


One in a Trillion:

The Gut Microbiome and
the Role of the Dietitian in
Protecting a Most Unique Asset

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About Me

- Clinical dietitian at Carolina's Hospital System in Florence, South Carolina
- My coverage includes the SICU, MICU, and CVICU
- This subject is a passion due to its relevance in my every day life



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Objectives

1. Discuss the role of the gut membrane and how dysbiosis occurs
2. Evaluate research on dysbiosis of the gut and systemic disease
3. Examine how medical interventions impact bacterial colonizations (including nutritive interventions)
4. Review the role of the dietitian in protecting this special asset



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Patients and Opportunities for Dietitian Intervention:

63 AAF admitted with SBO

- Placed on PPI
- S/P bowel resection
- Multiple antibiotics
- TF started once bowel function returned

43 yo GRAV2

- 100 kg
- Started on antibiotics 2/2 C-section
- Complications post surgery with baby kept away from the breast

8 yo WM with texture aversions with a consult for IBD 'low residue' diet



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What is the Gut Microbiome?

- Bacteria, archaea, viruses and eukaryotic microbes that reside in and on our bodies
- They contribute:
 - metabolic functions
 - protect against pathogens
 - educate the immune system
 - affect directly or indirectly most of our physiologic functions

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What is the Gut Microbiome?

- Mutualistic relationship
- Fecal microbiome
 - 100 trillion microorganisms
 - Outnumber human cells by a factor of 10
- Our gut is individualized
 - Compared with other parts of our body, the gut is more individualized
- Conversely, long-term suggested treatments for gut repair appears to be similar for most people

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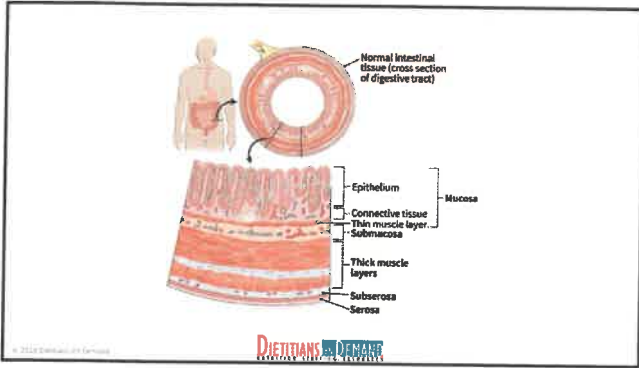


What is the Gut Membrane?

- The intestinal mucosa is the innermost of 4 concentric histological layers found throughout most of the intestinal tract
- The mucosa itself is further subdivided into 3 layers
 - The epithelium
 - The lamina propria
 - Muscularis mucosae


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What is Dysbiosis?

- Altered microbial communities
- Intestinal barrier impairment



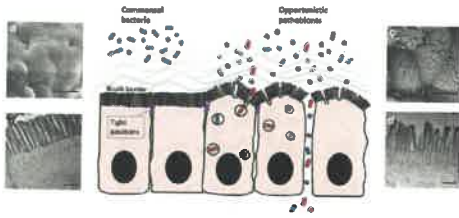
An endoscopic view of the colon showing significant inflammation and redness of the mucosal lining, characteristic of dysbiosis or inflammatory bowel disease. At the bottom, there is a logo for 'DIETITIANS ON DEMAND' and the text '© 2014 Dietitians On Demand'.

Terms important to dysbiosis

- **Dysbiosis:** a term used to refer to a microbiota community associated with a diseased state that can be differentiated from the microbiota community associated with a healthy control state
- **Richness:** the number of distinct members ("species") in the community
- **Diversity:** a measure of the richness and evenness characteristics of a community, often calculated as a specific diversity index

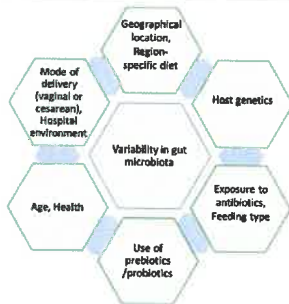
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Why is this Important?



