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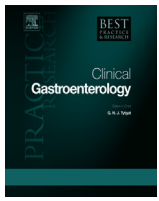

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Pharmacological and alimentary alteration of the gastric barrier

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A B S T R A C T

The gastric barrier contains several lines of defence which protect the epithelium from harmful microbes and toxins. Pre-mucosal defence mechanisms include secreted acid (HCl 0.1 mmol/L) and pepsin, which are capable of denaturing tissue. A tightly adherent mucous layer provides the next line of defence, and physically separates any potentially hazardous substance in the lumen from the mucosal surface. Apical secretion of HCO_3^- maintains a non-acidic microenvironment at the mucosal surface. Membrane-bound phospholipids repel soluble toxins, and sulphydryls scavenge reactive oxygen species. However, when noxious agents overwhelm these mechanisms, the epithelium is damaged. Herein, we discuss the pathological and physiological basis for several disease states which are associated with a breakdown in one or more components of the gastric barrier, including: *Helicobacter pylori*-associated gastritis, atrophic gastritis, stress-related mucosal disease, age-related gastropathy and portal hypertensive gastropathy. The effect of non-steroidal anti-inflammatory drugs and proton pump inhibitors on the gastric mucosa, is explored. Finally, we outline the alterations in mucosal defence caused by alcohol, caffeine, minerals and vitamins.

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Introduction

The stomach, in its capacity as a food reservoir whose role is to gradually deliver ingested food to the small intestine, is constantly exposed to toxins. The gastric barrier contains several lines of defence, including pre-mucosal, mucosal and post-mucosal elements (Fig. 1). When offensive agents, whether infectious or chemical in nature, overcome mucosal defence systems, the result is epithelial damage and ulceration. Although advances have been made in the study of the gastric barrier over the past decades, our understanding is still incomplete. A milestone in the 1970's was the description of the mechanism of action of non-steroidal anti-inflammatory drugs, and their implication as a cause of gastric ulceration [1]. Another milestone was the discovery of *Helicobacter pylori* (*H. pylori*) in 1982 [2]. The advent of histamine receptor antagonists in the early 1980's and proton-pump inhibitors in the late 1980's has dramatically reduced the burden of disease associated with decreased mucosal defence. In the current review, we describe the key components of the gastric barrier. The pathophysiological basis for diseases which affect the integrity of this barrier is examined. Finally, we discuss the effect of ingested substances – both food and drugs – on the function of the gastric barrier, while focussing again on pathophysiological mechanisms.

Key components of the gastric barrier

Acid

The primary secretory function of the stomach is production of hydrochloric acid. Acid is a key component of the gastric barrier and serves to prevent enteric infection and bacterial overgrowth. Additionally, gastric acid acts to potentiate absorption of iron, calcium and vitamin B12, as well as the conversion of pepsinogen to its active form, pepsin. Acid is produced by parietal

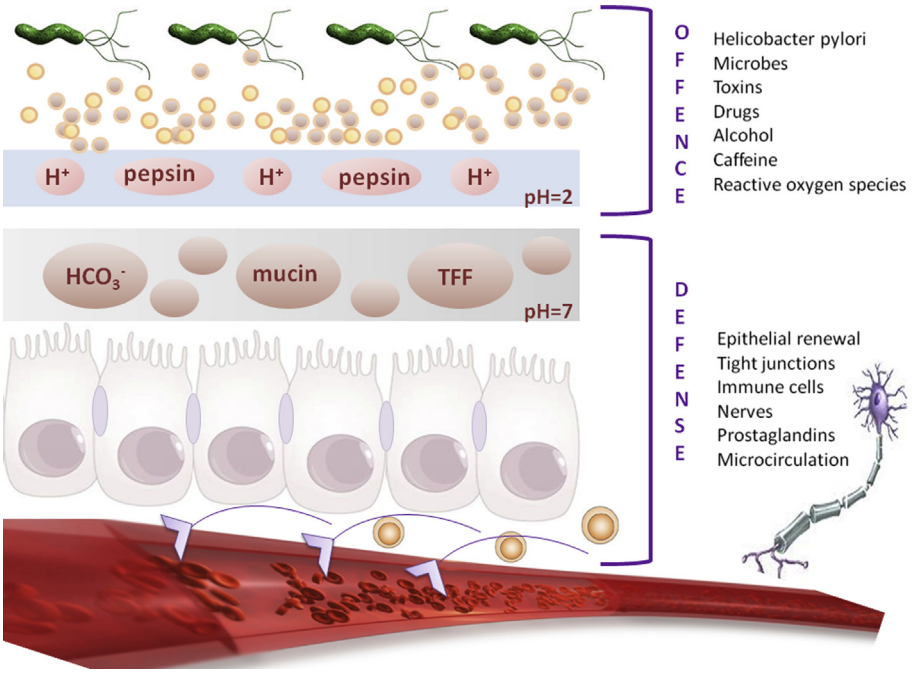

Fig. 1. The gastric barrier. A multi-tiered gastric barrier combines pre-epithelial, epithelial and post epithelial elements. When offensive agents overwhelm the mechanisms of gastric defence, mucosal damage and ulceration ensue. Abbreviations: TFF, trefoil factor.