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Stomach (P Malfertheiner, Section Editor)

Initiatives for a Healthy Stomach

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Abstract

Purpose of review The stomach is not only a major digestive organ, but also a sophisticated endocrine organ and an essential microbial defense organ. Stomach diseases, such as peptic ulcer diseases, stomach cancer, and functional dyspepsia, are important health burden worldwide. However, the public awareness about the stomach health and diseases are relatively low.

Recent findings To promote the awareness of medical professionals and also the general population on stomach health and diseases, the healthy stomach initiatives (HSI) was established in 2012. The HSI is very active in promoting international collaboration studies and public awareness events focused on stomach health and diseases. The HSI chose October 2 as the "World Stomach Day" to promote public awareness, to invite physician involvement, to increase scientific research, to apply government support, and to get industrial sponsorship. The first World Stomach Day was celebrated in Taipei in 2018 with very successful public educational activities.

Summary To promote the study of stomach diseases and the public awareness of stomach health is an important work. The HSI and the World Stomach Day will play essential roles in this work.

Introduction

The stomach is traditionally regarded as one of the major organs of digestive system, involving food digestion, nutrition absorption, control of secretion, and gastrointestinal motility, etc. However, recent evidence suggested stomach is also a sophisticated endocrine organ with sophisticated physiology, biochemistry, and immunology functions. Moreover, the rapid development of gut microbiota research has discovered the essential roles of the stomach in shaping gut microbial composition in the gastrointestinal tract.

The disorders of the stomach functions lead to several important diseases, such as peptic ulcer diseases, stomach cancer, and functional dyspepsia. Although the incidence rates of peptic ulcer diseases and stomach cancer have declined significantly in the past decades, they are still major health burden in specific populations, such as the elderly and East Asian populations. In contrast to the health burden, the public awareness of the stomach diseases is relatively low.

To promote the awareness of medical professionals and also the general population on stomach health and diseases, several leading scholars established the healthy stomach initiatives (HSI) in 2012. In the past years, HSI is very active in promoting international collaborations and public awareness events focused on stomach diseases. For further promoting the awareness about stomach health and diseases, HSI chose October 2, the day of first reporting the discovery of *Helicobacter pylori* in 1982, as the "World Stomach Day". The first World Stomach Day was celebrated in Taipei in 2018 with very successful public educational activities. In this article, the functions and diseases of the stomach will be first discussed. Then, the HSI and the World Stomach Day will be introduced.

Functions of stomach

Digestion

Digestion is the core function of the stomach. The key functions of stomach in digestion include food reservoir, acid and enzyme secretion, and its role in gastrointestinal motility. Once food is taken into stomach lumen, hydrochloric acid, the major component of gastric acid, is secreted by parietal cells. Hydrochloric acid, stimulated by gastrin, converts pepsinogen into pepsin. Pepsin digests proteins into smaller peptides, which will be further processed and absorbed in the intestine. The stomach itself contributes little to absorption of nutrients, except absorption of vitamin B12, iron, calcium and some drugs, such as aspirin.

Endocrine

In addition to digestion, stomach is also a sophisticated endocrine organ. Among these endocrine, gastrin is an important hormone secreted by stomach G cells. After food ingestion, gastrin is produced to regulate gastric acid secretion by binding to CCK2 receptors on stomach enterochromaffin-like cells to stimulate them to secrete histamine, which induces hydrochloric acid secretion by parietal cells [1]. Gastrin can be inhibited by somatostatin, which is secreted by D cells of the stomach and the intestine. In addition to regulate gastric acid secretion, gastrin is also important in regulating extracellular matrix proteins involving tissue remodeling, such as matrix metalloproteinase, tissue inhibitor of metalloproteinase, and urokinase plasminogen activator families [2•]. Another important endocrine, ghrelin, is also secreted in the stomach by ghrelinergic cells. It functions as a neuropeptide to regulate short-term appetite by influencing hypothalamus and vagal afferent signaling. Ghrelin also plays important roles in controlling energy homeostasis [3].

Motility

Stomach is also the coordinator of gastrointestinal motility. Stomach regulates the rate of emptying of ingested food and the following gastrointestinal tract motility. Recent evidence found two parallel neural circuits to inhibit (gastric inhibitory vagal motor circuit, GIVMC) or to accelerate (gastric excitatory vagal motor circuit, GEVMC) gastric emptying rate [4]. Several hormones regulate these two neural circuits. Cholecystokinin and GLP-1 inhibit gastric emptying by stimulating GIVMC. On the contrary, ghrelin and motility increase gastric emptying by stimulating GEVMC. The rate of gastric emptying is correlated with satiety sensation and food intake.

