

## Hypothesis

*Helicobacter pylori* infection transmitted sexually via oral-genital contact: a hypothetical model

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**Objectives:** To postulate that *Helicobacter pylori* infection may be transmitted sexually, using the human female vagina as a reservoir for transmission.

**Methods:** A literature search was performed using Medline, Embase, Biological Abstracts, and Currents Contents (January 1983 to August 2000). Relevant keywords were used and additional manual searches were made using the reference lists from the selected articles to retrieve other papers relevant to the topic.

**Conclusions:** *Helicobacter pylori* infection could be transmitted sexually with the vagina acting as a potential temporary/permanent reservoir given the right environmental conditions.

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Keywords: sexually transmitted infections; *Helicobacter pylori*; vagina; oral-genital contact

**Introduction**

*Helicobacter pylori* is the causal organism responsible for chronic gastritis and peptic ulcer disease. A recent meta-analysis of studies showed that the infection is also associated with a twofold increased risk of developing gastric cancer.<sup>1</sup> *H pylori* infection has also been associated with a number of extragastric infections.<sup>2</sup>

The route of transmission of *H pylori* infection has been widely hypothesised but the exact mode(s) of transmission is still unknown. Currently, several routes of transmission have been postulated including oral-oral, faecal-oral, iatrogenic, fomite, and vector borne, but no definite transmission pathway(s) has yet been identified. In addition to the human stomach, the potential reservoirs of *H pylori* include faeces, the cheek, saliva, and dental plaques. Animals, vomitus, water, and food are also candidates.<sup>3</sup> These potential reservoirs are obviously important when trying to determine possible routes of transmission of this fastidious organism.

There have been many reviews that have been published looking at possible transmission routes and reservoirs of *H pylori*.<sup>3–5</sup> However, no published papers have examined the possibility of sexual transmission via the vagina. The aim of this paper is specifically to postulate the idea that *H pylori* may be transmitted sexually and that the vagina may act as a reservoir.

**Hypothesis**

I would like to postulate that *H pylori* infection could be transmitted sexually with the vagina acting as a potential temporary/permanent reservoir under certain environmental conditions.

**Epidemiological evidence**

The natural acquisition of *H pylori* infection appears to occur mostly during childhood and is associated with low socioeconomic status and poor hygiene. Faecal-oral transmission may play an important part in this acquisition. However, the mode of transmission among

young adults and couples who continue to be infected, although at a low rate even with improved understanding and level of hygiene, remains to be elucidated.<sup>6</sup> The possibility of sexual transmission via the vagina in adults would contribute, in part, to the low rates.

Previous data have suggested that sexual behaviour may be important in the transmission of *H pylori*.<sup>7–9</sup> The majority of these studies have concentrated on the possibility of oro-anal transmission between male homosexuals.

Seroprevalence studies have shown that in cohabiting couples with a partner who is infected with *H pylori* the non-infected individual has an increased risk of contracting the infection. Studies have shown that prevalence rates were statistically significant between couples with and without *H pylori* infection (83.3% v 28.5%) respectively.<sup>10 11</sup>

Ethnicity may also be an important predictor of sexual transmission of *H pylori* infection. A number of studies have shown that the highest rates of sexually transmitted infections occur in ethnic minorities (Australian Aborigines, African-Americans, Hispanics, etc . . .).<sup>12 13</sup> The high prevalence of sexually transmitted infections correlates well with the high *H pylori* prevalence rates that exist among these ethnic groups.<sup>5 13</sup> It must also be remembered that there are differences in vaginal flora among different ethnic groups. This may in part be due to genetic or behavioural differences leading to altered vaginal flora. Sexual mixing (that is, mixing partners between ethnic groups) may increase the chance of transmission of *H pylori* between partners from a high prevalence ethnic group (for example, African American) to a lower prevalence ethnic group (European-American).

Molecular studies have produced evidence of *H pylori* transmission between spouses. Schutze *et al*<sup>11</sup> found that reinfection had been caused by the same *H pylori* strain and identified the spouses of the patients as carriers of the identical strain. This was supported by other studies.<sup>14–16</sup> Moreover, it has been shown

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that multiple strains of *H pylori* may infect the same individual.<sup>17 18</sup>

Vertical transmission may also occur during birth if *H pylori* is present in the vagina. Studies have shown that the prevalence of *H pylori* in pregnant women is about 20%.<sup>19 20</sup> In one case report, *H pylori* was isolated 6 days after birth from a neonate who had developed frequent vomiting, weight loss, and difficulty in suckling.<sup>21</sup> Moreover, the case findings of ulcerative oesophagitis and antral micronodular gastritis in such a short time after birth were surprising based on the assumption of contamination. Is it possible that this neonate might have been infected in utero?

