

# Upper Gastrointestinal Tract Motility Disorders in Women, Gastroparesis, and Gastroesophageal Reflux Disease



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## KEYWORDS

- Sex differences • Women's health • Gastrointestinal dysmotility • GERD
- Gastroparesis • Estrogen • Progesterone

## KEY POINTS

- Female ovarian hormones (ie, progesterone, estrogen) are one of the main causes for the observed sex differences in upper gastrointestinal motility.
- Men have increased stomach acid production and more physiologic gastroesophageal reflux (GERD) than women, possibly explaining the increased complication rates of GERD in men.
- Healthy women's stomachs empty out slower than men. Women also perceive fullness and nausea more quickly and for longer periods of time than men.
- Women with gastroparesis tend to be more symptomatic than men. Their symptoms are also less likely to improve over time compared with men.

## INTRODUCTION

There are known sex differences in gastrointestinal (GI) motility in both healthy and diseased states, likely due to the effect of female hormones. Both estrogen and progesterone receptors are found throughout the GI tract and likely influence its motility.<sup>1</sup> There are several mechanisms that may account for the influence of these hormones on GI motility. In vitro studies suggest that estrogen is needed to prime and enhance

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the inhibitory effects of progesterone.<sup>2</sup> These hormones also likely mediate GI motility effects by eliciting changes in nitric oxide-containing neurons in the myenteric plexus and by affecting the number and function of mast cells in GI mucosa.<sup>3,4</sup>

Given the fluctuations of these female hormones during the menstrual cycle, pregnancy, and menopause, including the perimenopausal transition, one may also expect significant differences in GI motility during each of these female hormonal stages. Such differences have in fact been found in some studies and are described in this article. During the menses stage of the menstrual cycle, estrogen and progesterone are at their lowest levels. In the follicular phase that follows, estrogen levels begin to increase. It is this increase that triggers ovulation. Once ovulation has occurred, estrogen levels peak a second time followed by an increase in progesterone levels during the luteal phase to prepare the uterus lining for possible fertilization. If the egg is not fertilized, the corpus luteum degenerates and no longer produces progesterone, followed by a decrease in estrogen levels. The menstrual cycle then repeats itself. Menstruation is considered an inflammatory state characterized by increases in proinflammatory cytokines (eg, tumor necrosis factor- $\alpha$ ) and other mediators before menstrual flow. Evidence suggests that the inflammatory response is linked to declining progesterone levels in the late luteal phase.<sup>5,6</sup> During pregnancy, there is a progressive and substantial increase in progesterone and estrogen. After menopause, the opposite occurs: estrogen and progesterone levels drop significantly. The age at which menopause occurs and the pattern of the drop in hormone levels are variable. This transition is referred to as the perimenopause phase.

Despite the growing evidence that sex differences exist, most practitioners continue to diagnose and treat conditions of GI dysmotility without acknowledging them. Providers often generalize associated risk factors and prognoses of GI dysmotility conditions to both men and women. The effect of female hormonal stages (ie, menses, pregnancy, menopause) on GI motility is also not factored into treatment plans. To more accurately and effectively manage conditions of GI dysmotility for both men and women, providers should better understand the sex differences in both healthy and GI dysmotility conditions. More studies need to be conducted to better understand these sex differences.

This article specifically reviews sex differences in esophageal and gastric motility, first for healthy participants and then for the most common dysmotility conditions. For esophageal conditions, it will focus on gastroesophageal reflux disease (GERD) and other esophageal motor disorders. For gastric conditions, it discusses gastroparesis and accelerated gastric emptying. Although limited by the currently available literature, this article describes any known differences in signs and symptoms during each female hormonal stage for each aforementioned healthy and abnormal condition.

## THE ESOPHAGUS

### *Sex Differences in Esophageal Anatomy and Motility in Healthy Participants*

**Table 1** summarizes the sex differences in esophageal anatomy, motility, sensation, and pH studies. Women may have shorter esophageal sphincter lengths than men.<sup>7,8</sup> In healthy participants undergoing esophageal manometry, women are more likely to have longer esophageal body contractile duration than men.<sup>9–11</sup> Studies investigating sex differences in esophageal mechanical pain thresholds have conflicting results, possibly due to differences in balloon distention methods.<sup>12–15</sup> Although no sex differences in esophageal thermal pain thresholds have been found, women report higher chemical pain thresholds and larger referred pain areas compared with men,

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