



Review article

Clinical and bacteriological characteristics of *Helicobacter cinaedi* infection

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ABSTRACT

Helicobacter cinaedi was first isolated from rectal cultures from homosexual men in 1984. In the 1980s to mid 1990s, the microorganism was mainly isolated from samples from homosexual men or immunocompromised patients; however, during the last two decades, *H. cinaedi* has been isolated from immunocompromised and from immunocompetent individuals worldwide. In Japan, the isolation of this microorganism was first reported in 2003. Since then, many cases have been reported in hospitals across the country. Despite many reports, the etiological properties and pathogenicity of *H. cinaedi* remain elusive; however, we are increasingly able to recognize some of the features and the clinical relevance of infection. In particular, a long incubation period is essential for detection in an automatic blood culture system and many of the recent isolates are resistant to both macrolides and quinolones. Furthermore, there is an association between infection and severe or chronic illnesses, such as meningitis or arteriosclerosis, in addition to mild diseases such as fever, abdominal pain, gastroenteritis, proctitis, diarrhea, erysipelas, cellulitis, arthritis, and bacteremia.

In this review, we introduce the current knowledge and our latest findings relating to *H. cinaedi*.

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1. Introduction

The genus *Helicobacter* is a gram-negative spiral bacterium, belonging to the family *Helicobacteriaceae* of the order *Campylobacteriales* within the class *Epsilonproteobacteria*.

Almost all members of genus *Helicobacter* show curved spiral (S-shape) or fusiform rods that are 0.2–1.2 × 1.5–10 μm. Spiral cells may be tightly or loosely wound depending on the species and on the culture age and condition. Cells in old cultures or those exposed to air become coccoid. Periplasmic fibers may be observed on the cell surface in certain species (Fig. 1).

Helicobacter cinaedi was first reported as a *Campylobacter*-like organism type-1 (CLO-1) in 1984 by Fennell et al. [1] They described three different types of CLOs—CLO-1, CLO-2 (later named “*Campylobacter fennelliae*”), and CLO-3 (still unnamed)—based on

biochemical traits (nitrate reduction and odor-producing ability) and membrane spot DNA–DNA hybridization results. The following year, Totten et al. [2] proposed the name “*Campylobacter cinaedi*” for CLO-1 organisms, although they demonstrated that there are two genetic groups within CLO-1 type, namely, CLO-1a and CLO-1b, with DNA–DNA hybridization values of 42–51%. Comparable values between CLO-2 and CLO-3 strains were far lower (less than 7%). These data and the lack of biochemical differences between CLO-1a and CLO-1b groups allowed the authors to include both within a single species. Thus, “*C. cinaedi*” is genetically diverse, involving at least two genomospecies. In 1991, “*C. cinaedi*” and also “*C. fennelliae*” were moved into the genus *Helicobacter* [3] as *H. cinaedi* and *Helicobacter fennelliae* [4].

To date, the validation of 33 species in genus *Helicobacter* has been proposed, but only seven species have been isolated from human clinical specimens (Table 1, Fig. 2). *Helicobacter pylori*, classified as a “gastric-*Helicobacter* species” [5], is the most well known species of the genus *Helicobacter*, although *H. cinaedi*, *Helicobacter bilis*, *Helicobacter canadensis*, *Helicobacter canis*, *H. fennelliae*, and *Helicobacter pullorum*, classed as “enterohepatic

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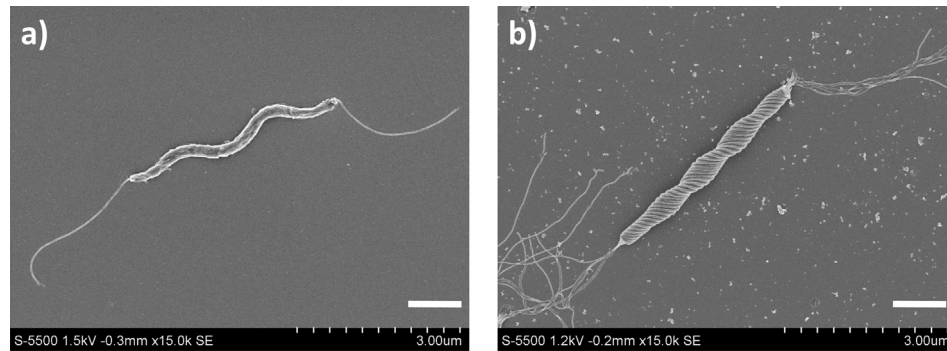


Fig. 1. SEM image of *Helicobacter* species. a) *H. cinaedi* (PAGU611; a whole genome determined strain) showing S-shaped and bipolar flagella. b) *H. bilis* (PAGU599^T) showing a fusiform cell body encircled by tightly wound periplasmic fibers and multiple sheathed flagella ($\times 15,000$, Bar = 1.0 μm).

Helicobacter species” [5], have also been isolated from human clinical specimens.

