

Brohée Lecture at Gastro 2009

Acid secretion in the developed world – now too much of a good thing ?

Kenneth E.L. McColl

Division of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, Scotland, UK.

There has been a remarkable change in the human stomach in the western world over the past few decades. Fifty years ago, most adults in the western world had their stomach colonized by *Helicobacter pylori* infection. The associated chronic mucosal inflammation caused a progressive loss of specialized parietal cells and a consequent reduction in acid secretion with increasing age. *H. pylori* has colonized the human stomach since at least the time our ancestors migrated from Africa 65,000 years ago (Fig. 1). Diminution in acid secretion with increasing age has therefore been a feature of the stomach since as long ago as we know. The very recent disappearance of *H. pylori* infection means that acid secretion is maintained throughout life and is thus now substantially higher in adults than it was in previous generations. One important question that needs to be addressed is whether the new pattern of acid secretion is suited to our current environment in the western world.

Gastric acid secretion is one of the most sophisticated and highly developed biological functions. It is an energetically expensive process, as it involves creating and sustaining a hydrogen ion concentration gradient of more than 1,000,000 : 1 across the gastric epithelium. For this reason, the parietal cells are full of mitochondria that generate the adenosine triphosphate (ATP) required to drive the proton pump. The production of gastric acid by the stomach is potentially dangerous. The acidic gastric juice and proteolytic enzymes are able to digest human tissue. Furthermore, the potentially damaging gastric secretions are separated from the rest of the body by an epithelium that is only a single cell thick. For that reason, there is a very complex system for controlling acid secretion and protecting the epithelium. Gastric acid secretion is highly conserved and is thought to have evolved 350 million years ago when land-roaming creatures first appeared (Fig. 2). All these characteristics of gastric acid secretion indicate that it must provide, or has provided, a function that was very important for human survival.

Gastric acid has a number of recognized functions. These include initiation of protein digestion, denaturation of potentially immunogenic proteins, facilitation of absorption of iron, calcium, and vitamin B₁₂, and killing of potentially pathogenic ingested microorganisms. The only one of these recognized functions that could justify the energy and risks associated with secreting gastric acid is the killing of potentially pathogenic micro-

organisms. Is this original critical function still relevant today, or has it become redundant ?

There have been profound changes in the human environment and the extent to which humans are exposed to ingested pathogens over recent decades and centuries. Approximately 20,000 years ago, humans learned how to control fire and started using it for cooking, and in this way reduced the risk of ingesting contaminated flesh. They became different from other carnivores and from what they had been like for the previous 50,000 or more years. Approximately 2000 years ago, the first sewage systems and clean drinking water appeared in parts of the Roman Empire and have now become standard throughout the developed world. Fifty years ago, food refrigeration appeared, with further improvement in food safety. Over the last 25 years, the production of food and its storage have become much more stringent and free from pathogenic contamination. There has therefore been a progressive and probably exponential decrease in human exposure to potentially pathogenic microorganisms over recent times. Gastric acid secretion evolved to allow survival in a very different environment from the relatively sterile one that now characterizes the western world.

A number of observations do suggest that acid secretion is redundant and no longer required for life in the western world. Marked long-term suppression of gastric acid with proton-pump inhibitors rarely causes infective complications. In addition, patients who develop autoimmune atrophic gastritis and associated complete achlorhydria rarely have problems, provided they receive the necessary vitamin B₁₂ supplements. Gastric acid secretion is certainly less important in the environment of the western world than it has been in the past.