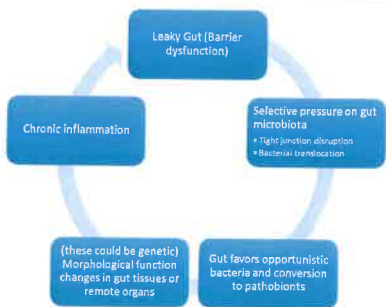
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Gestation, Birth, and Infant Feeding

- Diet in the womb
 - Mothers pass nutrients on to fetus
 - Variability in diet is encouraged
- C-section vs. vaginal birth
 - Vaginal seeding
 - Antibiotics
- Breastfeeding vs. formula feeding
 - Breast milk contains more than proteins, fat, carbs, and vitamins/minerals



Ingredient	Class of Ingredient	Function	Reference
Antiproteases (e.g., secretory immunoglobulin A and lysozyme inhibitors)	Enzyme	Inhibits breakdown of milk-lactative immunoglobulins and enzymes	Howell et al., 1986; [23], 1991
Acylalase	Enzyme	Degrades bacteriostats	Hansen et al., 1983
Cytolase	Enzyme	Degrades hydroxy peroxide, protects against bacterial invasion of intestinal barrier	Lachnath-Mannion and Alston, 2000
Flavonoids	Cytosin	May prevent defects in immunology	[23], 1991; Monstky et al., 1990
Free fatty acids	Lipids	Antifungal (antimicrobial) substances (Glandic, Zimovska)	Monstky et al., 1990
Gonocyte colony stimulating factor	Cytokine	Causes endothelial cell migration and proliferation	Wallace et al., 1997
Immunoglobulin inhibitor	Opioid	Prevents bacterial adherence	Hansen et al., 1983
Hydrolytic	Enzyme	Degrades bacteriostats	Hansen et al., 1983
Immunoglobulin G	Immunoglobulin	Immune protection	Howell et al., 1986; [23], 1991
Interleukin-1 beta	Cytokine	Activates T-cells	Monstky et al., 1990
Interleukin-4	Cytokine	Enhances immunoglobulin A and C-reactive protein production	Monstky et al., 1990
Interleukin-8	Cytokine	Chemotactic	Machamer et al., 2002
Interleukin-10	Cytokine	Decreases inflammatory cytokine synthesis	Goldman et al., 1996
Lactoferrin	Protein	Prevents microbial binding	Poterson et al., 2001
Lactoferrin	Carbin	Anti-lactoferrin may prevent iron from being bioavailable to microbes	Howell et al., 1986; [23], 1991



Ingredient	Class	Function	Reference
Lipases	Enzyme	Enhances bacteriostatic and bacteriocidal free fatty acids	Howell et al., 1986; [23], 1991
Lysozyme	Enzyme	Bactericidal	Howell et al., 1986; [23], 1991
Macrophage colony stimulating factor	Cytokine	Macrophage proliferation	Goldman et al., 1996
Mucin	Protein	Inhibits E. coli binding to gut epithelium	Poterson et al., 2001
Oligosaccharides, polysaccharides, gangliosides	Carbohydrates, glycoconjugates	Receptor analogs block binding of mucin bacteria growth promoters for Lactobacillus	Coyne et al., 1999; [23], 1991; Kevren-Liquid and Saramita-Olsson, 2001
Pectinases	Enzyme	Bactericidal	Howell et al., 1986; [23], 1991
Phenyl acetylating acetyl hydrolytic factor	Enzyme	Conjugal transfer activator factor	Futakawa et al., 1993
Prostaglandin E2, F2-alpha	Prostaglandin	Intestinal cytoprotection	Howell et al., 1986
Ribonuclease	Enzyme	Prevents viral replication	Nevalsky and Borens, 2002
Secretory immunoglobulin A	Immunoglobulin	Immune protection (broad spectrum antiviral, antibacterial, antimicrobial)	Howell et al., 1986; [23], 1991
Sialic acid	Cytokine	Alters adhesion of viral or other molecules to intestinal epithelium	Xygi et al., 2000
Transforming growth factor-beta	Cytokine	Produces immunoglobulin A and activates D-cells	Botschke et al., 2000
Tumor necrosis factor-alpha	Cytokine	Mobilizes amino acids	Monstky et al., 1990
Uric acid	Antibiotic	Antibiotic	Van Zanten-Orobos et al., 1994

