

The relationship between human *Campylobacter* iosis and broilers

Abstract

Campylobacter is the leading cause of bacterial foodborne diarrhoeal disease in the developed world, with raw and undercooked broilers (chicken meat) the primary source of sporadic infection. In this review we provide an update of the significance of *Campylobacter* infection and broilers.

Keywords: *Campylobacter jejuni*, broilers, poultry, illness, epidemiology

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Table Continued....

Year	Cases
2001	55,081
2002	48,133
2003	46,291
2004	44,577
2005	46,735
2006	46,853
2007	51,982
2008	50,006
2009	57,784
2010	62,686
2011	64,726
2012	65,032
Total	698,122

Source: Laboratory Reports in England and Wales reported to HPA.

Campylobacter and Illness

Antimicrobial treatment is usually not needed with human *Campylobacter* iosis, as it is normally self-limiting.⁸ The exceptions are severe cases with patients who are generally young, old, pregnant or immuno compromised. Human *Campylobacter* iosis is normally associated with watery and occasionally bloody diarrhoea, fever, abdominal cramps and vomiting lasting for roughly 5-7days. These symptoms usually develop 1-5days after exposure. Guillain-Barré syndrome (GBS) is a severe demyelinating neuropathy and *Campylobacter* iosis is the most common infection proceeding the onset of post-infectious GBS.⁶ Roughly 33% of global GBS cases are attributed with *Campylobacter* iosis.² Around 20% of GBS cases require intensive care and case-fatality rates in high income countries are 3-10%.² *Campylobacter* disease burden is also significantly increased by irritable bowel syndrome (IBS) and reactive arthritis.

Abbreviations: DALYs, disability-adjusted life-years; FQ, fluoroquinolones; GBS, guillain-barré syndrome; GLP, good laboratory practice; HACCP, hazard analysis critical control point; HPA, health protection agency; IBS, irritable bowel syndrome; LMIC, low- and middle-income countries; MLBs, multilamellar bodies; MLST, multilocus sequence typing; OMVs, outer membrane vesicles; PCR, polymerase chain reaction; ReA, reactive arthritis

Introduction

Campylobacter iosis has been the most frequently reported zoonotic disease in humans in the EU since 2005¹ (Table 1). The true frequency of gastroenteritis caused *Campylobacter* spp. is difficult to accurately determine due to underreporting, particularly in Low- and Middle-income countries (LMIC).² Several surveys have calculated the annual incidence to be between 4.4 and 9.3 per 1,000 population in high-income countries.² Recorded *Campylobacter* species in these studies are mostly the thermotolerant species *C. jejuni* and *C. coli*.¹ In general, reported *Campylobacter* infections are markedly higher in specific age groups; young children in particular (<5years of age).³ There are probably varied risk factors with different age groups.³⁻⁵ Outside areas other than Europe and North America, incidence reports are relatively rare, and frequently show low detection rates from human samples.⁶ In temperate regions human *Campylobacter* iosis exhibits particular seasonality trends.⁷ Environmental sources, e.g. livestock & wild birds, cause a higher incidence in young rural children in late spring.³ An extended summer peak linked with chicken strains has been found in adult populations,³ partially because of barbeques and summer holidays. International trade and travel influence public health globally by affecting patterns of antimicrobial use and resistance selection.²

Table 1 *Campylobacter* cases: 2000 to 2012 for England and Wales.^{40,41} Figures shown are for *Campylobacter* sp cases reported to the Health Protection Agency (HPA) for England and Wales. It includes patients with enteric and non-enteric infections and includes isolates from all body sites.

