Transmission of *Helicobacter pylori* infection

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G Oderda. Transmission of *Helicobacter pylori* infection. Can J Gastroenterol 1999;13(7):595-597. *Helicobacter pylori* infection is one of the most common bacterial infections worldwide. It is accepted as the major cause of chronic gastritis, peptic ulcer, carcinoma of the distal part of the stomach and gastric lymphoma. However, how and when the infection is acquired remain largely unknown. Identification of mode of transmission is vital for developing preventive measures to interrupt its spread, but studies focused on this issue are difficult to implement. From epidemiological studies, it is known that there are great differences in the prevalence of infection in different populations and in ethnic groups originating from high prevalence regions. This is likely related to inferior hygienic conditions and sanitation. In developing countries, infection occurs at a much earlier age. In developed countries, the prevalence of infection is related to poor socioeconomic conditions, particularly density of living. Humans seem to be the only reservoir of *H pylori*, which spread from person to person by oral-oral, fecal-oral or gastro-oral routes. Most infections are acquired in childhood, possibly from parents or other children living as close contacts. Infection from the environment or from animals cannot be entirely excluded.

Key Words: *Children; Fecal-oral transmission; Gastro-oral transmission; Helicobacter infection; Oral-oral transmission*

Transmission de l'infection à *Helicobacter pylori*

RÉSUMÉ : L'infection à *Helicobacter pylori* est l'une des infections bactériennes les plus fréquentes à travers le monde. On la considère comme la cause majeure de gastrite chronique, d'ulcère gastro-duodénal, de cancer de la partie distale de l'estomac et de lymphome gastrique. Cependant, il reste en grande partie à déterminer quand et comment l'infection s'acquiert. L'identification du mode de transmission sera cruciale pour le développement de mesures préventives visant à interrompre sa transmission, mais il est difficile de réaliser des études axées sur cette question. D'après des études épidémiologiques, on sait qu'il existe d'énormes différences dans la prévalence de l'infection chez différentes populations et groupes ethniques provenant de régions à forte prévalence. Ceci est vraisemblablement relié à des conditions d'hygiène et à des mesures sanitaires plus mauvaises. Dans les pays en voie de développement, l'infection survient à un âge beaucoup plus précoce. Dans les pays développés, la prévalence de l'infection est reliée à des conditions socioéconomiques insatisfaisantes, en particulier à la densité de la famille. Il semblerait que les humains soient l'unique réservoir de *H pylori*, qui se transmet d'individu à individu par voies orale-orale, fécale-orale ou gastro-orale. La plupart des infections s'acquièrent au cours de l'enfance, peut-être des parents ou d'autres enfants vivant dans l'entourage du malade. De plus, on ne peut totalement exclure l'environnement ou les animaux comme sources d'infection.

Iatrogenic transmission of *Helicobacter pylori* through sharing of nasogastric tubes (1), pH electrodes, and contaminated endoscopes or biopsy forceps is well documented (2). Increased infection in endoscopy staff (3) and viable *H pylori* isolated from gastroscope washing (4) demonstrate that contaminated equipment serves as a route of transmission. However, this accounts for only a small minority of infections. Volunteers infected by oral ingestion develop acute transient dyspeptic symptoms a few days after ingestion (5), but in the majority of subjects symptoms can be absent when primary infection occurs. There is little knowledge of the nature of symptoms at acquisition. This likely accounts for the difficulty in studying the mode of naturally occurring transmission.

Data on seroconversion show a low incidence of infection in adults that ranges from 0% to 0.6% per year (6), whereas a higher rate of acquisition is reported in children (7). This suggests that primary infection takes place mainly in childhood. Also, data on recurrence rates after eradication treatment confirm a higher frequency of reinfection in children (8) than in adults (9), particularly in younger children. However, the reason(s) for the higher susceptibility in children is unknown.

Evidence for person to person transmission comes from studies on patients living in institutions, where close contact is the rule and where the same *H pylori* strain is isolated from children living in the same room (10). Clustering of infection in families has been reported in several countries (11,12), and the same strain has been isolated within the same family (13). Attempts to prevent reinfection by treating all infected family members results in a greater probability of eradication one month after treatment (12). High

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density of living and bed sharing in childhood are risk factors for acquiring the infection (14-16). This confirms that close contact with infected parents favours spread through the person to person route, but a common source of infection cannot be entirely excluded. However, infection does not spread to all persons living in close contacts; clustering has not been confirmed in all studies, infected and noninfected family members are found in the same families, and children born from an infected Belgian mother did not get the infection in the first year of life (17). Therefore, other cofactors must also play a role in the transmission of *H pylori*, some protecting and some facilitating the infection.

