Why Campylobacter?
Campylobacter is one of the major foodborne pathogens of concern. C. jejuni and C. coli are the major causative agents, with C. jejuni accounting for approximately 90% of cases of Campylobacter-associated illness around the world (Tresse et al. 2017; Tam et al. 2003; Wieczorek et al. 2018). Campylobacteriosis caused by C. jejuni commonly causes severe diarrhoea, abdominal pain, fever, headache, nausea, and vomiting with some extreme cases resulting in Guillain–Barré syndrome (GBS) and acute flaccid paralysis (Havelaar et al. 2015; Ramos et al. 2021). Symptoms are severe in children below 5 years of age, the elderly, and immunocompromised individual. The infection is usually sporadic and self-limiting and thus does not require medication. Mortality due to Campylobacter infection is low (Mearelli et al. 2017). Campylobacteriosis caused by C. jejuni is endemic in certain parts of Africa, Asia, and the Middle East, especially in children under 2 years of age who often have repeated or chronic infections (Kaakoush et al. 2015; Pascoe et al. 2020). Campylobacter infections rarely cause mortality, though occasional deaths occur in the elderly, immunocompromised, or paediatric populations (Kaakoush et al. 2015; Havelaar et al. 2015).

Epidemiology of Campylobacter
Annually, approximately 800 000 cases occur in the United States of America alone, and the incidence in high-income countries varies from 4.4 to 9.3 per 1 000 people (Havelaar et al. 2015). In 2014, Europe reported a total of 240 379 confirmed cases from a total of 28 countries – an increase of 13% over the previous year (European Centre for Disease Control and Prevention 2017). In the Oceania region, Campylobacteriosis is the most reported foodborne infection in Australia in 2010, with 16 968 cases (Kaakoush et al. 2015). Although surveillance data from developing countries is greatly lacking, Campylobacteriosis is endemic in certain parts of Africa, Asia, and the Middle East, especially in children under 2 years of age, who often have repeated or chronic infections (Kaakoush et al. 2015; Pascoe et al. 2020). Campylobacter infections rarely cause mortality, though occasional deaths occur in the elderly, immunocompromised, or paediatric populations (Kaakoush et al. 2015; Havelaar et al. 2015).

Geographical impact of Campylobacter
Campylobacteriosis is considered to be indirect as countries with high average temperature ranges like Nigeria (18 °C [65 °F] to 37 °C [98 °F]) and countries with low average temperature ranges like Iceland (10 °C [50 °F] to 15°C [59 °F]) have reported cases of Campylobacteriosis, indicating that there is no correlation between temperature and the growth and spread of the Campylobacter species (Callicott et al. 2008). There are not many studies reporting the geographic, climate, and temperature impact on Campylobacter infections and the available studies do not show any significant correlation between weather and temperature on Campylobacter infection. However, Campylobacteriosis is considered to be indirect as countries with high average temperature ranges like Nigeria (18 °C [65 °F] to 37 °C [98 °F]) and countries with low average temperature ranges like Iceland (10 °C [50 °F] to 15°C [59 °F]) have reported cases of Campylobacteriosis, indicating that there is no correlation between temperature and the growth and spread of the Campylobacter species (Callicott et al. 2008). There are not many studies reporting the geographic, climate, and temperature impact on Campylobacter infections and the available studies do not show any significant correlation between weather and temperature on Campylobacter infection.

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The notorious case of Campylobacter spp.: an increasingly antimicrobial-resistant foodborne pathogen
With Campylobacter infections on the rise and treatment options disappearing because of growing antimicrobial resistance, how should the food industry respond?
... its genetic flexibility...

