

R E V I E W

***Helicobacter pylori*, transmission routes and recurrence of infection: state of the art**

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Summary. *Helicobacter pylori* (*H. pylori*) infection is one of the most common infection in humans, affecting more than half of the population. The prevalence of the infection varies widely in rural developing areas (more than 80%) compared to urban developed ones (less than 40%), as a consequence of different socioeconomic and hygienic conditions. *H. pylori* infection is usually acquired during childhood; infected people usually remain asymptomatic, but about 30% of individuals may develop mild to severe upper gastrointestinal diseases such as gastritis, peptic ulcer, gastric cancer or MALT lymphoma. The transmission route is not clear yet; the person-to-person transmission, especially within the same family appears to be prevalent, but also environmental contamination is possible. The eradication without a specific therapeutic regimen is very unlikely and the reinfection rate after an effective eradication therapy is quite rare. The reinfection rate will increase if there are family members affected. (www.actabiomedica.it)

Key words: *Helicobacter pylori*, epidemiology, prevalence, transmission, reinfection, recurrence

Introduction

Helicobacter pylori (*H. pylori*) is an organism that has been intimately associated with humans for many centuries, even though it was discovered only in the early 1980s (1). *H. pylori* infection is a significant cause of morbidity and mortality in humans as it has a crucial role in the development of chronic gastritis, gastroduodenal ulcer, and gastric cancer which may seriously affect the quality of life of the patients (2). Since 1994 *H. pylori* has been classified in the first group of carcinogenic agents by WHO (3). For these reasons, the eradication of *H. pylori* infection remains a worldwide public health concern. All features implicated in the pathogenesis of *H. pylori*-related diseases are not completely understood and epidemiological data in certain countries are discordant, as in the so-called "African enigma". African enigma describes the dis-

cordance between the prevalence of *H. pylori* infection and *H. pylori*-related gastric cancer: despite the prevalence of *H. pylori* infection is high, there is no expected correlation with related gastric disease. Similar observations have now been made in other geographical areas. These data are of great interest in relation to the pathogenesis of *H. pylori*-related diseases and should lead to a careful examination of host, environment and *H. pylori* virulence (4, 5). *H. pylori* infection is predominantly acquired during childhood, usually persists throughout life without a specific treatment and interpersonal contact seems to be the main route of infection. In countries where the socio-economic conditions have been improving, there is evidence that the prevalence of *H. pylori* infection is declining. However, large proportions of adult populations remain infected so the burden of infection manifesting as peptic ulcer disease and gastric cancer continues to be relevant (6).

Anyway, also in more developed countries infection rates are heterogeneous, with well-defined high-risk groups. These groups include the elderly, those who live in poor hygienic conditions, migrants from high prevalence areas, the institutionalized and possibly rural dwellers in some areas. For these reasons, effective eradication treatments are needed, with the aim to prevent complications. Furthermore, intrafamilial transmission should also be considered, screening all the parents of infected subjects (7).

The aim of the present review is to focus on transmission routes and recurrence of infection of *H. pylori*.

Transmission routes

The route of transmission of *H. pylori* is not completely understood. The only known reservoir is the human stomach (8) and since *H. pylori* appears to have a narrow host range, new infections are thought to occur as a consequence of direct human-to-human transmission or environmental contamination. Person-to-person transmission can be subdivided in two main categories: vertical and horizontal transmission. The vertical mode is infection spread from ascendant to descendent within the same family, while horizontal transmission involves contact with individuals outside the family or environmental contamination (9). Several studies in the literature focus on the relation between *H. pylori* infection and familial exposure. Most of them (10, 11) support the concept of intrafamilial clustering of *H. pylori* infection. They suggest that person-to-person transmission occur in the same family possibly because of close interpersonal contacts, moreover, family members share a genetic predisposition to *H. pylori* infection, finally, family members are exposed to a common source of infection and share the socio-economic status. Instead, in developed countries with low *H. pylori* prevalence, the infected mother is likely to be the primary source of infection in the children (12). In population with high *H. pylori* prevalence and poor socio-economic conditions, infected mothers are less involved in the transmission inside the family, while transmission among siblings as well as outside acquisition appears to play a major role in the transmission pathway. The person-to-person transmission may occur by three possible pathways: the gastro-oral, the

oral-oral and the fecal-oral routes, but no predominant mechanism of transmission has been yet identified.

Gastro-Oral Transmission

H. pylori is acquired in early life and the vomiting of achlorhydric mucus may serve as a vehicle for transmission. The transmission route could be via gastric juice, especially as a result of vomiting in childhood (13). Studies reported data about isolation percentage of *H. pylori* from gastric juice of symptomatic patients: the microbe appears to survive outside the human body in unbuffered gastric juice and is often present in high quantities in vomit. These results support the gastro-oral transmission, especially during childhood, in association with poor hygienic conditions.

