Does *Helicobacter pylori* infection modify lung development, height or simply reflect shared environmental exposures?

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The identification of *Helicobacter pylori* as a pathogen associated with gastric disease has led to serological assays that can establish exposure in larger study populations and hence exploration of associations with diseases epidemiologically. The paper by Sze *et al*,[1] is an elegant example of this process. The authors have used the data from the Lung Health Study, which is a large prospective cohort based on a randomised trial of a smoking cessation intervention coupled with an ipratropium inhaler[2] that evaluated data on 4765 patients with mild to moderate COPD at baseline, who were followed up for 11 years. The ascertainment of *H. pylori* status was made serologically after 5 years of follow-up, and then cross-sectional associations and longitudinal changes in lung function over 11 years were examined stratified by *H. pylori* status. The results are that absolute lung function is lower in individuals with evidence of exposure to *H. pylori* infection, but that per cent predicted lung function is not. This difference is accounted for by height which is a component of per cent predicted lung function, as those individuals with *H. pylori* positive serology were shorter than those who were not. Interestingly, exposure to *H. pylori* infection was also associated with higher systemic inflammation (as measured by C reactive protein) cross-sectionally, and lower educational attainment. The latter is considered a measure of socioeconomic status in childhood, suggesting that early life environment may be important. There was no association between *H. pylori* status and rate of decline of lung function, which suggests that this is not a modifiable risk factor that can be considered for lung preservation strategies in this population. Finally, there was an excess mortality from cardiovascular mortality in the patients who were seropositive for *H. pylori*, although it is not clear if this analysis was adjusted for age (the mean age of the *H. pylori* positive group was almost 2 years older than the *H. pylori* negative group).

These observations are generally similar to those from our population-based study of 2361 individuals from Nottingham, UK, where evidence of *H. pylori* serological exposure was associated with lower lung function, again as a consequence of smaller stature,[3] and *H. pylori* exposure was also associated with lower measures of socioeconomic status and increased systemic inflammation.[4]

There are two questions for epidemiologists with regards to the interpretation of observational data. 'Is this a causal effect?' and 'is it important?' *H. pylori* appears to be associated with smaller stature, and hence smaller lungs. Demonstrating that *H. pylori* infection is the casual agent that impairs lung development to the level of proof needed to support intervention is a challenging prospect. Future areas of research could consider measuring *H. pylori* status in child development cohorts that include measures of lung function and have access to multiple measurements of *H. pylori* status from early life onwards. However, this issue is complicated by the fact that some children can change from seropositivity back to a seronegative status. In a population-based birth cohort in Ethiopia, 17% of children who had evidence of *H. pylori* infection using a faecal antigen assay at age 3 years, ceased to be positive at the age of 5 years.[5] The issue of fluctuating exposure status is a big challenge for the study of the impact of *H. pylori* infection on children's health and development.

While the prevalence of *H. pylori* infection was 18% in the study by Sze *et al*, there is a strong cohort effect, with birth cohorts from recent decades having a markedly lower prevalence of infection in the UK than those born before the 1960s.[3] Hence, even if this is a true association, the relative importance is decreasing in developed countries like the UK at least. In addition, as populations develop economically, better nutrition and healthcare in early life is associated with an increase in height and presumably lung function. In societies where exposure to environmental insults such as tobacco smoke and other forms of air pollution from conception onwards decreases, lung function can be expected to improve for those who are young enough to benefit from these changes. Hence, even if there is a causal association between *H. pylori* infection and growth, the relative importance of this compared with other factors that modify growth and lung development can be expected to decrease for children born in recent years.

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