

# Emergence of MDR *Campylobacter jejuni* bacterium

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hi, I'm Sarah Gregory, and today I'm talking on the phone with Dr. Bruno Lopes, a postdoctoral research fellow at the University of Aberdeen in the UK. We'll be discussing his article about an antimicrobial-resistant strain of *Campylobacter jejuni* in poultry. Welcome, Dr. Lopes.

[Bruno Lopes] Thank you, Sarah.

[Sarah Gregory] What is *Campylobacter jejuni*?

[Bruno Lopes] So, *Campylobacter jejuni* is a gram-negative bacterium, and it is a spiral S-shaped bacterium, or a curved bacterium, that is found in poultry.

[Sarah Gregory] Do animals or people get this infection, or...or both? I guess you just said poultry, so that would be animals. Do people get it?

[Bruno Lopes] The main source of *Campylobacter jejuni*, or from where, basically where this bacterium is found is in animal hosts otherwise. And this includes poultry, ruminants, pigs, and even wild birds. But poultry is the main source of *Campylobacter jejuni* because...because, you know, there is a direct source to, there is a direct link between the infection between the source to the human cases.

[Sarah Gregory] Can people get this illness from eating contaminated meat? And if so, how can we protect ourselves?

[Bruno Lopes] So, basically, people can get it. People can get infected by maybe washing their raw poultry, for instance, because when you wash the raw poultry, the...the water that sprinkles out from it, it basically contains *Campylobacter* and it contaminates other surfaces and it can also contaminate other fruits and vegetables that are lying around. But you can also get the illness if you are on a farm visit, for instance, and...and also if you have, like, direct order supplies, which are often contaminated by feces from ruminant hosts. So even...even raw milk can be a source of *Campylobacter* infection.

[Sarah Gregory] Okay, so yes, raw milk is something that we worry about here at CDC, and...and I'm just going to reinforce this message that washing poultry before you cook it is not a good idea, right?

[Bruno Lopes] That's right.

[Sarah Gregory] Okay, how...how widespread is this illness?

[Bruno Lopes] This illness, it's about...the W...according to the WHO, you can see that one in 10 people are infected every year because of *Campylobacter*. And it is...it is quite widespread and it is very noticeable in the West, especially in the UK or in European countries and even in America. The other reason for that is because the poultry consumption, especially in the UK, is almost like 33 kgs per...per capita per year. So, basically each person consumes 33 kgs of poultry meat each year, and because poultry is the main...main source of infection, it...the person can get easily infected with...with *Campylobacter*.

[Sarah Gregory] Your study identified that one particular strain of *C. jejuni* can be resistant to multiple types of antibiotics. Why is this and how did this happen?

[Bruno Lopes] It is basically because of the farming practices that are going on in the country. And it's very important because this is...this is a big problem because we need antibiotics to treat patients and the same antibiotics are being used in the farm environment in order to...in order to provide measures to prevent diseases in poultry. But sometimes the antibiotics are being misused in the sense that even if the poultry is not infected, or a batch is not infected, still the antibiotics are given in order to just improve their health. So, what happens is, because *Campylobacter* is like a normal flora in the poultry, inside the poultry host reservoirs, like chicken or turkey, what will happen is the bacterium will start becoming resistant to these antibiotics because it wants to survive. And with the process of natural evolution it will gain a resistance to various different classes of antibiotics that are being used in the poultry environment. And because...because poultry is like a food source, there is direct link between farm to fork transmission of disease and the humans can get *Campylobacter* if they eat poultry that has been not cooked properly or if they touch a poultry or wash it, for instance.

[Sarah Gregory] Okay, so I think from your study I gathered that a lot of antibiotic resistance is initially caused by a random mutation in the bacteria's DNA. This is quite a scary thing that bacteria can share these mutated genes with one another, spreading antibiotic resistance. Can you kind of explain how this works to us?

[Bruno Lopes] So, mutation is like one...one of the mechanisms by which a bacterium can become resistant. There are also other mechanisms, which is known as plasmid-associated mechanisms, which are basically genes. The first time we'll talk about mutations. So what happens is when, when a bacterium develops a mutation that is beneficial to...to the bacterium, it can resist the antibiotic and it can survive various stresses. And similarly, if the bacterium acquires a gene from outside, from some other bacteria, for instance, this particular gene can even hydrolyze, or it can basically cut down all the antibiotics or degrade antibiotics that are being thrown at it.

