DISEASES CAUSED BY CAMPYLOBACTER JEJUNI, THE RELEVANCE OF THEIR DETECTION AND TREATMENT

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Abstract. A common zoonotic bacterium that commensally colonizes the guts of numerous bird species is *Campylobacter jejuni. C. jejuni* is a significant foodborne pathogen in humans. Human infection results in small intestinal campylobacteriosis, which is the primary cause of bacteria-dependent gastroenteritis cases globally. The majority of *C. jejuni* infections are specifically caused by consuming undercooked rooster meat, raw milk, contaminated water, and cross-contamination of ready-to-eat food after handling raw chicken meat. The Guillain-Barré, Miller Fisher, and Reiter syndromes are among the post-infection disorders of the nervous system and joints that infected people may later experience along with watery and/or bloody diarrhea accompanied by stomach pain. Reducing *C. jejuni* colonization in poultry farms using vaccination, bacteriocins, and phage therapy procedures is one therapeutic approach. Following strict hygienic guidelines is one of the preventative measures used during the production of poultry meat. Additionally, employing well-established mice and in vitro cell model systems, significant advancements have been made recently in the fight against campylobacteriosis. In this sense, particular elements linked to *C. jejuni* colonization and pathogenicity were regarded as preferred treatment structures, focusing on bacterial mobility, host cell interaction, intracellular survival, and bacterial multiplication and spread. In order to lessen *C. jejuni*-induced epithelial cell damage, inflammation, and apoptosis in infected mice, several pharmacological substances have been added to this. In order to lessen the effects of acute campylobacteriosis and post-infection sequelae in humans, we examine these innovative treatment and preventative strategies as well as "One World-One Health" initiatives.

Keywords. *Campylobacter jejuni,* probiotics, phytochemicals, bacteriophages, gut microbiota, epithelial barrier, One Health, and vaccines

Introduction. *Campylobacteriosis,* one of the most common gastroenteritis in the world, is caused by *Campylobacter jejuni* and *coli*. The consumption of raw or undercooked meat or unclean water is the main cause of this foodborne illness. The majority of the time, intestinal infections have minimal symptoms and are self-limiting. Children, newborns, and those with impaired immune systems may exhibit more severe manifestations. Although uncommon, extraintestinal localizations are conceivable.

Late consequences including reactive arthritis and Guillain-Barré syndrome, which are mostly caused by a prior Campylobacter infection, are of great clinical significance. Over the past few decades, antibiotic resistance in poultry populations has alarmingly increased. A multi-step strategy involving pre- and post-harvest interventions is needed to effectively control Campylobacter. These interventions include the use of particular food additives, adherence to and improvement of biosafety and hygiene standards, and the creation of an effective vaccine [1-5]. Major infectious diseases known as zoonoses are spread by bacteria, fungi, viruses, parasites, and prions to both people and animals. Approximately 75% of infectious diseases are initially spread from animals to people, sometimes through tainted food. The World Health Organization reports that foodborne illnesses account for about 550 million cases of illness each year, including 220 million very young children under the age of four. The two genera of pathogens that predominate in bacteria-dependent zoonotic illnesses in the human gut are *Salmonella* and *Campylobacter*. According to reports from the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (2024), salmonellosis and campylobacteriosis are the two most prevalent human zoonoses in 16 European nations. Even if there has been a slight decline in the total number of *Salmonella* cases recorded globally in recent years, *Campylobacter* infections are still very common and cause serious health issues. The annual expenditures of campylobacteriosis were estimated to be around 2.4 billion euros for the European Union and up to 11.3 billion dollars for the United States [6-11]. As a result, Campylobacter is a common foodborne and zoonotic infection that has a significant financial impact on societies. *Campylobacter species* are frequently found in a variety of natural environments, such as surface water and the digestive tracts of birds and other essential agricultural animals. Furthermore, two common subspecies of Campylobacter can coexist as commensal microorganisms with chickens and other farm animals. As a result, bacterial contamination frequently happens during slaughter, which invariably results in the transfer of *C. jejuni* to meat. Therefore, eating rooster meat products that are positive for *C. jejuni* is the primary way that the disease spreads to people. Unpasteurized milk and tainted water were also mentioned as potential origins of the virus. After entering the body through the fecal-oral pathway, *C. jejuni* colonizes the lower small and large intestines after passing through the upper gastrointestinal tract. At a few hundred bacteria, the infectious dosage is very low. After penetrating the intestinal epithelium, *C. jejuni* activates the human innate immune system, causing acute inflammatory reactions. As a result, the course of campylobacteriosis varies from moderate, self-limiting, slightly inflammatory symptoms to severe, highly inflammatory, and blood-containing diarrhea, depending on the immunological status of the infected individual. These symptoms can be linked to severe stomach pain, which typically lasts for a week or more [12-18]. Bacteremia and immunologically-mediated post-infectious illnesses with an autoimmune component can occasionally be brought on by *C. jejuni* infections. These include joint inflammation linked to Reiter's syndrome (RS) or reactive arthritis, which can happen weeks after *C. jejuni* clearance, as well as neurological conditions such the Guillain-Barré and Miller-Fisher syndromes (GBS and MFS). Furthermore, *C. jejuni* infections may cause bouts of chronic inflammatory bowel illness including Crohn's disease and ulcerative colitis, as well as the development of post-infectious irritable bowel syndrome (PI-IBS). Nevertheless, there is still much to learn about the molecular causes of these illnesses. Therefore, a deeper understanding of human health and disease pathways related to domestic animals and wildlife is urgently needed. Therefore, one possible tactic for guaranteeing improved management of zoonotic infectious illnesses is the "One World-One Health" approach. Additionally, in recent years, novel medication treatments, bacteriophages, and vaccinations against campylobacteriosis have been developed. Inhibiting *C. jejuni's* inflammatory and cell damage responses is another goal of current treatments, which may provide protection against secondary disorders including GBS, MFS, and other chronic inflammatory processes. The present state of anti-Campylobacter therapies and recent advancements in this crucial area of human health protection are covered in this review paper [19-25].

