Commentary: A unifying mathematical hypothesis for the epidemiology of *Helicobacter*-associated diseases—plurality should not be assumed without necessity

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In the latest of a series of papers on the epidemiology and disease associations of *Helicobacter pylori*, Sonnenberg\(^1\) provides a mathematical basis for observations that have been made in many countries over the past 150 years. In a nutshell, several
authors have noted that the peak incidence of gastric ulcer occurred for a birth cohort born (in Britain) around 1880 and the peak for duodenal ulcer was ~20 years later. These relationships hold true for several other countries for which mortality data exist as far back as the mid-19th century. A summary of the age-standardized cohort mortality presented on linear axes gives a striking result (shown in Figure 1c).

In a new analysis, Sonnenberg shows that the observed data can be modelled by an algorithm, which assumes that gastric ulcer occurs mainly in persons who acquire H. pylori before the age of 15 years whereas duodenal ulcer is more likely if H. pylori was acquired after the age of 15 years. The reason for these associations might be because early acquisition, more likely in a developing country where the incidence is very high, predisposes to atrophic gastritis with modest or declining acid secretion in adulthood. Lower incidence, with later acquisition of H. pylori, might predispose to robust acid secretion in adulthood, perhaps even with higher than normal basal acid secretion.

As a non-epidemiologist, it immediately strikes me that the data upon which this analysis is based were generated 50–100 years ago, when differentiation between duodenal ulcer and gastric ulcer might have been inexact. However, Sonnenberg has addressed this by using age-related mortality statistics, which might have similar accuracy during the time span of the data. In addition, these data would capture the ultimate demise which might have similar accuracy during the time span of the underlying data. Immediately one recalls the important introduction of aspirin by the Bayer Company in 1900, an undoubted cause of increased gastro-duodenal bleeding for any ulcer sufferer. Similarly, as pointed out by Sonnenberg, pyloric and antral ulcers are commonly called gastric type, but really have a clinical pattern more like duodenal ulcers.

The paper ascribes a recent ‘epidemic’ of ulcer in central Europe between 1965 and 1985 as a duplication of the early 20th century improvement of living standards. Anecdotally, I can recall seeing a patient who married into an ulcer family and then developed duodenal ulcer. Spousal transfer of H. pylori in adulthood, to a Helicobacter-naive partner might be another way later transmission might occur.

If Sonnenberg is correct, his hypothesis implies an increased ulcer risk for people born in developing countries whose H. pylori acquisition age is in transition. The novelty of Sonnenberg’s paper is that his mathematical analysis provides a unifying hypothesis explaining phenomena observed for both gastric and duodenal ulcer.

Early serological data in the 1980s suggested that H. pylori was acquired throughout life since it was far more prevalent in older persons. Further studies demonstrated that very few persons actually acquired H. pylori in adulthood so that adult infections really reflected childhood acquisition many years earlier. Graham proposed the different clinical outcomes for H. pylori, i.e. duodenal ulcer (high acid state) vs gastric cancer (low acid state) by invoking environmental factors related mainly to socioeconomic status.2 These included age of acquisition, diet, and strain characteristics. Aspects of this theory have been discussed in many papers since, and Graham has wavered in his opinion, more recently discounting the proposal on the basis of dissimilarity between the epidemiology of H. pylori and other infections such as hepatitis A and polio.3

The concept of differential exposure of birth cohorts as an explanation of the observed age-related prevalence of H. pylori developed around 1990 and has held up to this day. The subject is complicated and, since none of us has a time machine, the truth may never be known. However, as Sonnenberg claims, his may be the closest approach to an ‘Ockham’s razor’ for the changing clinical epidemiology of gastric and duodenal ulcers, the two most prevalent H. pylori-associated diseases.

References