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Gastric acid secretion: Changes during a century

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A B S T R A C T

The advances in knowledge of gastric physiology within the past century have been the most exciting and important in this area of interest for many decades.
The aim of this presentation consists of a comprehensive review of the extensive recent literature on this topic in order to highlight milestones in the field of gastric physiology, in particular in gastric acid secretion, gastric pathophysiology, acid-related diseases and use of acid regulatory drugs. Moreover, in the 21st century there have been many epidemiologic changes as well as a decrease of *Helicobacter pylori* infection and gastric cancer together with an increase of gastroesophageal reflux disease and the related increase of pomp proton inhibitor wide use.

Introduction

The present review is focusing on gastric acid secretion and its changes during the last century. In particular, we will analyse the role of *Helicobacter pylori* (*H. pylori*) infection and IL1 beta in acid-related diseases such as peptic ulcer disease and gastroesophageal reflux disease (GERD), as well as the development of new techniques in the measurement of gastric acid secretion.

Moreover, in gastroenterology, as in other medical specialities, new potential therapies, both pharmaceutical and invasive, continually appear on the horizon, always with great initial enthusiasm.

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Over time, these either will prove to be failures or will find their appropriate level of use in our therapeutic armamentarium. When faced with promising new therapies, we should always wonder whether they are effective and safe and whether they are really better than the current ones. Although acid suppression therapy has stood the test of time, the final chapter on the pharmacological treatment of acid-related diseases has not yet been written.

Which factors could change gastric acid secretion?

Environmental factor: H. pylori *infection*

In 1910 was "no acid, no ulcer", since 1984 it became "no *H. pylori* no ulcer" following the discovering of the role of *H. pylori* [1].

As a classic example of epidemiology, John Snow was able to identify tainted water as the cause of the London cholera epidemic in 1854, because disease occurrence clustered amongst households served by a singular water pump at Broad Street [2]. Similarly, the recurrent clustering of deafness among subjects born shortly after rubella epidemics led to the discovery of rubella embryopathy [3]. The frequent occurrence of gastric cancer among coal miners in Europe was partly related to their high salt intake as a means to cope with profuse sweating while working underground [4,5]. Other such examples abound. The present review is focused on clustering in time and especially on the historic period and cohort effects of gastrointestinal diseases associated with *H. pylori*.

The incidence and mortality of many diseases increase with age. Because of the cumulative exposure to environmental risk factors over time and the age-related decline in physiological repair, older people are more prone to develop most types of disease and die from them. After becoming infected with *H. pylori*, it takes decades for the gastric mucosa to develop intestinal metaplasia, gastric atrophy, mucosal dysplasia and, ultimately, gastric cancer [6,7]. The increased incidence of a disease in a particular age group can also point at time when the risk exposure to an environmental agent was especially high. Nowadays, gastric and duodenal ulcers tend to occur in older people, who were more likely to have been exposed to *H. pylori* in their childhood than recently born generations [8]. Period effects are caused by environmental influences that change during a given time period and simultaneously affect most or large portions of the population. Acute ulcer attacks became more common, for instance, during the air raids of London by the German air force during World War II or after earthquakes in Japan [9,10]. Period effects are also brought forth by the introduction of new diagnostic techniques, public health measures or medical therapies, which typically affect all age groups at the same time. Therefore, period effects tend to reveal themselves as rise or fall occurring in all age groups alike during the same time period. In contradiction to period effects, the concurrence of divergent trends among period-age contours of consecutive age groups is generally suggestive of underlying birth-cohort effects. Cohort effects are caused by risk exposure during early childhood that influences subsequent disease behaviour throughout life. The acquisition of *H. pylori* infection during early childhood and the ensuing risk for the future development of peptic ulcer or gastric cancer represents a typical example for a cohort effect in digestive diseases.

The recent decline in peptic ulcer and gastric cancer is easy to explain by similar trends of *H. pylori* infection in the general population. Although the route of transmission of *H. pylori* has still remained somewhat of a mystery, the drop in infection rate is generally assumed to have resulted from increasing standards of hygiene [11,12]. The initial rise in the occurrence of peptic ulcer and gastric cancer has remained the true mystery. *H. pylori* is found to have infected all human populations worldwide, and there appears to be no population free of any *H. pylori* infection. Based on genetic analysis of *H. pylori* obtained from populations throughout the world, its origin can be traced back to Africa, and it is now assumed that *H. pylori* migrated inside the stomachs of the first humans out of Africa [13]. If this is true, how could there have been any sudden rise in the occurrence of *H. pylori* -related diseases throughout the nineteenth century?

As its competitors vanished, the ecologic niche of *H. pylori* in the stomach and upper gastrointestinal tract expanded, resulting in more ulcers and gastric cancers. Subsequently, further improvements in hygiene ultimately led also to the downfall of *H. pylori* and its associated diagnoses. It has been suggested, for instance, that pasteurisation of milk eliminated acidophilic lactobacilli as potential gastric