The question remains, why hasn't a *Helicobacter* species been recovered from the female vagina when so many vaginal swabs have been done to culture organisms like *Neisseria gonorrhoea*? One of the reasons may be that *Helicobacter* species are difficult to grow in culture because of its fastidious nature and the correct culture techniques have not been employed to grow it. For optimal growth the organism requires a microaerophilic environment (5–7% oxygen); selective media (although it can grow on most types of media); temperature between 33°C and 40°C; 98–100% humidity, and 2–7 days' incubation.<sup>22</sup> A second reason may be that in a routine laboratory, microbiologists look for certain organisms based on the clinical information provided and not "one off" organisms which they would more than likely consider to be "contaminates" or "not clinically significant."

#### Preliminary experimental studies

A few studies have been conducted in an attempt to isolate *H pylori* from the vagina. Early attempts produced negative results.<sup>23 24</sup>

Recently, de-Argila *et al*<sup>25</sup> conducted a study which attempted to find *H pylori* in vaginal secretions by taking vaginal brushings and using polymerase chain reaction (PCR), culture, and Gram stain. However, the diagnostic methods used failed to detect *H pylori*. This may be because the testing time might be important and the sampling methods used may not have been adequate.

In order to determine if any studies had been conducted looking at *H pylori* and sexual transmission I conducted an extensive literature search using the major electronic databases, including Medline, Embase, Biological Abstracts, and Currents Contents (January 1983 to August 2000). The keywords used for the search included *Helicobacter pylori* (*Campylobacter pylori* and *Campylobacter pyloridis*), sexual transmission, sexually transmitted disease, sex workers, prostitutes, vagina, micro-organisms, and epidemiology. Additional manual searches were made using the reference lists from the selected articles to retrieve other papers relevant to the topic.

I found that no studies have been conducted to determine if the prevalence of *H pylori* infection is increased in female sex workers when compared with the general population. This would be an important population to assess for sexual transmission of *H pylori*.

However, a case report which was published a year before Warren and Marshall's now famous original paper on "spiral bacteria in the stomach" may have found strains of *Helicobacter* in a woman's vagina associated with vaginitis. The article reports finding comma-shaped rods (1–4 µm in length), with a characteristic corkscrew motility having between four and eight flagellae.<sup>26</sup> Some of the organisms were cultured under microaerophilic conditions and cultured after 72 hours' incubation at 37°C. The biochemical profile of these unknown organisms matched very closely with that of *H pylori*, although definitive tests such as urease activity were not undertaken. Could this unknown organism have been a *Helicobacter* species?

#### *H pylori* in the vaginal niche

*H pylori* normally lives in the stomach of humans and has the unique ability to survive in extreme acidic conditions. Can *H pylori*'s ability to exist in such a niche enable it to live in other acidic environments? The acidic nature of the vaginal tract may provide an adequate milieu for the survival of *H pylori*. Assuming that the acidic environment is adequate for *H pylori*, the length of colonisation may be lifelong; however, this may depend on other vaginal flora (and sexually transmitted diseases) and how they interact with *H pylori*, as well as physical removal of the organism during menstruation.

To consider that *H pylori* would not grow in the vagina because it is not a microaerophilic environment would be incorrect. The vagina supports the growth of a number of microaerophilic organisms as both normal flora and during pathological processes (lactobacilli, *Trichomonas vaginalis*, *Actinomyces israelii*).<sup>27–29</sup>

Other factors that may affect the sexual transmission of *H pylori* might include a particular sexual practice or the coexistence of other venereal diseases (which cause disruption of the normal integrity of skin and mucosa and local aggregation, as well as systemic stimulation, of lymphocytes). Moreover, the possibility of other coexisting infectious and nutritional conditions (increase the level of infectivity and shorten the interval or generation time).

#### Symbiosis between *H pylori* and yeast

Siavoshi *et al*<sup>30</sup> showed that *H pylori* has a unique symbiotic relationship with yeast where the yeast may protect *H pylori* against adverse environmental conditions. *H pylori* penetrates the yeast and resides in a vacuole where it can survive heat (100°C for 15 minutes), dehydration (37°C for 3 months), and chlorination (2 ppm). This symbiotic relationship may prolong the viability of *H pylori* and play a crucial part in sexual transmission.