Oral-Oral Transmission

The saliva is another possible source of *H. pylori*, since the gastric microbiome can reach and colonize the mouth after regurgitation or vomiting. *H. pylori* has been cultured directly from saliva and the DNA has been frequently amplified from saliva, subgingival biofilm and dental plaque (14). Based on these reports, the mouth might be a reservoir of *H. pylori* (15). The oral-oral transmission involves especially the mother-child transmission: the oral secretions of the mother, which may be contaminated with *H. pylori*, can be directly transmitted to the infant. Negative arguments against the oral-oral transmission include the discordance of strains type between mother and child (16, 17), although this is controversial, as other reports demonstrate the presence of common strains infecting couples (18). These data suggest that although saliva might work as a vehicle of transmission, the oral-oral transmission is not the main modality of transmission of *H. pylori*, at least in adults.

Fecal-Oral Transmission

H. pylori DNA has been frequently detected in human feces (19, 20) but attempts to culture *H. pylori* from feces have had limited success because the bacterium persists there predominantly in a non-culturable (cocoid) form.

Transmission by water

The exact way by which *H. pylori* gains access to the human stomach is unknown and also environmental contamination should be considered. When hygienic conditions are poor, household contamination of treated water cannot be ruled out. Some authors hypothesize that water plays a role both as an environmental reservoir of infection and as a medium in the fecal-oral transmission of *H. pylori* infection. It was demonstrated that children living in houses with an external water supply, or those consuming raw vegetables, which are often irrigated with untreated sewage water, had a higher prevalence of *H. pylori* infection (21, 22). The association of serum antibodies against *H. pylori* with serum antibodies against two known waterborne pathogens (*Hepatitis A virus*) (23) and *Giardia* (24), suggests that the infection may be waterborne or related to poor hygienic conditions.

Transmission by Food

As it happens with water, food products may also be contaminated while being handled under poor hygienic conditions. Several studies address the role of food in the transmission of *H. pylori*. Food products analyzed are mainly milk, meat and vegetables. Among these milk products are the most studied, probably because the infection is mainly acquired during childhood and milk is mostly consumed during this period (25).

Recurrence of infection

Recurrence of *H. pylori* is thought to occur via two distinct mechanisms: recrudescence and reinfection. Recrudescence reflects the reappearance of the original strain of *H. pylori* following its temporary suppression rather than successful eradication. Instead, true reinfection occurs when, after successful eradication, a patient becomes infected with either the original strain or a new strain of *H. pylori* (26). Many investigators have found that recurrence rates during the first 3-12 months after cure are due to late recrudescence. A documented *H. pylori* negativity for 1 year after treatment is a reliable indicator of successful eradication without

recrudescence. It seems that low-efficacy therapy does not actually cure *H. pylori* infection in the gastric mucosa, but only temporarily suppresses it without eradicating it completely from the host (27-29).

H. Pylori reinfection after successful eradication is an important problem in the management of this disease. Recrudescence rather than reinfection is likely to be responsible for most recurrent cases because the recurrences decrease with time, declining sharply after the first year, and identified strains (before and after therapy) are usually genetically identical. Reported "true" reinfection rates in adults generally varied from 0 to 23.4%. The annual "true" reinfection rates were much lower than the reported annual recurrence rates within the first years after eradication (26). Intrafamilial transmission could be also involved in the reinfection of *H. pylori*; its presence among asymptomatic family members may facilitate the transmission within households (7). The reinfection rate after eradication therapy for *H. pylori* is extremely low in developed countries such as Europe and the USA. The annual reinfection rates reported by Zendehdel et al. were around 1% (29). In contrast to the low rates of *H. pylori* reinfection reported in western populations, high recurrence rates have been reported in developing countries (30-33). Therefore the high prevalence of *H. pylori* infection may possibly be associated with high recurrence of infection after eradication because of the high risk of re-exposure (34). Genetic factors may also play a role, susceptible individuals who have eradicated *H. pylori* may be prone to reinfection when they are exposed to *H. pylori*-positive people (7).

Several articles dealing with the occupational risk of infection by *H. Pylori* have been published. Matysiak-Budnik (35) showed an association between occupational exposure and an increased risk of infection. Williams (36), too, stated that there were increased occupational risks for endoscopy personnel.

Conclusion

The prevalence of *H. pylori* is closely related to socio-economic conditions and accordingly, this infection is more common in developing than in developed countries. Intrafamilial transmission is a modality of

infection and reinfection, which should never be forgotten. The close contact among family members appears to be a key route responsible for the transmission of *H. pylori* (37, 38). Therefore, all family members of infected people should always be screened, regardless of their symptoms. In this way, by reducing the undiagnosed patients, the risk of development of the *H. pylori*-related diseases could be reduced, decreasing the risk of reinfection within the family and then limiting the spread of *H. pylori*. Its recurrence in the first year after eradication therapy is likely due to a mixture of recrudescence of infection and reinfection. The reinfection is predominant in the subsequent years after eradication while the risk of recurrence tends to decrease. Since the early age at acquisition of *H. pylori* infection may result in more intense inflammation and the early development of atrophic gastritis and subsequent risk of gastric ulcer, gastric cancer, or both, health education programs within the family (washing of hands and mouth, brushing teeth, no sharing of food plates or drinking glasses, no sharing of spoons in feeding children) should be implemented. Then, to optimize eradication rate of *H. pylori* infection, not only the choice of antibiotics should be considered, possibly based on culture and antibiogram, but also the geographic site, the demographic factors, and the local infection recurrence rate should be analyzed.

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