Microbial defense

The acidic environment of the stomach not only helps in digestion, but also creates an important defense for microbes. Most microbes taken into the stomach with food or saliva are killed or inhibited in the very acid environment. *Helicobacter pylori* (*H. pylori*) is the first microbes found in this harsh environment by producing urease, which transforms urea in the stomach into carbon dioxide and ammonia, which neutralize the acid [5]. The infection status of *H. pylori*, and its related gastric inflammation, combined with stomach acidity shaped the microbial composition in the stomach [6]. Surgery, such as subtotal gastrectomy with highly selective vagotomy, reducing gastric acid secretion and increasing bile influx into stomach dramatically change stomach microbiota [7].

Diseases of stomach

Peptic ulcer diseases

Peptic ulcer diseases (PUD) are one of the major stomach diseases, including gastric ulcer and peptic ulcer. PUD is the mucosal break reaching the submucosa. Previous estimation of the lifetime prevalence of PUD in the general population is about 5–10%, and the annual incidence is about 0.1–0.3%; however, the incidence has declined significantly in the past decades [8]. The declining trends can be explained by the discovery of PUD risk factors, such as *Helicobacter pylori* (*H. pylori*) infection, smoking, increased dietary salt intake, and the widely applied *H. pylori* eradication in clinical practice [9].

In our previous nationwide population-based study, we found admission rates reduced 42–48% for both uncomplicated and complicated gastric ulcer diseases (with bleeding or perforation) within 10 years. The admission rates reduced 41–71% for both uncomplicated and complicated duodenal ulcer diseases. In the same period, we found *H. pylori* eradication therapy increased twice and proton pump inhibitor (PPI) use increased 10 times [10]. Despite the declining trends for PUD, the aging population leads to higher risk of peptic ulcer bleeding due to increased prevalence of comorbidities, such as coronary heart diseases, liver cirrhosis, or end-stage renal diseases (ESRD). In our previous nationwide studies, we found cirrhotic patients or patients with ESRD had significantly higher risk of peptic ulcer rebleeding [11, 12].

Stomach cancer

Gastric cancer is another major stomach disease. Both gastric cancer incidence and mortality have declined significantly in the past decades. Up until the mid-

1990s, gastric cancer remains the most common cause of cancer-related mortality worldwide [13••]. The ranking of global cancer-related mortality for gastric cancer declined to the 2nd leading cause in 2008 and 3rd leading cause in 2018. In 2018, there are over 1,000,000 new stomach cancer cases and an estimated 783,000 stomach cancer-related death [14]. Even though gastric cancer is rapidly declining, it remains an important health burden in East Asian countries, such as Japan, Korea, and China. It is estimated that more than 60% of stomach cancer cases were diagnosed in these three countries [14]. Several risk factors, such as higher prevalence of *H. pylori* infection, diet, environmental factors, and genetic factors may contribute to the significantly higher risk of stomach cancer in East Asia [9].

As early as 2001, meta-analysis of nested cancer-control studies had suggested that *H. pylori* infection was associated with 5.9-fold increased risk of noncardia gastric cancer [15]. In 2009, our nationwide cohort study showed that early *H. pylori* eradication therapy significantly reduced risk of gastric cancer [16]. A recent meta-analysis based on observational studies and clinical trials found *H. pylori* eradication was associated with 47% gastric cancer risk reduction [17].

Functional dyspepsia

Functional dyspepsia is one of the most prevalent stomach diseases. Functional dyspepsia is a disease presented with upper abdominal discomfort or pain, but without organic causes. Functional dyspepsia can be classified into three subtypes: post-prandial distress syndrome (PDS), epigastric pain syndrome (EPS), and overlapping PDS and EPS syndrome. Functional dyspepsia can be caused by disturbed gastric motility, gastric hypersensitivity, or stomach chronic inflammation [18]. Genetic factors and psychiatric comorbidities are also suggested to correlate with functional dyspepsia, but the specificity needs more evidence to support. Recent studies have discussed the roles microbial compositions in functional dyspepsia, but the small sample sizes of the studies and the relatively preliminary observations were still not definite enough to make conclusions [19, 20].

The healthy stomach initiative

What is healthy stomach initiative?

Although peptic ulcer diseases and stomach cancer have declined in the past decades, both diseases remain important health burden worldwide. To promote the awareness to medical professionals as well as the general population on stomach functions and diseases, the healthy stomach initiatives (HSI) was created in 2012 by the following leading scholars: Peter Malfertheiner, Francesco Di Maria, Francis Megraud, and Richard Hunt. HSI has received endorsement by the European Helicobacter Study Group (EHSG), World Gastroenterology Organization (WGO), and the European Association of Gastroenterology, Endoscopy, and Nutrition (EAGEN) as well as several national societies.

