Microflora of the Human Gastrointestinal Tract

First Runner Up, Science

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Abstract

The human body plays host to a large and diverse group of microbial inhabitants. The intestinal system is certainly no exception. Extending from the esophagus to the anus, the human gut provides varying environments in which microorganism can exist and often thrive. Obtaining samples of these microbes to examine can be difficult, and much of what is known about the human gut has been learned from studying other animals. Among the most common genera of intestinal microbes inhabiting both humans and animal are Bacteroides, Clostridium and Bifidobacterium. Each of these genera exists within their own niche and has a symbiotic relationship with the digestive system and with each other. The gastrointestinal tract offers environments varying in pH, movement, and oxygen and nutrient availability, all of which affect which type of microbe may colonize an area. This composition of gut flora can also be affected by antibiotics which can lead to detrimental effects on the digestive system of the host. The host may also suffer should another part of the body become infected with an intestinal microbe. Despite their potential to cause harm, microorganisms play a crucial role in the human gut environment and have proven to be an integral component to human metabolism and healthy functioning.

The human gastrointestinal tract is essentially a tube that extends from the mouth to the anus. Its function, with the aid of digestive organs such as the liver, gallbladder and pancreas, is to break down ingested food into increasing smaller constituents allowing for their absorption and distribution to the rest of the body. Beginning with the oral cavity, food passes through the oropharynx and laryngopharynx to the esophagus before being expulsed into the stomach. The partially digested food (now called chyme) then passes through the anaerobic sections of the gut—the duodenum, jejunum and ileum of the small intestine—and is expelled out of the body through the anus after passing through the caecum, the colon, and the rectum of the large intestine (Wilson, 2005). Distinct microflora are found in each section of the gut; its lumen (interior) holds a number of microbial cells that is approximately 10 times larger than the number of eukaryotic cells in the human body (Bengmark, 1998). This number includes an estimated 300-500 different species of bacteria (Simon, Gorbach, 1984) spanning the entire gut (esophagus to anus) through its varying environmental conditions.

How gut environments vary from one region to another can be affected by several factors. The movement of food through the gut is one such factor. This movement is often achieved by peristalsis,

where circular muscles surrounding the food bolus constrict, pushing it down, and longitudinal muscles below it contract, thereby expanding the volume area below the bolus and allowing it room to descend. This peristaltic activity is found in the esophagus, stomach and small intestine and is an important clearance mechanism that rapidly propels fluid and particulate matter. This rapid movement of matter hinders microbial colonization of the mucosal surface (Wilson, 2005).

This mucosal surface of the gut is another example of how gut environments vary. The mucus found throughout the gut is thickest (highest in mucin content) in the stomach and thinnest in the colon (where it has a lower mucin content). The mucus layer's function is mostly a protective one; it shields the underlying tissue from microbial colonization, acid and digestive enzymes, and forms a barrier which decreases the friction between the underlying tissues and the matter passing through the gut.

pH is another feature that affects gut environment, especially in the stomach. The median intragastric pH is 1.4 but pH is influenced by factors including age, diet (Finegold *et al*. 1974) and whether food or drinks have recently been ingested. Meals can cause pH to rise, often ranging from 1 to 5 (Hills, Marsh, 1989). Chyme entering the small intestine is very acidic, but its pH is increased quickly by the alkaline fluids present in the small intestine, becoming neutral by the time it reaches the ileum (Wilson , 2005). Oxygen availability also varies along the gastrointestinal tract, from the aerobic environment of the stomach to the anaerobic large intestine.

Studies of the flora of the human intestine are complicated by the problems of obtaining samples of intestinal contents. Most of the intestinal tract is normally inaccessible for examination. Therefore, many studies of the intestinal flora are by necessity studies of the bacteria found in feces. Unfortunately, the microorganisms found in this type of sample accurately represent only the flora of the rectum. Abdominal surgery is another sampling option, but it has been found that the fasting required, the anesthesia, and the stimulation of the gut through the surgery itself cause changes in the composition of gut flora (Drasar, Barrow, 1985). Capsules swallowed to minimize the invasiveness of surgery have the problem of allowing microflora to incubate, protected within the capsule itself, until the capsule is passed. Fistulae have the drawback of excess mucus production at the entrance site, inhibiting microfloral growth (Drasar, Barrow, 1985). Because of these complications, much of what we know about the intestinal flora of humans has been gleaned from research on animals, and new research techniques are continually adapted.

An organism's initial inoculum of microorganisms is usually derived from the mother at birth. Its composition will change over an individual's lifespan and also varies among geographic regions, but there are certain indigenous flora that are commonly isolated. Numerically, the most important genus of intestinal bacteria in animals and man is *Bacteroides*. These are all non-motile, Gram-negative, anaerobic, non-sporing rods, although some may show varying degrees of polymorphism (Drasar, Barrow, 1985). Although anaerobic, *Bacteroides* are among the most oxygen tolerant of all anaerobes. Their nutritional requirements are simple and consist of vitamin B_{12} and an iron derivative of

hemoglobin. Ammonia is their primary source of nitrogen. Energy, electron and carbon sources are mainly carbohydrates and polysaccharides, including starch, cellulose, and pectin gained from human ingestion. The major end products of *Bacteroides*' carbohydrate metabolism are succinate, propionate and acetate (Wilson, 2005).

