Oral Campylobacter species: Initiators of a subgroup of inflammatory bowel disease?

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Abstract

In recent years, a number of studies detected a significantly higher prevalence of Campylobacter species such as Campylobacter concisus (C. concisus) in intestinal biopsies and fecal samples collected from patients with inflammatory bowel disease (IBD) compared to controls. Most of these Campylobacter species are not of zoonotic origin but are human oral Campylobacter species. Bacterial species usually cause diseases in the location where they colonize. However, C. concisus and other oral Campylobacter species are associated with IBD occurring at the lower parts of the gastrointestinal tract, suggesting that these Campylobacter species may have unique virulence factors that are expressed in the lower parts of the gastrointestinal tract.

Key words: Campylobacter concisus; Oral Campylobacter species; Inflammatory bowel disease; Crohn’s disease; Ulcerative colitis

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Core tip: The human oral cavity is a reservoir of a number of Campylobacter species. Accumulated evidence suggests that some oral Campylobacter species such as Campylobacter concisus may be initiators of a subgroup of human inflammatory bowel disease.

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INFLAMMATORY BOWEL DISEASE

Inflammatory bowel disease (IBD) is a group of chronic relapsing inflammatory diseases of the gastrointestinal tract. The most common clinical types of IBD are Crohn’s disease (CD) and Ulcerative colitis (UC); the two forms of IBD differ in clinical presentation, distribution of inflammation in the gastrointestinal tract, endoscopic appearance and histology[1]. The cause of IBD is not well understood. It is thought...
that the disease occurs in individuals with genetic predisposition when triggered by environmental factors\[6\]. The incidence of IBD is increasing worldwide\[6\]. Epidemiological studies suggest that environmental factors play a particularly important role in the increased incidence of IBD\[6,\, 5\].

**BACTERIAL FACTORS ASSOCIATED WITH IBD**

Studies have shown that microbes in the gastrointestinal tract play a key role in the development of IBD. Colitis did not occur in animal models of IBD when raised germ-free, and the intestinal inflammation resolved in patients with CD after faecal stream diversion\[6,\, 7\].

Extensive research has been conducted to search for the identities of the bacterial species that might contribute to the development of IBD. These include analyses of gut microbiome and investigations of associations between individual bacterial species and IBD. Studies of gut microbiome, which were performed by sequencing 16S rRNA genes, detected reduced bacterial species diversity and changed relative abundance (dysbiosis) in inflamed mucosal tissues of patients with IBD\[6,\, 9\]. Recent studies suggest that such changes were due to the impact of host inflammatory responses on the resident microbes\[10,\, 11\]. Indeed, bacterial species have different abilities in resisting the responses of the immune system and some may even use the by-products of inflammatory responses to boost their growth\[10,\, 12\].

A number of individual bacterial species were found to be associated with patients with IBD, which were summarized in a recent review by Hold et al\[13\]. Whether the gut bacterial dysbiosis and individual bacterial species that are associated with IBD contribute to the pathogenesis of IBD are still under investigation.

**DIFFERENTIAL ROLE OF BACTERIAL SPECIES IN THE PATHOGENESIS OF IBD**

The generally accepted concept is that IBD is caused by multiple bacterial species. This concept may require some refinement in order to more clearly define the role of different bacterial species in the pathogenesis of IBD.

It may be more informative to divide bacterial species that are involved in the pathogenesis of IBD into two broad categories, initiators and exacerbators. The initiator bacterial species are those that instigate the inflammation in the early stage of IBD, while the exacerbator bacterial species are those that contribute to the on-going inflammation after the intestinal epithelial barrier is breached by a direct action of the initiators or by the inflammation initiated by the initiators. The dominant intestinal resident bacterial species, which have co-evolved with the host’s mucosal immune system, most likely are exacerbators in the pathogenesis of IBD.

IBD is a group of diseases that have similar clinical manifestation and histopathology. Given this, the initiators of IBD may consist of several agents that have some common virulence factors. Individual cases may be initiated predominantly by one initiator bacterial species or by more than one initiator. The chronic and recurring nature of IBD suggests that IBD patients are frequently exposed to these initiators. CD can occur at any part of the gastrointestinal tract, suggesting that some initiators are present in the upper gastrointestinal tract. Accumulated evidence suggests that Campylobacter concisus (C. concisus) and a number of other oral Campylobacter species are possible initiators of a subgroup of human IBD.

