The Uses and Dangers of Probiotics
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Objectives
- Describe and define probiotics
- List common products on the market
- Review possible mechanisms of action that may be beneficial
- Identify common uses and briefly discuss current evidence
- Identify less common uses and briefly discuss current evidence (or lack there of)
- Recognize potential dangers of probiotic use
PRO-BIO-TIC₁

- Pro: derived from Greek, meaning “promoting” or “for”
- Bio: life
- Tic: pertaining to

QUIZ TIME!₂

- Who was the FATHER of probiotics?
  A. Louis Pasteur
  B. Al Gore
  C. Elie Metchnikoff
  D. Hippocrates
  E. William Proctor
The FATHER of Probiotics

- A Russian scientist
- Proposed theory that toxic bacteria in the gut were a cause of aging
  - Drank rotten milk (lactic acid) to kill these harmful bacteria
- Wrote a book, that led to the future development of probiotics

PRO-BIO-TIC

- AKA
  - “Normal flora”
  - “Good bacteria"
  - “Helpful bacteria"
  - “Friendly bacteria”
- Individual bacteria identified by:
  - Genus
  - Species
  - Strand (number)
Your Normal Flora

- Contains around 400 strains of bacteria, fungi, and parasites
- TRILLIONS of bacteria live in our digestive tracts
- Common bacteria found in supplements:
  - Lactobacillus species
  - Bifidobacteria species
  - Saccaromyces boulardii

Products available

- Over 100 products are commercially available
Examples:
- Florajen
- Proviva
- Culturelle
- Align
- Bacid
- Activia
- Florastor

There is NOT generic equivalence with probiotic strains/products due to variability.
- Products have different:
  - Manufacturing methods
  - Storage requirements
  - Species related differences
- Try to stick with specific products that have shown benefit in CLINICAL STUDIES

Possible Mechanisms

- Colonization resistance
  - Competitive exclusion
- Metabolic effects
  - Bacteriocins
  - Decrease pH
  - Quorum sensing
- Modulation of signal transduction
- Probiotics

Maintain barrier function
- Reduce macromolecular permeability and bacterial translocation
- Maintain tight junctions (ZO-1, claudin)

Innate/Adaptive Immuno modulation
- Enhance cytokines (IL-6, TNF)
- Increase mucin production

(http://ncp.sagepub.com/content/24/1/10/F1.large.jpg)
Common Uses
- Irritable Bowel Syndrome
- Infectious Diarrhea
- Antibiotic-Related Diarrhea
- Traveler’s Diarrhea

Less Common Uses
- Allergies
- Immunity
- Dental health
- Cancer prevention
- Genitourinary health
- Antihyperlipidemia
Rumor Has It...

DID YOU HEAR WHAT THEIR SAYING ABOUT PROBIOTICS?

OH MY! DO TELL...

Rumor vs Truth

Probiotics can lower your cholesterol
Conflicting

- Studies have shown modest reductions in Total cholesterol and LDL while other have shown no effect
- Meta-analysis found overall decreases of total (-6.40 mg/dL) and LDL cholesterol (-4.90 mg/dL)

- Inhibit intestinal cholesterol absorption
  - Occurs through binding of and incorporation of cholesterol in bacterial cells

- Suppress reabsorption of bile acids
  - Synthesized by cholesterol

Rumor vs Truth

Probiotics are effective in newborns with intestinal infections
YES! But...

- This has only been studied in preterm infants
- There has been some evidence showing the use of probiotics in infant prevents necrotizing enterocolitis
  - NEC may be due to abnormal bacterial colonization
    - Diclofor
    - Culturelle
    - Florastar
    - Infloran
    - Bifidobacterium
- A number of commercial product infant mild formulas contain probiotics

Rumor vs Truth

Probiotics are recommended for antibiotic-associated diarrhea
*TRUTH*

- Several meta-analysis have showed reductions in risk for development of antibiotic associated diarrhea (AAD)
  - Results: Relative risk reduction of 32%
  - Number needed to treat: 13
  - Consistent across subgroup analysis
- Other sources say approximately 60-65% reduction in AAD incidence (cite source)-see refere
- Most commonly studied species included: Lactobacillus, Saccaromyces boulardii, and bifidobacterium

### RECENT NEWS

- PLACIDE study
  - Conducted in Wales and northeastern England
  - Involved 5 hospitals, 68 different medical and surgical units, and more than 17,000 patients aged 65 years or older.
  - Showed no benefit, with increased risk for flatulence and bloating
How much, how long???

