PREBIOTICS & PROBIOTICS

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What we already know ......

Functional Foods

- foods that provide a health benefit beyond the traditional nutrients it contains.....

*American Dietetics Association, 1995*

- specific minerals, vitamins, fatty acids, dietary fiber or bioactive substances such as phytochemicals, antioxidants, probiotics and prebiotics etc.
Microbiology turns inwards

Human Genome project and Meta Hit project reveals that the gut micro flora has more than 1000 species and 100 trillion organisms....

Metabolic activity of the gut flora is like a virtual organ within an organ......
The Gut Microbiota and its influence on health

<table>
<thead>
<tr>
<th>Protective functions</th>
<th>Structural functions</th>
<th>Metabolic functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogen displacement</td>
<td>Barrier fortification</td>
<td>Control IEC differentiation and proliferation</td>
</tr>
<tr>
<td>Nutrient competition</td>
<td>Induction of IgA</td>
<td>Metabolize dietary carcinogens</td>
</tr>
<tr>
<td>Receptor competition</td>
<td>Apical tightening of tight junctions</td>
<td>Synthesize vitamins e.g., biotin, folate</td>
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<tr>
<td>Production of anti-microbial factors e.g., bacteriocins, lactic acids</td>
<td>Immune system development</td>
<td>Ferment non-digestible dietary residue and endogenous epithelial-derived mucus</td>
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<td></td>
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<td>Ion absorption</td>
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<td>Salvage of energy</td>
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</table>

Commensal bacteria

Dietary means for the Restoration of the gut microflora

**Probiotics**

“Probiotics are live microorganisms, which, when administered in adequate amounts, confer a health benefit on the host.” (FAO/WHO 2002)

**Prebiotics**

*Prebiotics are non-digestible food ingredients that have a beneficial effect through their selective metabolism in the intestinal tract.* G.R. Gibson et al. (2004)

**Synbiotics:** Combination of Prebiotics and Probiotics
Prebiotic & Probiotic Concept

**PROBIOTICS**
- Intestinal Microbiota
  - Live Bacteria
  - Exogenous Bacteria
- Barrier Function
  - Suppression of Pathogenic Bacteria
  - Immune Function

**PREBIOTICS**
- Endogenous Bacteria
- Non-absorbable oligosaccharides
Characteristics of a Prebiotic

- Resistant to gastric acidity and hydrolysis by mammalian enzymes and GI absorption
- Can be fermented by intestinal micro flora
- Selectively stimulates the growth and/or activity of intestinal bacteria associated with health and well being
Prebiotics

- Lactulose
- Inulin type fructans
- Trans Galacto oligosaccharides

**OTHER PREBIOTICS**

- Poly dextrose
- Soy bean Oligosaccharides
- Lacto Sucrose
- Iso malto oligosaccharides
- Glucans
- Xylo oligosaccharides

**MISCELLANOUS**

- Pectic Oilgo saccharides
- Manno oligosaccharides
Prebiotic – Mechanism of action

- Changes in composition and functionality of the microbiota
- Selective stimulation of beneficial bacteria
- Facilitating competitive exclusion of pathogens
- Immunomodulation and enhancing host defense
Evidence for the efficacy of Prebiotics

- In-vitro Studies
- Animal Studies
- Observational Human Studies
  - Experimental Human Studies
    * Randomized Controlled Studies
    * Other types of trials
Clinical Application of Prebiotics

- Inflammatory Bowel Disease
- Antibiotic Associated Diarrhoea
- Traveller’s diarrhoea
- Calcium absorption and bone health
- Colon cancer
Prebiotic Products

Ecomos (Prebiotic poultry food supplement – Polchem Hygiene Labs.)

Naturon FOS (Sugar free prebiotic syrup – FOS – Agron India Pvt. Ltd.)

Stimup Flora (Probiotic and Prebiotic capsule – Naticon Research Labs)

ALOE MAXim – Aloevera Juice (Aloe Juice, Fenugreek Fiber, Prebiotic Oligosaccharides, Vit- C – Prist Herbochem)

FOS (Superior quality Fructo Oligo Sacharide: FOS – high fibre – Arun & Co.)
Changing Perception on Probiotics

- **Low dose food supplement**
  - Inactive
  - e.g. yoghurts

- **Old generation**
  - Not scientifically backed
  - Doubtful efficacy
  - e.g. yeast

- **New generation**
  - Scientifically backed
  - Efficacy demonstrated
  - Clear proof of concept

**WHO DEFINITION of Probiotics**
"Live microorganisms which, when administered in adequate amounts, confer a health benefit on the host"
What makes a probiotic???

