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Your digestive Health: A Heealthy Gut From the start

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# Intestinal Microbiome In GI Health

eubiosis

dysbiosis

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- 1- Dysbiosis of the gut microbiota in disease, Simon Carding, Kristin Verbeke, Daniel T. Vipond, Bernard M. Corfe and Lauren J. Owen.
  Published online 2015 Feb 2. doi: 10.3402/mehd.v26.26191. PMCID: PMC4315779PMID: 25651997
- 2- Willie Textbook of pediatric GI disease

### Gut Microbiota



• The collection of bacteria, fungi, viruses, and yeasts in the GI tract, termed gut microbiota, can be considered a microbial organ placed inside the GI tract.

- Gut microbiota offers many benefits to the host through a range of physiologic and metabolic functions, 1- maintaining gut integrity,
  - 2- providing protection against pathogens,
  - 3- regulating host immunity.

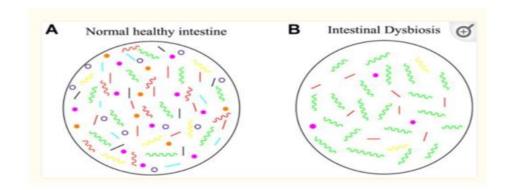
- It is estimated that 500 to 1000 bacterial species exist in the human body at any one time, and the number of subspecies is far greater.
- Each strain of bacteria has its own genome composed of thousands of genes,
- That is 100 times more genetic diversity than the human genome,



- In humans, 386 strictly anaerobic species were identified to be localized around mucosal regions of the oral cavity and GI tract.
- We are learning that each individual has a unique microbiome, and there are great differences between individuals.



- Disruption of normal gut microbial environment
- & Imbalance in gut microbiota



## **Gastrointestinal Tract Colonization**

- Traditionally the intestinal tract has been considered sterile at birth; however, emerging data suggest that colonization begins in utero, because the presence of microorganisms has been identified in amniotic fluid, fetal membranes, umbilical cords, placentas, and meconium.
- with the birthing process colonization continues, with the gut microbiota of newborns closely resembling the microbes encountered during birth.
- Vaginally delivered infants acquired bacterial communities resembling their own mother's vaginal microbiota, which was dominated by Lactobacillus, Prevotella, or Sneathia spp.



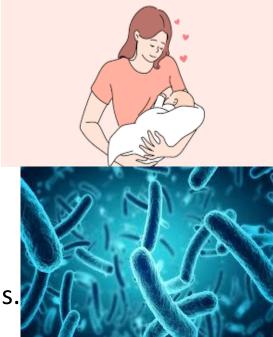


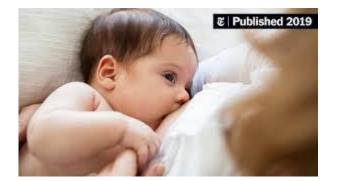
 In contrast babies birthed by C-section harbored bacterial communities that resembled those of the skin, comprising Staphylococcus, Corynebacterium, and Propionibacterium spp.

 Because C-section babies do not receive that first vaginal maternal inoculum, it not only affects the development of the GI microbiota increased vulnerability to certain pathogens infection with methicillin-resistant Staph. aureus (64% to 82% of C - section ) higher incidence of atopic diseases, allergies,

### Infant Feeding Method's Effect on the Gut Microbiota

- Meeting all nutritional and physiologic requirements, breast milk is the optimal food for infants.
- Human milk contains protein, fat, and carbohydrate, Ig, endocannabinoids.
- Breastfeeding enrich vaginally acquired, lactic acid–producing bacteria in the baby's intestine.
- Breast milk is not sterile and contains as many as 600 different species of bacteria, including beneficial Bifidobacterium species B. breve, B. adolescentis, B. longum, B. bifidum, B. catenulatum, and B. dentium.
- All of these Bifidobacterium species may promote healthy microbiota development





- The carbohydrate component of human milk, in addition to lactose, also contains
   oligosaccharides serve as prebiotics by selectively stimulating growth of members of the
   genus Bifidobacterium:
- strengthening gut mucosal protection through activities against pathogens
- > modulation of the intestinal immune system,
- production of immunoglobulin A

 Increased proportion of Bifidobacteria is noted in breast-fed infants compared with those fed formula. Aerotolerance seems to differ between breast-fed and formula-fed infants.

