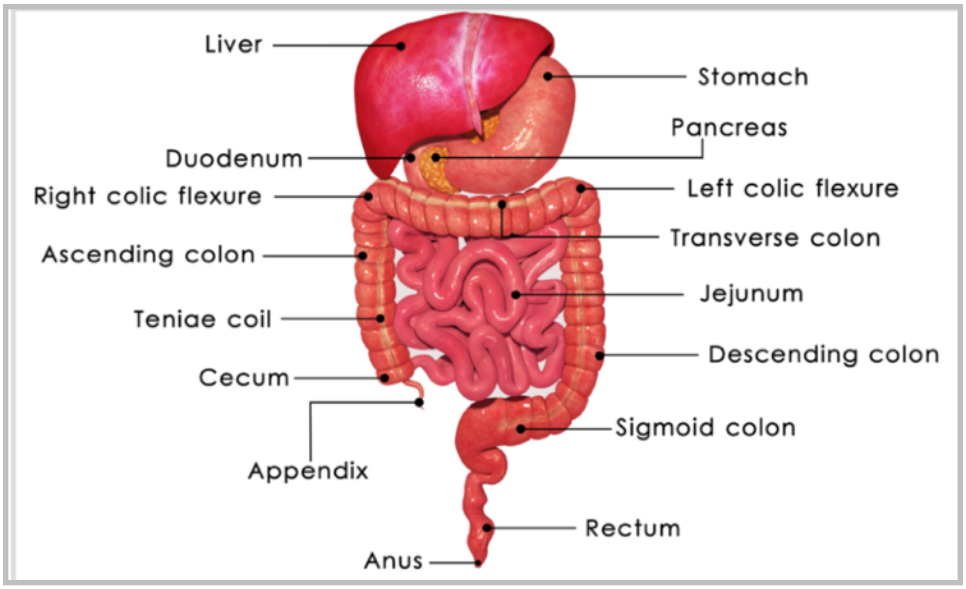
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Gut Basic Physiology Review



The GI tract is a hollow tube starting with the mouth and ending with the anus, consisting of the mouth, the pharynx, the esophagus, the stomach and intestines, the rectum, and the anus, as well as the accessory organs that assist the GI tract like the salivary glands, liver, gallbladder, and pancreas.

The GI tract has two primary purposes:

1. Breaks food into nutrients, which are then absorbed to provide us with energy.
2. Serves as a barrier system that protects against antigens and keeps foreign substances from getting inside the bloodstream and the body.

COMPONENTS OF THE GI TRACT:

1. Oral cavity:
    - Amylase begins to break down complex carbohydrates.
    - Salivary glands also produce immune substances that can assist us in fighting microorganisms that we might be exposed to.
2. From the mouth, the food passes through the pharynx.
3. The esophagus then transfers substances to the stomach.
4. The stomach is a J-shaped organ divided into four regions: the cardia, the fundus, the body, and the pylorus.
    - The primary functions of the stomach are:
        1. Short-term storage of food

2. Mechanical breakdown of food
3. Chemical digestion of food via stomach acid and enzymes
4. Killing of microorganisms that we swallow, also by stomach acid
5. Absorption of some substances like alcohol

5. From the stomach, chyme, which consists of food mixed with stomach acid and enzymes, passes into the small intestine.
6. The small intestine is composed of three sections, listed here in descending order:
   - Duodenum combines enzymes produced in pancreas and bile salts from the liver
   - Jejunum is where the majority of digestion and absorption occurs
   - Ileum is the longest segment; it empties into the cecum, which is the first section of the colon

The small intestine overall performs a majority of the digestion and absorption of nutrients.

THE LIVER:

The liver is situated in the upper-right quadrant of the abdomen.

Its main role in digestion is the production of bile and the metabolism of nutrients. All nutrients that are absorbed by the gut pass through the liver, where bile salts break down lipids into smaller particles so that they can be acted on by pancreatic enzymes.

THE GALLBLADDER:

Its main function is the storage and concentration of bile produced by the liver.

THE PANCREAS:

The primary function of the pancreas is the production of enzymes to break down food.