- non pathogenic and non toxic
- contains a large number of viable cells
- exerts a beneficial effect when consumed
- has the capacity to metabolize and survive in the gut
- retains its viability during storage and use

<table>
<thead>
<tr>
<th>Genus</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive bacteria</td>
<td></td>
</tr>
<tr>
<td>Bacillus</td>
<td>coagulans, subtilis</td>
</tr>
<tr>
<td>Bifidobacterium</td>
<td>adolescentis, animalis, bifidum, breve, infantis, lactis, longum, thermophilum</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>faecium</td>
</tr>
<tr>
<td>Lactobacillus</td>
<td>acidophilus, brevis, casei, delbrueckii, fermentum, helveticus, johnsonii, lactis, paracasei, plantarum, reuteri, rhamnosus, salivarius</td>
</tr>
<tr>
<td>Lactococcus</td>
<td>lactis</td>
</tr>
<tr>
<td>Propionibacterium</td>
<td>freudenreichii</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>thermophilus</td>
</tr>
<tr>
<td>Gram-negative bacteria</td>
<td></td>
</tr>
<tr>
<td>Escherichia</td>
<td>coli</td>
</tr>
<tr>
<td>Yeasts</td>
<td></td>
</tr>
<tr>
<td>Saccharomyces</td>
<td>cerevisiae var. boulardii</td>
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</table>
Probiotic - Mechanism of action

Probiotics:
- **Potential obesity-related & infection benefits**
  - Blood endotoxin ↓
  - Improved mucosal integrity
    - Gram negative bacteria ↓
- **Pathogen inhibition**
  - Oral tolerance ↑
  - IgA secretion ↑
- **Constipation benefit**
  - Improved enterocyte energy source
  - Pathogen inhibition improved
- **Food tolerance**
  - Digestion of food antigens ↑

**Allergic response**
- IBD ↓
- Pro-inflammatory cytokines ↓
- Anti-inflammatory cytokines ↑

**Improved immune response to infections**
- Increased CD4+ and CD8+ T cells

**Pathogen adhesion**
- Mucin synthesis ↑
- Blocking adhesion sites

**Constipation benefit**
- Faecal microbiota mass ↑

**Risk of certain cancers**
- Binding or breakdown of carcinogens & toxins
- Bacteria and enzymes associated with carcinogen production
Clinical Applications of Probiotics

- Gastrointestinal disorders
  - Diarrhoea
  - Constipation
  - Irritable Bowel Syndrome
  - Inflammatory Bowel Disorder
- Prevention of allergic disorders
- Prevention of cancers
- Reduction of respiratory diseases
- Immune stimulation
- Vaginal diseases
- Possible role in Obesity and autism???
# Evidence for various indications

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<tr>
<th>Indication</th>
<th>Study Design</th>
<th>Conclusion</th>
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<tr>
<td>Acute Infectious Diarrhoea</td>
<td>63 RCT and quasi RCT with total of 8014 participants</td>
<td>Duration of diarrhoea was reduced by 25 hours. Risk of diarrhoea lasting 4 days or more by 59%. Probiotics appear to be safe and show beneficial effects in shortening the duration and reducing stool frequency.</td>
<td>Allen SJ et al 2010.</td>
</tr>
</tbody>
</table>
| Constipation                      | Systematic review of 5 RCT’s (n=377) to evaluate the safety and efficacy of various probiotic strains in adults | *Bifidobacterium lactis* DN-173 010, *Lactobacillus casei* Shirota and *Escherichia coli* Nissle 1917 are effective on defecation frequency and stool consistency in adults.  
In children, *Lactobacillus casei rhamnosus* Lcr 35 showed a beneficial effect. | Chimielewska et al. 2003        |
| Irritable Bowel Symptoms (IBS)    | 19 RCT’s in 1650 patients were conducted                                     | Significant effect in reducing IBS symptoms is shown by probiotic treatment.  
There was no difference between the different types of probiotics that were used, with *Lactobacillus* (three trials, 140 patients), *Bifidobacterium* (two trials, 422 patients), *Streptococcus* (one trial, 54 patients) all showing a trend towards benefit. | Moayyedi P. et al. 2010         |
## Evidence for various indications