#### **Breast milk**

 Aerobic organisms more common in the feces of breast-fed infants,



#### Formula

- Anaerobic and facultatively anaerobic organisms, which preferentially use anaerobic glycolysis, are more frequently identified in feces of formula-fed
- More Bacteroides and Clostridia colonization

### Solid Food



- The second transition in gut colonization occurs when the diet transitions to solid foods.
- Changes the relative ratio of bacterial phyla in the GI tract from an unstable community dominated by Actinobacteria and Proteobacteria
   to a stable mixture dominated by Firmicutes and Bacteroidetes, similar to adult-like microbiota (by three years of age)
- This adaption achieved by incorporating genes from bacteria in the environment

## Ecology of a Healthy Gastrointestinal Tract

- The gut microbiota differs in numbers and composition along the length of the GI tract,
- Chemical, nutritional, and immunologic gradients along the gut affect the diversity and density of the gut microbiota.
- Although the saliva may contain up to 109 microbial cells/mL, low gastric pH limits bacterial numbers in the stomach and duodenum .
- In addition, due to bile and peristalsis, the jejunum is typically colonized only by relatively simple, rapidly growing, facultative anaerobes
- In the ileum, microbial numbers and diversity increase as peristalsis and acidity decrease.
- The colon is where the numbers and diversity are greatest, Overall microbiota vary between individuals, but
- up to 1011 to 1014 primarily anaerobic bacterial cells/g of feces are commonly detected in the colon.
- Prevotellaceae, Lachnospiraceae, and Rikenellaceae have been shown to dominate in the colon

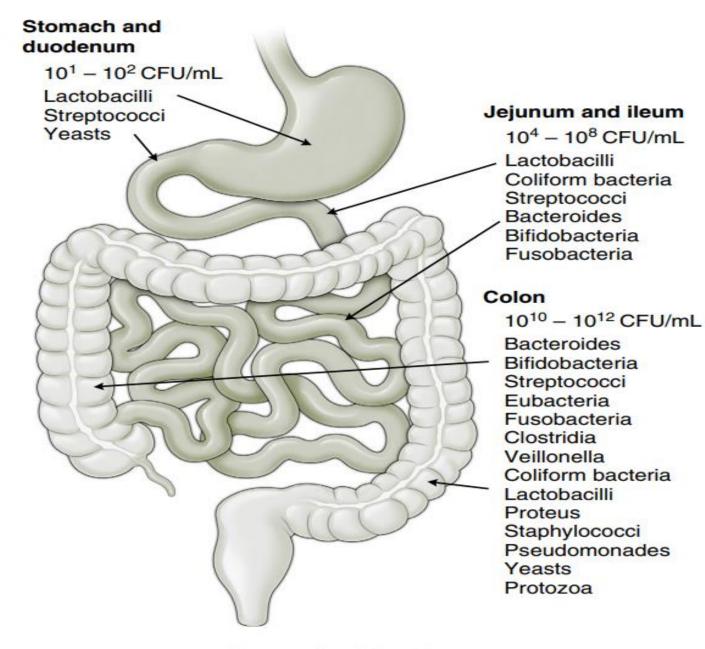
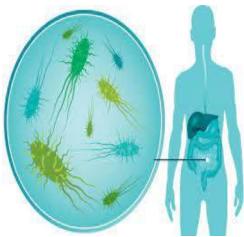


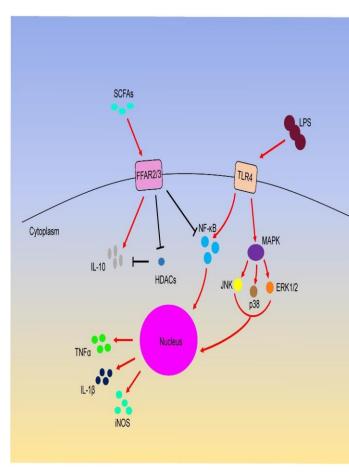
Fig. 4.1 Gut Microbiota.