One of the most abundant of the *Bacteroides* spp. is *B. thetaiotaomicron* (Wilson, 2005). Its genome has been sequenced, with various findings indicating its ability to sense and respond to changes in the environment. In addition, this species is able to horizontally transfer genes that encode antibiotic resistance and virulence factors (Morrison, 1996). *Bacteroides* spp. have a high pathogenic potential and account for nearly two-thirds of all anaerobes isolated from clinical specimens—the most frequently isolated being *B. fragilis*, which is often the cause of peritoneal infection. In addition to being oxygen-tolerant, this species of *Bacteroides* has a number of virulence factors, a major one of which is its capsular polysaccharide, which allows it to evade host defense systems (Wilson, 2005).

Another key genus of the intestinal microflora in humans in *Clostridium*. This genus is the most ubiquitous of the spore-forming bacteria isolated from the human gut. They are Gram-positive, motile, and obligately anaerobic prokaryotes. They are chemoorganoheterotrophic rods, often found in pairs or short chains. Most are fermentative or protein-degradative (proteolytic) species that will produce acetate and butyrate as products of carbohydrate metabolism, and acetone and butanol as fermentative products (Wilson, 2005).

Many species of the genus *Clostridium* are pathogenic, causing disease in humans and animals. They may be involved in polymicrobial infections such as peritonitis, intra-abdominal abscesses, and septicemia (Wilson, 2005). *Clostridium perfringens* is a normal component of the human gut flora, but may contribute to those polymicrobial infections, and may also cause gas gangrene. *Clostridium difficile*—so named due to the difficulty in isolating it and growing it in vitro (Fox, 2007)—is another pathogenic species that may cling to the microvilli of the gut and proliferate when other gut flora are wiped out by antibiotics. It is a natural resident of some individuals' gut flora, but many acquire *C. difficile* nosocomially (during hospital visits). *C. difficile* can cause pseudomembranous colitis (inflammation of the colon) in humans (Fox, 2007).

Bifidobacterium spp. are another group of bacteria comprising normal human gut microflora. They may be, in fact, the first important microorganism to contribute to healthy functioning in infants. (Tissier, 1906). They are non-sporing, non-motile, pleomorphic Gram-positive rods and may be found singly, in chains, or in clumps (Wilson, 2005). They metabolize glucose, producing acid (acetate and lactate), but can ferment other sugars and hydrolyse polysaccharides, proteins and peptides. They gain their carbon, energy, and electrons from simple compounds, mainly mono- and polysaccharides. They also utilize ammonia, and produce large quantities of amino acids and vitamins such as thiamine, folic acid, and cyanocobalmin (Wilson, 2005). *Bifidobacterium* spp. are tolerant of low pH levels and can inhibit the growth of other microbes due to their acid production.

Bifidobacterium spp. are very rarely implicated in human infections and have been shown to produce a broad-spectrum antibiotic that inhibits the growth of *C. difficile*, *B. fragilis,* and other enteropathogens such as *Vibrio cholorae*, *Salmonella* spp., *Campylobacter* spp. and *Escherichia coli* (Wilson, 2005). Microorganisms such as *Bifidobacterium longum* may inhibit the growth of other members of the microflora, not only though the production of antimicrobial substances, but also by consuming an essential nutrient, occupying space for adhesion or by creating an environment that is unsuitable for the growth of other microorganisms.

The genome of *B. longum* has been sequenced, in part to help understand its optimal growth conditions due to the overwhelming health benefits of this species to humans. *B. longum* has been associated with diarrhea prevention in antibiotic-treated patients, cholesterol level reduction, alleviation of lactose intolerance symptoms, improved immune functions, and cancer prevention via protection from several types of carcinogens (including methyl quinolones, heterocyclic amines, nitrosamine, and azomethane [Joint Genome Institute 2011]).

Probiotics are dietary supplements that are ingested to restore beneficial bacteria to the host, and are often recommended after taking a course of antibiotics. The genus *Bifidobacterium* includes several well-studied species, known to be probiotics, which may have antagonistic effects on the colonization of other microorganisms. *Bifidobacterium* are GRAS microbes: "generally regarded as safe" by the United States Food and Drug Administration. According to Wilson (2005), probiotics for intestinal use should be naturally found in humans, be harmless, be able to be manufactured; should withstand passage through the gut, should eventually colonize the gut, and should exert their benefits quickly. The field of probiotics is a rapidly growing one, and some of their supposed benefits are not yet fully understood.

Each of the genera *Bacteroides*, *Clostridium,* and *Bifidobacterium* exists within their own niche and has a symbiotic relationship with the digestive system and with each other. These are only a few examples of the many microbes that exist within the human gut. There is much left to learn about the intestinal microflora, and this field of research remains an important and growing one, despite difficulties in sampling. Through varying conditions and environments from the esophagus to the anus, the microflora of the human gastrointestinal tract play a crucial role in the human gut environment and have proven to be an integral component to human metabolism and healthy functioning.

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