There is an invalid species name related to the genus *Helicobacter* known as “*Flexispira rappini*” (sometime referred as “*Helicobacter rappini*”). “*F. rappini*” was first proposed by Bryner et al. [6,7] for a strain group of ultrastructurally distinct, urease-producing strains isolated from lambs, dogs, canine, ovine, and humans. Since this first study, strains have been identified as “*F. rappini*” by 16S rRNA gene sequence comparison, despite notable morphological and phenotypic differences [8–10]. In 2000, Dewhirst et al. [11] reported that “*F. rappini*” strains represent at least 10 *Helicobacter* taxa, and then Hänninen et al. [12,13] fell into each taxon as a valid *Helicobacter* species (Table 2). Only taxon 7 (one strain isolated from dog stomach) and taxon 10 (three strains isolated from cotton-top tamarin) have not been clear their taxonomic positions. Indeed, the title of the 16S rRNA gene sequence information under the DDBJ/NCBI/EBI accession number M88138 (ATCC43879) is still ‘*Helicobacter* sp. “*Flexispira* taxon 8” 16S ribosomal RNA gene’. This information may be a cause of misunderstanding and the researcher should carefully read both the title and

the annotated text. Other provisional names, “*Helicobacter westmeadii*” [14] and “*Helicobacter* sp. strain Mainz,” have been assigned to *H. cinaedi* [15].

H. cinaedi was first isolated from rectal swabs obtained from homosexual men with proctitis, proctocolitis, and enteritis [1], but the number of reports of *H. cinaedi* infection has been steadily growing throughout the last two decades. Because early reports mainly described the isolation of these microorganisms from homosexual men or immunocompromised patients, and their presence was attributed to human immunodeficiency virus infection, agammaglobulinemia, or some other underlying disease [16–21], the organisms were thought to be related to specific hosts. Recently, however, given that increasing numbers of infections have also been reported in immunocompetent patients [22–25], the patient group affected by *H. cinaedi* is larger than originally thought.

In Japan, the first report describing the isolation of *H. cinaedi* was published in 2003 [26]. Since then, isolation of this microorganism has been reported in patients regardless of gender and within a wide age range, from newborns to the elderly, by many

Table 1

All validity proposed members of the genus *Helicobacter*.

Species	Host animal	Valid year	Species	Host animal	Valid year		
<i>Enterohepatic Helicobacter</i> ^a			<i>Gastric Helicobacter</i>				
1	<i>H. cinaedi</i> ^b	Human, Hamster	1991	21	<i>H. pylori</i> ^b	Human, Monkey	1989
2	<i>H. canis</i> ^b	Dog, Human	1994	22	<i>H. acinonychis</i>	Cheetah	1993
3	<i>H. bilis</i> ^b	Mouse, Dog, Human	1997	23	<i>H. aurati</i>	Hamster	2002
4	<i>H. canadensis</i> ^b	Human	2002	24	<i>H. baculiformis</i>	Cat	2008
5	<i>H. fennelliae</i> ^b	Human	1991	25	<i>H. bizzozeronii</i>	Dog	1996
6	<i>H. pullorum</i> ^b	Chicken, Human	1995	26	<i>H. cetorum</i>	Dolphin, Whales	2006
7	<i>H. cholecystus</i>	Hamster	1997	27	<i>H. cynogastricus</i>	Dog	2006
8	<i>H. ganmani</i>	Mouse	2001	28	<i>H. felis</i>	Cat, Dog	1991
9	<i>H. hepaticus</i>	Mouse	1994	29	<i>H. heilmannii</i>	Monkey	2012
10	<i>H. mesocricetorum</i>	Hamster	2000	30	<i>H. mustelae</i>	Ferret	1989
11	<i>H. muridarum</i>	Mouse, Rat	1992	31	<i>H. nemestrinae</i>	Monkey	1991
12	<i>H. pametensis</i>	Bird, Swine	1994	32	<i>H. salomonis</i>	Dog	1997
13	<i>H. rodentium</i>	Mouse	1997	33	<i>H. suis</i>	Pig	2008
14	<i>H. trogontum</i> ^c	Rat	1996				
15	<i>H. typhlonius</i>	Mouse	2002				
16	<i>H. anseris</i>	Goose	2006				
17	<i>H. brantae</i>	Goose	2006				
18	<i>H. marmotae</i>	Woodchuck, cat	2006				
19	<i>H. mastomyrinus</i>	Rodent	2006				
20	<i>H. equorum</i>	Horse	2007				

^a “Enterohepatic-Gastric” categories were basically according with Solnick et al. [5].

^b Only seven species has been isolated from human specimen. Some reports described the detection of *H. suis*, *H. felis*, *H. hepaticus*, or *H. ganmani* using genetic methods but there is no report, to our knowledge, has isolated the organism.

^c Two isolation cases of *H. trogontum* from human clinical specimen have been reported on the Japanese Society for Clinical Microbiology Meeting (Journal report has not been yet).

Besides these species, “*Candidatus Helicobacter bovis*” (gastric helicobacter) has been proposed in 1999 [95].

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