**MOST OF THE CAMPYLOBACTER SPECIES DETECTED IN PATIENTS WITH IBD ARE NOT OF ZOONOTIC ORIGIN BUT ARE HUMAN ORAL CAMPYLOBACTER SPECIES**

To date, four studies have examined the intestinal prevalence of Campylobacter species in patients with CD and controls using Campylobacter genus PCR; three of which have detected a significantly higher intestinal prevalence of Campylobacter species in patients with CD as compared with the controls\[14-\, 17\]. Three studies have examined the intestinal prevalence of Campylobacter species in patients with UC and controls using Campylobacter genus PCR, two of which detected a significantly higher intestinal prevalence of Campylobacter species in patients with UC compared with the controls\[16-\, 18\].

At the single species level, three studies found a significantly higher intestinal prevalence of C. concisus in patients with CD as compared to controls\[14-\, 16\]. Two studies found a significantly higher intestinal prevalence of C. concisus in patients with UC as compared to controls\[16,\, 18\]. Furthermore, Mukhopadhya et al\[18\] detected a significantly higher intestinal prevalence of C. ureolyticus in patients with UC as compared to controls.

In these studies, a total of eight Campylobacter species were detected, including C. concisus, Campylobacter showae, Campylobacter hominis, Campylobacter gracilis, Campylobacter rectus, Campylobacter jejuni, Campylobacter curvus and Campylobacter ureolyticus\[16\]. C. concisus was the most commonly detected species\[14-\, 18\]. The majority of Campylobacter species detected in these studies were not of zoonotic origin but were previously reported human oral Campylobacter species (Table 1). These Campylobacter species do not have strong abilities in resisting the antimicrobial effects of bile, suggesting that the
Table 1 Most of Campylobacter species detected in the intestinal biopsies and fecal samples collected from patients with inflammatory bowel disease and controls are not of zoonotic origin but are human oral Campylobacter species

| Campylobacter species | Human oral bacteria | 2% ox-bile resistance | Urease activity | Motile |
|-----------------------|---------------------|-----------------------|----------------|-------|
| C. concisus           | Yes                 | 14%-50%               | -              | Yes   |
| C. showae             | Yes                 | -                     | -              | Yes   |
| C. hominis            | No                  | 60%-93%               | -              | No    |
| C. gracile            | Yes                 | -                     | -              | No    |
| C. jejuni             | No                  | 60%-93%               | -              | Yes   |
| C. ureolyticus        | Yes                 | -                     | 50%-100%       | No    |
| C. curtus             | Yes                 | -                     | -              | Yes   |
| C. rectus             | Yes                 | -                     | -              | Yes   |

Information was obtained from[14,15,17,18,19]. Campylobacter jejuni (C. jejuni) refers to C. jejuni subsp. jejuni. C. ureolyticus has been isolated from various clinical sources including dental samples. - indicates 0%-11% positivity.

intestinal tract is not an optimal colonization site for these Campylobacter species in general (Table 1). C. concisus has a better ability in resisting bile compared to other oral Campylobacter species, about half of the C. concisus strains were able to grow in the presence of 2% ox bile (Table 1). Some C. ureolyticus strains are urease positive (Table 1). Of the six oral Campylobacter species detected in intestinal tissues, four species are motile (Table 1).

PATHOGENIC MECHANISMS OF C. CONCISUS AND OTHER ORAL CAMPYLOBACTER SPECIES

We hypothesized that some oral C. concisus strains may play a role in the development of IBD in 2010 and conducted continuous research to investigate this in the following years[19]. If C. concisus is involved in IBD, it is most likely an initiator. Indeed C. concisus does not appear to have strong abilities in resisting an inflammatory environment; there was a lower prevalence of this bacterium in areas with more severe inflammation compared to areas with less severe inflammation[14,20]. However, these Campylobacter species live in the human oral cavity, they may repeatedly colonize the lower parts of the intestinal tract.