- Lactobacillus or Bifidobacterium spp:
  - Most studies conducted with 3-5 billion CFU/day BID
- Saccharomyces boulardii:
  - 500 mg BID if standardized to (30 billion/G)
- Should try to use formulations/species that were used in clinical trials

Rumor vs Truth

Probiotics reduce your risk of cancer
Maybe

- β-glucuronidase: Produced by pathogenic bacteria in the GI tract
  - ↑ levels increase tumor growth
  - ↑ production of blood vessels that feed the tumor
  - Convert certain molecules into procarcinogens
    - Colon cancer
    - Bladder cancer
    - Breast cancer

Rumor vs Truth

Probiotics can prevent travelers-diarrhea
Possibly…8,9

- Mixed results
- Meta-analysis in 2007 showed a 15% relative risk reduction for traveler’s diarrhea
- Saccaromyces boulardii and mixture of lactobacillus and bifidobacterium showed most benefit

Rumor vs Truth

Probiotics can help decrease risk of developing allergies
It's Promising!  
- *Ureaplasma urealyticum*  
  - Colonize the human genital tract  
- Women taking probiotics during pregnancy  
  - ↓ in the incidence of childhood eczema in infants  
  - May show some positive evidence for asthma  
- L. rhamnosus GG

Rumor vs Truth

Probiotics can be used to prevent Lung infections
YES!

- Several clinical trials have evaluated probiotics for preventing respiratory tract infections
  - Common cold
  - Sinusitis
  - Pharyngitis
  - Acute otitis media

Rumor vs Truth

Probiotics can be used to treat and prevent irritable bowel syndrome
Perhaps yes, perhaps not

- Conflicting evidence
- May decrease symptoms of Irritable Bowel Syndrome-Constipation
  - ↓ abdominal discomfort
  - ↓ bloating
  - ↓ difficult bowel movements
- Primarily evidence for Bifidobacterium

Rumor vs Truth

Probiotic promote female reproductive and bladder health
Yes and No

- May be helpful in bacterial vaginosis
  - Lactobacilli produce hydrogen peroxide and lactic acid
    - which lower vaginal pH and may help prevent the overgrowth of other bacteria
- A number of studies have failed to demonstrate protection
  - UTIs
  - Yeast infections
    - Does not seem to reduce the risk of vaginal candidiasis infection following use of antibiotics

Rumor vs Truth

Probiotics prevent tooth decay
YES! But…11,12

- Systemic review of 23 randomized clinical trials assessing use of probiotics on oral health
  - In two-thirds of the selected papers, probiotics demonstrated a capacity to reduce *S. Mutans* counts in saliva and/or plaque.
  - But to date, RCTs on this topic are insufficient to provide scientific clinical evidence.

Probiotics and oral protection11,12

- Has been shown to prevent
  - Dental caries
  - Periodontitis
  - Oral fungal infections
  - Halitosis
Probiotics and Teeth\textsuperscript{11,12}

- Probiotics may inhibit bacteria *S. Mutans* from forming biofilms in our mouths
  - Preventing adhesion of bacteria
  - Competing for nutrients
  - Enhance immune responses

Rumor vs Truth

Probiotics can treat and prevent infectious-diarrhea
TRUTH!

- May **duration** of infectious diarrhea by 30.5 hours
- Primarily due to Rotovirus

### Theoretical Dangers of Probiotics

- **Ability to cause infection**
- **Transfer of antibiotic resistance to the GI flora**
- **Toxic effects to the GI tract**

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**Graph:**

Duration of diarrhea (hours)

- **Phreatophyte**
- **Lactobacillus**
- **Enterococcus**
- **Bifidobacterium**

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Dangers of Probiotics\textsuperscript{15,16}

- Risk of bacteremia & fungemia
  - *Bifidobacterium*
    - Endocarditis
  - *Lactobacilli* Species
    - Sepsis
    - Endocarditis
  - *Saccharomyces boulardii*
    - Fungemia

### Proposed Risk Factors for Probiotic Bacteremia/Fungemia\textsuperscript{15,16}

<table>
<thead>
<tr>
<th>Major risk factors</th>
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<tbody>
<tr>
<td>1) Immune compromise, including a debilitated state or malignancy</td>
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<tr>
<td>2) Premature infants</td>
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<table>
<thead>
<tr>
<th>Minor risk factors</th>
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<tbody>
<tr>
<td>1) Central venous catheters</td>
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<tr>
<td>2) Impaired intestinal epithelial barrier, eg, diarrheal illness, intestinal inflammation</td>
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<td>3) Administration of probiotic by jejunostomy</td>
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<td>4) Concomitant administration of broad spectrum antibiotics to which probiotic is resistant</td>
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<tr>
<td>5) Probiotics with properties of high mucosal adhesion or known pathogenicity</td>
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<tr>
<td>6) Cardiac valvular disease (<em>Lactobacillus</em> probiotics only)</td>
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Dangers of Probiotics

- *Lactobacillus* species
- Contain plasmids for antibiotic resistance
  - Tetracyclines
  - Erythromycin
  - Chloramphenicol
- Transfer to other bacteria is rare

Dangers of Probiotics\textsuperscript{15,16}

- Potential risk of GI toxicity
  - GI tract breaking down lactic acid bacteria
    - Lactic acidosis
  - Probiotics prevent deconjugation of bile salts
    - Malabsorption
When Choosing a probiotic

- Check the label
- Beware of the internet
- Pick certified probiotics
- Storage

Finally…

- Scientific evidence supporting specific uses is still lacking
- The FDA has not approved any health claims
- Probiotics do not replace any proven treatments
- Monitor closely if any serious underlying health problems
Summary

- Probiotics have many potential uses
- There are vast amounts of information about probiotics and much of this information is conflicting
- It is important to weigh the potential risks and benefits based on individual patient factors

References
References