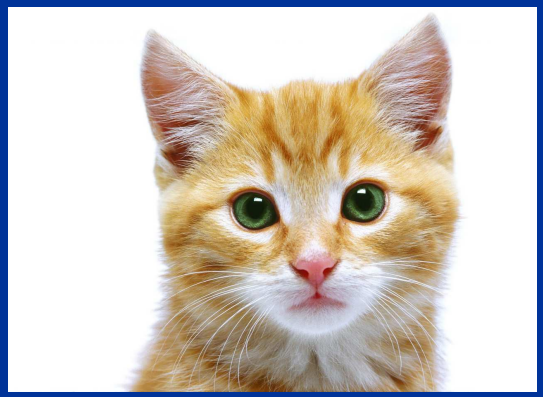
Lactobacillus

Types of Probiotics

Lactobacillus Species	*Bifidobacterium* Species	*Saccharomyces* Species	*Escherichia coli* Species
L. acidophilus *L. casei* *L. fermentum* *L. gasseri* *L. johnsonii* *L. lactis* *L. paracasei* *L. plantarum* *L. reuteri* *L. rhamnosus* *L. salivarius*	*B. animalis* *B. bifidum* *B. breve* *B. lactis* *B. longum*	*S. boulardii*	*E. coli Nissle 1917*

Strain is Important

E. coli **Nissle 1917 vs.** ***E. coli*** **0157:H7**



Same species, different strain = different performance!

Synbiotic

- Synbiotic:
  - The combined use of prebiotics and probiotics.

+

Bifidobacteria

Inulin

Probiotic Bacteria in Dietetic Products for Infants: A Commentary by the ESPGHAN Committee on Nutrition

ESPGHAN Committee on Nutrition: *Carlo Agostoni, †Irene Axelsson, ‡Christian Braegger, §Olivier Goulet, ‖Berthold Koletzko, #Kim F. Michaelsen, **Jacques Rigo, ††Raanan Shamir, ‡‡Hania Szajewska, §§Dominique Turck, and ‖‖Lawrence T. Weaver

Journal of Pediatric Gastroenterology & Nutrition (2004)

- **Level of Evidence: C**
  - **There is a lack of published evidence that indicates the long term clinical benefit of using formulas supplemented with probiotics.**
  - **In addition, there is a lack of safety data.**

Probiotics in infants for prevention of allergic disease and food hypersensitivity (Review)

Osborn DA, Sinn JK

Cochrane Database of Systematic Reviews, 2007, Issue 4

- **Level of Evidence: C**
  - **There is insufficient evidence to recommend the addition of probiotics to infant feeds for the prevention of allergic disease or eczema.**

Probiotics for treating infectious diarrhoea (Review)

Allen SJ, Okoko B, Martinez E, Gregorio G, Dans LF

Cochrane Database of Systematic Reviews, 2003, Issue 4

- **Level of Evidence: A**
  - **Probiotics appear to be a useful adjunct therapy for treating acute infectious diarrhea in adults and children.**
  - **Probiotics reduced the duration of diarrhea by about 30 hours and decreased stools by 1.5 hours/day.**
  - **Lactobacillus *rhamnosus* GG**

Probiotics for the prevention of pediatric antibiotic-associated diarrhea (Review)

Johnston BC, Supina AL, Ospina M, Vohra S

Cochrane Database of Systematic Reviews, 2007, Issue 2

- **Level of Evidence: A**
  - **The current data is promising, but it is premature to routinely recommend probiotics for the prevention of AAD in children.**
  - ***Lactobacillus GG* and *S. Boulardii* strains administered at a dosage of between 5 – 40 billion cfu/day appeared most effective.**

Probiotics for prevention of necrotizing enterocolitis in preterm infants (Review)

AlFaleh K, Bassler D

Cochrane Database of Systematic Reviews, 2008, Issue 1

- **Level of Evidence: A**
  - **Enteral supplementation of probiotics reduced the risk of severe NEC and mortality in preterm infants. The analysis supports a change in practice in premature infants >1000 g at birth.**

Cancer?

Level of Evidence: D

- No trials in children
- Prevention Radiation Induced Diarrhea
  - Pelvic radiation - VSL #3 (Delia et al, 2007)
  - Pelvic radiation - Lactobacillus acidophilus (Marteau et al, 2001)
- Prevention of Colon Cancer
  - Lactobacillus BB12 and GG with inulin (Rafter et al., 2007)

Yogurt

- Two starter cultures common to all yogurt - *Streptococcus thermophilus and Lactobacillus bulgaricus*
- Other species are added after the fermentation process.
- Studies using yogurt show promising health benefits.

Adolffson et al. (2004)

Yogurt

- Proven Health Benefits:
  - Diarrheal disease in children
  - Therapeutic effects in IBD
  - Constipation
  - Lactose Intolerance

Yogurt

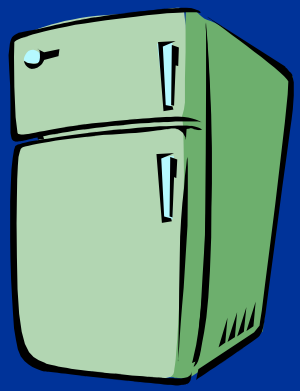
Bifidobacterium lactis DN-173 010

***L. casei* DN-114 001**

Dosage & Administration

- Formulations are administered orally either in capsule, powder or drop form.
- A daily dose of 10^9 to 10^{10} (one to ten billion) colony forming units (cfu) of viable bacteria are needed for health effects (Sanders et al, 1996).
- No known reports of toxicity associated with exceeding dose.
- Probiotics do not permanently adhere to the intestinal cells and must be taken long term.

Storage



- Keep out of heat and light.
- After opening, keep away from moisture.
- Keep refrigerated to prolong shelf life.
- Check expiration dates.

Culturelle®

- *Lactobacillus casei* GG
- Guaranteed 10 billion cfu/capsule
- Dosage: 1 package/day
- www.culturelle.com

VSL#3®

- Mixture of 8 different strains of probiotic bacteria
- 450 billion cfu/packet
- Dosage: 1-4 packets/day
- Available from: http://www.seaford.ca/SiteProducts.aspx

Florastor®

- *Saccharomyces boulardii* lyo
- 250 mg/package = 5 billion cfu)
- Dosage: 1-2 packages/day
- Available from most drug wholesalers

Probiotic Safety

- High risk patients:
  - Central venous catheters
  - Artificial heart valves
  - Low WBC count
  - ELBW infants
  - HIV infected patients
  - Transplant patients
  - Severely malnourished
  - Autoimmune disorders

Conclusion

- Probiotics have great potential in pediatrics.
- Scientific evidence is increasing yearly.
- Future work needs to focus on strain, dosage and mode of administration.
- More research is needed!

Royal University Hospital

Thank–you!

University of Saskatchewan