

# Populations Dynamic Trends of *E. coli*

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

[Sarah Gregory] Hi, I'm Sarah Gregory, and today we have back with us Dr. Johann Pitout, an EID associate editor and medical microbiologist at the University of Calgary in Canada. We'll be discussing trends of antimicrobial resistance in *E. coli*.

Welcome, Dr. Pitout.

[Johann Pitout] Thank you, Sarah. Thank you for the invitation.

[Sarah Gregory] Your study is about antimicrobial resistance (or AMR) among *E. coli*. Tell us about the importance of global AMR to the public?

[Johann Pitout] So, antimicrobial resistance has always been sort of the...the area where it hadn't really caught the attention of the public. For sure, it hasn't really. However, during the last sort of 5 years it got the attention of politicians, especially the U.S. Senate for example, has put some...some things together to fight antimicrobial resistance. So, today we...we consider antimicrobial resistance as a global health threat, this is...that has been classified by the World Health Organization (WHO) as a global health threat. And probably the best analogy that I can use is that antimicrobial resistance is very much like global warming. It's not particularly fast, a slow-moving process. Not everyone is buying into this antimicrobial resistance as...as a global threat. But it is coming. And if we don't really...if we don't stop the spread of antimicrobial resistance, medical practice as we know it today will change forever. For example, chemotherapy or major surgery will cease to exist due to the risk of antimicrobial resistance to...to patients. Patients would more likely be...if...if it continues to spread as it is now, patients will die due to overwhelming bacterial infections if you...if you use chemotherapy or major surgery on them.

[Sarah Gregory] Well, that is certainly horrifying.

[Johann Pitout] It is. It...it's not covert, Sarah, it's not like covert in your face. It's more like a silent assassin, global warming, in the background. But it's not going away.

[Sarah Gregory] How does AMR spread among bacteria?

[Johann Pitout] So...and I'm going to specifically talk about the genes that are responsible for producing a mechanism bacteria will use to become resistant to antimicrobial agents. So, there's really...although it's a relatively complicated situation, there's really only two ways that antimicrobial resistant genes can move. The first method is where there's another group of genes. These are called mobile genetic elements (or MGEs). They basically capture these antimicrobial resistance genes and then they move them within the bacteria or between bacteria. And the very common one that most people know about are plasmids. This is where plasmids play a big role in moving these genes around bacteria—different bacteria. These bacteria don't even have to be the same type of bacteria. These...these genes move...it's like a highway where bacteria sort of live and breathe and then these genes move between them the whole time.

Now, interestingly enough is these genes (these antimicrobial resistant genes), they can find their way onto certain clones. And this is what we will be talking about a lot today—these clones, certain clones, that seem to...to be a little bit more successful than, say, other clones. And I'll hopefully will be able to explain that as we carry on. They have different names in the literature.

The most common name that I've seen is...these are called high-risk clones, but I think for the sake of this presentation we'll just call them successful clones. And these clones, when the genes reach them, they act as hoarders and spreaders of these antimicrobial genes. So, they hold onto these genes but they also have the ability to spread them to other bacteria. So they play a really big role in...in the spread of antimicrobial resistant genes. So, those are the two mechanisms. First is mobile genetic elements, and then they find their way onto these special or successful clones and then they tend to keep...keep hold of them and then spread them to other bacteria as they...they grow up.

[Sarah Gregory] Ok. So, tell us a little bit more about really what a successful bacteria clone is. What is a clone?

[Johann Pitout] Ok. So, I'll...I'll try and explain this. And to do this, the best way that I know of is to use an analogy of...of motor manufacturing. So, say if you can imagine you have this motor manufacturer. And I just want to put a disclaimer as I'm not a car freak, so it's not really something that I personally...you know, I don't drool over cars a lot. I just use it as it's a very good...it's a very good analogy to...to use. So, and I will use BMW because most people know what a BMW car is, and I also have a BMW so it's easy for me to sort of explain how this all works. If we...if we think that the BMW manufacturing in this analogy, they would represent the *Enterobacteriales* (or the *Enterobacteriaceae* as it used to be known). So, you have different models of BMW, for example the 2, the 3, the 5, 7M series. So these will then represent different species of the *Enterobacteriaceae* in this analogy. Now, I will take the X series, because again I have an...have an X3 BMW, so it's easy for me to relate to that. If we take the X series to represent *E. coli* (*Escherichia coli*), there's X1, there's X2 all the way...I think they're down to X8 nowadays, I'm not quite sure. You can see that they all look similar, but they are not identical. They are a little bit different.