### The Gut Microbiome – Host Mutualistic Relationship

- The gut microbiota and its host have a mutualistic rather than a commensal relationship
- The gut microbiota are involved with
- > Enzyme production and synthesis of essential nutrients
- > Defend against colonization by opportunistic pathogens
- Support intestinal immune function and integrity.
- > Vitamin synthesis such as folate, vitamin K, biotin, riboflavin, and cobalamin
- Stimulate normal development of the humoral and cellular mucosal immune systems
- Interestingly, germ-free mice show extensively underdeveloped gut-associated lymphoid tissue and antibody production,



- For instance, dietary polysaccharides that indigestible by the host reach the gut microbiota in the colon -----> fermented by the gut microbiota ----> short -chain fatty acids (SCFAs), acetate, propionate, and butyrate.
- SCFAs
- > an energy source for the colonocyte and are rapidly absorbed
- > play a role in gut motility, gut barrier maintenance,
- glucose homeostasis, and energy harvesting
- Decreased luminal PH ----> decreased growth of E. coli
- & Enterobacteriaceae



### Factors Impacting the Gut Microbiota

- By the age of 3 years the gut microbiome resembles that of an adult, where humans acquire stable gut microbiota maintained in well -balanced host -microbiota symbiotic states called enterotypes.
- Enterotypes : classified into three types Bacteroides, Prevotella, other Firmicutes.

However, many environmental factors can influence the diversity and composition of the microbiome, including :

diet, medications, psychological stress

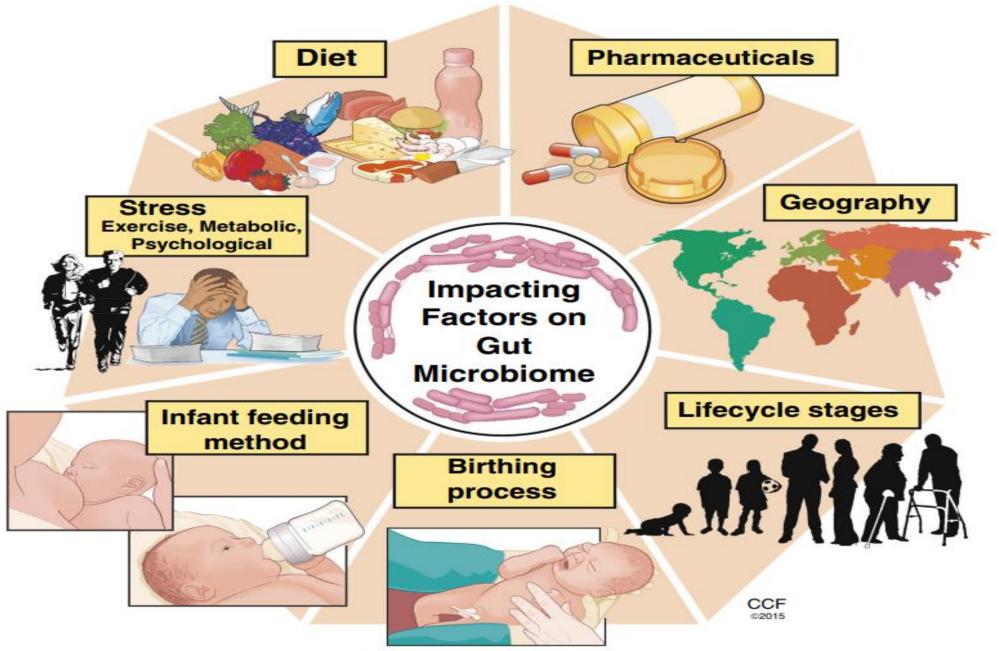


Fig. 4.2 Factors Impacting Gut Microbiota.

### Food Supply

 Significant and meaningful changes in the gut microbiota have been associated with dietary alterations

Mediterranean Diet : Rich in fruits, vegetables, whole grains, and heart-healthy fats, ----> more diversified microbiome

Western diet, rich in fat, sugars, and animal protein and depleted of fiber -----> lower diversity of microbiome -----> increasing incidence of obesity, coronary vascular disease, metabolic syndrome, and certain malignancies

Vegetarian diet ----> lower microbial counts of Bifidobacterium, Bacteroides, Escherichia coli, and Enterobacteriaceae species and lower stool pH compared with omnivores.