The main purpose of the presented manuscript is to provide a brief overview of the relevance of diseases caused by *Campylobacter jejuni*, their diagnosis and treatment based on the results of reputable scientific research.

Microbiology of *Campylobacter jejuni*. Gram-negative, curved or spiral-shaped, motile, microaerophilic bacilli that do not form spores are known as campylobacters. Temperatures between 37

and 42 degrees Celsius are ideal for their growth. There are now 57 species in the genus Campylobacter, which can be divided into 5 phylogenetic groupings. There is a taxonomy list of every species of Campylobacter that is currently known. But at the moment, *Campylobacter jejuni* is the genus's most clinically relevant species. Two subspecies of *Campylobacter jejuni* can be distinguished: *Campylobacter jejuni* subspecies jejuni and *Campylobacter jejuni* subspecies doylei. They cause acute febrile enteritis in humans. Up to 25% of human Campylobacter-associated infections are caused by *Campylobacter coli*, another extremely common species. *C. sputorum, C. upsaliensis, C. ureolyticus, C.* lari, and *C. hyointestinalis* are more newly discovered species. The gastrointestinal systems of many animals, including birds, chickens, dogs, and cattle, frequently contain these microbes as commensals. The fecal–oral route is the most common way for humans to contract an infection from contaminated food, water, or milk; zoonotic transmission by direct animal contact is less frequent [11-21].

Epidemiology of Campylobacteriosis. One of the most common causes of infectious diarrhea in the globe is campylobacteriosis, which is brought on by an infection with Campylobacter jejuni or coli. The prevalence of infection seems to be rising in recent decades, despite the constraints imposed by insufficient national surveillance in many African, Asian, and Middle Eastern nations. The Centers for Disease Control and Prevention (CDC) estimate that there are 1.5 million instances of infection in the US each year, with a total economic effect of between 1.3 and 6.8 billion dollars. Over 60% of all zoonoses recorded in Europe are caused by Campylobacter, which is also the most common cause of bacterial enteritis and the primary cause of foodborne sickness. Only Japan, Korea, and Singapore have national surveillance in Asia; the epidemiological data from these nations are in line with those seen in other high-income countries [5-11]. In Australia and New Zealand, campylobacteriosis is the most common cause of bacterial enteritis. This infection exhibits bimodal incidence patterns: young adults experience the second peak, while preschool-aged children under the age of five experience the first and greater peak. Infections in children under five make up about 13% of all cases reported in Europe. The warmer months see a rise in cases in temperate zones. A causal association between increased consumption of undercooked foods and decreased cold chain integrity is strongly suggested by the seasonal trend. However, this distinct seasonal pattern may be influenced by host gene expression [22-27].