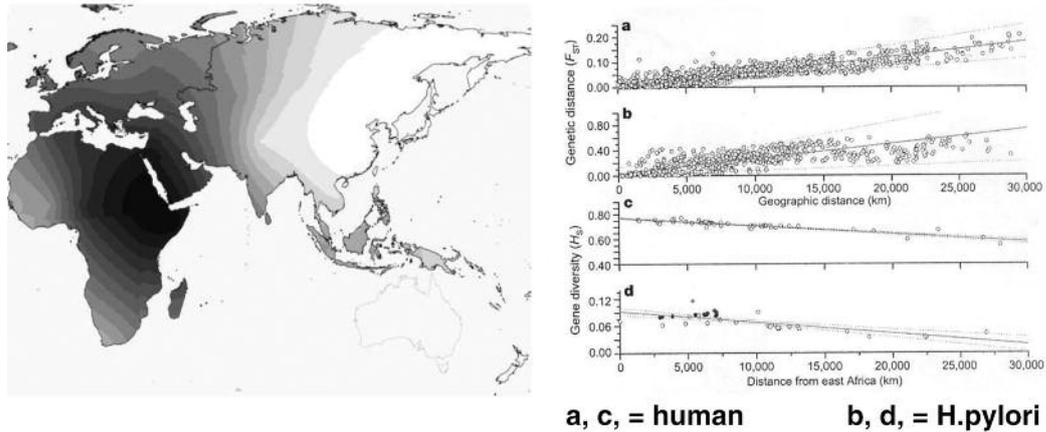
Paradoxically, the environmental changes that have made acid secretion less important have also increased the amount of acid produced. Previously, when everyone

Correspondence to : K.E.L. McColl, Professor of Gastroenterology, Division of Cardiovascular and Medical Sciences, University of Glasgow, Western Infirmary, Glasgow, Scotland, UK. E-mail: K.E.L.McColl@clinmed.gla.ac.uk

Reproduced from: McColl K.E.L. Acid secretion in the developed world – now too much of a good thing ? World Gastroenterology News, March 2010, 5-7 (with permission).

Submission date : 13/04/2010

Acceptance date : 13/04/2010

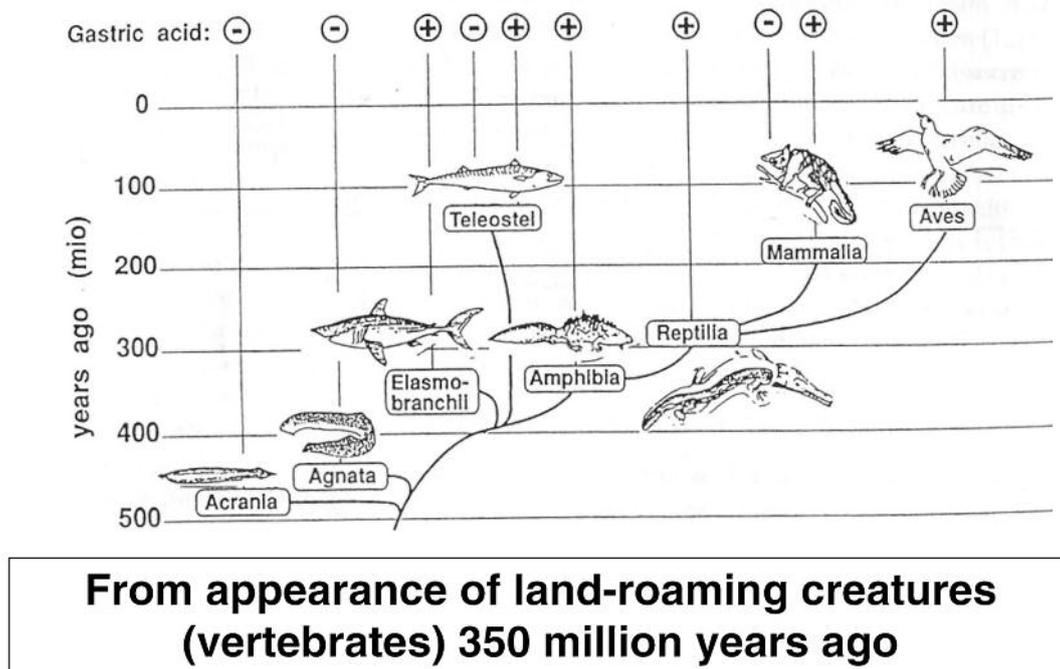


***H. pylori* travelled in humans out of Africa
~ 65,000 years ago**

(Linz et al. Nature 2007;445:915-918)

Fig. 1. — Evidence for long and intimate association between humans and *H. pylori* infection
© Nature, 2007. Reproduced with permission.

