

GIT:

- Normal GIT contains > 500 microbial spp (intestinal flora) and 100 trillion (10¹⁴) bacteria cells (mostly in colon) = gut microbiota or microbiome
- Microbial cells in human GIT = 10x the number of human cells in the body
- Each person has their own unique bacterial composition which is influenced by:
 - Individual genotype
 - Colonization at birth
 - Mother's milk: nutrients, prebiotics

WHAT CAUSES MICROBE DEPLETION?

- Stress
- Infection
- C section
- Antibiotics
- Environment

ALTERATIONS IN MICROBIOME:

- In GIT diseases, such as: IBS, IBC, *C. difficile*
- There is an imbalance (or dysbiosis) of the gut microflora

BIOTICS:

- **Biotics:** of, relating to, or caused by living organisms
- **Antibiotic:** against life
- **Probiotic:** for life
 - Stimulate growth of other organisms

PREBIOTICS:

- Dietary substances that nurture a selected group of microorganisms living in the gut
- Favour growth of beneficial bacteria over harmful
- Examples of fermentable carbs:
 - Oligofructose, inulin, galacto-oligosaccharides (GOS), lactulose
 - Found in cookies, cereals, chocolate, dairy products, mother's milk (GOS)
- Example: fermentation of oligofructose in colon
 - Increase number of bifidobacterial
 - Increased calcium absorption
 - Increased fecal weight
 - Shortening of GIT transit time

PROBIOTIC USES:

- Prevent and treat conditions caused by pathogenic bacteria
 - Treatment & prevention of AAD, acute infectious diarrhea
- Eradication of *H. pylori*
- Boost immune response, prevent URTIs
- Improve IBD, IBS, lactose intolerance
- Decrease cholesterol levels
- Assist in weight loss
- And more...

PROPERTIES OF AN IDEAL PROBIOTIC:

- High adherence to intestinal wall
- Stable against gastric acid, bile, O₂, enzymes
- Non-pathogenic
- Able to co-aggregate as part of the natural gut flora
- Resistant to the effects of an antibiotic
- Evidence for a health benefit

MECHANISMS OF PROBIOTIC/HOST INTERACTION:

Theory 1	<p>Restore balance to intestinal flora</p> <ul style="list-style-type: none"> • Counteract disturbances by recolonizing the intestine & crowing out "bad" bacteria • Compete for adhesion helping to enhance epithelial barrier
Theory 2	<p>Anti-microbial effects</p> <ul style="list-style-type: none"> • Produce substances [lactic/acetic acid, peroxides or bacteriocins (toxins)] to block colonization of pathogens
Theory 3	<p>Stimulate immune function *</p> <ul style="list-style-type: none"> • Stimulants antibody (IgA) secretion and natural killer cell activity; down-regulates inflammatory cytokine production • Improve phagocytic activity <p>* only found in healthy individuals; not people with immune system hypersensitivity</p>

MAIN MICROORGANISMS USED IN PROBIOTIC FORMULATIONS:

Lactobacillus	<ul style="list-style-type: none"> • 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 • Ued to ferment milk to make yogurt • Also referred to as: Acidophilus, Acidophilus Bifidus, Acidophilus Lactobacillus, <i>L. Acidophilus</i>, <i>L. Casei</i>, etc
Bifidobacteria	<ul style="list-style-type: none"> • Gram +ve rods, classified as anaerobes • Mostly colonize in the colon • Appear to be the most important organism in intestine for <u>providing a microbial barrier</u> to infection • Also a lactic acid bacteria • Predominant intestinal flora of breast-fed infants • Also known as: <i>B. bifidum</i>, <i>B. infantis</i>, <i>B. Lactis</i>, <i>Bifidus</i>
Saccharomyces boulardii	<ul style="list-style-type: none"> • A non-pathogenic yeast; believed to be a strain of <i>Saccharomyces cerevisiae</i> (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	<ul style="list-style-type: none"> • Occurrence of diarrhea: 5-35%; caused by disruption of gut microbiota caused by antibiotic therapy <ul style="list-style-type: none"> ○ 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 <i>S. boulardii</i> and <i>L. rhamnosus GG</i> (ATCC 53103) – 42 – 56% lower risk <ul style="list-style-type: none"> ○ 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	<ul style="list-style-type: none"> • 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) • <i>L. rhamnosus</i>, <i>LGG</i> (<i>Culterelle</i>) most often used; some evidence for <i>S. boulardii</i> • Doses used: at least 10 billion organisms/day
IBS	<ul style="list-style-type: none"> • Promising evidence for treating IBS but overall evidence is weak • Some evidence for <i>B. infantis</i> 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: logo = 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 logo yogurts!

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

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
 - a. Check expiry date
 - b. Make sure label says "contains live active cultures"
- Combined strains does not necessarily mean more effective

SUMMARY FROM NATURAL MEDICINES:

Type of Diarrhea	Likely Effective	Possibly Effective
Rotaviral	Lactobacillus GG	Bifidobacteria
AAD	<i>S. boulardii</i>	Lactobacillus
Traveler's		Bifidobacteria Lactobacillus <i>S. boulardii</i>
IBS	Peppermint	Bifidobacteria Lactobacillus

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

SOURCES AND ACTION:

Enzyme	Breaks down	Source derived from
Protease (papain, bromelain)	Protein	Bovine or porcine (extract trypsin & chymotrypsin), papaya, pineapple stems
Lipase	Fat (in butter, sauces)	Bovine or porcine
Amylase	Starch (in beans, lentils, grains, bread, corn)	Bovine or porcine; fungus (<i>Aspergillus oryzae</i>)
Lactase (β-galactosidase)	Milk sugar (lactose)	Yeast (<i>K. lactis</i>)
Alpha-galactosidase	Complex sugars (grains, beans, nuts, broccoli, cabbage)	Fungus (<i>Aspergillus niger</i>)
Pancreatin is a mixture of pancreatic enzymes (protease, amylase & lipase) – used when secretions are deficient		

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**