***Campylobacter jejuni* interacts with host cells and virulence factors.** Infection of cultured cell lines, a variety of animal model systems, and clinical investigations have all been used to study the molecular pathways of *C. jejuni* pathogenesis. Intestinal epithelial barrier breakdown and inflammation brought on by immune cell infiltration are the hallmarks of campylobacteriosis. Under the direction of chemotactic receptors, the invasive bacteria move very effectively with the help of their pushing flagella. Then, using certain bacterial adhesion factors, *C. jejuni* colonizes the mucus layer and adheres to intestinal epithelial cells. The adhesins FlpA and CadF, in particular, have been extensively described as binding factors of the extracellular matrix protein fibronectin and related integrin receptors [6-13]. According to reports, the capacity of *C. jejuni* to infiltrate these cells is ultimately linked to the close attachment of bacteria to the epithelium. Effector proteins called Campylobacter invasion antigens, which are produced through a type-III secretion system (T3SS) that is also expressed by the flagellum, facilitate host cell entrance by C. jejuni. CadF, FlpA, and CiaD have been shown to work synergistically to increase host guanine exchange factors, which in turn activate small Rho GTPase members to cause actin polymerization and *C. jejuni* invasion. Surprisingly, it has been demonstrated that *C. jejuni* can endure in vacuoles that form inside epithelial cells. While the reception of *C. jejuni* by macrophages results in the creation of lysosomes and the pathogen's ultimate death, it appears that *C. jejuni*-containing vacuoles stray from the classical endocytosis route, which dampens its transport to lysosomes. This could account for the variation in LOS linked to distinct illness outcomes following infection with distinct bacterial strains. For instance, sialylation of LOS's oligosaccharide component increases TLR4 binding and activation, which causes acute inflammation. Lastly, gangliosides in the human brain are similar to the sialylated oligosaccharide chains seen in *C. jejuni* LOS. Individual LOS structural variations may therefore cause the human host to produce anti-ganglioside antibodies, which may then result in axonal damage linked to GBS and MFS [20-27].

Strategies for prevention and therapy. Contaminated food is the most common way that *C. jejuni* is spread to people, with poultry and cattle being the main sources. The consequences of *C. jejuni*

contamination may be lessened by complex biocontrol of food processing at every stage, from harvesting and slaughter to storage and delivery to consumers. Additionally, by applying multiple intervention measures at the same time, it is possible to drastically minimize the emission of Campylobacter into the environment, which is responsible for the bacterial persistence. Although *C. jejuni* infections typically don't need medical attention, antibiotic treatment is advised in severe situations. The worldwide rise in antibiotic resistance poses a significant risk of common antibiotics losing their ability to treat *Campylobacter infections* due to inappropriate use of antibiotics in both humans and animals. The majority of the medicinal molecules listed below are naturally occurring substances made by bacteria or plants, and extensive study has been conducted to explore alternate preventative and treatment options. Most of these substances have just recently been studied for their capacity to stop *C. jejuni* from growing, mostly in mice trials and *in vitro* in cell lines. There is currently relatively little information about their use in humans because most of those papers were just published. As a result, we classified those possible medicinal substances as promising [19-26].

The "One Medicine" approach, which proposed the creation of an interdisciplinary cooperative research alliance of human and veterinary medicine to better control specific diseases, was the source of the "One World-One Health" (or simply "One Health") concept. It was first proposed by Calvin W. Schwabe approximately 40 years ago. The goal of this project is to have a deeper comprehension of both human and animal health and illness. In this regard, the Wildlife Conservation Society developed the "Manhattan principles," which summarize common criteria and useful approaches. The World Health Organization (WHO), the World Organization for Animal Health (WOAH), and the Food and Agriculture Organization of the United States (2025) have also released the so-called "Tripartite Concept Note," which is a strategic paper for a partnership. It focuses on the health risks associated with human interactions with domestic animals, wildlife, and natural ecosystems, including the fight against antimicrobial resistance and specific microbial diseases [1-9]. These concepts, which also involve environmental health, have been further refined in recent years as a possible approach for improved control of zoonotic infectious illnesses. In order to sustainably balance and enhance the health of people, animals, plants, and the environment, the WHO, the WOAH, the FAO, and the United Nations Environment Programme (UNEP) recently expanded this idea into the "Quadripartite collaboration on One Health." For Campylobacter, a significant zoonotic pathogen in the bacterial kingdom, the One Health idea is very crucial. The PAC-Campy partnership, which was established under the supervision of the Federal Ministry of Education and Research, serves as an illustration of its application. Furthermore, PAC-Campy offered effective intervention strategies to the public health service and industry. In supplementary study, the research network created infection models in mice that were tested with several of the medicinal chemicals mentioned above in order to discover novel strategies for preventing human infections and tracking the progression of outbreaks [11-19].