And bacteria have also evolved other strategies like efflux pumps, by which they can just pump out all the antibiotic outside the bacterial cell. And...and the more antibiotic you threw at the bacterium, the more resistant it can become. It will evolve mechanisms to become resistant to various classes of antibiotics. And there are other processes, like, for instance, transformation or transduction, in which a bacterium can pass on the parent gene to the...to the progeny. So the genes can be passed on from ancestors to the...to the progeny via vertical transmission, which is basically from the parent to the...to the sibling...to the son or daughter's cells.

[Sarah Gregory] Okay, so your article...I guess this touches on a little bit of what we're already talking about...your article theorizes that this strain of *C. jejuni* evolved in a "stepwise" manner. What does this mean?

[Bruno Lopes] Stepwise manner is basically that there are...there are several steps in which the bacterium has become resistant to antibiotics. And in this particular article, I'm saying that it has both acquired resistance to what is known as aminoglycosides types of antibiotics, then it has got a mutation in one of the genes and it has become resistant, it has developed resistance to...to the fluoroquinolone class of drugs. After that, it has acquired another gene, which is a tetracycline resistance gene and it has become tetracycline-resistant. And later on, it's the same with the beta-

lactamase gene, as well. It might have acquired this gene, and there is a mutation in one of the regions in the...in the beta-lactamase gene, because of which very high levels of beta-lactamase, or the enzyme that's being produced, which can degrade the beta-lactam classes of antibiotics. For example, penicillin is a beta-lactam class of antibiotics.

So...this, this basically shows that there is a stepwise evolution of this particular bacterium and this has occurred because of, for instance, if you look at the veterinary medicine directorate review, you will see that tetracycline and beta-lactams are one of the highly used drugs in the poultry industry, and this is something that has triggered the process of mutations or acquisition of genes because of which resistance has developed in this particular bacterium or strain.

[Sarah Gregory] Your study analyzed samples of *C. jejuni* from poultry and human stool samples in Northeast Scotland. Where did you get these samples, and what were you looking for?

[Bruno Lopes] We got the human stool samples from patients from Aberdeen Royal Infirmary, which is one of the hospitals that is associated with the University of Aberdeen. So the medical or the laboratory staff that are there, they isolated the strain, or they isolated *Campylobacter* from these stool samples and they archived it and gave it to us, which we whole...later on whole-genome sequenced. We also collected samples like poultry, poultry samples or poultry meat samples from various supermarkets, for instance, or the major retailers in the UK, in order to look at *Campylobacter* that is present in the poultry environment. And because ruminants are kind of a secondary source of infection, we also isolated *Campylobacter* from ruminant feces that came from other farms across...across Aberdeenshire. And some wild bird samples, or wild bird feces, were collected by bird ringers from which *Campylobacter* was isolated as well.

[Sarah Gregory] You made a type of family tree for how this strain acquired resistance genes over time. How did you do that?

[Bruno Lopes] I made this tree in a software called BioNumerics and what this software does is basically it will group all the related isolates next to each other based on their genetic sequence. And with this you can understand, or better understand, the relationship between the ancestors, which can be...which can be related to the...to the strain which has evolved, for instance.

[Sarah Gregory] What did you find?

[Bruno Lopes] When, when, when I analyzed around four different groups of major strains that are related to ST5136, which is the strain of this study, I found that most of these groups were kind of developing resistance to various different classes of antibiotics. But one major thing that I observed was that the immediate ancestor of ST5136, which is ST464, which, which I will call as a parent strain of ST5136, this particular strain had acquired resistance to a lot of antibiotics. And I can say that maybe around 50 percent of the population was resistant and 50 percent was not so resistant, but as, as the time went on, this particular ancestral strain of ST5136, which is strain ST464, this had acquired resistance to almost four different classes of antibiotics. And from this particular strain ST5136 has emerged, and it has...it has already got resistances to antibiotics on the chromosomes, so basically it has got stable mechanisms by which it can resist various classes of antibiotics.

[Sarah Gregory] How would you like to see this information used? Can it be helped to prevent or treat sickness?

