
GUT HEALTH

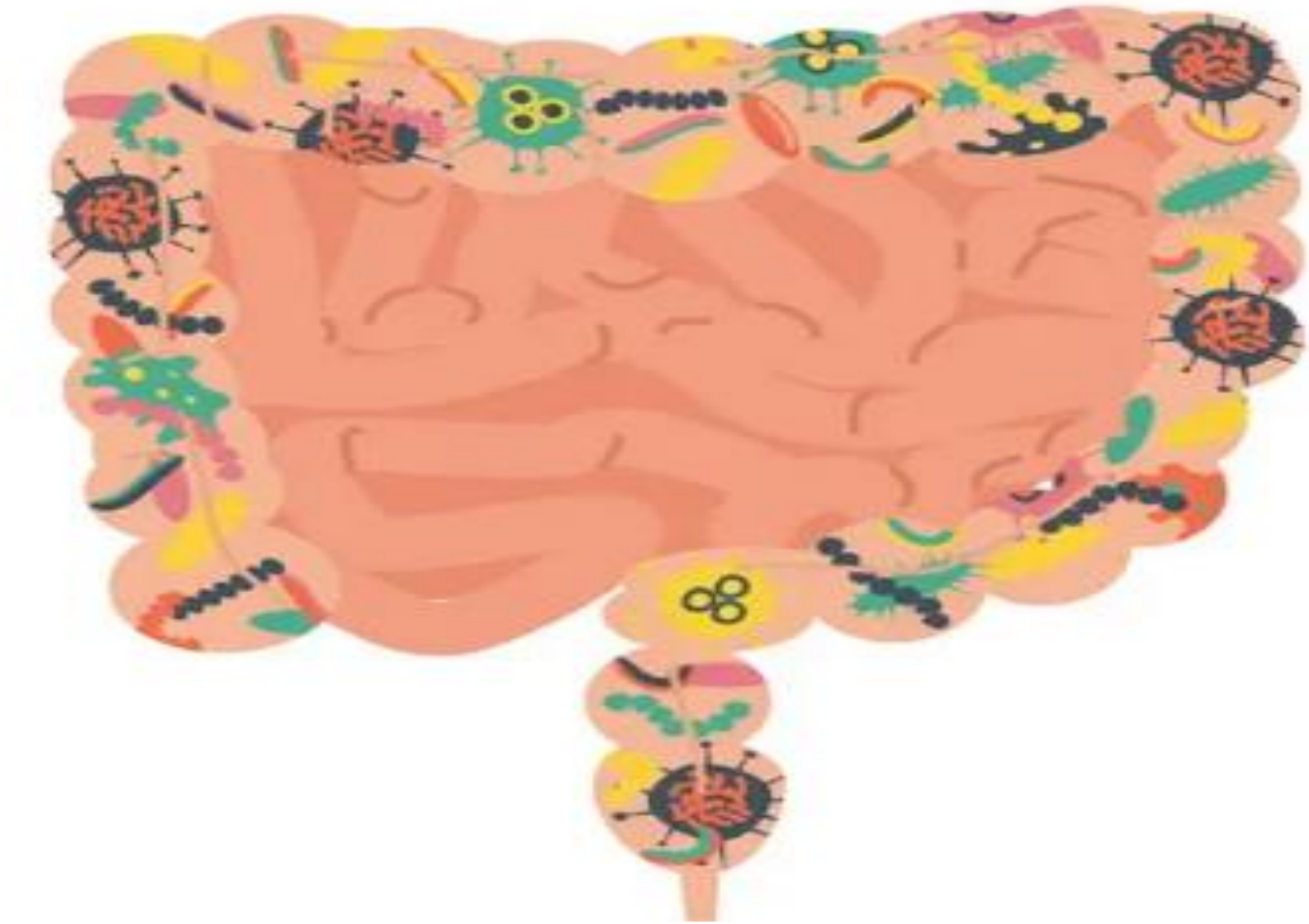
Definition:

- A healthy gut contains healthy bacteria and immune cells that ward off infectious agents like bacteria, viruses and fungi.

- A healthy gut also communicates with the brain through nerves and hormones, which helps maintain general health and well-being.



INTRODUCTION



- The alimentary tract represents an interface between the external environment and the body.

- Within it exists a complex polymicrobial ecology that interacts with the internal and external environment and has an important influence on health and disease.

- The properties of isolated microorganisms do not explain how the polymicrobial community functions or why its organisms can grow under conditions that should be deadly to them .

- An understanding of how microorganisms interact with each other, their host, and the luminal contents is expanding rapidly.