If we now take in...take the X3 series, they are all identical. They, at a certain point of time of course, motor manufacturers do change these models over time. But at a specific time when they produce X3's, they are all identical to each other. That will represent a clone. So, if we can think about an identical *E. coli* on a molecular as well as on the phenotypic scale that is what a clone is. So, when it comes to a successful clone, a good...good way to think of it is that this manufacturing process that normally produces all these different models suddenly starts producing only this one model—the X3. And this represents now the clone that we're going to be talking about as we carry on. And they produce this clone or make a lot of these clones....these different models (this one clone). And it sort of takes over the population after a period of time. It becomes the dominant clone. We will call that a successful clone. And if this clone then has the ability to also be antimicrobial resistant—that we refer to as antimicrobial resistant high-risk or successful clone. And these clones are extremely important—key players in the global emergence of antimicrobial resistance, and now very common among certain bacteria, especially *Staph. aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *E. coli*. We see a lot of these antimicrobial AMR high-risk clones or successful clones among those species. So, there's obviously something that makes them special. We don't quite yet understand why, but they play a very important role and they become the dominant part of a population.

[Sarah Gregory] So, AMR is...is very common then among *E. coli*?

[Johann Pitout] Actually, AMR is not that common among *E. coli*. This is what's so interesting. So, if you look at *E. coli* from the 1980s, the 1990s and the early 2000s, antimicrobial resistance was not really a big issue. I remember that going to all these conferences on antimicrobial resistance, *E. coli* very rarely in those times would actually have a session on...within the antimicrobial resistance field. However, here in the mid to late 2000s (especially since 2010) antimicrobial resistance exploded in *E. coli*. And very interestingly, we saw two groups of antimicrobial agents to which this *E. coli* became specifically resistant to the fluoroquinolones, which ciprofloxacin is probably the most well-known example, and the cephalosporins, which the 3rd generation cephalosporins such as ceftriaxone....this is...this is especially which this...the *E. coli* became resistant to. And the problem was is that these two groups of antibiotics was often used (and still often used) to treat serious infection due to *E. coli*, and it just exploded and today, the WHO has actually added *E. coli* to one of the antimicrobial resistance problem bacteria to which new therapies are urgently required, and especially those that are fluoroquinolone-resistant and cephalosporin-resistant. So, to summarize, not a big issue in...before 2000, and here from about 2010 it became a major problem in *E. coli*.

[Sarah Gregory] So why is this *E. coli* clone, ST131, so important? You say in your article, and I'm quoting, "Global expansion of antimicrobial drug-resistant *E. coli* sequence type 131 is unrivaled among human bacteria." Is this why you did this study?

[Johann Pitout] So, if we go back to this explosion of antimicrobial resistance since 2010, a lot of people did some genomic studies and then what we found out...I'm not the only one, there's lots of other people that also work...found out that this global resistance—this spread of fluoroquinolone resistance and cephalosporin resistance—is mainly due to this one clone (*E. coli* ST131). If we look at the population structure of *E. coli* causing infections, which look at that causing infections outside the gastrointestinal tract, there are certain clones which are very common but they are not antimicrobial-resistant. Then there are other clones that are antimicrobial-resistant but they are not specifically common in this *E. coli* population. And then there's ST131. It is unique in that it is antimicrobial-resistant and it is one of the most common clones among *E. coli*. So, there's something very special about this ST131. And this clone—this is the other thing that is hard to get your head around—it was...it is a global clone. It came in here from about 2008 and it's...it emerged from different regions in the world seemingly at the same time, which is really unusual for these....these clones or these type of high-risk clones to happen. Normally, it is in a certain country and then it will spread from one country to the others through whichever way. But ST131 was different. It emerged seemingly....it emerged across the globe at the same time. So, this makes it unrivaled among any other antimicrobial-resistant clone that we know about.

So, I can summarize this Sarah, is I'm pretty sure that when *E. coli* children talk to their parents they probably tell them, "I want to be like ST131 when I grow up."

[Sarah Gregory] Ok, oh dear. Tell us a little bit more about this...the emergence of this AMR clone.