[Bruno Lopes] This information is very important because this information can inform, for instance, policymakers in order to draw this legislation to make food secure to the...to the general public in order to prevent various diseases that impact public health. Because, although there are being efforts made at reducing the antibiotics that is used in the farm environment, I don't think there are very strict food-related laws, for instance, by which one can...one can say that, that the food one is eating is safe. So this particular information informs the policymakers of the government in order to draft and develop policies which can...which can lead to improvement in public health and will be very important in order to prevent evolution of pathogens, for instance, in...in the...in the food chain.

[Sarah Gregory] What kind of measures would prevent this spreading further?

[Bruno Lopes] For instance, if a...if a retailer, or if a...if an abattoir, or if a company is told to produce *Campylobacter*-free chicken, for instance, then...then the company will have to take measures in order to...in order to do that. And that would involve, like, significant, for instance, biosecurity measures in order to...in order to make the flock *Campylobacter*-free. Obviously there is a cost related to that, but the end result of that is you're making food more secure to the general public, by which you are decreasing the health-associated costs, because currently *Campylobacter* costs the UK economy almost one billion pounds each year.

[Sarah Gregory] Oh my goodness. Okay, you already touched on this a little bit, but what are countries like the UK doing now to prevent the spread of antibiotic-resistant strains of bacteria in poultry or anywhere?

[Bruno Lopes] Yeah. So, alliances like the British Poultry Council and Responsible Use of Medicines in Agriculture, and they are basically looking into it, and they are...they have cut down the antibiotic usage significantly. But I think there is more to do and more needs to be done in order to tackle the problem of resistance. Currently, the progress is very good, excellent, but sometimes we don't understand how bacteria can become quickly resistant to antibiotics, because all antibiotics act in a different way. Sometimes there are those for a bacterium to become resistant to. One antibiotic is very small, very tiny, but in other cases, it can be very large. For instance, a very good example of this is fluoroquinolone resistance. Now, fluoroquinolone is not a drug that is usually used, used in the poultry environment, but it is especially used, or it was used at least until 2016, in day-old chicks, which were given fluoroquinolone. And what we see in this particular story or in this particular article, is that the bacterium has developed resistance to fluoroquinolones, as well, although it has not been used so abundantly, compared to tetracyclines and beta-lactam classes of antibiotics, which are the major drugs. So, we really have to see what kind of drugs we are using and how much of these drugs are we using. So, I think there has to be...there has to be some kind of risk profiling of all the drugs, you know, so that...so that we are not left with a situation where we have got rid of all the drugs and there is nothing that we can use to treat patients. Because these are all very important antibiotics. Actually, fluoroquinolone is one of the critically important antibiotics, which is listed by the WHO. So, to preserve this antibiotic is the challenge of today.

[Sarah Gregory] Fluoroquinolone ...is that Cipro?

[Bruno Lopes] Yes, yeah, that is Ciprofloxacin, yeah.

[Sarah Gregory] Your article mentions “positive antimicrobial usage.” I guess you were sort of just talking about that. What is...what is that?

[Bruno Lopes] So, positive antimicrobial usage is basically when you are using the antibiotic only to treat a particular infection in the farm environment, if that is the case, and not using antibiotics just as you please in order to improve the health of the animals. Because, because by doing that, all you’re doing is you are creating a favorable environment for the bacteria to become resistant to these antibiotic types that you’re constantly throwing at them. And, because these bacteria can end up in the food chain, we will...we will not be having any drugs by which we can treat the patient. So, really we have to observe that we are using the antibiotics very wisely and in an effective way, in order to preserve this antibiotic for the future generation.

[Sarah Gregory] This is a pretty dire scenario. Are you optimistic about the future of these diseases and the meat industry, in general?

[Bruno Lopes] I think, given that, microbial resistance is increasing, I would say that our help is in our hands at the end. And there are...there are certain things that we can’t do anything about it. Like, for instance, we don’t know...we may not know some of the food from where it is stored. But sometimes, the government, for instance, in various countries, is implementing schemes. For example, the “red tractor” scheme, which has been implemented here in the UK, looks at how the food can be made more secure, it can be made more safe, and it can be produced responsibly, with minimum use of antibiotics. So, if these measures are taken into account and if the public or if we as people are aware about the resistances and various pathogens that can infect us, then I think we can decrease the levels of resistances.