- A major advance in understanding the function of the intestinal microbiota has been the development of techniques that permit a detailed assessment of the composition of the flora and its distribution throughout the alimentary tract.

- One of the methods to visualize single bacterial species within complex communities is called ribosomal RNA fluorescence in situ hybridization (FISH).

EVOLUTION'S ROLE IN THE DISTRIBUTION OF INTESTINAL MICROBIOTA



- Animals have developed multiple mechanisms to control bacteria that enter the digestive tract, which can be broadly divided into those that suppress their growth (eg, salivary lysozyme, gastric acid, secretion of defensins) or those that separate them from the host by creating a physical barrier (eg, the mucus barrier).

- Polymicrobial communities such as exist in the intestine are much more resilient to these defenses than bacterial monocultures.

- They exhibit a coordinated response to environmental challenges, resist antibiotics, and can evade the host's immune response and are thus able to persist under extreme conditions.

- As a result, the control of bacterial growth by the host is never absolute and the intestine is never sterile.
- The occurrence, composition, and organization of intestinal microbiota in each gut segment depend upon whether suppression or separation dominates.
- In gut regions with active suppression of microbiota, the bacteria are occasional, of variable composition, and of low concentration.
- A complete separation of bacteria from the mucosa and low levels of suppression lead to the development of an intestinal reservoir in which bacteria can grow and reach high concentrations. Bacteria are indigenous to these intestinal regions.

- The balance of suppression and separation mechanisms depends upon the evolutionary impact of bacteria on promoting health or causing disease.

- As an example, plant-feeding animals use microorganisms to digest cellulose, which would otherwise be indigestible. Thus, bacteria that digest cellulose are indigenous to the rumen of these animals.
- On the other hand, the nutrients resulting from bacterial degradation in ruminates are resorbed in the small intestine where bacteria would be clear competitors and are therefore suppressed. Thus, bacteria are occasional and present in only low concentrations in the small intestine.

- Similarly, bacteria in the colon are important for maintaining the health of colonic enterocytes and for digesting nutrients that could not be absorbed in the small bowel. As a result, bacteria exist in high concentrations in the colon.

BACTERIA IN THE UPPER GASTROINTESTINAL TRACT



Mouth :

- Microorganisms from the external world first contact the alimentary tract in the mouth.

- Bacteria can be found in high concentrations on food remnants, the dental surface and within or attached to desquamated epithelial cells, and suspended in oral secretions.

- There are also high concentrations of bacteria in saliva .

- Despite the high concentration of bacteria in the oral cavity, samples taken from the stratified epithelium of the mouth and saliva taken directly from the salivary duct are virtually sterile in healthy persons.

- This reflects defensive mechanisms working in concert to suppress bacterial adhesion and growth.

Tonsils :

- Similar to the rest of the oral cavity, no constant pattern of colonization can be found on the surface of the tonsillar epithelium .

- Most of the epithelial surface of tonsils is free of bacteria even in tonsillectomy specimens obtained from individuals with chronic tonsillitis .

- When bacteria were found, they were localized either to circumscribed regions of diffuse infiltration, within macrophages, superficial infiltrates, singular purulent fissures, or abscesses.

Stomach and duodenum :

- Cultures of fluid from the stomach or duodenum of healthy volunteers contain bacterial concentrations of 10^3 to 10^4/mL, depending in part upon the composition of digested food.
- Fluorescence in situ hybridization (FISH) demonstrates that bacteria in the stomach and duodenum are localized strictly within the intestinal lumen and separated from the mucosa by a mucus layer.
- Their composition is variable, reflecting the heterogeneous composition of the ingested flora.
- In healthy individuals, the mucosa and the mucus layer of the stomach and duodenum are free of bacteria.

- In patients with *Helicobacter pylori* infection, the mucosal surface of the stomach is covered with a bacterial biofilm in which *H. pylori* is predominant

Pancreatic tract :

The microflora of the normal pancreatic duct has not been extensively studied, since samples available from healthy individuals are not readily available.

FISH analysis of pancreatic duct biopsies obtained during ERCP from patients with benign or malignant obstruction of the pancreatic duct have demonstrated islands of bacterial adhesion in approximately 70 percent of the biopsies.

The anatomically normal pancreatic duct epithelium is generally sterile. Thus, bacterial islands appear to be located in regions of disturbed duct anatomy.

Bacterial species in the pancreatic duct are diverse and highly variable among individuals.

Biliary tract :

- Biopsies of healthy bile ducts are not readily available and thus the microflora of the biliary epithelium in health has not been extensively evaluated.