[Johann Pitout] Ok, so to understand this we need to go back to our BMW analogy of clones and car manufacturing, and in that analogy, we...we used the X3 to represent ST131. Now, if you go back...you know, the X3 are all identical. However, within them the manufacturer will put different colors—they will have, say, a blue model and they will have a yellow one and a green

model. And this is what happens with ST131. So, among ST131 they are different colors. For example, we have—and these are called clades within the name—so, ST131 are not all identical. Although they seem to be identical, if you look a little bit further you'll find out that they actually have different colors. So, you have different clades. So the clade A, for example, will be the blue color. This is the older and ancestral form of ST131 emerged around about the mid to late 1800s a long time ago. Then we have another clade, ST131 B (clade B), which we will have a yellow color for...for the example from forward on. This basically split from the A clade (the blue clade) here in the early 1900s. And then the...the multidrug-resistant clade (which is the C clade) which will be the green color for our example, this split from clade B in the 1980s to 1990s. And very interestingly, this then became the most dominant clade among ST131 globally. So for this expansion of ST131 from being nowhere really in the 1950s and 1960s to become a very dominant clone within *E. coli*, this happened due to one clade and this happened probably in the early 1980s to 1990s.

So, the other thing to remember about the C clade...unfortunately they're not all the same green color, so they have different shades of green. For example, there's the C1 clade, this will be a lighter green (if I can put it that way) and then you have the C2 clade which is then the darker green. So, even within clades we have different subclades and they are different colors, shades of the same color.

[Sarah Gregory] What geographic area does your study cover and why there?

[Johann Pitout] So, we...we performed our study in Calgary, which for those of you that don't know, Calgary is in Alberta which is just above Montana. I think that will put the U.S....the U.S. population or the U.S. listeners will understand, it's just north of...of Montana, close to British Columbia which is on our west side—this is for the Canadians, but they will know...Canadian listeners will know where Alberta is. This is the oil place, by the way. This is where all the...all the drama is at the moment about pipelines and so on. We have this issue in Alberta, and there's one pipeline going south to the U.S. as well, which will probably a hot topic in your next election. But I'm not going to talk about pipelines today.

What makes Calgary interesting or unique is that we have a centralized laboratory system. What that means is we...we have one laboratory system that performs all the microbiology within the Calgary region. And this is a population of just about 1.6 or 1.8 million people, and that such a system makes it an excellent model for performing population-based studies. And why it is so...so important is that within such a well-defined human community, the overall selection bias is minimized. So, we will include all patients, not only those from the hospital or only those from the community. We will include everybody. And the risk factors for pathogen acquisition in such a region is reasonably consistent over time. So that makes it really...makes it a real-world model of what is going on with an infection or with anything else, not necessarily just infection. If you look at cancers or something like that, that would be the same thing—you have a real-world model.

Now, we've done previously studies in Calgary looking at ST131 from basically in a time before...before it was actually known as ST131. So, we've been interested in...in tracking this clone for a long, long, long time. And then, we found from an earlier study from 2016 that ST131 in Calgary is our most common and our most antimicrobial-resistant clone among *E. coli* that cause bloodstream infections. So, we know that...that this is a very important pathogen

within our region. That's why we decided to see what happens to this clone over a period of time. Does it change or not? What characteristics are associated within such a well-defined human population? So, that's why we decided to do this study in Calgary.

[Sarah Gregory] And what period of time did you cover and why did you choose this timeframe?

[Johann Pitout] So, we decided to go back as far as 2006 and then we included 2012 and 2016. And the reason why...and we would have liked to have gone back to...to the early 2000s, but in our...remember I mentioned it's a centralized laboratory, so as part of our quality assurance we freeze all our isolates from blood cultures, so those that cause bloodstream infections, for a period of 10 years. When we woke up to this type of study, unfortunately the isolates from 2005 and earlier had already been discarded. So, the earliest isolate that we could find was from 2006. We would have liked to have done from 2006, 2007, 2008, and so on and so on and so on, up to 2016. However, there's a cost...there's a cost problem here. If you do every *E. coli* from blood in Calgary for every year, it will cost a fortune to do whole-genome sequencing on them. That's a...it's a relatively expensive thing. So, we choose then 2006, 2012 because we know that we...from our previous studies we...we knew that this is where *E. coli* or ST131 was at its peak, and we wanted to see what happens then in 2016. So that's why we chose those time periods.