But it is becoming increasingly difficult nowadays because bacteria are developing resistances on their chromosomes, and chromosomes being an integral part of the bacterium, you can’t get rid of the resistances as you like, for instance. Plasmid, it was something that was a...outside the chromosome was so...it was not associated with the normal genes that are there on the bacterial chromosome. And a bacterium can lose its plasmid and it can lose its resistance mechanism. But, here, as you observe in this particular story, the bacterium has developed resistances, and all the resistances are on the chromosome. The chromosome provides a nice, stable environment for the resistances or the resistant genes to be there, or the mutations to be there. So, reversing that can be a significantly difficult task.

But, saying that, if we take measures to prevent ourselves from getting the infection in the first instance, then we can prevent the impact of the resistances that can affect the human body through...through this antibiotic resistant bacteria and the human health or the public health can be improved in that way.

[Sarah Gregory] What about eggs? Can eggs...like, the shells of eggs...get this?

[Bruno Lopes] I don’t think the shell of eggs will have *Campylobacter* on it because, once the egg is released from the chicken, the shell of the egg doesn’t provide a suitable environment for this bacterium to be present on it, so that is another thing. Because *Campylobacter* needs a specific environment and, like, moisture is one of the major contributors for the *Campylobacter* to survive. It also requires, like, other gases, like nitrogen and carbon dioxide, and very, very little oxygen, because this bacterium is classed as microaerophilic. So, especially the skin of the chicken...there are loads and loads of *Campylobacter* in the skin of the chicken, because it has

this...it kind of mimics the porous environment, or there are pores present on the skin, you know, so it can thrive very well on that. And it is quite moist, as well.

[Sarah Gregory] A lot of people keep chickens now. Do you keep chickens?

[Bruno Lopes] I don't keep any chickens—I live in the city. But my grandmother used to keep chickens when I was...when I was a kid, you know, which was like maybe 20, 30 years back.

[Sarah Gregory] Ahhh. Okay. Well, tell us about your job and your particular areas of interest.

[Bruno Lopes] So, basically, I am a postdoctoral research fellow, as you said. And I look at lots and lots of genomes of foodborne pathogens, *Campylobacter* being the most important one or the one on which I focus on. And I also like another bacterium called *Acinetobacter baumannii*, which is a hospital-acquired infection bug, which is also a critical priority pathogen, which is listed by the WHO. And I'm looking at finding different mechanisms of resistances and various genes that are associated with specific strains of *Campylobacters* or even *Acinetobacters*, and how they have a role in developing antimicrobial resistance or host-pathogen interaction or even in virulence. And the ultimate goal is to find out, for instance...the data that will be also created with this and hopefully with this we can, we can prevent diseases or inform policymakers and draft new policies, for instance, in...related to *Campylobacter*, for instance.

[Sarah Gregory] Well, hopefully any future studies you do, you'll be submitting to the *EID* journal, huh?

[Bruno Lopes] Yeah, yeah.

[Sarah Gregory] On a completely personal note, Scotland is such a beautiful country for outdoor activities. Do you do any walking or hiking?

[Bruno Lopes] Yeah, I have done a lot of walking and hiking, actually. In fact, I have walked to Arthur's Seat from my home. So, I like to climb all the mountains over here and the various hills. And my PhD was actually in Edinburgh, and I have also climbed some hills over there. And now, in Aberdeen, I go out with friends to explore the various nice places in Scotland.

[Sarah Gregory] I know a lot of people that keep track of what they call "bagging the munros," the hills. Do you do that?

[Bruno Lopes] Yeah, yeah. I have not done a munro walk as such, but have climbed, like, small hills, like Clachnaben or Scolty hill. And even forests, there are a lot of forests over there, so I do quite a lot of forest walks, as well, like Kirkhill Forest is one of the main forests in Aberdeenshire, so that is quite nice.

[Sarah Gregory] Well, you're very lucky to live in such a gorgeous area.

[Bruno Lopes] Yeah.

[Sarah Gregory] Well, thank you so much for taking the time to talk with me today, Dr. Lopes.

[Bruno Lopes] Thank you, Sarah.

[Sarah Gregory] And thank you, listeners, for joining me. You can read the July 2019 article, Nationwide Stepwise Emergence and Evolution of Multidrug-Resistant *Campylobacter jejuni* Sequence Type 5136, United Kingdom, online at [cdc.gov/eid](http://cdc.gov/eid).

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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