#### Medications

• Antibiotics



- The gut microbiome is an ecosystem,
- Meaning that microorganisms can be co-dependent on each other
- for \_\_\_\_ > provision of nutrients and other metabolites
  - or for the removal of toxic waste products



- In adults, repeated antibiotic treatment can leave a lasting imprint on the gut microbial community long after the medication is removed.
- The use of antibiotics early in life negatively impacts the gut microbiota, decreasing the overall diversity and shifting the composition toward higher abundance of Proteobacteria

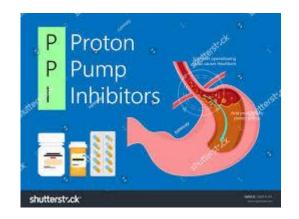
and lower actinobacteria

### Others,

- Nicotine-based product --- > gut dysbiosis and increased gut permeability
- Genetic background,
- Health status (infections, inflammation)
- Lifestyle habits
- Hygiene.
- Xenobiotics (antibiotics, drugs, food additives (overgrowth of proteobacteria )

Tomas Hrncir. Gut Microbiota Dysbiosis: Triggers, Consequences, Diagnostic and Therapeutic OptionsMicroorganisms. 2022 Mar; 10(3): 578

#### Proton Pump Inhibitors.



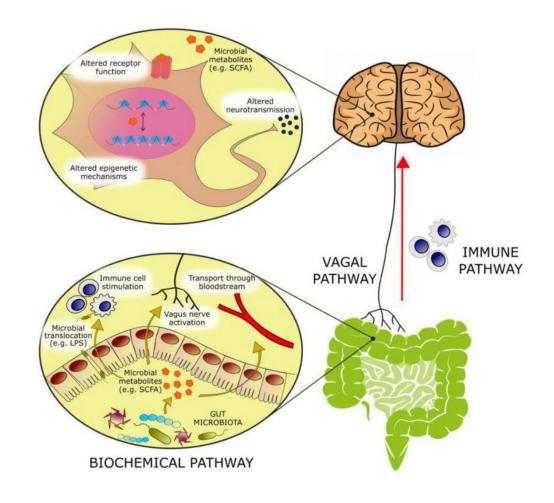
- Increasing the gastric pH ----- affect the gut microbiome in pediatrics gastric microenvironment by directly targeting bacterial, fungal and pathogenic bacteria
   ---> Increased risk of enteric infections
- Suppression of normal gastric flora -----> relative excess of Streptococcus, irrespective of Helicobacter pylori status and may explain the persistence of dyspeptic symptoms & development of peptic ulcer disease
- Overgrown with pathogenic species (dysbiosis)

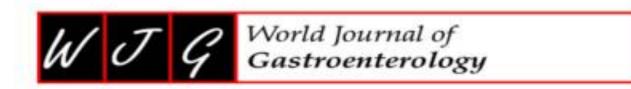
### **Psychological Stress**

- Stress, whether acute or chronic,
- ----> dysbiotic gut microbiome
- ---- > may induce anxiety and depression.
- Gut microbiota -----> metabolite

----> effect on neurotransmitter metabolism

----> modulate brain biochemistry and behavior





World J Gastroenterol, 2022 Feb 28; 28(8): 878–880. Published online 2022 Feb 28. doi: <u>10.3748/wjg.v28.i8.878</u> PMCID: PMC8900572 PMID: <u>35317102</u>

"Role of exercise in preventing and restoring gut dysbiosis in patients with inflammatory bowel disease": A letter to the editor

Neasa Mc Gettigan, Aoibhlinn O'Toole, and Karen Boland

#### Abstract

World J Gastroentero

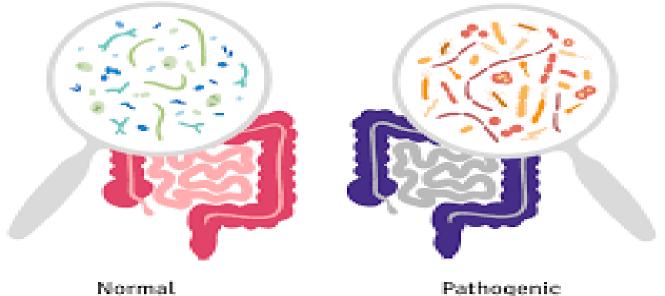
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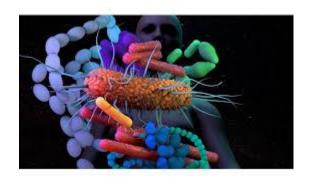
Exercise-induced changes of the microbiome in inflammatory bowel diseases (IBD) is a promising field of research with the potential for personalized exercise regimes as a promising therapeutic adjunct for restoring gut dysbiosis and additionally for regulating immunometabolic pathways in the management of IBD patients. Structured exercise programmes in IBD patients of at least of 12 wk duration are more likely to result in disease-altering changes in the gut microbiome and to harness potential anti-inflammatory effects through these changes along with immunometabolic pathways.