[Sarah Gregory] And what population did you investigate? Adults? Or teenagers and adults? Or everyone?

[Johann Pitout] We included everyone. That's the beauty of a population-based surveillance system where you have a well-defined population. We included everybody and we included people with a bloodstream infection due to *E. coli*. That was your inclusion criteria, and you had to be a Calgary resident. If you come from another region, for example, and you were on holiday here and you're unlucky enough to get an *E. coli* infection or bloodstream infection during your holiday, you would be excluded. So, it was specifically Calgary, bloodstream infection, everyone that's a Calgary resident. So, Sarah, I just want to make sure that people understand this includes everyone—those from the community, those from hospitals, those that attend clinics...every person in this region of 1.6 million people with a bloodstream infection due to *E. coli* was included in the study.

[Sarah Gregory] Ok, got it, alright. So, what were you looking for?

[Johann Pitout] So, we had some...some questions that we asked ourselves before we started with this...with this study. The first thing, due to the fact that we could do population-based studies, we could then determine the incidence rate per 100,000, which is a really good indicator of disease or infection. So, we wanted to see were there an increase of ST131 from 2006 to 2016 (the incidence rate). The second thing is, as I mentioned to you when I was explaining about the different X3 models with different colors and different shades of colors, we also wanted to look within this centralized or this well-defined population what happens to the...the different clades of ST131 over time. Are they all the same? Are they just the proportion of clades changed over time? And then the third thing we wanted to look at is we wanted to characterize these clades, combine the susceptibility data we have with the genomic data and with clinical data that we have, and we wanted to see if there's anything specific for the different clades. Are they all the same or are they different? So, those are the three things we were looking for.

[Sarah Gregory] And you talked about whole-genome sequencing, and so what kind of data did you use?

[Johann Pitout] So, I'll explain the study...a quick overview on the study. So, we took all the *E. coli* from blood, 2006, 12, 16. First thing we did is we took about, I would say, an average of just about 5–700 isolates a year. So, we first took them and then we screened them with a PCR, which is a...just an amplification test which is specific for ST131. So, we knew that among those isolates, so many of them are ST131. And it turned out to be about 20...so, 20% of these *E. coli* turned out to be ST131. Then we took that...those ones that were PCR-positive and we sent them in for whole-genome sequencing. What we did here is we used short-read sequencing, specifically Illumina was the one that we used here because it's really the most cost-effective one, and we sequenced the whole genome of these ST131. Basically, you get everything that you can...you can go and sequence, and then afterwards you need to find somebody to help you to what you were looking for. You can find out resistance factors, you can look at virulence factors...there's so many things that you get, but it's basically the whole genome that we sequenced. And then we combined the clinical data. We...we went to different databases in Calgary which we have here because it's a centralized region, we could then at the time of when the patient presented with infection, we could look at their different clinical...clinical presentations, we could look at either hospital or community infections, and we could look at, you know, the age groups and everything. So, we combined all of this. We had susceptibility data that we...that we do in Calgary to provide physicians with information about treatment, and we had the genomic data and we combined it all in one file and then we...we analyzed that. And that was really what the study was all about.

[Sarah Gregory] Ok. So after all of that, what did you find?

[Johann Pitout] So, the first thing is, as I mentioned, we wanted to look at the incidence rate increase over time. So, it increased from 4.91 per 100,000 people (that was in 2006) up to 10.212 in 2016. That is a significant increase of ST131 over time. We found that the ST131 belonged to those three different clades. We had clade A (which is the blue clade) was about 10% of the ST131 with blue, about 9% of ST131 with the B clade (which was the yellow one), and then the remainder one—the 81%—this was the C clade, which is the green clade.

We then looked at different clinical susceptibility and genomic characteristics, and we saw that each of these clades were associated with...with certain clinical and also genomic characteristics. And for those people that are interested in, can go and look at the paper. I'm not going to mention as there's so much data that we created with this whole-genome...genome sequencing, just wanted to mention that the clades A and clades B (this is now the blue and the yellow ones), they were the most antimicrobial-susceptible of these clades and they would tend to be more in the community. They are associated with community (strictly community) infection in younger patients. The C clade (which is the green one), this is the most common clade as I mentioned but it's also the most antimicrobial-resistant clade, and this tends to be more infections in older people, people that have been in contact with the healthcare system some or another time in the past 6 months. We saw that quite a bit with the C clade.