- Gallbladder resection specimens obtained from patients who did not receive preoperative antibiotics are free of bacteria, indicating that the bile duct epithelium is normally not colonized.

Gallstones :

- A similar trend of the bacterial biofilm vanishing after local deposition of organic substances can be observed in gallstones.

- Because gallstones are essentially foreign bodies, they should be permanently colonized.

- Bacteria can indeed be found in loose brown pigment stones and sludge, which are an initial stage in the formation of gallstones.

Small intestine :

- The epithelial surface of the small intestine in a healthy human is not colonized.
- Occasional groups of bacteria can be found in low concentrations of 10^5 or less.

- Pathologic conditions with altered microbiota in the small intestine include
  - acute and chronic infections
  - bacterial overgrowth
  - inflammatory bowel disease.

- Common to all of these conditions are :
  - ✓ disruption of the mucus barrier
  - ✓ loss of bacterial separation between mucosa and lumen
  - ✓ bacterial adherence
  - ✓ Invasion
  - ✓ translocation

BACTERIA IN THE COLON

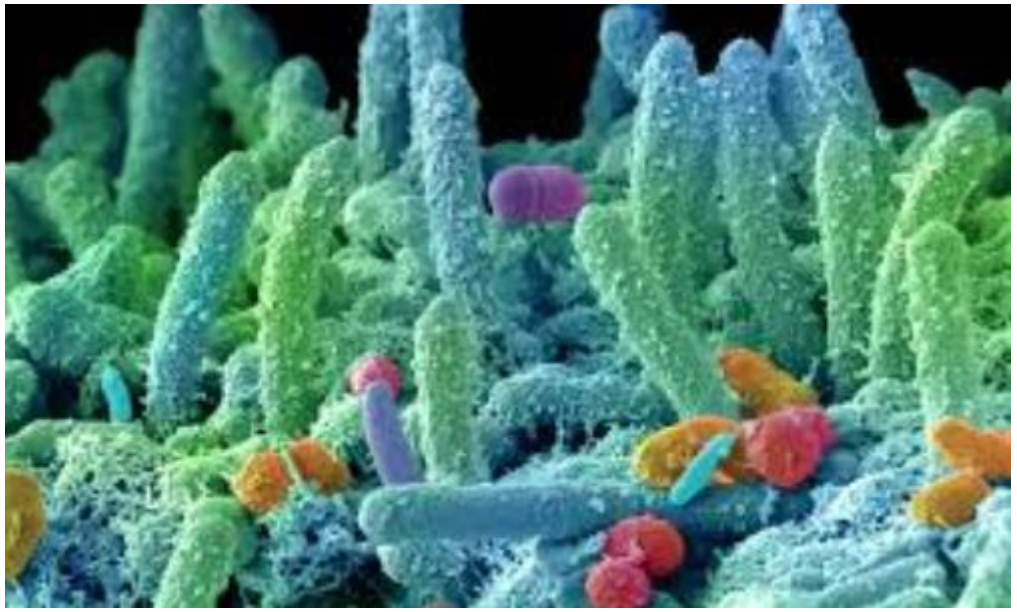


The role of microbiota in colonic function

- The large intestine is a bioreactor in which the host uses bacteria to degrade indigestible leftovers. Bacteria produce valuable substances such as vitamins and short fatty acids by degrading waste products.
- In humans, resorption in the large intestine is restricted mostly to water and electrolytes. Bacteria in the human colon are mainly responsible for the reduction of the fecal mass.
- Which bacterial species are responsible for these processes are not well known. However, a reasonable assumption is that the numerically predominant bacteria are indispensable for the biochemical processes that occur in the colon.
- *Eubacterium rectale* (*Roseburia* spp), *Faecalibacterium prausnitzii*, and *Bacteroides* groups comprise each 10 to 30 percent and cumulative 70 percent of the total microbiota in humans .
- Although the fecal flora is one of the most well-characterized microbiota, many of the bacterial species inhabiting the large intestine are unknown. Strict anaerobic species predominate, although the diversity of bacteria is high and consists of approximately 3000 to 5000 species