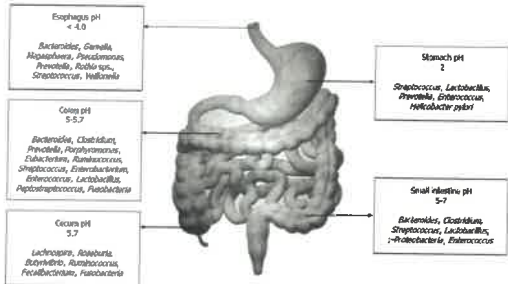


Childhood and Adulthood

- Antigen permeability
 - Poor diet or other factors
- Systemic inflammation
 - Crohn's or UC
- Protein intolerance
 - Celiac disease
 - Can be any number of conditions, however
- Anatomy changes secondary to surgery
 - Gastric bypass
 - Colectomy

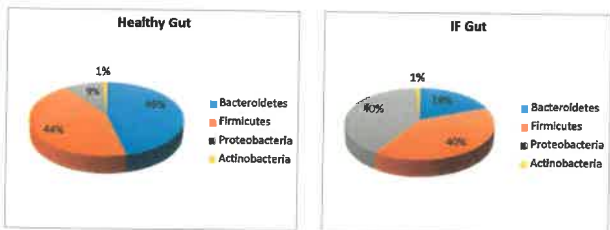


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Gut Microbiome and Intestinal Failure



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Prolonged Starvation

- Atrophy of the gut
- ASPEN recommendations – first 48 hours
 - Try to assess true patient stability – vasopressors, paralytic, hemoglobin, distension
- Reduced oral intake may have impacts on gut as well
 - Thinning of mucous
 - When added to medications, weakened gut may occur

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Diet

- We are removed from our food production
- Western diet
 - High Omega-6
 - Low fiber – this is SO vital
 - Lack of diversity
 - Added emulsifiers, sugar, and alternative sweeteners

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Fiber:



Benefits:



- Decreased gut transit time
- Increased stool bulking
- Decreased diarrhea (soluble)
- Decreased constipation (insoluble)

Effects on microbiome:

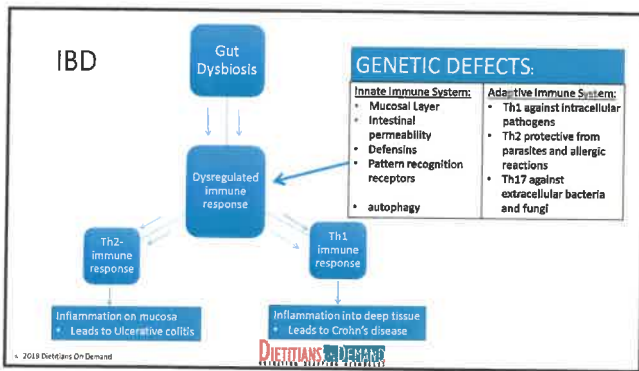
- SCFA production
- Decreased inflammation
- Immune homeostasis/microbiome composition
- Decreased permeability

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 <p>High fiber, lower Omega-6 increases:</p> <ul style="list-style-type: none"> • Microbiota diversity • Microbiota richness • SCFA • Bifobacteria • Prevotella • Bacteroides <p>Decreases in:</p> <ul style="list-style-type: none"> • Firmicutes • Zonulla • Enteric pathogens 	 <p>High fat, low fiber, high salt increases:</p> <ul style="list-style-type: none"> • Firmicutes • Zonulin • Enteric pathogens <p>Decreases in:</p> <ul style="list-style-type: none"> • Microbiota diversity • Microbiota richness • SCFA • Bifobacteria • Neuroelasticity
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IBD

- Therapies
 - Prebiotics
 - Probiotics
 - Fecal transplantation
- May be an easier and safer alternative to immunosuppressants



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IBD

- The low fiber white diet is antiquated
- Oat bran, wheat bran, germinated barley vs. psyllium and low residue
- We see that again, the recommendations for most humans are very similar
 - Real food, mostly plants, in moderation

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Food Additives

- Carrageen
- What are our tube feeding formulas made of?