Then, the next thing we found is that...very interestingly is that the prevalence of the clades changed over time. For example, we had the...the C clade...specifically the C1 clade (which was the light green clade), this was common in 2006. However, by 2016 the C2 clade (which is the

darker green one), that became the most common clade. So, these clades...the proportions of them do change over time. And we also saw, for example, the...the blue and the yellow clade also changed over time. So, it seems like in a well-defined population as Calgary, these proportions of clades do not...do not remain the same. So, I think that, Sarah, was probably the most important result that we found in the study.

[Sarah Gregory] Do we know what has caused this increase in the microbial resistance? And also, why the clades change?

[Johann Pitout] Sarah, so it turned out to be that the C2 clade (which is the darker green one)...this is the one that increased over time but it tends also to be the most antimicrobial resistant subclade among ST131. So, it wasn't only increasing over time, it is the most resistant one to antibiotics. And that's pretty worrying. And we don't really know why that happened. We don't understand why this dark green clade...why the C2 clade, why it increased over time. But we need to obviously find out why that is happening, but we don't understand. It seems to be a community clone. It's not really associated with long-term care centers like some of...some of the ST131 publications from other parts of the world, which show that this...this clone is very prevalent in long-term care centers. However, we find in Calgary that this C2 (the dark green one) is not a long-term care center one. It seems to be in the community. We don't really know why. We probably believe that it is...it is in the region of Calgary where there's a lot of ex-pats, people from the Indian subcontinent (which is India), and it's possible that they travel and pick up this clade while they are traveling and then bringing it back. However, we don't have good information about this and we were planning a study that will look at their risk factors of this...of this C2, the dark green clade

[Sarah Gregory] So, without actually knowing what's causing the increases, is there a way to stop this?

[Johann Pitout] At this moment in time, we...we cannot really stop the spread of this clade if we don't understand what exactly is the risk factor. So, as soon as we do our next study, we will hopefully be able to find out what...what is...what is the main factors that's driving this clade within Calgary, and then we can start looking at how to stop it from increasing over time.

[Sarah Gregory] Were there any challenges or limitations to this study?

[Johann Pitout] This is a...the challenge that we find (or the limitation if I can put it this way) is with all of these type of studies, when you look at blood culture or serious infections due to *E. coli*, you only really include patients that actually went to the laboratory and had a serious enough infection to have a blood culture taken. So, this really excludes those patients that are younger and feel that they don't really need to go to the hospital or to a doctor's office to get tested for. So, we don't really know what happens with milder *E. coli* infections. So, we only have data on those very serious infections. So, it's most likely that the incidence rate of our study is conservative and it's probably higher for ST131 than...than what we reported. So that's probably the biggest limitation of this type of study.

[Sarah Gregory] What are the next steps or future studies that you would like to see? I think you already mentioned a couple, right?

[Johann Pitout] So as I mentioned, yeah, we will do the specific risk factors associated with the darker green (the C2) clade. I think that's a study that we need to do, and we are planning to do

one. The other thing that we are also planning to do is...I don't think I stressed this enough in my introduction, but this clone (this ST131) is really a model for other special or high-risk clones in other bacteria. It is the most common one and it's the most important one. And by figuring out what makes ST131 so unique, so special. And how it evolved over time from blue to the green clades, we can use that information to predict how other super clones emerge in other species, and maybe we can then find out how to prevent these clones from emerging. So, we really do need to look at what makes this *E. coli* clone so special. And it's probably due to the fact that when ST131 becomes...it evolves from one clade to a more multidrug-resistant clade, it maintains somehow its fitness. And that I think is the secret here. We need to figure out what did this clade do to maintain its fitness as it becomes antimicrobial-resistant. Because normally when bacteria become resistant to antibiotics this is associated with a huge fitness cost, and it seems to us that ST131 has the ability to become resistant but it doesn't have the fitness cost that's associated with that. And I think finding that out would be very, very important.

And then the last thing we do need is we also need some rapid diagnostic tests for ST131, especially in the community. We need to be able to have a test that we can go and find these people that are infected or colonized with ST131 in the community so that we can figure out how does this clone spread within the community setting. Because in the community, you don't have the traditional hospital risk factors associated with spread of antimicrobial resistance. Here the antimicrobial usage is much lower than you would find in a hospital setting. So, there's obviously something that this clone does in the community, and we need to figure out how it gets around. Otherwise, we will never be able to control the spread of this clone. So, those are the three things that I think we need to do.