Resistance mechanisms in the context of Campylobacter food poisoning

Campylobacter’s dynamic adaptation is attributed to its genetic flexibility, which benefits the organism with rapid evolution. The innate error-reading mechanisms, the genome’s vulnerability to mutation, and the exposed cells that make it possible to receive horizontal genes collectively promote selection in Campylobacter for adaptability to colonize hosts and to develop antimicrobial resistance. C. jejuni to determine the antibiogram associated with molecular resistance mechanisms shows that resistance to fluoroquinolones (55.8%) and tetracyclines (49.7%) was high (Elhadidy et al. 2020). Previous studies show that resistance to ciprofloxacin and tetracycline has exponentially increased (Wieczorek et al. 2018) with a growing trend of treatment complications in infants who are commonly treated with antibiotics for non-self-limiting diarrhoea and systemic Campylobacteriosis (Schiaffino et al. 2019; Dai et al. 2020). DNA gyrase mutation C257T in the gyrA gene and the tetracycline resistance tetO gene is detected in the majority of the clinical isolates, but few isolates seem to have also developed physiologic resistance. The tetracycline resistance tetO gene is transferred horizontally from poultry sources (Avaran et al. 2004). Approximately 2% of Campylobacter isolates from diarrhoeal patients were resistant to macrolides and contained ermB coding for efflux pump, pld, and rplV genes in the 23s rRNA mutation of 50S ribosomal subunit resistance genes (Elhadidy et al. 2020). This highlights the need for future exploration of physiologically resistant populations of Campylobacter spp. in human infections. Thermotolerant communities of Campylobacter with higher antibiotic resistance were encountered in poultry and bovine meat (Di Giannatale et al. 2019). Gas-trointestinal pathogens require thermostolerance and other physiological resistance to acids or salts to survive and to flow between hosts along the food chain. Such tolerance mechanisms may be attributed to the phenotypic resistance to antibiotics, which requires further study.

Morphophysiological characteristics of Campylobacter

Campylobacter bacteria are small, gram-negative, non-spore-forming, oxygen-sensitive, highly mobile curved or spiral-shaped rods that grow best in micro-aerobic conditions. They have a polar flagellum at one or both ends of the cell, they are catalase- and oxidase-positive, and they are urease-negative. They are fastidious organisms which belong to a distinct group, designated “rRNA superfamily VI”, and have been reported to change into coccoid forms upon exposure to adverse conditions, especially oxidation. In general, these bacteria are fragile and easily destroyed by heat, acidity, desiccation, and disinfectants.

There is an overwhelming increase in Campylobacter’s antimicrobial resistance, especially to fluoroquinolones...

Campylobacter virulence factors

Enteric Campylobacters likely express several virulence factors when colonising the intestines, allowing for their survival against food processing and resistance to physiological stress (Bolton 2015). The different virulence-related mechanisms include invasive properties (facilitating binding and entry into host cells), bacterial adherence to intestinal mucosa, oxidative stress defenses, heat shock, toxin production (e.g., cytotoxins and cytolethal distending toxin that cause cell death), iron acquisition (for nutrition), and the ability to remain in a viable but non-culturable (VBNC) state (Backert et al. 2013). Other Campylobacter virulence factors entail secretion of certain sets of proteins, translocation capabilities, chemotaxis (to traverse chemical gradients), and flagella-mediated motility (enabling movement into the mucus layer) (Biurer et al. 2011).

Impact of Campylobacter Anti-microbial Resistance

There is an overwhelming increase in Campylobacter’s antimicrobial resistance, especially to fluoroquinolones; this is perhaps unsurprising given the alarming increase in resistance to fluoroquinolones on a global level. This limits the usefulness of fluoro-
Ingestion of 500–800 bacteria can result in human disease.

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Campylobacter bacteraemia has a very low detection rate, accounting for less than 1% of European patients with gastroenteritis. This can be attributed to many factors such as under-diagnosis and the lack of routine blood cultures for gastroenteritis patients (Mearelli et al. 2017). Campylobacter bacteraemia is very serious in patients with immunodeficiency, particularly HIV/AIDS, antimicrobial-resistant strains being more likely to manifest as a single course of treatment failure for diarrhoeal disease. Campylobacter bacteraemia, the presence of resistant strains in the food chain will have an impact on human health (Wieczorek et al. 2018).