Year	Cases
2000	58,236

(ReA) sequelae.⁹ Studies indicate that ReA occurs with 1-5% of campylobacteriosis cases. A shortage of clear diagnostic and classification criteria make the true extent of ReA challenging to accurately determine. Around 25% of ReA cases can develop into chronic spondyloarthropathy. People with more severe acute enteric disease are more likely to develop IBS within 1-2 years after having campylobacteriosis; IBS develops in up to 36% of patients.² The median estimated costs to patients and the National Health Service in the UK from 2008-2009 were; *Campylobacter* £50million (£33m-£75m), norovirus £81million (£63m-£106m), rotavirus £25m (£18m-£35m).¹⁰ The costs per case were approximately £30 for norovirus and rotavirus, and £85 for *Campylobacter*, which was mostly borne by patients and caregivers via lost income or out-of-pocket expenditure. *Campylobacter*-related GBS hospitalisation cost around £1.26million (£0.4m-£4.2m). The number of years lost due to disability caused by *Campylobacter* related sequelae [disability-adjusted life-years (DALYs)] are also used to calculate disease burden.^{6,9,11} Recent estimates range from 1,568 DALYs in New Zealand,¹² 3,633 in The Netherlands,⁹ 18,222 in Australia¹¹ and 22,500 in the USA.⁶ The economic costs of efforts to control *Campylobacter* in agriculture, food production are also significant and need to be considered.¹⁰

Poultry and *Campylobacter*

Many sources of campylobacteriosis have been identified, e.g. raw milk and pets, but broilers and broiler meat are the most important.¹³⁻¹⁶ *Campylobacter* in urban areas has been associated with broilers, but less so in the countryside [8]. The European Food Safety Authority estimated that chicken meat consumption accounts for 20%-30% of campylobacteriosis in the EU, with 50%-80% of cases linked to the chicken reservoir as a whole.¹⁷ Between 2000-2014, global chicken meat production rose from 58.5million tonnes to 95.5million tones,⁸ and has continued to increase, putting more pressure on public health agencies and the poultry industry to lower poultry/ chicken-associated human campylobacteriosis.⁸ To survive under environmental conditions encountered along the food chain, i.e., from poultry digestive tract its natural reservoir to the consumer's plate, *Campylobacter* has developed adaptation mechanisms.¹⁸ Among those, biofilm lifestyle has been suggested as a strategy to survive in the food environment and under atmospheric conditions.¹⁸ *Campylobacter* prevalence in poultry, as well as the contamination level of poultry products, varies between different countries; from 0.6% to 13.1% in the Finland, Norway and Sweden, and up to 74.2%-80% in several other countries;¹⁹ one Northern Ireland study from 2009 showed a prevalence on poultry meat of 91%.²⁰

The stages in the broiler production and processing chain consist of primary production at rearing farms, transport to slaughter, the slaughter process, followed by the processing of chicken meat products, selling products at the retail level, and handling and consumption of chicken meat products at home and in public places such as restaurants.⁶ In order to implement effective interventions that reduce the probability of *Campylobacter* colonisation of broiler flocks, it is essential to understand the risk factors involved.¹⁶ All of these different phases have a role in the transmission of *Campylobacter* from farm to fork. Production chain conditions vary between countries, and this is also reflected in the annual number of *Campylobacter*-positive chicken flocks.⁸ Contamination and resulting colonisation of broiler flocks in farms normally results in the transmission of *Campylobacter* along the poultry production chain and in contamination of poultry meat at retail.⁸ During the slaughter process, plucking and evisceration can lead to carcasses contamination, whilst transport appears to have a

lesser effect on the contamination of carcasses.¹⁷ A large variety of poultry products ranging from fresh, frozen, cooked, whole carcasses and smaller portions with different infection risks are globally commercially available. Lower *Campylobacter* counts have been recorded from skinless portions of meat, e.g. breast fillets.¹⁷ Good hygienic practices and applying control measures based on Hazard Analysis Critical Control Point (HACCP) principles are important for effective post-harvest control.² Decontamination of carcass by chemical or physical methods as part of these measures have proved successful.² Quality surveillance data is vital to identify disease outbreaks, to detect sporadic cases for case-control studies, to provide isolates that can be used in attribution models based on isolate subtyping, and to furnish data for constructing and calibrating risk assessment models and to document the success of control programmes.² Surveillance data also advises national decision-making by: determining the relative importance of campylobacteriosis compared with other enteric infections; showing which animals are the primary reservoirs for infection; and helping to identify the most common transmission pathways. *Campylobacter* surveillance is practised more in countries with higher incomes.²