Data from a study in Gambian children suggest that specific immunoglobulin (Ig) A in breast milk is a factor protecting against infection. Children born from infected mothers with high IgA titres in their milk were infected later (18). Previous antibiotic use for other minor infections has been reported in noninfected children in southern China and in Germany (19,20). Poor nutritional status may facilitate spread of the infection. In particular, levels of vitamin C, which inhibit *H pylori* urease activity in vitro (21), are lower both in plasma and in the gastric juice of patients who do not eradicate the infection even if they are compliant with the treatment (22). Indicators of poor nutritional status, including low serum protein levels, packed red cell volume, and impaired height and weight, are found in *H pylori*-infected Peruvian children (23). However, it is unclear whether these changes are a cause or a consequence of the infection.

Infected children in Scotland have a diminished growth compared with that of their noninfected school mates (16). In contrast, in Italy, short children are of a low socioeconomic status, which appears to be one of the main causes of their diminished growth; *H pylori* infection is simply a marker of their social disadvantage (24). Other factors that may facilitate the spread of *H pylori* are rapid intestinal transit and/or low gastric acidity of infected patients. Viable *H pylori* were cultured from feces of children with diarrhea (and thus rapid intestinal transit) and from an adult with achlorhydria (25). Studies in an animal model showed that *Helicobacter mustelae* is easier to culture from ferret stools after administration of a proton pump inhibitor (26).

One other unsolved problem is understanding how person to person transmission occurs – is the pathway oral-oral or fecal-oral?

Some observations favour the oral-oral route. A higher prevalence of *H pylori* is found in Chinese Australians who use chopsticks, which are sometimes used to share food (27). *H pylori* DNA encoding 16S rRNA is found by polymerase chain reaction (PCR) in dental plaque (28) and saliva samples of infected patients (29,30). Viable *H pylori* has also been cultured from dental plaque (31). On the other hand, *H pylori* 26 kDa surface protein has been found by PCR in noninfected patients (32), and the urease C gene has not been found in dental plaque (33). However, contamination of PCR testing equipment should be considered in some studies.

Evidence of the possible person to person transmission through the oral-oral route comes from studies showing an increased prevalence of infection in spouses of infected patients with *H pylori* duodenal ulcers, where the increase was associated with the duration of cohabitation (34). Moreover, about half of the infected spouses harbour the same ribopattern of their partner (35). However, other studies do not confirm these findings. More recently, it has been suggested that the oral cavity is not an important reservoir for *H pylori*. A seroepidemiological study performed in an Italian rural area where an association with Epstein-Barr virus infection was compared in the same setting showed that concordance between the two infections was no better than by chance. Furthermore, multiple logistic regression analysis did not show any risk factor shared by both infections (36).

The other possible pathway accounting for spread of the infection is the fecal-oral route of transmission. Indeed, infections transmitted by the fecal-oral route spread more readily among young children, in whom *H pylori* is most commonly acquired. Some experimental findings favour this route of transmission; *H pylori* has been cultured from human feces (25), the *ure*-A and *cag*A gene can be detected in the feces of infected patients (37) and some studies show a positive association with hepatitis A virus infection known to be spread by the fecal-oral route (38). However, no association with hepatitis A virus was found in Chinese children living in a rural area (39) nor, more recently, in rural Italian adults (40).

Some studies suggest that *H pylori* infection may also be acquired from the environment, either from water or from animals. Transmission via water may occur; coccoid forms of the microorganisms have been found to survive for up to one year in river water, and spiral forms for up to 10 days in cold river water (41). Epidemiological studies seem to confirm this possibility; among Peruvian children drinking water from a cistern, the prevalence of infection is much higher than in children drinking tap water (23). In Chile, an increased prevalence of infection is associated with the consumption of uncooked vegetables (42). However, viable *H pylori* have never been cultured from water.

The possibility of zoonotic transmission was suggested by the early finding of an increased prevalence of infection in abattoir workers (43) and veterinarians (44), and, more recently, by the detection of *H pylori* in domestic cats (45). A model for studies on mode of transmission may be *Helicobacter heilmannii*. Recently, an increased prevalence of *H heilmannii* infection has been found in patients living with cats, pigs and dogs (46). More recent findings suggest that houseflies may be a vector for transmitting the infection from individual to individual (47). However, these data are still highly controversial (48).

An intriguing hypothesis is that the infection may be transmitted through a gastro-oral route via refluxed gastric content or vomitus (49). Indeed, attempts to culture *H pylori* from feces or saliva have met with difficulties, the infection is easily transmitted by gastric intubation and acute infection is characterized by achlorhydric vomiting. Mucus may

serve as vehicle for transmission in refluxate or vomitus. A high prevalence of infection with the same strain has been found in mentally retarded cohabiting children with frequent gastroesophageal reflux (10).

CONCLUSIONS

How transmission of *H pylori* occurs is still largely unknown. Infection tends to be acquired at a young age. There is a possibility that infection is transmitted by different pathways; person to person transmission potentially occurs by the fecal-oral and/or gastro-oral routes in children, and by the oral-oral route in adults. In developing countries, infection may occur via water. Cultural practices and environmental factors may well influence the mode of transmission in different human populations.

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