An international group of highly ranked, well-known specialists from 35 countries have joined the committee of the HSI to support is task. HSI members meet frequently in several important international conferences, such as

International Workshop of European Helicobacter and Microbiota Study Group (EHMSG), United European Gastroenterology Week (UEGW), Digestive Disease Week (DDW), and Asia-Pacific Digestive Week (APDW).

What has healthy stomach initiative done?

HSI is very active in promoting international collaborations in stomach health-related research. For example, HSI is promoting staR (gastric cancer Research) study to identify genetic risk variants and corresponding genes for stomach cancer in the European population through genome-wide association studies (GWAS) and through the incorporation of already available omics-data world-wide. This will be helpful to identify biomarkers for the prediction of disease course and treatment outcome.

In addition to promote scientific research collaboration, HSI is also very active in holding public awareness events to educate general population, such as HSI public awareness event 2012 in Treviso, 2013 in Berlin, and 2014 in Vienna. For the educational purpose, HSI made a 6 × 4-m interactive walk-able stomach model, which can be disassembled, transported, and then assembled to be used in educational or public events. This model provides an excellent stomach walk-in experience to understand the structure, function, and diseases of the stomach.

World Stomach Day

Why we need World Stomach Day?

HSI has devoted many efforts to increase public awareness about stomach health. To make the general population education more effective, Chun-Ying Wu proposed the idea of "World Stomach Day" in the HSI meeting at Vienna in 2016 during UEGW. The reasons to have the "World Stomach Day" is to have the specific day for promoting public awareness, inviting physician involvement, increasing scientific research, applying government support, and getting industrial sponsorship. The idea got fully supported by the HSI members, especially Peter Malfertheiner.

In the following HSI meeting at Chicago in 2017, Chun-Ying Wu proposed October 2 as the "World Stomach Day" because Barry Marshall and Robin Warren, the Nobel Laureates in Physiology or Medicine 2005, first reported the discovery of *Helicobacter pylori* on October 2, 1982. October 2 is also the holiday of India to celebrate the birth anniversary of Mohandas Karamchand Gandi. Finally, the HSI members decided October 2 as the "World Stomach Day" after discussion.

Fair of the World Stomach Day

Since Chun-Ying Wu proposed the idea of "World Stomach Day", Peter Malfertheiner gave Taiwan the privilege to celebrate the first "World Stomach Day". In 2018, The Gastroenterological Society of Taiwan (GEST) held a fair in Taipei to celebrate the first "World Stomach Day" during the Taiwan Digestive Disease Week. In the fair, Ming-Hsiang Wu, the President of GEST, Chun-Ying Wu, Yi-Chia Lee, and Jyh-Ming Liou initiated the launching ceremony of "World Stomach Day." Chun-Ying Wu dressed up as a "Stomach Protection Superman" to defend our stomach health (Fig. 1). In the fair, GEST arranged

Fig. 1. Chun-Ying Wu dressed up as a "Stomach Protection Superman" to defend our stomach health in the 1st World Stomach Day, 2018.

several interactive activities to educate the health and diseases of the stomach. For example, the kids could make key chains with "stomach protection superman" logo by themselves. There was also a huge air balloon with the "stomach protection superman" logo to increase the awareness of the general population. These first World Stomach Day celebration activities were widely reported by many electronic and print media.

In 2019, Taiwan kept celebrating of "World Stomach Day" and invited worldwide leading scholars to make "Taipei Consensus of *Helicobacter pylori* eradication and stomach cancer prevention". Taiwan's Vice President, Chien-Jen Chen, attended the World Stomach Day press conference and strongly supported the World Stomach Day activities (Fig. 2). In addition to Taiwan, many countries also held many activities to celebrate "World Stomach Day." Wish

Fig. 2. Media Conference of the 2nd World Stomach Day, 2019, in Taipei and the Taipei Consensus of *Helicobacter pylori* eradication and gastric cancer prevention.

these activities contribute to increase public awareness about stomach health and diseases.

Conclusion

Stomach is an essential organ for digestion, endocrine, and also microbiota. Stomach diseases, especially peptic ulcer diseases and gastric cancer, remain important health burden worldwide. More international collaboration studies and public awareness events are crucial to reduce disease burden and to improve stomach health. The HSI plays important roles in these activities, and the World Stomach Day, October 2, provides a specific day for promoting public awareness, inviting physician involvement, increasing scientific research, applying government support, and getting industrial sponsorship.

Compliance with ethical standards

Conflict of interest
Chun-Ying Wu declares that he has no conflict of interest.

Human and animal rights and informed consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
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