- In the colon, bacteria reach concentrations of up to the 10^{11}/mL and compose up to 90 percent of the fecal mass.
- Such high bacterial concentrations can be achieved only under active facilitation of bacterial growth. Bacterial growth is facilitated by peristalsis (which extensively mixes bacteria with fibers), and maintenance of optimal viscosity and temperature.
- It was initially believed that the immune system was tightly regulated to respond to pathogenic intestinal bacteria while tolerating commensal bacterial. However, it is increasingly recognized that bacterial residents of the large bowel cannot be easily divided as being pathogenic or nonpathogenic.
- Many of indigenous bacteria are known pathogens. As examples, *Escherichia coli* cause sepsis, *Bacteroides* cause abscesses, Enterococci cause endocarditis, and *Clostridium histolyticum* causes gas gangrene. These bacterial groups are considered normal inhabitants of the human colon because they can be found in every healthy person.
- Fluorescence in situ hybridization (FISH) analysis of the mucosal flora has clearly demonstrated that the host does not tolerate the indigenous microbiota but separates them from contact with the mucosa

Mucus barrier



- Colonic and ileal biopsies from healthy persons are covered with mucus that is free of bacteria.

- The separation of fecal bacteria from the mucosa by mucus can be seen in sections of normal appendices, which were resected for suspected acute appendicitis and found to be normal.

- In healthy humans, the separation of bacteria from the mucosa is equal in the proximal and distal colon and bacteria are never found in crypts.

Composition and Volume of GI Gas



- The GI tract normally contains a relatively small amount of gas.
- The volume of gas within the intestinal lumen is determined by the balance between gas input and output, a highly dynamic process.
- Gas input may result from swallowing, chemical reactions, bacterial fermentation, and diffusion from the blood
- Gas output involves belching, bacterial consumption, absorption into the blood, and anal evacuation.
- Despite this variety of factors, the volume of gas within the GI tract is remarkably constant and similar among healthy persons, suggesting that it is under homeostatic control.
- Measurements of intestinal gas volume have been performed using a specifically designed CT technique.
- Data acquisition is relatively simple, but analysis is fairly elaborate and has been carefully validated. This technique has confirmed previous measurements showing about 100 to 200 mL of gas in the fasting state and somewhat larger volumes (65% increase) after ingestion of a meal



- Five gases—N_2, O_2, CO_2, H_2, and methane (CH_4)—were found to account for more than 99% of intestinal gas; many additional gases were present in trace concentrations.

- N_2 was usually predominant
- O_2 was present in low concentrations
- the concentrations of CO_2, H_2, and CH_4 were highly variable.

- GI gas is distributed in 3 compartments: stomach, small intestine, and colon.
- In each compartment the volume and composition of gas depend on gas metabolism and diffusion of gas between the lumen and blood.
- Excess gas in 1 compartment is propelled by peristalsis to the next, and the end product is evacuated per anus.

Metabolic Activity of Colonic Microflora



- The composition of the colonic microflora (and therefore, the amount of gas produced on a given diet) varies considerably among individuals, depending on early environmental conditions as well as factors encountered later in life, such as antibiotic and dietary exposures.
- In the colon, luminal microflora produce and consume intestinal gases.
- The colon harbors large numbers of gas-producing microorganisms that ferment undigested substrates, with the release of H 2 and CO 2
- Bacterial metabolism seems to be the sole source of intestinal H 2 .
- Three types of microorganisms consume H 2 : acetogens, sulfate-reducing organisms, and methanogens.
- Acetogens consume H 2 and CO 2 to synthesize short-chain fatty acids.
- Sulfate-reducing microorganisms use H 2 to reduce sulfate to sulfide.
- Methanogens use H 2 to reduce CO 2 to CH 4 .This last reaction uses 5 moles of gas to produce 1 mole of CH 4 and therefore results in a reduction in bowel gas.

