

## Review

# Pathophysiology of *Campylobacter jejuni* infections of humans

Trudy M. Wassenaar<sup>a</sup>, Martin J. Blaser<sup>b\*</sup>

<sup>a</sup>Johannes Gutenberg University, Institute of Medical Microbiology and Hygiene, Hochhaus am Augustusplatz, D-55101 Mainz, Germany

<sup>b</sup>Division of Infectious Diseases, Vanderbilt University School of Medicine and VA Medical Center, Nashville, Tennessee 37232, USA

**ABSTRACT** – *Campylobacter jejuni* and closely related organisms are major causes of human bacterial enteritis. These infections can lead to extraintestinal disease and severe long-term complications. Of these, neurological damage, apparently due to the immune response of the host, is the most striking. This review examines current knowledge of the pathophysiology of the organism. Diversity of *C. jejuni* isolates in genotypic and phenotypic characteristics now is recognized and clinically relevant examples are presented. Expected future directions are outlined. © 1999 Éditions scientifiques et médicales Elsevier SAS

*Campylobacter* / microbial pathogenesis / bacterial toxins / enteric diseases / emerging infections

## 1. Introduction

More than twenty years ago, microbiologists became aware of the importance of the Gram-negative bacteria *Campylobacter jejuni* (figure 1) and the closely related *C. coli* as causative agents of human enteritis. Since then, substantial insights have been gained about the ecology, environmental spread, epidemiology, and pathogenicity of the organisms. Nevertheless, this knowledge has not (yet) resulted in a reduction in the incidence of campylobacteriosis in most countries, which is one of the goals of future research. Moreover, it now is recognized that *Campylobacter* infections pose a risk of extraintestinal sequelae that can be life-threatening. Better insight into the pathogenesis of these diseases may result in improved prevention and therapy. This review considers the heterogeneity amongst *C. jejuni* strains, and *Campylobacter*-induced diseases, the bacterial virulence factors that have been recognized to be pertinent, the host responses that have been discovered, and the directions in which future research should head.

## 2. Diversity of *C. jejuni*

*C. jejuni* isolates are strikingly diverse compared to many other enteropathogens. Both phenotypic and genotypic diversity have been described (table I). The two generally applied serotyping schemes detect a wide diversity in serotypes: the extended heat-labile typing scheme

of Lior [1] now recognizes over 100 serotypes of *C. jejuni*, *C. coli*, and *C. lari*. The heat-stable typing scheme of Penner and Hennessy, based on lipopolysaccharide O-antigens, detects more than 60 serotypes [2]. Genotypic diversity has been demonstrated by several genetic methods, e.g., pulsed-field gelelectrophoresis [3–8], Restriction fragment length polymorphism analysis of the PCR-amplified flagellin locus [9–13], random arbitrarily primed DNA PCR [14–17], ribotyping [18, 19] and amplified fragment length polymorphism [20, 21]. The bacterial subtypes recognized by one phenotypic or genotypic technique mostly do not correlate with those determined by the other techniques [22–30], which demonstrates even further the complexity within the species.

Diversity between *C. jejuni* strains has also been observed at the phenotypic level for almost every characteristic that has been implied in pathogenicity. However, by comparison of clinical and nonclinical isolates, this phenotypic variation does not always coincide with observed or predicted differences in virulence. Examples of phenotypic diversity observed with *C. jejuni* isolates are plentiful and a selection is given here. Adherence to intestinal cells, as determined in vitro with cultured HeLa cells, as well as invasion into HEp-2 cells, varies among isolates of *C. jejuni* [31, 32]. Toxin production was found extremely variable, either in the type of toxin produced or in the degree of toxicity detected [33–38]. Most *C. jejuni* isolates are serum sensitive; however, different degrees of serum resistance have been demonstrated for *C. jejuni* isolates [39]. The potential to colonize chickens, which are a major vehicle of transmission to humans, also varies between *C. jejuni* strains [40].

\* Correspondence and reprints