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Antibiotics

- Kill the good and bad bacteria
- Particularly offensive category: fluoroquinolones
 - Increase chances of pathogenic infections (*C. diff*)



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Other Medications

- Proton pump inhibitors
- Opiates
- Antipsychotics
- Statins
- NSAIDs



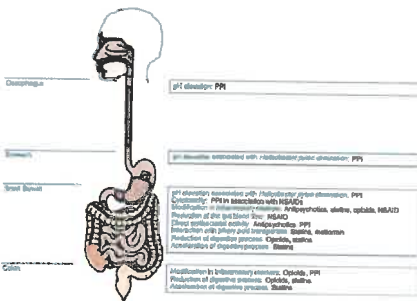


FIGURE 2 Proposed mechanisms by which drugs influence the gut microbiome



Proton Pump Inhibitors

- Used to protect the stomach
- May have unintended consequences in the small intestines
- Alteration to luminal contents
 - Could interfere with nutrient absorption
 - Amount or location of bacterial food substrates
- Does increase pH and inhibit growth of Gram-positive and Gram-negative bacteria
 - *H. pylori*
- However changes in dietary protein entering the large intestines
- Possible increase in chance of *C. difficile*



Opiates

- Paralyze the gut
 - Gut barrier disruption – Increased risk for translocation
 - Decreased transit time = more time for toxins to remain in system
- Taxonomic changes
- *E. faecalis* 100% ↑ vs. placebo
- Eating patterns for patients addicted to opiates may be poor

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Antipsychotics

- Weight gain is a common side effect
- Risperidone associated with:
 - Higher BMI
 - Lower Bacteroidetes:Firmicutes ratio



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Statins

- Number two most prescribed drug class
- Common side effects:
 - Nausea
 - Vomiting
 - Constipation
 - Diarrhea



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NSAIDs

- Changes in numbers not diversity
- Platelet aggregation inhibitors positively associated with *streptococcus anginosus* and *streptococcus parasanguinis*
- Appears to be more influenced by long-term use

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Metformin

- Some research shows that metformin increases *Bifidobacterium bifidum* and SCFA
- Possible enhancement of the intestinal mucosal barrier
- Mechanism could be related to inhibition of reabsorption of bile acids secondary alteration of the function of sodium-dependent intestinal bile acid transporter

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Long-term Impacts of Dysbiosis

- Gut-Liver Axis
 - The liver and intestine communicate extensively through the biliary tract, portal vein and systemic mediators
 - Liver products primarily influence the gut microbiota composition and gut barrier integrity
 - Intestinal factors regulate bile acid synthesis, glucose and lipid metabolism in the liver.
 - TMA (trimethylamine) to TMAO (trimethylamine N-oxide)
 - Pro-atherogenic – CVD

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Long-term Impacts of Dysbiosis

- Gut-Brain Axis
 - Nitric oxide
 - Gene regulation
- Cognitive function
 - HPA (hypothalamus-pituitary-adrenal) axis
- Campylobacter jejuni → change in GABA expression → anxiety

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What Can We Do As Dietitians?

- Be the support system
 - Listen, support, educate, comfort
- Practice best practice
 - Stay up to date on research and implement it
- Speak up!
 - Have the hard conversations
 - This needs to happen in inpatient and outpatient settings

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What Can We Do As Dietitians?

- Set 'Big Picture' Goals
 - Real vs. processed food vs. good and bad foods
 - Focus on small goals for long-term big change
 - Consistent eating
 - Try to keep patients healthful enough to not need as much medications
- Set the example
 - Eat well; self-care
 - Be realistic
- Advocate for change
 - Speak for your community
 - Educate yourself on gentrification and access to healthful choices
 - Advocate for legislative changes that improve dietitian's control over nutritive care

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Quiz

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Question 1

Which of the following is not a noted benefit of breastfeeding (when compared to formula feeding)?

- A. Definitive resistance against obesity
- B. Microbial seeding
- C. Breast milk containing diverse components other than CHO, fats, and PRO
- D. Teaching proper fullness cues



Question 2

Which of the following was not mentioned as a potential source of impact for the gut microbiome?

- A. Birth method
- B. Paternal diet
- C. Antibiotic use
- D. Patient PO diet

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Question 3

By what time frame does ASPEN recommend gut stimulation in critical care?

- A. 1-2 hours after admission
- B. Within 24-48 hours of admission
- C. Within a week of admission
- D. When the patient has full bowel function

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Question 4

Which type of medication shows some promise for enhancing the intestinal mucosal barrier?

- A. Risperidone
- B. Lipitor
- C. Oxycodone
- D. Metformin

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Question 5

Which of the following was associated with s-nitrosylation?

- A. Diabetes
- B. Cancer
- C. Heart disease
- D. Parkinson's
- E. Of other the above

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Answers to Questions

- 1. A
- 2. B
- 3. B
- 4. D
- 5. E

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