**Source and transmission pathways in Campylobacter**

The colonization of different animal reservoirs by Campylobacter poses an important risk to humans through shedding of the pathogen in livestock wastes and contamination of water sources, the environment, and food (Igwaran and Okoh 2019). Campylobacter bacteria colonize the gastrointestinal tract, often causing a wide variety of disease, including foodborne illness, diarrhea, and dehydration.

Ingestion of 500–800 bacteria can result in human disease. However, there are reports of 100 Campylobacter cells or fewer causing infections in humans (Ferdich et al. 2017). Acute diarrhoea (including traveller’s diarrhoea and children’s diarrhoea) is the most common symptom caused by a Campylobacter infection. Watery or bloody diarrhoea, accompanied by fever, stomach cramps, abdominal pain, nausea, and vomiting are common. Bloating, headache, and muscle pain may also occur in some patients.

**Clinical manifestations of Campylobacter infection in humans**

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Current guidelines to tackle the Campylobacter and their drawbacks

The epidemiology of Campylobacteriosis is consequential for public health, not only because of increasing Campylobacteriosis prevalence but also because of the increasing number of human infections where antimicrobial-resistant Campylobacter has been identified. In humans, Campylobacter spp. account for 50% of all reported foodborne illnesses (220,682 confirmed cases) in the most recent annual report on zoonoses, zoonotic agents, and epidemic outbreaks of foodborne illnesses from the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) (2019). These findings were consistent with previous studies that identified Campylobacter as a leading cause of infectious diarrhea and foodborne illness, primarily occurring in Europe (EFSA & ECDC, 2019). The guidelines for controlling Campylobacter colonization in the food chain are established according to EFSA research and Commission Regulation (EU) 2017/1495 of August 23, 2017, that amended Commission Regulation (EC) No 283/2005 of 17 February 2005. The most important challenges are standardizing validation measures, implementing improved biocontrol methodologies in the poultry sector (principally, mitigating the source of Campylobacter transmission to humans), and promoting innovation and efficacy among all ecosystem actors. These actions must occur in parallel with policies for control and contamination notification and they must increase consumer protection.

Recent interventions

Multiple strategies have been implemented to reduce Campylobacter colonization in the food chain. Recent- ly, scientists have started looking at alternatives to antibiotics to address multidrug-resistant Campylobacter. Scientists have also explored probiotics as a supplement to prevent Campylobacter colonization in the guts of animals, though the findings were inconsistent (Dai et al. 2020). Researchers have also focused on the use of chemical-based antimicrobials such as trisodium phosphate (TSP), peracetic acid (PAA), acidified sodium chlorite (ASC), and cetylpyridinium chloride (CPC). These chemicals are usually applied as spray or surface sanitizers in poultry farms and in the sites where boiler chickens are processed (Johnson et al. 2017). Major investigations are currently underway to improve antimicrobial intervention methods in poultry processing. Processing plants cannot rely on the integrity of cold transportation to retailers and, therefore, must prioritize the advancement of antimicrobial interventions. There are many factors driving industrial changes but one of the most prominent factors is pressure from the public for safer poultry (MacRitchie et al. 2016). Producers are exploring alternative and novel methods to kill these microbes, including electrostatic spraying, cold plasma treatment, and bacteriophage-based methods (Soro et al. 2020).

Conclusions

Campylobacter is notorious for its rapid spread and colonization in animals and humans through food and excreta. There is debate regarding the administration of antimicrobial treatments in the management of uncomplicated Campylobacter infections because these infections are usually self-limit- ed and most patients recover without the need for antibiotics. Antibiotics should be reserved for severe cases of C. jejuni, which include symptoms such as bloody diarrhea, fever, worsening symptoms, or a large number of stools. The AMR Insights Ambassador Network consists of an integrated global and cross-professional community discussing, devising, and driving actions to combat AMR. The Network aims to inspire, connect, and empower our Ambassadors to take individual and collective actions to curb AMR.

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