The enzymes include things like carbohydrases, which are enzymes that break down carbohydrates; lipases that break down fat; nucleases that break down nucleic acids; and proteolytic enzymes, which break down protein.

We have ten times more microbes in the human body than human cells!

Gut microbes are absolutely crucial to health; they promote normal GI function, protect against infection, regulate metabolism, and are home to a majority of the immune cells in our body.

An altered gut microbiome is implicated in just about every chronic inflammatory disease.

For example, there is a link between the gut and the brain. Problems in the gut, like inflammation, can lead to a higher risk of problems associated with the brain, such as dementia, autism spectrum disorders, neurological conditions, depression and/or anxiety.

INFANTS:

- Research has shown that the location of the infant's initial microbiome exposure strongly affects the composition of the infant's gut for several years after, and perhaps permanently. This explains why children who are born via C-section are at greater risk for asthma, obesity, type 1 diabetes, and several other conditions.
- Babies that are exclusively formula-fed are known to have significant differences in gut microbiota compared to fully or partially breastfed babies. This is important because pioneer bacteria, which are the first bacteria to colonize the infant gut, have been shown to alter gene expression to create a more favorable environment for themselves and a less favorable environment for later bacteria.

ADULTS:

There are several factors that are known to influence the gut microbiota, including:

- Diet proteins, fats, and especially carbohydrates and fiber, or fermentable carbohydrates
- Medications, particularly antibiotics and NSAIDS
- Chronic stress
- Chronic infections
- Physical inactivity

THE GUT MICROBIOTA HAS THREE PRIMARY FUNCTIONS:

1. Metabolic
    - Bacteria in the gut break down dietary compounds that might otherwise cause cancer; synthesize vitamins like biotin, folate, and vitamin K; convert non-digestible carbohydrates to short-chain fatty acids like butyrate, which play an important role; provide energy and benefit cells lining the gut; and help with the absorption of minerals like calcium, iron, and magnesium. Microbes also determine how we process and store the food we eat. We know that certain patterns of gut microbes increase energy storage and lead to obesity, whereas other patterns have the opposite effect and tend to lead to a lean phenotype.
2. Structural
    - Bacteria ferment carbohydrates to produce short-chain fatty acids like butyrate or propionate. Short-chain fatty acids then stimulate the growth and differentiation of epithelial cells. They also inhibit cell proliferation in the colon.
    - Dysbiosis can lead to the production of endotoxins like lipopolysaccharide (LPS), which activates zonulin, a protein that regulates intestinal permeability via its effect on the tight junctions. This LPS production can make the gut barrier more permeable.

3. Protective
    - The mucosal lining is the primary interface between the gut and the external environment. The gut contains the gut-associated lymphoid tissue (GALT), which comprises 70 to 80 percent of the immune cells in our body. The microbial composition of the gut has been shown to affect the composition and function of the GALT.

GUT PERMEABILITY:

The protein zonulin, discovered by Alessio Fasano, plays a major role in increasing intestinal permeability. Zonulin levels have been shown to be high in celiac disease, type 1 diabetes, MS, rheumatoid arthritis, inflammatory bowel disease, and other autoimmune conditions. Researchers have found that you can induce type 1 diabetes in mice almost immediately by exposing them to zonulin. These mice develop leaky gut and then begin producing antibodies to cells that are responsible for making insulin.

There are several known factors than can increase gut permeability, including:

- Diet. For example, an increase in gut permeability is seen in celiac disease and even non-celiac gluten sensitivity.
- Flour, sugar, and seed oils have been shown to alter the gut microbiota, resulting in increased production of lipopolysaccharide, which causes the release of zonulin, triggering leaky gut.
- Things like SIBO; chronic stress; infections like H. pylori, parasites, or bacteria like Clostridium difficile; excess alcohol consumption; and medications, particularly aspirin, antibiotics, and acid-blocking drugs like PPIs or NSAIDs can all contribute to leaky gut via their effect on the microbiome.
- Environmental toxins like bisphenol A (BPA) and heavy metals have been shown to contribute to leaky gut.