Studies suggest that the enteric pathogenicity of C. concisus may be determined by both the characteristics of individual strains and an individual's intestinal environment. C. concisus normally colonizes the human oral cavity[16,21], some individuals are colonized with multiple oral C. concisus strains, which was more often seen in patients with active IBD[22]. C. concisus strains are very sensitive to low pH; most of the swallowed C. concisus bacteria are likely to have been killed by the acidic gastric juice. Bile is also a great inhibitor to the growth of C. concisus[23].

These observations in part explain the low isolation rate of C. concisus from fecal samples despite the bacterium being transported from the oral cavity to the lower parts of the gastrointestinal tract through swallowed saliva or food[24,25]. The inhibitory effect of bile to C. concisus growth is dose dependent[23]. This may be one of the reasons why C. concisus was more often detected in intestinal biopsies collected from descending colon and rectum of patients with IBD in a previous study by Mahendran et al[16]. A small number of oral C. concisus strains have greater abilities in resisting the antimicrobial effects of low pH and bile. The association between these strains and different phenotypic variants of IBD are under investigation.

In addition to gastric acid and bile, another environmental factor that may affect the colonization of C. concisus in the intestinal tract is H2 gas. H2 gas has a great impact on C. concisus growth. In laboratory cultivation, C. concisus does not grow under microaerobic conditions but has a very slow growth under anaerobic conditions[26,27]. The presence of H2 gas enables C. concisus to grow under microaerobic conditions and markedly increases its growth under anaerobic conditions[26]. The atmospheric conditions in the human intestinal tract are microaerobic to anaerobic. Given this, C. concisus is likely to establish an intestinal colonization in individuals whose intestinal environment is able to provide a constantly available H2 for C. concisus to use in their growth.

Normally, bacterial species cause disease in the location where they colonize. In contrast, C. concisus has an unusual disease association; it uses the human oral cavity as its natural colonization site, but is associated with IBD occurring at the lower parts of the gastrointestinal tract[14,16,18]. This unusual disease association pattern suggests that C. concisus may have unique virulence factors that are expressed in the intestinal environment. We previously identified a number of putative prophages in C. concisus genome[21], one of which is CON_phi2. CON_phi2 contains a gene that encodes zonula occludens toxin (Zot)22]. Recently we detected the expression of Zot in C. concisus and found that C. concisus Zot has biological effects on Caco2 cells[28]. Whether enteric environmental factors affect the release of C. concisus Zot toxin and the pathogenic mechanisms of C. concisus Zot are current under investigation, which will shed lights on further understanding why C. concisus, an oral commensal bacterium, may contribute to inflammatory diseases in the lower parts of the gastrointestinal tract. The zot gene was also detected in C. ureolyticus strains isolated from amniotic fluid and vagina[29]. Whether C. ureolyticus strains isolated from the oral cavity of patients with IBD have the zot gene and the pathogenicity of C. ureolyticus Zot are currently under investigation, which may reveal a common pathogenic mechanism shared by a number of Campylobacter species.
KOCH’S POSTULATES AND THE ROLE OF C. CONCISUS IN IBD

A question that we have often encountered in examining the role of C. concisus in IBD was whether the relationship between this bacterium and IBD has fulfilled Koch’s postulates. In 1880s, Robert Koch proposed some criteria, which were called Koch’s postulates, to determine the causative relationship between a microbe and a disease. Despite its contribution to the development of microbiology, these postulates have limitations, which have been discussed by other researchers[30]. IBD is not a single disease and C. concisus is not a typical pathogen. C. concisus is a bacterium that is present in everyone’s oral cavity and some strains have acquired additional virulence factors such as toxins encoded by prophages. The pathogenicity of this bacterium is determined not only by the virulence of individual strains but also an individual’s gastrointestinal environmental factors. Given this, Koch’s postulates are not suitable to assess the relationship between C. concisus and IBD.

