

The Esophageal and Gastric Microbiome in Health and Disease



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KEYWORDS

• Esophagus • Stomach • Microbiota • Gastric acidity • Health • Disease

KEY POINTS

- The esophagus and stomach are host to their own population of bacteria, which differs in health and disease.
- *Helicobacter pylori* uniquely colonizes only gastric mucosa, but an increasing number of bacteria is now isolated from the gastric juice and gastric mucosa, including *Lactobacillus*, which also colonizes gastric mucosa.
- The presence of *H pylori* alters the populations of other gastric bacteria with a marked reduction in diversity.
- Alterations in intragastric acidity may be the cause or the consequence of changes in the microbial populations of the stomach.
- Esophageal inflammation is associated with an altered microbiota in gastroesophageal reflux disease, Barrett's esophagus, eosinophilic esophagitis, and cancer.

INTRODUCTION

The microbiota of the esophagus and stomach have been the least systematically studied in the organs of the gastrointestinal tract and, until recently, most publications have reported phenomenological observations and associations rather than underlying physiologic or pathophysiologic mechanisms. The discovery of *Helicobacter pylori* by Marshall and Warren in 1982¹⁻³ has focused attention over the last 30 years on the unique characteristics of this bacterium to colonize and alter the immunologic and physiologic functions of the host.

The widely held view was that the gastric secretions of hydrochloric acid and the proteolytic enzyme pepsin ensured a sterile stomach despite numerous observations

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by scientists from the late nineteenth century describing bacteria in the acidity of the stomach.⁴ This may have influenced the commonly held view that *Helicobacter* species are the only organisms capable of colonizing the human stomach. *H pylori* research has increased the understanding of how it can modify its own microclimate, and it is now clear that other organisms also occupy the gastric mucosa and lumen.

Indeed, further investigations with modern techniques have shown that the microbiota of the stomach involves hundreds of phylotypes with a microbial density of between 10^1 and 10^3 colony-forming units (CFU)/g.⁵⁻⁷ There are unique anatomic and physiologic features of the stomach that differentiate the microbiota here from that elsewhere in the gastrointestinal tract and especially the esophagus.

It is important to appreciate that the definitions and basic concepts and methodology for identifying bacteria and other microorganisms that constitute the microbiome and their interactions with the immune response, are covered earlier in this issue and also apply to the upper gastrointestinal microbiota. The terms microbiome and microbiota comprise the bacterial, fungal, viral, and potentially prion populations. However, this review addresses the bacterial components of the esophagus and stomach and the inherent differences that require consideration.

THE ESOPHAGEAL MICROBIOME IN HEALTH

Esophageal Microbial Flora

Under normal physiologic conditions, the esophagus acts as a conduit and does not retain food contents, which is in contrast to the oral cavity or the stomach and colon. Culture studies based on washings from the esophagus suggested that bacteria that were obtained from the esophagus were either swallowed from the oral cavity or reached the distal esophagus during reflux from the stomach.⁸ A study of the bacterial flora of the oral cavity and the upper and lower esophagus, obtained by esophageal brushings and biopsy samples, revealed that *Streptococcus viridans* is the most common bacterium.⁹ Methods of bacterial detection, which are independent of culture, are increasingly reported and characterize the diversity of the esophageal microbiota. In a group of healthy individuals, using broad-range 16S rDNA polymerase chain reaction (PCR) applied to esophageal biopsies, Pei and colleagues¹⁰ found a range of microbial diversity with the most prevalent organisms being *Streptococcus*, *Prevotella*, and *Veillonella*. Fillon and colleagues¹¹ studied the esophageal microbiome by sampling with a new technique, the Enterotest capsule, an esophageal string test and an oral string and nasal swab. They found that the diversity at the phylum level was similar, and the most common genera were also *Streptococcus*, *Prevotella*, and *Veillonella*, similar to those found by Pei and colleagues.¹⁰ In a study using PCR of biopsies from the distal esophagus in healthy volunteers, patients with either esophagitis or Barrett's esophagus (BE), Yang and colleagues¹² found that *Streptococcus* dominated in the healthy esophagus, whereas gram-negative anaerobes dominated in both esophagitis and BE. They further designated this division into 2 distinct types: type I and type II, respectively, for the 2 conditions.

THE ESOPHAGEAL MICROBIOME IN DISEASE

Several studies have reported changes in the microbiota of the lower esophagus in a variety of diseases, including reflux disease, BE, and esophageal carcinoma, in addition to eosinophilic esophagitis in a pediatric population.¹³⁻¹⁵

In patients with severe gastroesophageal reflux disease (GERD), Dunbar and colleagues¹⁶ reported histologic changes characterized by T-lymphocyte predominant inflammation with papillary and basal cell hyperplasia with no loss of surface cells.

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