further consideration, apart from the relationships of pCTL frequencies reported here.

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References


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Paternal and Maternal Infection Status and Helicobacter pylori in Their Children

To the Editor—We read with interest the study by Rothenbacher et al. [1], which showed a strong association between parental Helicobacter pylori infection status and that of their children in a population-based sample of 1074 children and their fathers or mothers. Unfortunately, the following points, partly raised in the discussion section, negate the authors’ hypothesis that the mother plays a key role in transmitting H. pylori to the child.

The role of paternal infection status was not sufficiently investigated because of the limited sample size. In fact, 947 mothers and 127 fathers accompanied the children. The prevalence of H. pylori infection was 24.6% and 33.9% in the 329 and 62 children whose mothers and fathers were currently infected with H. pylori, respectively, and 1.9% and 6.2% in the 618 and 65 children whose mothers and fathers were not infected. The odds ratio (OR) for H. pylori infection of children whose mothers were infected was 16.5 (95% confidence interval [CI], 8.9–30.8) and 7.8 if the child’s father was infected (95% CI, 2.5–24.2). With the same prevalence rates of H. pylori infection, if a sample of 947 fathers with their children was investigated, the 95% CI would change from 2.5–24.2 to 5–12, possibly reaching statistical significance (i.e., >1) after adjusting for potential confounders (95% CI, 0.8–19.1 with the study sample).

The prevalence of H. pylori infection in the group of children accompanied by their fathers was significantly higher than in children accompanied by their mothers (25 [19.7%] of 127 vs. 93 [9.8%] of 947, respectively; OR, 2.25; 95% CI, 1.3–3.7; P = .001). This clearly indicates different exposures for H. pylori within the two groups and suggests that comparisons of independent variables may be misleading.

The father’s infection status may be related to the mother’s infection status. This suggests that simultaneous measurement of both maternal and paternal infections are needed to ascertain the relative association with the child’s infection status and to speculate on intrafamilial H. pylori transmission.

The study design is not suitable for the exclusion of sources outside the home, such as day care centers or kindergarten, which are major determinants of H. pylori interpersonal spread among children of these two very different paternal and maternal groups.

Collectively, the above issues indicate that this study is not valuable for differentiating maternal from paternal infection status as major risk factor for H. pylori infection and is even less so for supporting a key role of the mother in the transmission of H. pylori to the child.

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Reply

To the Editor—We thank Luzza and Pallone [1] for their interest in our recent work [2]. However, most of the issues they raise were addressed in the article; others may relate to a misunderstanding of our epidemiologic methods.

First, Luzza and Pallone noted correctly that assessment of the role of the paternal infection status was limited by the small sample size of accompanying fathers, and we commented on this observation in detail. We believe the points made in the Discussion section may explain why the estimate regarding the role of paternal infection status did not reach statistical significance, although the point estimate indicated an increased risk of infection for the children.

Second, the issue that the crude prevalence of Helicobacter pylori infection in children accompanied by fathers was higher than in children accompanied by mothers is explained by the
differing nationalities of the two groups (nationality was a strong determinant of *H. pylori* infection in our population). This was described in our Results section. Therefore, the method used by Luzza and Pallone to compare the two crude prevalence figures is misleading because it does not take into account the differences in nationality and other relevant determinants. In our study, we provided only the estimates of the multivariable analysis that were controlled for the main determinants of the *H. pylori* infection status of the children, among them nationality. This method makes a careful comparison of the two odds ratios for *H. pylori* infection of children according to current infection status of mother or father less problematic. Also, we pointed out in the Discussion that the children accompanied by mothers differed somewhat from the group accompanied by fathers, an issue that was taken into account when we formulated our conclusions.

Third, as we noted and as correctly rephrased by Luzza and Pallone, the father’s infection status may be related to the mother’s infection status, and therefore further studies, including simultaneous measurement of both maternal and paternal infection, are needed to further clarify the role of parental infection status. However, epidemiologic theory allows the assessment of the consequences of the possible association between maternal and paternal infection. The implications of this eventual association are (as outlined in the second to the last paragraph of our Discussion section) that the described association between infection of parents and children may be confounded by the mother’s infection status, resulting in an overestimation of the role of paternal *H. pylori* infection status or vice versa. These issues were clearly discussed and taken into consideration when we formulated our conclusions.

Nevertheless, although the association of the weaker of two predictor variables (in our case, paternal *H. pylori* infection) with a dependent variable (in our case, the child’s *H. pylori* infection status) may, in theory, be due entirely to confounding by the stronger predictor variable (in our case, maternal *H. pylori* infection), the opposite scenario is not possible. Furthermore, the key role of the mother in transmitting *H. pylori* to the child seems quite plausible, because in our society she usually has the closest contact with the child.

Fourth, in Germany most children attend kindergarten (e.g., 97% of our study population did so). In kindergarten, children are together regardless of parental infection status. It would be extremely unlikely that the strong associations observed between infection status of children and parents would persist if considerable transmission of infection occurred outside the family. Attendance of day care facilities by children below kindergarten age was less common but was not associated with *H. pylori* infection in our study population. The same was true for other potential sources of infection, including siblings or pets.

In summary, this and our earlier studies [3–6], which Luzza and Pallone seem not to have taken into consideration, strongly suggest that *H. pylori* infection may be acquired early in life—before kindergarten age—and that parent-child transmission, in particular mother-child transmission, plays a key role.

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Modulation of the Pro- and Antiinflammatory Cytokines by Amphotericin B

To the Editor—We read with great interest the article by Rogers et al. [1] reporting the activation by amphotericin B of human genes encoding for the proinflammatory cytokines tumor necrosis factor (TNF) and interleukin (IL)–1β and for the anti-inflammatory cytokine IL-1 receptor antagonist (IL-1RA). Amphotericin B is still a major component of antifungal therapy, but its use is limited by severe adverse effects such as fever, chills, and hypotension. It has been hypothesized that these adverse effects of amphotericin B treatment are mediated through induction of pyrogenic proinflammatory cytokines [2–5]. The increase of the mRNA expression of these genes reported by Rogers et al. represents a strong argument that amphotericin B induces production of cytokines through transcriptional mechanisms, and this information may prove valuable in finding strategies to combat this deleterious side effect of the drug.