IMPORTANCE OF IDENTIFYING BACTERIAL SPECIES THAT INITIATE IBD AND SUGGESTIONS TO CONSIDER C. CONCISUS AND OTHER ORAL CAMPYLOBACTER SPECIES AS A TARGET IN MANAGEMENT OF HUMAN IBD

Due to the unknown identities of bacterial species that initiate the disease, the treatment of IBD is predominantly symptomatic management, involving anti-inflammation and suppression of patient’s immune system. As a result, relapse in IBD is frequent and in some cases, surgery is required. As IBD is a group of diseases, it is important to identify initiators that are responsible for individual cases, which will enable the development of treatment strategies that are suitable for individual patients to reduce relapse and surgery.

Some strategies targeting C. concisus and other oral Campylobacter species may be incorporated into IBD management. One suggestion is to reduce the load of C. concisus and other Campylobacter species in the oral cavity using topical treatments. Oral cavity is the natural colonization site of C. concisus and a number of other Campylobacter species detected in the intestinal tissues of patients with IBD. Reduction of the load of C. concisus and other Campylobacter species in the oral cavity reduces the possibility of these bacteria colonizing the lower parts of the gastrointestinal tract. The main advantage of this strategy is that it is non-invasive and unlikely to disturb the balance of intestinal microbiota.

The second suggestion is to eradicate C. concisus and other oral Campylobacter species using antibiotics in patients with IBD, particularly in patients with frequent relapses and multiple surgeries. We previously found that C. concisus was not detected in saliva samples collected from IBD children who received metronidazole or ciprofloxacin one month prior[31]. However, C. concisus was detected in most of saliva samples (6/7, 86%) collected from IBD children who had antibiotics treatment two months prior[31]. These data showed that the two antibiotics that were used in treatment of some cases of IBD, metronidazole and ciprofloxacin, only had inhibited the growth of oral C. concisus or eradicated it from the oral cavity temporarily. An effective antibiotic therapy that can be used to eradicate C. concisus needs to be developed. Prior to using a given antibiotic to treat patients with IBD, whether the antibiotic induces C. concisus and other oral Campylobacter species to produce prophage toxins should also be examined.

FUTURE STUDIES

Accumulated evidence suggests that translocation of C. concisus and other Campylobacter species from their natural colonization site, the oral cavity, to the lower parts of the gastrointestinal tract may initiate mucosal inflammation there. Further studies investigating the unique pathogenic mechanisms of C. concisus and other oral Campylobacter species are needed, which will shed light on the understanding of how oral Campylobacter species may initiate the development of chronic mucosal inflammatory conditions such as IBD. Diagnostic methods that can accurately identify IBD cases which are caused by translocation of C. concisus or other oral Campylobacter species should be developed. In addition, effective therapies in reducing or eradicating oral Campylobacter species should be established. These strategies will provide useful information in assisting the clinical management of individual IBD cases.

REFERENCES

1 Podolsky DK. Inflammatory bowel disease. N Engl J Med 2002; 347: 417-429 [PMID: 12167685 DOI: 10.1056/NEJMra020831]
2 Sartor RB. Mechanisms of disease: pathogenesis of Crohn’s disease and ulcerative colitis. Nat Clin Pract Gastroenterol Hepatol 2006; 3: 390-407 [PMID: 16819502 DOI: 10.1038/ncpgasthep0528]
3 Molodecky NA, Soon IS, Rabi DM, Ghali WA, Ferris M, Chernoff G, Benchimol EI, Panaccione R, Ghosh S, Barkema HW, Kaplan GG. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology 2012; 142: 46-54.e42; quiz e30 [PMID: 22001864 DOI: 10.1053/j.gastro.2011.10.001]
4 Jayanthi V, Probert CS, Pinder D, Wicks AC, Mayberry JF. Epidemiology of Crohn’s disease in Indian migrants and the
indigenous population in Leicestershire. *Q J Med* 1992; 82: 125-138 [PMID: 1620813]

5. Montgomery SM, Morris DL, Pounder RE, Wakefield AJ. Asian ethnic origin and the risk of inflammatory bowel disease. *Eur J Gastroenterol Hepatol* 1999; 11: 543-546 [PMID: 10755259 DOI: 10.1097/00042737-199905000-00013]

6. Mizoguchi A. Animal models of inflammatory bowel disease. In: Conn PM, editor. Animal Models of Molecular Pathology, 2012: 263-320