Farm epidemiology

In developed countries, each broiler rearing house in farms generally contains between 10,000-30,000 birds, with several houses usually present in each farm.⁸ These high numbers facilitate high levels of *Campylobacter* amplification, the rapid spread between broilers within houses,⁸ and cross-contamination between separate houses on farms. Even with improving farm biosecurity levels the *Campylobacter* colonisation of broilers is extremely difficult to prevent.^{20,21} After approximately two weeks poultry flocks are frequently colonised with *C. jejuni* without any apparent symptoms.¹ Vertical transmission, from parents to progeny, is not a significant *Campylobacter* source.⁸ Better biosecurity intervention strategies in farms have reduced broiler *Campylobacter* colonisation, decreasing subsequent campylobacteriosis cases in several countries.⁸ In broiler farms, longer downtimes between flocks, older broiler houses (> five years), no separate ante-room or barrier in houses, and the use of the drinker nipples with cups or bells compared with nipples without cups, have all increased the risk of *Campylobacter* colonization.¹⁶ Increasing the slaughter age of birds (from 36days, to >40days), laughtering in summer months (June, July and August), thinning broiler flocks, and an increasing amount of rearing houses on farms are all significant factors for producing *Campylobacter* positive broilers.^{19,22,23} Farms with poorer biosecurity measures have been linked with having broilers with more strains of *Campylobacter*.²⁴ There is limited knowledge about how *Campylobacter* persists in broiler litter and faeces.²⁵ *C. jejuni* survives significantly longer in faeces, with a minimum survival time of 48 hours, compared with 4 hours in used broiler litter. *C. jejuni* survival is significantly enhanced at 20°C in all environmental conditions in both broiler litter and faeces, compared with survival at 25°C and 30°C. Survival is greater in microaerophilic compared with aerobic conditions in both sample matrices. The persistence of *Campylobacter* in broiler litter and faeces under various environmental conditions has implications for farm litter management, hygiene, and disinfection practices.²⁵

The colonisation of broilers with *Campylobacter* in drinking water may be partly due to *Campylobacter* resisting disinfection inside waterborne protozoa.²⁶ *Campylobacter jejuni* inside amoeba can infect broilers.²⁷ *Campylobacter* survive for prolonged periods of time both within, and in the presence of, different protozoa, including amoeba and ciliates.²⁶ Some protozoa package and excrete bacteria

into multi-lamellar bodies (MLBs), increasing the risk of persistence of *C. jejuni* in the environment and possible transmission between different reservoirs in food and potable water through packaging.²⁸ The protection of *Campylobacter* from disinfection within protozoa and/or biofilms has important implications for water safety.²⁹ Whilst *Campylobacter* is present in the faeces of wild mammals (mice, rats, badgers, foxes, and rabbits), pets (dogs and cats), insects, and wild birds, are all frequently present in the vicinity of farms, the evidence of actual transmission, either direct source contamination from house entry or via environmental faecal contamination, to broilers is contradictory, sparse and unclear.³⁰ Relatively low *Campylobacter* isolation rates have been recorded from Dipteran flies.²¹ However, in the summer the potential of broiler *Campylobacter* colonisation from this potential reservoir could in theory rise when fly populations increase.²¹ Certain investigations have shown no significant overlaps in the *Campylobacter* populations in poultry and wildlife.³⁰ The incorporation of ecological data into studies of *C. jejuni* in wild birds has the potential to resolve when and how wild birds contribute to domestic animal and human *C. jejuni* infection, leading to the improved control of initial poultry contamination.³¹ The antibiotic resistance of *C. jejuni* and *C. coli*, particularly with macrolides and fluoroquinolones (FQ), has raised concerns about the evolution of antibiotic resistance and has major implications for animal and human treatment.¹⁴ Using FQ to treat poultry correlates with high levels of resistance to these drugs.² Resistant bacteria may transfer between farms, as farms with no record of using FQ have had FQ-resistant *Campylobacter* detected on them.¹⁵