[Sarah Gregory] And what's the most important public health message, do you think, in your study?

[Johann Pitout] So, we've shown that...that within ST131 there are certain clades that are antimicrobial-resistant and that are emerging over time significantly. If we...if we remove this clade from the population of *E. coli* in causing bloodstream infections, this will cause...this will cause a substantial decrease in the overall incidence rate as well as the antimicrobial burden among *E. coli* causing bloodstream infections in Calgary. So, removing this clone, finding something that we can maybe treat or give a patient, and eliminate ST131 will have a huge public health removal of a burden. That will be a huge...huge overall benefit to...to public health in the Calgary region. And—this is the other thing Sarah, I need to mention—this is not only a Calgary problem. This is a global problem. We are just doing the study, but ST131 is doing this likely everywhere where you find *E. coli* causing bloodstream infections. So, eradicating ST131, either maybe getting a vaccine because it does have a certain envelope that is specific to this clone. Or there's now lately there's a lot of talk about using bacterial phages to decolonize people. So, if you can find a bacterial phage that is specific for ST131 and you can give it for people to swallow and you eradicate ST131, it would lead to considerable public health benefits for Calgarians and probably the world as well.

[Sarah Gregory] So, right now with this rampant AMR clade, is there...if a person gets *E. coli* ST131, what happens to them? Is there any kind of treatment available?

[Johann Pitout] So, luckily we still have a very big group of antibiotics called the carbapenems, which has still has very good activity against ST131. And this is now used to treat ST131 in



serious infections, for sure. However, the clock is ticking. There's no doubt about that. ST131 is slowly but luckily not that quickly, but it is becoming resistant to the carbapenems. So...so although we have a very good group of antibiotics that's still active, we need to be very careful because it's on its way. And then as I said for the future, we really do need a vaccine for ST131 like we have for certain *Streptococcus pneumoniae*, for example, serotypes. We need the same thing for ST131. Or we need...somebody needs to look at bacteriophages as well as a possible treatment.

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

[Johann Pitout] Carbapenems is imipenem and meropenem. Those are the two big ones. Cipro is a fluoroquinolone.

[Sarah Gregory] Ok. What are the best ways that people can just protect themselves from getting *E. coli*?

[Johann Pitout] So, I'm not going to talk about *E. coli* as...as a whole because that's a huge...that's a lecture on itself. However, as far as ST131 goes, how do you protect yourself against this? And I think that's a...that's a very difficult question to answer at this moment in time. Until we figure out how it moves and what is the risk factors (travel, long-term care centers, that type of thing), we don't...I cannot really give you good advice on how to prevent or how to protect yourself from ST131. But I can promise you that what we're doing for COVID at the moment is probably going to decrease also ST131 (handwashing and that sort of a thing).

[Sarah Gregory] And back to your very dire comment at the beginning about antimicrobial resistance taking hold and then making it impossible for people to get cancer treatments, or at least chemotherapy and such. What does that mean? What's going to happen then?

[Johann Pitout] Sarah, all I can tell you is the clock is ticking and we really need to find ways to stop antimicrobial resistance from spreading among bacteria. You know, we're lucky enough at this moment in time they are slowly coming, new antibiotics are coming onto the market, and we are a little bit still ahead of the curve, but we are starting to slowly lose the battle because the number of new antibiotics (especially for gram-negative such as *E. coli*) are becoming less and less and less. So, we really do need good funding like we are having at the moment for COVID. But we also need this for antimicrobial resistance. We need people to look at ways to limit the spread. I don't think it will ever stop the spread of antimicrobial resistance, because this is part of normal evolution. But we really need studies to show how can we stop this or limit the spread of antimicrobial resistance. Otherwise, as you say, this is a dire, dire thing if you cannot have surgery anymore (or major surgery anymore) because of the...of the fear for antimicrobial resistance.

[Sarah Gregory] Well, on that note, tell us about your work and what you enjoy about it.