### Diseases induced by dysbiosis





- IBD
- Metabolic disorders
- Obesity
- Type 2 diabetes (T2D)



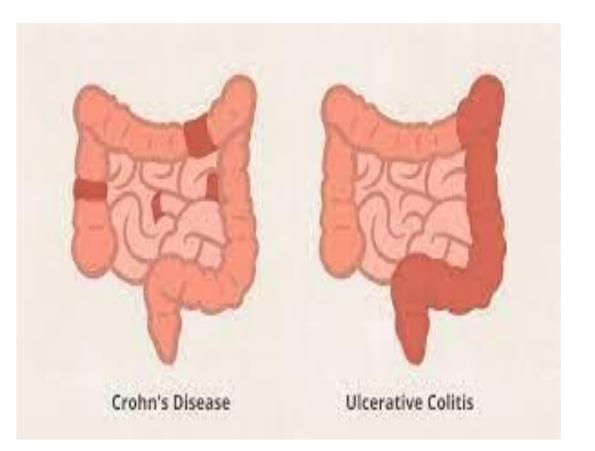
- Irritable bowel syndrome (IBS) In IBS, changes in microbiota composition the different subtypes of disease compared to healthy individuals
- Celiac disease interaction between host genetics and microbiota composition
   Celiac disease results from CD4 T-cell reactivity to dietary gliadin,
   Some bacterial species being able to digest gliadin and perhaps
   reduce the immunopathogenicity of ingested gliadin

• Colorectal cancer (CRC) alterations in microbiota composition with increased diversity observed compared to control

### IBD

• Inflammatory bowel disease Crohn's disease (CD) and ulcerative colitis (UC)

 Although the aetiology of both diseases is unknown, there is increasing evidence that intestinal microbial dysbiosis has a role



### Metabolic disorders

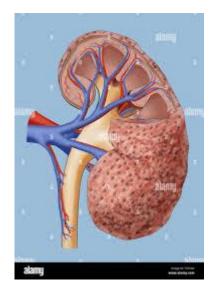


Two observations :

• one, that the transfer of microbiota from lean donors into individuals with metabolic syndrome can increase insulin sensitivity and overall amelioration of symptoms of metabolic disease

• Two, dietary changes in humans leads to rapid and reversible changes in the relative abundance of dominant members of the intestinal microbiota

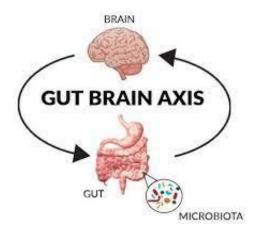
### Kidney diseases



- Between the large intestine and the kidney, a bi-directional functional relationship exists.
- Uremia influences the colonic microbial metabolism.
- Whereas microbial-related metabolites are involved in the progression of the kidney disease

### Dysbiosis and CNS-related disorders

- Intestinal microbial dysbiosis may impact on the 'gut-brain-axis' to affect the CNS and behavior and cognitive function.
- Early colonization of the intestinal tract by microbes is important for the post
   -natal development of the enteric nervous system



Dysbiosis of the gut microbiota in disease, Simon Carding, Kristin

- Autism spectrum disorder (ASD) : Evidence of a possible causal role of the intestinal microbiota maternal immune activation (MIA) mouse
- Chronic depression in humans : by increased immune response (serum IgM and IgA responses) directed against lipopolysaccharide (LPS) products of gram negative gut enterobacteria Hafnia alvei, Pseudomonas aeruginosa, Morganella morganii, Pseudomonas putida, Citrobacter koseri, and Klebsiella pneumonia
- Alzheimer's dx and parkinson