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<td>Inflammatory Bowel Disorders (IBD)</td>
<td>Meta-analysis of 13 RCT - seven studies - remission rate and eight studies - recurrence rate, two studies - both remission and recurrence rate</td>
<td>Probiotic treatment was more effective than placebo in maintaining remission in ulcerative colitis.</td>
<td>Sang L. et al 2010.</td>
</tr>
<tr>
<td>Allergic Disorders</td>
<td>Meta-analysis of 12 studies on therapeutic effect of probiotics of which 4 studies were conducted on children</td>
<td>Nine of the 12 articles showed benefits from the use of probiotics in allergic rhinitis showing a reduction in symptom severity, recurrence of episodes and use of medication for rhinitis but not for asthma.</td>
<td>Vliagoftis et al. 2008</td>
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Randomized controlled field trial at National Institute of Cholera and Enteric Diseases (NICED) Kolkata - Role of *Lactobacillus casei* strain Shirota in preventing diarrhoea

- Double blind RCT involving 3758 children between 1 and 5 years was conducted in an urban slum community in Kolkata
- Probiotic group - 1802 children, Nutrient group - 1783 children
- Intake period - 12 weeks, Follow up - 12 weeks
- Incidence of diarrhea in the probiotic group (0.88/child/year) was significantly lower in the probiotic group than in the placebo group (1.029/child/year).
- Protective efficacy - 14% (95% CI, 4-23%, p<0.01)
Gaps and Recommendations

- The safety and clinical effects of one strain cannot be extrapolated to another strain

- Need for well designed randomized controlled trials

- Validated clinical outcome measures

- Optimal dose

- Long term safety of pro and prebiotics
Probiotic Drugs

✓ Enterogermina
✓ VSL#3
✓ Sporlac
✓ Darolac
✓ Bifilac
✓ Econorm

Bacillus subtilis
(8 Strains) 450 billion live lactic acid bacteria, 3 strains of Bifidobacteria

B. coagulans

Lactobacillus acidophilus,
Lactobacillus rhamnous,
Bifidobacterium longum,
Saccharomyces boulardii

Streptococcus faecalis, T-11,
Clostridium butyricum, Bacillus mesentericus, Lactobacillus sporogenes

Saccharomyces boulardii
Probiotics Food Sources

✓ Usualy found in fermented dairy products
• Yakult
• Nesvita
• B-Activ
• Nutrifit
Dairy as delivery vehicles

- Viability
- Refrigeration encourages probiotic survival in product
- Low pH of the product
- Deliver functional nutrition
- Good option for incorporating beneficial bacteria
- Compliance - Food vs. Pill
ICMR - DBT guidelines for Probiotic foods in India

Label -

Genus, species, strain designation

Minimum viable number of the probiotic strain to be specified at the level at which efficacy is claimed and at the end of shelf life

Evidence Based Health claims

Proper storage conditions
Regulations governing production and distribution of functional foods

Japan - FOSHU

- “Foods for Specified Health Uses” (FOSHU) is a regulatory system to approve the claims made on food labels in 1991.

- Safety and efficacy has been scientifically validated.

- FOS, Soy bean oligosaccharides, soy protein, probiotic bacteria such as Lactobacillus casei strain Shirota, Bifidobacteria breve.
Percentage of FOSHU per Type of Food

- Cholesterol: 1102 (11.9%)
- Body fat: 35 (4.1%)
- Middle chain fatty acids: 29 (3.3%)
- Blood sugar level: 128 (15.0%)
- Blood pressure: 107 (12.5%)
- Calcium: 42 (4.9%)
- Dental hygiene: 65 (7.6%)
- Probiotics: 71 (8.3%)
- Prebiotics: 239 (28.0%)
- Others: 35 (4.1%)

853 foods (100%)

Fig. 3 Number of functional foods recognized as FOSHU in Japan as of 2 June, 2009
The vision for India

- A Fundamental change in perception
- Developing a diet based intervention strategy
- Formulating foods tailored to meet specific health need
- Concept to get ingrained in the public health system without being seen as a medicine
Thank You