[Johann Pitout] As you mentioned, I'm a medical microbiologist. So, I do...I do half of my time...I do clinical microbiology where I am (diagnostics and in that area). I'm mostly proficient in susceptibility testing and also testing for antimicrobial resistance. That is my real job, if I can put it that way. Then I have also a university appointment. You mentioned I'm from the University of Calgary, I have a research appointment there. And in my research, I think the best way to describe me is that I'm a...I'm a tracker of antimicrobial resistance determinants and also, specifically, clones. I love to track them and see what happens to them over time. Where do they

go? What do they do? Do they change over time? That...that for me is a big, big thrill to look at that. And hey, they really keep me very busy because it's not only *E. coli* that's...that's got these clones, as I mentioned before. I also love to look at *Klebsiella* clones. They are another big favorite of mine, chasing after clones. So, the big thing I think we need is, we need easy and cheap diagnostics to track these clones. Because, you know, we can track a clone in a...in a first-world country as much as we want, but we need for people in lower and middle-income countries to also be able to track these clones. Otherwise, they are just coming over to us the whole time. So, I...my big passion is to...to develop cheap and easy-to-do diagnostics to track these clones. And that's really what keeps me...keeps me busy in the research side.

[Sarah Gregory] On top of that, you're also an associate editor for the EID journal. Would you tell us what that involves?

[Johann Pitout] So yes, I am the gram-negative associate editor for *Emerging Infectious Diseases*. So, I look after most of the antimicrobial-resistant papers for gram-negative that come in...that are submitted to *Emerging Infectious Diseases*. These...these submissions are then forwarded to me on a daily basis, and what I do then first up is I...I have a look at the quality of the study, see if it's relevant to *Emerging Infectious Diseases*. And we are pretty...relatively strict, because it...it's a very high-impact journal. So, I look for something that's very novel, and then something that's emerging because it's called *Emerging Infectious Diseases*. That's what I'm really interested in for the journal. And...and then I decide if it's worthy to send out for reviews. If not, then we will let the authors know that this...this manuscript is probably not relevant for this journal and you can maybe try a more specialized journal. Otherwise, I will find reviewers and I use a lot of different reviewers from all over the world, and then they review these manuscripts for me. And I also sometimes review it myself if I can't find people, and then we make a decision if this...if this manuscript is worthy for *Emerging Infectious Diseases*. And I try...I think the one thing that I've really tried to do since I've joined as an associate editor is to turn...to get the turnaround time quicker for *Emerging Infectious Diseases*. I think it's fair only to authors to get the response back as soon as possible. So, that's basically what I do at *Emerging Infectious Diseases*.

[Sarah Gregory] And it doesn't seem like you could possibly actually have any free time, but if you do and when you do, what do you enjoy doing?

[Johann Pitout] Now Sarah, I must say that free time is pretty limited. However, I try and...and have a...have a very active lifestyle. Coming originally from South Africa where an active lifestyle is sort of part of...part of our growing up, I try and do as much activity as I possibly can—weather permitting, of course, being in Calgary. Just to tell you, I'm looking out of the window and there's snow everywhere. So, it's hard to have a very active lifestyle here if you're not into the winter sports. So, I try...I do a lot of cross-country running. I do mountain biking as well (I do trails, mostly). To stay flexible, I do yoga on a weekly...not daily, but yoga every now and then. If the weather goes bad, I go out to do my workouts in a local gym. However, I must say now with COVID, the local gyms are out so I haven't been back there for a while. And then, as far as nonactive things, I do collect red wines from Bordeaux...especially from, you know, Bordeaux in France. I also like the Brunellos from Tuscany and Riojas from Spain. However, I am finding that it's hard with these wines...it's hard to actually...if you collect them for such a long period of time, it's hard to actually open the bottle at the end of the day and then drink it.

So, I find you get so attached to these things that I'm not sure if it's actually worth my while to collect them and at the end of the day actually drink them. So, I...I am thinking of maybe not collecting them so much anymore because it's no use if they become like children. So, that's really what I try and do outside my...my professional life.

[Sarah Gregory] Yeah, the collecting of wines. It's something I used to do, but I...I just basically don't even drink anymore. So, like I have all of these bottles of wine and I'm like, now what? Right?

[Johann Pitout] Yeah, I agree.

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

[Johann Pitout] It's a pleasure, Sarah.

[Sarah Gregory] And thanks for joining me out there. You can read the December 2020 article, Trends in Population Dynamics of *Escherichia coli* Sequence Type 131, 2006–2016, online at [cdc.gov/eid](http://cdc.gov/eid).

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

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