Highly Conserved



**From appearance of land-roaming creatures
(vertebrates) 350 million years ago**

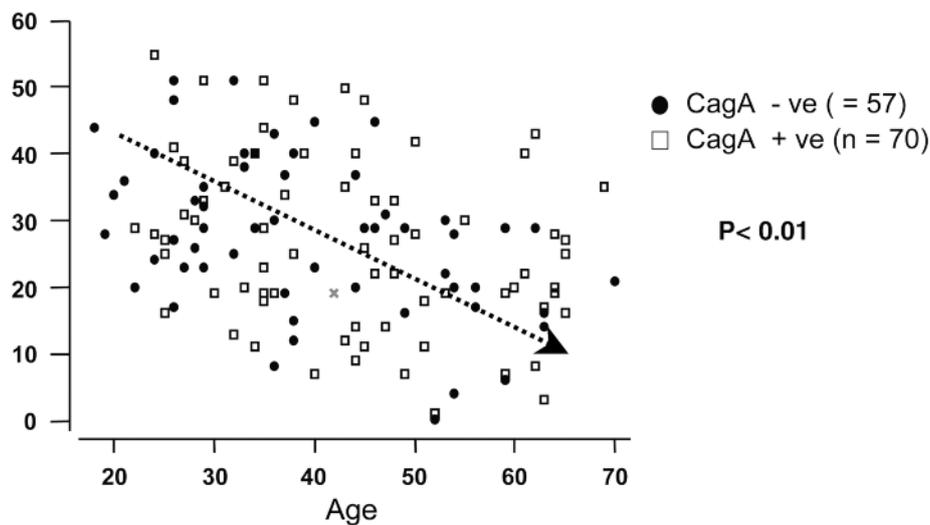
Fig. 2. — Gastric acid secretion

was infected with *H. pylori*, there was progressive damage to the gastric mucosa with increasing age and a progressive decrease in acid-secreting capacity (Fig. 3). Nowadays, the stomach retains its capacity to secrete acid into old age, and that capacity may even increase as one gets older. The degree of atrophy developing in

H. pylori-infected individuals was also greater in previous generations due to the increased salt intake and lack of fruit and vitamin availability throughout the year.

There has therefore been a profound change in the balance between the amount of acid we need to protect us from bacteria and the amount of acid we are

Maximal Acid Output (mmol/h) - decreases with age



(Derakhshan et al *J.Clin.Path.* 2006;59;1293-1299)

Fig. 3. — Acid output in *H. pylori* infected subjects decreases with age

© *J. Clin. Pathol.*, 2006. Reproduced with permission..

producing. Our acid secretion has increased, while our need for acid has actually decreased. Borrowing Churchillian language, we might say that “Never before in the history of human–microbial conflict has so much acid been produced by so many humans to kill so few bacteria”.

Is there evidence for the recent increase in acid secretion being potentially damaging? There is now good evidence that increasing acid secretion does result in upper gastrointestinal disease, and it comes from studies of the effect of proton-pump inhibitor therapy. Although such therapy reduces gastric acid secretion during treatment, it also results in a marked rebound acid hypersecretion following discontinuation of treatment. Consequently, for a month or more after discontinuing such therapy, acid secretory capacity is approximately 50% more than it was prior to starting the treatment. Studies in previously asymptomatic healthy volunteers have now shown that this increase in acid secretion is associated with development of new-onset upper gastrointestinal symptoms, which are probably related to gastroesophageal reflux. An increase in gastric acidity can make previous physiological volumes of gastroesophageal reflux become pathological. Further evidence that we may now be producing more acid than is good

for us is the high prevalence of gastroesophageal reflux disease and its complications and also the significant proportion of the population now taking acid-suppressive therapy.

In conclusion, I think there is now substantial evidence that the level of acid secretion in human adults in the developed world is doing more harm than good. However, it should be recognized that the level of acid secretion in young children and particularly toddlers may be appropriate, as their acid secretion may not be that different from that of previous generations and also because their requirement for it may remain high due to their ingested exposure to environmental pathogens. Their environment may not be that dissimilar from that of distant ancestors or other acid-secreting creatures.

Finally, a word of caution is required. Gastric acid secretion evolved approximately 350 million years ago and has been carefully conserved ever since. It must therefore have served our ancestors well over these many years. The relatively sterile environment of the western world is a very recent phenomenon and may be transient. Humans will need acid to survive in the future if we return to a more typical environment. We should therefore be slow to dismiss what nature has provided for our good and which has served us well for a very long time.