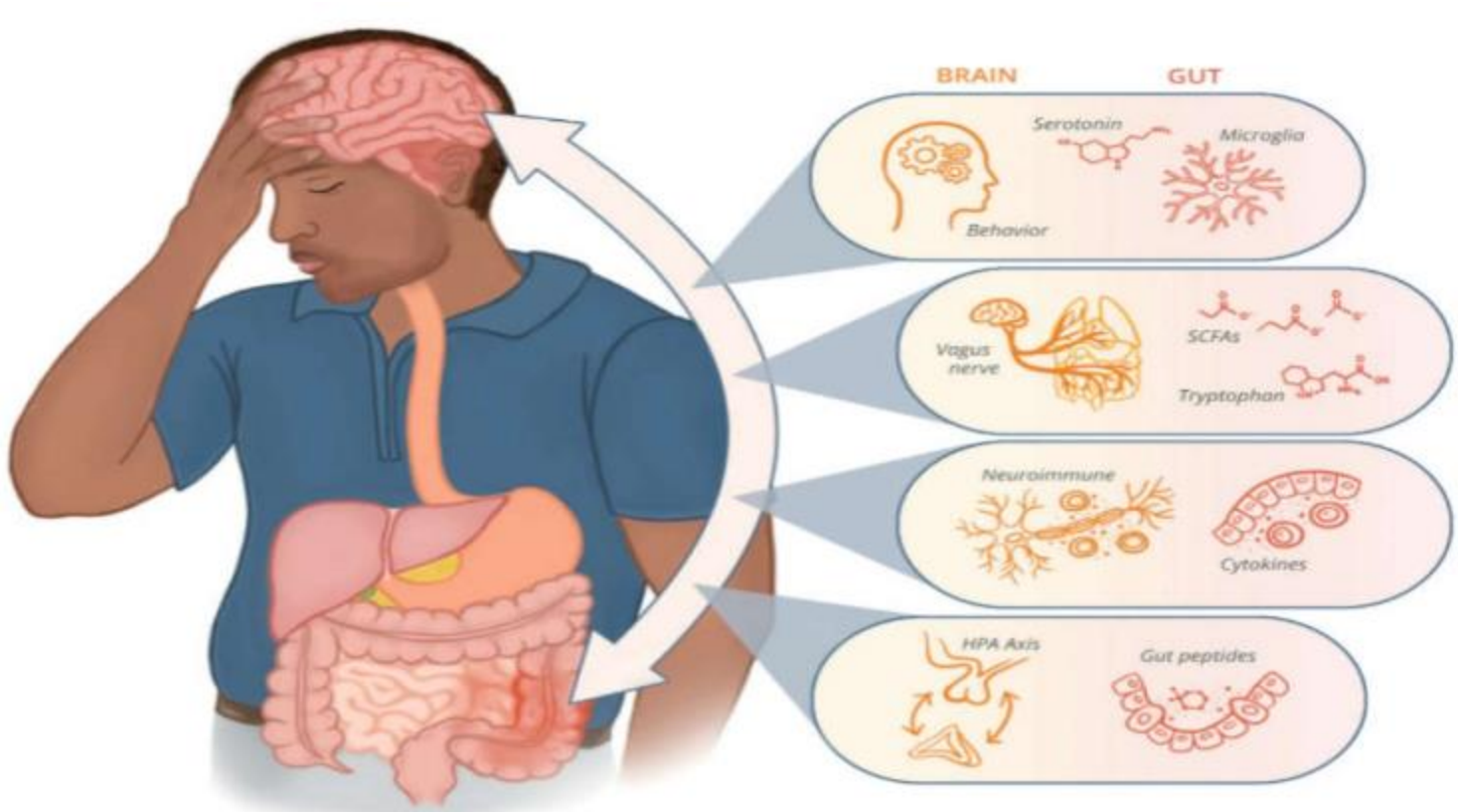
- Only about 40% of adults have sufficient concentrations of methanogens to yield detectable breath CH 4 concentrations.

- Sulfate-reducing bacteria and methanogens compete for H 2 ; methanogens tend to locate in the distal colon, and if methanogens are abundant, sulfate-reducing bacteria are confined to the proximal colon.

Gut-brain axis



- Many people with gastrointestinal disorders – such as irritable bowel syndrome (IBS) and inflammatory bowel disease – perceive pain more acutely than others because their brains are more responsive to pain signals from the GI tract.
- Research is showing that the gut is deeply connected to the brain, and one influences the other in positive and negative ways.
- “Things are being absorbed, things are being excreted. But someone with IBS will perceive those processes as pain and bloating – as symptoms. There is some type of amplification from your gut to your spine and from the spine to the brain.
- “It all refers to the gut-brain axis,” . “We’re now learning that our GI tract has a brain of its own.”
- Traditional thinking has always been focused on how the brain impacts the gut. In reality, the two mutually affect and depend on each, thus the gut-brain axis.
- In other words, the gut and the brain “talk” to each other. The trillions of microbes in our gut “talk” to our brain via blood circulation, the gut’s nervous system and the gut’s immune system. In turn, the brain “talks” to our gut using the same pathways.
- People often say, “I have a gut feeling” or “I just feel it in my gut.” That’s because when you feel anxious, scared, excited or nervous, you feel it first in your gut.
- The cool thing is we can influence how the brain in the gut operates through our own behaviors.”


BRAIN
GUT
Serotonin
Microglia
Behavior
Vagus nerve
SCFAs
Tryptophan
Neuroimmune
Cytokines
HPA Axis
Gut peptides



Healthy GUT Healthy YOU



Tanks for your Attention