7. Rutgeerts P, Gobbes K, Peeters M, Hiele M, Penninckx F, Aerts R, Kerremans R, Vantrappen G. Effect of faecal stream diversion on recurrence of Crohn’s disease in the neoterminal ileum. *Lancet* 1991; 338: 771-774 [PMID: 1681159 DOI: 10.1016/S0140-6736(91)90066-A]

8. Gevers D, Kugathasan S, Denson LA, Vázquez-Baeza Y, Van Treuren W, Ren B, Schwager E, Knights D, Song SJ, Yassour M, Morgan XC, Kastner-DF, Bennett KW. A comparison of Bacteroides ureolyticus isolates of different ethnic origin and the risk of inflammatory bowel disease. *PLoS One* 2012; 7: e14594 [PMID: 22848538 DOI: 10.1371/journal.pone.0014594]

9. Rautema R, Jarvis GA, Marnila P, Meri S. Acquired resistance of Escherichia coli to complement lysis by binding of glycoprophosphoinositide-anchored protein (CD55). *Infect Immun* 1998; 66: 1928-1933 [PMID: 9573071]

10. Hold GL, Smith M, Grange C, Watt ER, El-Omar EM, Mukhopadhyay I. Role of the gut microbiota in inflammatory bowel disease pathogenesis: what have we learnt in the past 10 years? *World J Gastroenterol* 2014; 20: 1192-1210 [PMID: 24574795 DOI: 10.3748/wjg.v20.i5.1192]

11. Zhang L, Man SM, Day AS, Leach ST, Lemberg DA, Dutt S, Stormon M, O’Loughlin EV, Magoffin A, Ng PH, Mitchell H. Detection and isolation of Campylobacter species other than *C. jejuni* from children with Crohn’s disease. *J Clin Microbiol* 2009; 47: 453-455 [PMID: 19052183 DOI: 10.1128/JCM.01949-08]

12. Man SM, Zhang L, Day AS, Leach ST, Lemberg DA, Mitchell H. Campylobacter concisus and other Campylobacter species in children with newly diagnosed Crohn’s disease. *Inflamm Bowel Dis* 2010; 16: 1006-1016 [PMID: 19885905 DOI: 10.1002/ibd.21157]

13. Mahendran V, Riordan SM, Grimm MC, Tran TA, Major J, Kaakoush NO, Mitchell H, Zhang L. Prevalence of Campylobacter species in adult Crohn’s disease and the preferential colonization sites of Campylobacter species in the human intestine. *PLoS One* 2011; 6: e25417 [PMID: 21966525 DOI: 10.1371/journal.pone.0025417]

14. Hansen R, Berry SH, Mukhopadhyay I, Thomson JM, Saunders KA, Nicholl CE, Bisset WM, Loganathan S, Mahdi G, Kastner-Cole D, Barclay AR, Bishop J, Flynn DM, McGrogan P, Russell RK, El-Omar EM, Hold GL. The microaerophilic microbiota of de novo paediatric inflammatory bowel disease: the BISCUIT study. *PLoS One* 2013; 8: e58825 [PMID: 23554935 DOI: 10.1371/journal.pone.0058825]

15. Mukhopadhyay I, Thomson JM, Hansen R, Berry SH, El-Omar EM, Hold GL. Detection of Campylobacter concisus and other Campylobacter species in colonic biopsies from adults with ulcerative colitis. *PLoS One* 2011; 6: e21490 [PMID: 21738679 DOI: 10.1371/journal.pone.0021490]

16. Zhang L, Budimcan V, Day AS, Mitchell H, Lemberg DA, Riordan SM, Grimm M, Leach ST, Ismail Y. Isolation and detection of Campylobacter concisus from saliva of healthy individuals and patients with inflammatory bowel disease. *J Clin Microbiol* 2010; 48: 2965-2967 [PMID: 20519479 DOI: 10.1128/jcm.02391-09]

17. Macuch PJ, Tanner AC. Campylobacter species in health, gingivitis, and periodontitis. *J Dent Res* 2000; 79: 785-792 [PMID: 10729981 DOI: 10.1177/002203450079001301]