Dangerous consumer behaviour

There is a high prevalence of unsafe behaviours (undercooking and poor hand washing technique) when cooking poultry and eggs, and a great need for improvement in consumer behaviour and education.³² Many consumers still do not follow recommended food safety practices for cooking poultry and eggs, which can lead to exposure of pathogenic *Salmonella* and *Campylobacter*.³² In the USA, nearly 70% of consumers rinse raw poultry before cooking it and the majority of consumers (>80%) incorrectly store raw poultry in refrigerators.³³ This is extremely unsafe behaviour because of the potential cross-contamination of *Campylobacter* to other kitchen surfaces and other foods, especially ready-to-eat foods.³³ In the UK, outbreaks of *Campylobacter* infection are increasingly attributed to undercooked chicken livers, yet many recipes, including those of top chefs, advocate short cooking times and serving livers pink.³⁴ It is estimated that 19%-52% of livers served commercially in the UK fail to reach 70°C, and that predicted *Campylobacter* survival rates are 48%-98%. These findings indicate that cooking trends are linked to increasing *Campylobacter* infection case numbers.³⁴ Collectively, using information from research studies and effectively monitoring and examining consumer behaviour will improve the effectiveness of science-based education of schemes to lower the frequency of human campylobacteriosis cases.³³

Conclusion & future approaches

Chicken meat is the main global source of *Campylobacter*.¹ Reducing *Campylobacter* colonisation, carriage and transmission in broiler chickens, and related products, would lower human campylobacteriosis levels. Because of the epidemiological complexity of this problem, including geographical variations, the solution cannot be achieved by a few simple intervention strategies.² *Campylobacter* control and intervention strategies need to be tailored

to reflect and adapt to regional variations, possibilities, practicalities and preferences, by the effective implementation of multiple stepwise interventions on the farms and in processing facilities.^{2,8} From an epidemiological and risk assessment perspective, further knowledge should be obtained on *Campylobacter* prevalence and genotype distribution in primary production.³⁵ Effective quality assurance schemes, including Good Laboratory Practice (GLP), which includes continuous monitoring and improvement, are vital for cogent diagnostic laboratories.² In developed countries molecular methods, e.g. real-time PCR, could be applied to quantify *Campylobacter* spp. directly from chicken droppings and thus avoid culture-associated bias resulting from failure of recovery from viable but non-culturable states previously described in *Campylobacter*.³⁶ Intervention methods which are effective in the pre-harvest stages in farms include application of strict biosecurity measures, good animal husbandry, and health measures.³⁴ The elucidation of the seasonal components of human campylobacteriosis epidemiology would improve with increasing the integration molecular subtyping.³ Temporal patterns in human infections do not always correlate with those found in poultry.⁸ Community socioeconomic and environmental factors are important to consider when assessing the relationship between possible risk factors and *Campylobacter* infection.⁷ Overseas travel has been linked as being a significant source of the disease, especially for northern European residents.⁸

Despite numerous trials and studies, there are currently no available vaccines commercially available to remove or reduce *Campylobacter* intestinal load in poultry.³⁷ Feed additives (pre and probiotics) have potential to reduce *Campylobacter* infection in flocks.³⁵ Probiotics, e.g. *Lactobacillus salivarius* SMXD5, may exhibit an anti-*Campylobacter* activity in vivo and partially prevent the impact of *Campylobacter* on the avian gut microbiota.¹ In future it will be important to identify, characterise, develop and promote new vaccine antigens, with more robust economics funding models which enable vaccine developers to hedge against the risks of market volatility.^{37,38} The oral vaccination of poultry with modified outer membrane vesicles (OMVs) could be a promising option for future vaccine development.³⁹ With well organised and multidisciplinary and coordinated approaches between countries in these and other areas, the disease burden on *Campylobacter* should hopefully be reduced in the future.

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Conflict of interest

The author declares no conflict of interest.

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