

Is the Coccoid Form of *Helicobacter pylori* Viable and Transmissible?

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Helicobacter pylori (*H. pylori*) is one of the most common infectious diseases in the world. It colonizes about 50-60% of the world's population. *H. pylori* infection is an important cause of chronic gastritis; it promotes peptic ulceration, and is a risk factor for gastric adenocarcinoma and maltoma. Major route of transmission is either oral to oral or fecal to oral pathway. Although *H. pylori* DNA has frequently been detected by PCR from saliva, dental plaques, and feces, rarely has *H. pylori* been cultured from these sources.¹ This is because the spiral form of *H. pylori* has the propensity to become a coccoid form under stressfully environmental conditions such as exposure to oxygen, alkaline pH, high temperature, nutrient starvation, prolonged culture, and treatment with proton pump inhibitor or antibiotics.^{2,3}

The role of the coccoid form of *H. pylori* has been a matter of dispute. Some authors consider the coccoid form to be a degenerative or dead form of *H. pylori*,⁴ while others consider it a dormant form and viable.^{2,5} The viability of the coccoid form is an interesting topic because these coccoid forms may be responsible for the transmission of infection if they are viable, whereas their role would be negligible if there were a degenerative form with no infectious capability.

There are various methods to evaluate the viability of coccoid form directly or indirectly, including capacity to synthesize proteins, cultivability, integrity of DNA and ribosomal RNA, nucleic acid contents, urease activity, adherence ability,⁶ vacuolating cytotoxicity,⁶ antigenic and ultrastructural changes, infectivity on animal model, and host immune response. The article by Wang *et al.*⁷ in this issue describes how they used genomic analysis to demonstrate that the sequence of *vacA* gene in coccoid form is almost the same as that in spiral form and could express its product-VacA protein. The authors suggest that the coccoid form which they collected after antibiotics treatment was viable because these coccoid forms maintained the integrity of their nucleic acid con-

tents and active protein synthesis. The finding is consistent with previously published data. Sisto *et al*⁵ have demonstrated that coccoid form obtained after prolonged incubation in a liquid medium had decreased DNA and RNA levels after 31 days but were not degraded and still expressed the urease, cytotoxic island and vacuolating toxin genes.

Successful colonization by a non-culturable coccoid *H. pylori* in BALB/c mice was reported,⁸ whereas Eaton *et al.* could not achieve this in a gnotobiotic piglet model.⁹ These conflicting results may reflect different viability of coccoids or different host species specificity. Some investigator has suggested that coccoid forms are morphologically divided into 2 types with different transformation processes and consist of the dying bacteria, the living ones with culturability and the viable but non-culturable ones.¹⁰ However even if coccoid forms are viable, they could not play an important role in the transmission of infection by surviving in water or in the environment because coccoid forms can only survive for a short period of time outside their protected niche. There is a very interesting and instructive report from Parsonnet *et al.*¹¹ showing that *H. pylori* could be cultivated uniformly from vomitus, and occasionally, from saliva and cathartic stools. They suggested that *H. pylori* is potentially transmissible during episodes of gastrointestinal tract diseases, such as enteritis or vomiting, by fecal or oral shedding of *H. pylori* from healthy carrier. In such situation, the *H. pylori* are fresh and high-quantity in spiral form, and thus are highly contagious rather than the non-culturable coccoid form.

REFERENCES

1. Kabir S. Detection of *Helicobacter pylori* in faeces by culture, PCR and enzyme immunoassay. *J Med Microbiol* 2001;50: 1021-9.

2. Mizoguchi H, Fujioka T, Kishi K, Nishizono A, Kodama R, Nasu M. Diversity in protein synthesis and viability of *Helicobacter pylori* coccoid forms in response to various stimuli. *Infect Immuno*. 1998;66:5555-60.
3. Janas B, Czkwianiane E, Bak-Romaniszyn L, Bartel H, Tosik D, Planeta-Malecka I. Electron microscopic study of association between coccoid forms of *Helicobacter pylori* and gastric epithelial cells. *Am J Gastroenterol* 1995;90:1829-33.
4. Kusters JG, Gerrits MM, Van Strijp JAG, Vandenbroncke-Grauls CM. Coccoid forms of *Helicobacter pylori* are the morphologic manifestation of cell death. *Infect Immuno* 1997; 65:3672-9.
5. Sisto F, Brenciaglia MI, Scaltrito MM, Dubini F. *Helicobacter pylori*: ure A, cag A and vac A expression during conversion to the coccoid form. *Int J Antimicrob Ag* 2000;15:277-82.
6. She FF, Su DH, Lin JY, Zhou LY. Virulence and potential pathogenicity of coccoid *Helicobacter pylori* induced by antibiotics. *World J Gastroenterol* 2001;7:254-8.
7. Wang XF, Wang KX. Cloning and expression of vacA gene fragment of *Helicobacter pylori* with coccoid form. *J Chin Med Assoc* 2004;67:549-56.
8. Cellini L, Allocati N, Angelucci D, Iezzi T, Di Campli E, Marzio L, et al. Coccoid *Helicobacter pylori* not culturable *in vitro* reverts in mice. *Microbiol Immuno* 1994;38:843-50.
9. Eaton KA, Catrenich CE, Makin KM, Krakowkas S. Virulence of coccoid and bacillary forms of *Helicobacter pylori* in gnotobiotic piglets. *J Infect Dis* 1995;171:459-62.
10. Saito N, Konishi K, Sato F, Kato M, Takeda H, Sugiyama T, Asaka M. Plural transformation processes from spiral to coccoid *Helicobacter pylori* and its viability. *J Infect* 2003; 46:49-55.
11. Parsonnet J, Shmueli H, Haggerty T. Fecal and oral shedding of *Helicobacter pylori* from healthy infected adults. *JAMA* 1999;282:2240-5.