It should also be remembered that, owing to the ubiquitous distribution of yeast, it also represents a significant proportion of the normal flora of the human female vagina and the external genitalia.<sup>31 32</sup> Studies have shown that the prevalence of yeasts and/or *Candida albicans* in the normal vagina of healthy, non-pregnant women is between 5% and

30%.<sup>33</sup> Yeasts have also been isolated as normal flora from the human mouth with 75% of yeasts found in the mouth being *C albicans*, with other *Candida sp* making up the rest.<sup>34</sup>

The role of yeast in acting as a vector for the transmission of *H pylori* may be a significant one owing to the fact that vulvovaginal candidiasis is a common condition and 10–20% of women have an asymptomatic yeast infection.<sup>35</sup>

Moreover, bacterial vaginosis affects 25–35% of adult women and ~50% of lesbians (who may be a high risk group with some studies stating that bacterial vaginosis may be easily sexually transferred between lesbians).<sup>36–37</sup> Further research needs to be undertaken to elucidate the mechanisms of transmission among lesbians and to determine if any species of *Helicobacter* play a part in bacterial vaginosis.

### Proposed transmission mode

Transmission to the female genital tract would occur during sexual activities such as oro-genital sex. Because *H pylori* has been found and cultured from the saliva and mouth there exists a possibility that *H pylori* may be transmitted from infected person to non-infected person via kissing or other sexual activities.<sup>38–39</sup>

Namavar *et al*<sup>39</sup> detected *H pylori* from the saliva, tongue, palate, and cheek. Normally, *H pylori* colonises the columnar epithelium of the stomach, but if *H pylori* can survive on the squamous epithelium in the mouth, then is it not possible that it may also inhabit the squamous epithelium of the vaginal tract? Anatomical changes such as cervical ectropion (columnar epithelium on the exocervix) may enhance the possibility of *H pylori* colonisation.<sup>40</sup>

Fisk and Riley<sup>41</sup> presented a case where a common oral bacterium (Group A  $\beta$  haemolytic streptococci) was transmitted during fellatio causing pathology. Some individuals may permanently harbour *H pylori* in their mouth, which may act as a reservoir for future reinfection. There are conflicting studies with regard to the importance of the oral cavity in the transmission of *H pylori* infection.<sup>42</sup>

*H pylori* may then colonise or pseudocolonise the vagina (it may not be necessary for *H pylori* to attach itself to the vaginal epithelium); however, it may survive in the moist mucus which envelopes the vaginal space. Transmission may be made without penetrant sexual intercourse. Previous studies have all concentrated on the possibility that transmission occurs because of penetrant sex.

The time *H pylori* remains viable in the vagina may vary, however, for those individuals who engage in sexual activities more frequently (such as female sex workers); the risk of transmission is greater even if *H pylori* is not viable for long periods of time.

The natural infectious dose of *H pylori* is unknown; however, based on the epidemiology of other enteric organisms, it would suggest that the infectious dose of *H pylori* is small.<sup>43</sup> Moreover, the infective dose provides a greater

understanding of the mechanism of transmission and thus if the infective dose for *H pylori* is small, this would suggest spread via person to person.

Because of the anatomy of the female genitalia and the close proximity to the anus, one must also consider the possibility of a “red herring” where *Helicobacter* in the faeces could be transmitted by hand contact with the perineum or during “wiping” after defaecation.

### POSSIBLE METHODS OF SEXUAL TRANSMISSION OF HELICOBACTER PYLORI

- (1) Oro-anal (rimming)
- (2) Oro-genital, direct transmission (cunnilingus)
- (3) Oro-genital, indirect transmission (fellatio followed by sexual intercourse)
- (4) Oro-oral, kissing (erotic)
- (5) Masturbation (using infected saliva as a lubricant)
- (6) Fomites (sex toys).

Once the organism has established a niche in the vagina it may be transmitted again from the vagina to the mouth of a non-infected male or female during oral sex or via intercourse which may then be followed by oral sex with that partner. The potential pathways are only as diverse as a person’s sexual practices.

Because of an increasing world population, especially of younger age groups, increasing travel, and mixing of populations and the alteration of social values and increasing promiscuity there has been an astronomical increase in sexually transmitted diseases over the past four decades.<sup>44</sup>

### Future research

If *H pylori* could exist in such a niche as the female genital tract, would the organism produce any pathology? Would infection produce similar pathology as seen in an infected stomach—that is, ulcers, atrophy, cancer? How would we diagnose and treat such cases?

Further studies would be needed to determine the exact mechanisms by which *H pylori* might be transmitted. If the female genital tract could be a possible and plausible reservoir for *H pylori*, then these studies would concentrate on the individuals who are more sexually active and more likely to have multiple partners. Also, an appropriate sample size and adequate sampling methods should be applied.

### Note added at proof stage

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