18. Zhang L, Lee H, Grimm MC, Riordan SM, Day AS, Lemberg DA. Campylobacter concisus and inflammatory bowel disease. *World J Gastroenterol* 2014; 20: 1259-1267 [PMID: 24574800 DOI: 10.3748/wjg.v20.i5.1259]

19. Mahendran V, Tan YS, Riordan SM, Grimm MC, Day AS, Lemberg DA, Octavia S, Lan R, Zhang L. The prevalence and polymorphisms of *zoona* occluden toxin gene in multiple *Campylobacter* concisus strains isolated from saliva of patients with inflammatory bowel disease and controls. *PLoS One* 2013; 8: e75525 [PMID: 24086553 DOI: 10.1371/journal.pone.0075525]

20. Ma R, Sapwell N, Chung HK, Lee H, Mahendran V, Leong RW, Riordan SM, Grimm MC, Zhang L. Investigation of the effects of pH and bile on the growth of oral Campylobacter concisus strains isolated from patients with inflammatory bowel disease and controls. *J Med Microbiol* 2015; 64: 438-445 [PMID: 25657299 DOI: 10.1099/jmm.0.000013]

21. Engberg J, On SL, Harrington CS, Gerner-Smidt P. Prevalence of Campylobacter. *Arcoabacter, Helicobacter*, and *Sutterella* spp. in human fecal samples as estimated by a reevaluation of isolation methods for *Campylobacter*. *J Clin Microbiol* 2000; 38: 286-291 [PMID: 10618103]

22. Nielsen HL, Ejlertsen T, Engberg J, Nielsen H. High incidence of Campylobacter concisus in gastroenteritis in North Jutland, Denmark: a population-based study. *Clin Microbiol Infect* 2011; 17: 9243 [PMID: 21219646 DOI: 10.1111/j.1469-0691.2010.03186.x]

23. Lee H, Ma R, Grimm MC, Riordan SM, Lan R, Zhong L, Raftery M, Zhang L. Examination of the Anaerobic Growth of Campylobacter concisus Strains. *Int J Microbiol* 2014; 2014: 476047 [PMID: 25214843 DOI: 10.1155/2014/476047]

24. Vandamme P, Dewhirst FE, Paster BJ, On SLW. Genus I. Campylobacter. In: Garrity GM, Brenner DJ, Krieg NR, Staley KT, editors. Bergey’s Manual of Syst Bacteriol. 2 ed. New York: Springer, 2005: 1147-1160

25. Lee H, Liu F, Mahendran V, Zhang L. Detection of the zoona occludens toxin expressed in Campylobacter concisus strains isolated from patients with inflammatory bowel disease. *J Gastroenterol Hepatol* 2014; 29: 10-10

26. Bullman S, Luiz G, Corcoran D, Sletor RD, Lucey B. Genomic investigation into strain heterogeneity and pathogenic potential of the emerging gastrointestinal pathogen Campylobacter ureolyticus. *PLoS One* 2013; 8: e71515 [PMID: 24026611 DOI: 10.1371/journal.pone.0071515]

27. Fredricks DN, Relman DA. Sequence-based identification of microbial pathogens: a reconsideration of Koch’s postulates. *Clin Microbiol Rev* 1996; 9: 18-33 [PMID: 8665474]

28. Wong SM, Day A, Lemberg D, Riordan SM, Grimm MC, Budimcan V, Mitchell H, Ismail Y, Zhang L. Antibiotic susceptibility of Campylobacter concisus isolated from patients with inflammatory bowel disease. *J Gastroenterol Hepatol* 2010; 25: A80-A80

29. Duerrden B, Eley A, Goodwin L, Magee JT, Hindmarsh JM, Bennett KW. A comparison of Bacteroides ureolyticus isolates from different clinical sources. *J Med Microbiol* 1989; 29: 63-73 [PMID: 2724326]
Zhang L. Oral Campylobacter species and IBD

Lastovica AJ, On SLW, Zhang L. The Family Campylobacteraceae. In: Rosenberg E, Delong EF, Loy S, Stackebrandt E, Thomas F, editors. The Prokaryotes. Fourth Edition ed. London: Springer, 2014: 308-326

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