### Lecture 23: Evidence for Efficacy?

**NOTE:** Evidence of health benefits should be attributed to the strain (slide 25 shows strains).

#### MAIN MICROORGANISMS USED IN PROBIOTIC FORMULATIONS:

| Lactobacillus | Gram +ve rods, classified as anaerobes
|---------------|----------------------------------|
|               | ** Able to survive gastric conditions better than bifidobacterial = do not require enteric coating**
|               | Can latch on to intestinal wall for ≥ 1 week
|               | Lactic acid producing
|               | Used to ferment milk to make yogurt
|               | Also referred to as: Acidophilus, Acidophilus Bifidus, Acidophilus Lactobacillus, L. Acidophilus, L. Casei, etc

| Bifidobacteria | Gram +ve rods, classified as anaerobes
|----------------|----------------------------------|
|                | Mostly colonize in the colon
|                | Appear to be the most important organism in intestine for providing a microbial barrier to infection
|                | Also a lactic acid bacteria
|                | Predominant intestinal flora of breast-fed infants
|                | Also known as: B. bifidum, B. Infantis, B. Lactis, Bifidus

| Saccharomyces boulardii | A non-pathogenic yeast; believed to be a strain of Saccharomyces cerevisiae (baker’s yeast)
|------------------------|----------------------------------|
|                        | Mostly colonize in the colon

**NOTE:** Evidence of health benefits should be attributed to the strain (slide 25 shows strains → brand products in Canada)

### EVIDENCE FOR Efficacy?

- **Challenge in interpretation:** pooled data; lack of clear understanding of what specific strains are more effective

#### AAD

- Occurrence of diarrhea: 5-35%; caused by disruption of gut microbiota caused by antibiotic therapy
  - Episodes can range from mild (stopping when abx stop) to serious (bowel perforation, death)
  - Increased risk with: age, co-morbidity, broad-spectrum antibiotics, length of treatment
- Good evidence for *S. boulardii* and *L. rhamnosus GG* (ATCC 53103) – 42 – 56% lower risk
  - 5-40 billion cfu/d shown to be effective (with higher dosage range more effective)
  - Take for same duration as antibiotic (and 1-2 weeks longer); space doses by 2 hrs (theoretical)
- Evidence isn’t sufficient enough to support routine use of probiotics; consider if history of AAD or frail

#### CDAD

- Overall, good evidence it decreases incidence of CDAD by 66%; and moderate quality evidence it reduces risk (prevention) by 64%
- Specific strain, length of treatment, and safety in immunocompromised is not known
- Take for same duration as antibiotic (and 1-2 weeks longer)
- *L. rhamnosus, LGG (Culterelle)* most often used; some evidence for *S. boulardii*
- Doses used: at least 10 billion organisms/day

#### IBS

- Promising evidence for treating IBS but overall evidence is weak
- Some evidence for *B. infantis 35624*
YOGURT VS. NHP?
- Available in fermented dairy foods
  - Some yogurts contain encapsulated powdered bacteria
- Stability is an issue (should be refrigerated)
  - Short shelf life
- Some studies exist on yogurt products
- Pharmaceutically based delivery systems are more reliable
  - Example yogurt: Iogo = BB-12 + LA-5 > 1 billion cfu/100g
  - Example NHP: Bio-K+ = L. acidophilus CL1285 + L. casei LBC80R
    - Comes as 30 billion & 50 billion cfu = 30-50 Iogo yogurts!

ADVERSE EFFECTS:
- Very well tolerated
- Common side effects (transient): bloating, diarrhea, abdominal discomfort
- May down-regulate immune function in immunocompromised patients
  - Best to avoid

HOW DO I SELECT A PRODUCT?
- Recommendation should be based on:
  1. Demonstrated efficacy for specific indication
  2. Defined strain of bacteria
  3. Correct dose for a specific condition
  4. Ensure product contains viable bacteria
    - Check expiry date
    - Make sure label says “contains live active cultures”
- Combined strains does not necessarily mean more effective

OTHER NHPS: PEPPERMINT OIL:
- Leaves contain 2.4% essential oil (35-70% menthol)
- Used in IBS due to its antispasmodic effects
  - ↓ slow-wave frequency in small intestine (↓ peristalsis)
  - Relaxes GI smooth muscle through CCB properties

SUMMARY FROM NATURAL MEDICINES:

<table>
<thead>
<tr>
<th>Type of Diarrhea</th>
<th>Likely Effective</th>
<th>Possibly Effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotaviral</td>
<td>Lactobacillus GG</td>
<td>Bifidobacteria</td>
</tr>
<tr>
<td>AAD</td>
<td>S. boulardii</td>
<td>Lactobacillus</td>
</tr>
<tr>
<td>Traveler’s</td>
<td></td>
<td>Bifidobacteria</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lactobacillus</td>
</tr>
<tr>
<td>IBS</td>
<td>Peppermint</td>
<td>Bifidobacteria</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lactobacillus</td>
</tr>
</tbody>
</table>

DIGESTIVE ENZYMES:

WHAT ARE THEY?
- Aid in digestion of proteins, fats, and carbs
- Can take them as supplements that are animal or plant/microbe derived
- Well studied for pancreatic enzyme replacements (animal sources)

SELECT THE RIGHT ENZYME:
- Evidence for digestive relief in people without pancreatic disease is lacking and mixed (trials are very small)
- Select a supplement that provides the enzyme(s) specific to the food causing the digestive problem(s)
  - i.e. bloating/gas after high fat meals, try lipase

CONCERNS WITH DIGESTIVE ENZYMES:
- Pancreatin may inhibit folic acid absorption (supplement with folate)
- Allergy to the source (papaya, pineapple, porcine protein)
- Bromelain – believed to have anti-platelet activity
- Excessive dosing may cause transient GI upset
- Broken down by stomach acid – use enteric coated

Sources and Action:

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Breaks down</th>
<th>Source derived from</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protease (papain, bromelain)</td>
<td>Protein</td>
<td>Bovine or porcine (extract trypsin &amp; chymotrypsin), papaya, pineapple stems</td>
</tr>
<tr>
<td>Lipase</td>
<td>Fat (in butter, sauces)</td>
<td>Bovine or porcine</td>
</tr>
<tr>
<td>Amylase</td>
<td>Starch (in beans, lentils, grains, bread, corn)</td>
<td>Bovine or porcine; fungus (Aspergillus oryzae)</td>
</tr>
<tr>
<td>Lactase (B-galactosidase)</td>
<td>Milk sugar (lactose)</td>
<td>Yeast (K. lactis)</td>
</tr>
<tr>
<td>Alpha-galactosidase</td>
<td>Complex sugars (grains, beans, nuts, broccoli, cabbage)</td>
<td>Fungus (Aspergillus niger)</td>
</tr>
<tr>
<td>Pancreatin</td>
<td>Protein</td>
<td>Bovine or porcine (extract trypsin &amp; chymotrypsin), papaya, pineapple stems</td>
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