Discussion. Globally, campylobacteriosis is a major cause of foodborne disease and infectious diarrhea. Consumption of contaminated food, particularly raw meat or untreated water, contact with diseased animals or polluted settings, and contact with poultry—the main reservoir and source of human transmission—are the main ways that campylobacter infections are spread. There are two main types of Campylobacter jejuni/coli infection symptoms: extraintestinal and gastrointestinal. Miller Fisher syndrome, Guillain-Barré syndrome, and reactive arthritis are examples of late consequences [1,2,5,9,11]. Campylobacteriosis is most common in children between the ages of 0 and 4. International standards concur that certain antimicrobial medication should be used for serious intestinal infections. Malnutrition, immunodeficiency, and cancer are examples of host variables that can affect the choice of treatment. Due to growing resistance to FQs or macrolides, the Centers for Disease Control and Prevention (CDC) has classified antibiotic resistance in Campylobacter as a "significant public health threat." Despite the fact that many vaccinations have been suggested recently to lessen poultry intestinal colonization, none of them have demonstrated enough effectiveness to offer a conclusive remedy [6-11]. Human campylobacteriosis, one of the most common bacterial gastroenteritis in the world, is a serious public health problem even though the infection is frequently asymptomatic in poultry. The infection is self-limiting and has a low fatality rate, but because of its high prevalence, hospital expenses are very high. Pre-harvest and post-harvest treatments are the two primary stages of the control measures. Improving

environmental hygiene to reduce *Campylobacter* exposure by cleaning and replacing the farm's soils and vegetation, minimizing the mixing of different species, and restricting interaction with other potential reservoirs like wild animals are the main biosecurity methods. It is crucial to put strict biosafety and biosecurity procedures in place for farm workers. Food additives, such as probiotics and prebiotics, have not been able to effectively reduce the colonization and spread of the germ despite multiple experiments. To address the growing issue of multidrug resistance in avian populations, it is also imperative to create a vaccination and alternate antibiotic therapy. The entire production chain, including farms, transportation, and final goods like carcasses and egg shells, is thoroughly cleaned as part of post-harvest protocols [12-17]. A comprehensive approach is required to develop and implement successful containment methods due to the convergence of factors such as growing poultry production, worldwide travel, the advent of antibiotic resistance, and the widespread presence of Campylobacter. Effective Campylobacter control requires a multifaceted approach that includes better hygiene standards, biosafety precautions, the synergistic use of food additives and probiotics, vaccine research, and increased public health awareness [22-27].

Conclusions. *C. jejuni* is a significant zoonotic pathogen that is widely dispersed around the world and highly contagious in humans. The virus is one of the four main causes of diarrheal illness in the world and has not yet been successfully removed from the chicken food chain. From a medical and socioeconomic perspective, this pathogen poses a major threat to humanity due to its high prevalence of the disease and the possibility of late sequelae. Therefore, in order to prevent the prevalence of the bacterium in animals and reduce contamination during food production, "One World-One Health"-based control systems and intervention strategies have recently been established. For instance, improved cleanliness at the fattening, slaughtering, and processing stages should be aided by novel technology decontamination techniques.

At the same time, public education programs are needed to increase the general public's awareness of foodborne pathogens like *C. jejuni.* When processing raw poultry meat products, which may even spread the disease to other foods, kitchen hygiene should be the main priority. The molecular underpinnings of *C. jejuni* pathogenicity have also been thoroughly uncovered in recent years, and these processes are currently being used to create new treatments, phage regimens, and vaccines to prevent campylobacteriosis.

In order to lower the C. jejuni load in the gut and to prevent related inflammation and apoptosis, future research should focus more on finding and studying novel anti-bacterial and anti-inflammatory compounds. This could not only lessen diarrhea but also help protect against secondary diseases caused by the pathogen, such as GBS, MFS, RS, or various chronic inflammatory processes in humans.

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