

00:00:05:08 - 00:00:37:20

Clare

Hello and welcome. I'm Clare and you're listening to Microbe Talk, the podcast by the Microbiology Society. This month, I'll be taking a deep dive into the methods of wastewater monitoring. After reading an article in Microbial Genomics about how wastewater monitoring was integral to mapping and understanding COVID, I was interested to find out more. So I spoke to Professor Steve Patterson about how he and his team turned genetic information in our sewers into data that was integral to understanding the spread and evolution of COVID in the UK.

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Anne Leonard

So my name's Steve Patterson, I'm professor of genetics at the University of Liverpool and director of the Natural Environment Research Council Environment Omics Facility.

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Clare

Awesome, awesome. And so you obviously have got very involved in the sort of wastewater monitoring, specifically in COVID. How did you get into that? How did that happen?

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Steve Patterson

Way back in March 2020, like a lot of us, COVID suddenly hit us, threw their lives up in the air and with colleagues here- So we run a genomics facility. There were some samples that came in from a pilot study to take wastewater samples and look for coronavirus within that. I was asked, would I be able to generate sequence data from that?

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Steve Patterson

So that started off as quite a large program. And so I mean that kind of wastewater based epidemiology. If you not come across it before, some of the kind of advantages of that of that are - well the way that I put it - so is that not everyone takes a test. You know, those swabs that you're sticking up, your nose it's all the time and everyone hated.

00:01:50:09 - 00:02:08:07

Steve Patterson

Not everyone takes a test, but everyone has to take a poo. All of that goes down into the sewer system. And it's a way of possibly sampling a population. And it's particularly good if you've got asymptomatic individuals. So, you know, the shedding, but they might be going to work, etc., because they don't know that they've that they are infected.

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Steve Patterson

And there's also some communities that were hesitant about going for testing. You know, if you're in 0 hours contracts, getting a test at the time that was positive meant that you couldn't work, that you couldn't, you know, pay the rent and so on. So there were large, you know, sort of communities there that the testing program wasn't reaching but could be reached using the wastewater based epidemiology.

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Clare

Yeah. Yeah, definitely. Was this the sort of monitoring wastewater? Was that something that was brand new to COVID or had you done it previously?

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Steve Patterson

So my Lab works a lot with environmental samples, applying genomics to that. And so one of the things that you do, for example, is you go and sample pond water. Look at the biodiversity of organic bacteria that are in that as it's basically the same kind of methods for that. But just applied to pathogens and... I mean, wastewater, based epidemiology

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Steve Patterson

So people have used that, for example, for polio for quite a while.

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Clare

Yes, I'd read that report. Yeah. I suppose the first question would be how do you find that there's COVID present?

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Steve Patterson

So the process that we - so the samples taken, actually those were usually done in something... So it was taking samples every hour over a 24 hour period and keeping them cool those would go to the lab down in Exeter and nucleic acid would be extracted from that. And then the, the kind of detection bits would be done by quantitative PCR.

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Steve Patterson

It's a very sensitive method to detect the pathogen there, based on amplifying up a small region of its genome. Then detecting that we would also get that nucleic acid up to our lab. And then similarly use a PCR based method to generate little segments of the of the virus genome, then put those through sequencing machines and then then the analysis of of that to see what variants of what mixture of variants are there within that data.

00:04:17:01 - 00:04:27:18

Clare

Okay. So it's not necessarily specifically sensitive to COVID. You could monitor it kind of generally and see any pathogen present in wastewater, is that correct?

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Steve Patterson

Yeah. I mean, if you got the assays, you can do potentially most, most pathogens. So for example, we've been trying to sort of create a kind of a legacy of this, what comes after COVID, you know, so looking at designing assays for things like measles, for influenza, RSV and so on, and I was I was actually in Kenya a few weeks ago on sort of there within a LMIC then I see it's perhaps got an attractive way to detect what kind of pathogens are out there.

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Steve Patterson

So, you know, you can imagine that being applied to, you know, things like polio or to other things like that.

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Clare

Yeah. Yeah. And I suppose in my research, one of the big great things about wastewater monitoring is it's the breadth. You can sample lots of people and treat them as a smaller of population, basically, and monitor through those populations. And do you find that that's potentially a limitation as well? The fact that it's so kind of broad?

00:05:32:18 - 00:05:52:18

Steve Patterson

Yes. I mean, so you can have some of the sort of criticisms are that, you know, you don't get down to, you know, individual level. I mean, some of the some of what we were trying to do within cities to, you know, lift the manhole covers and sort of trying to get it down to particular areas was trying to get it within a sort of a general community.

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Steve Patterson

But, you know, there are limitations, for example, in terms of, you know, you know, to put it crudely, do you have a poo at home or do you have a poo at work? You know, all of those kinds of considerations. There's been been some interest, for example, in applying wastewater to borders to check the the the wastewater that comes off airplanes or from airports to see whether we can detect pathogens as they're coming into the country.

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Steve Patterson

Again, you know, with the sort of caveats about, you know, being able to sort of sample individuals from that.

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Clare

Yeah. Yeah. It's interesting. So I spoke to actually was excited. I was excited about having a chat with you and speaking to my friends about it. And their first kind of response was just from like, from like a surveillance perspective. They were perhaps, maybe this is information that's being gathered about me that I don't know, that's being gathered.

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Clare

Was that kind of their initial worry, which I was quite surprised at? And kind of what is your sort of thoughts on that? What would you say to that kind of feeling?

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Steve Patterson

You know, there's no there's no individual information associated with it. You know, we're not able to get, you know, an individual pathogen status for an individual, you know, And we're not we're not able to we're not even trying to sort of sequence any of the human DNA within the wastewater, not that there really is much there at the end of it.

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Steve Patterson

I mean, it's just I mean, during the COVID pandemic, all of a sudden mobile phone data was being used. I mean, it was not at an individual level, but looking at sort of in a sort of general sort of movement between cities and, you know, what times people were active and and things like that. So, I mean, I think you know, I think if you're on the Internet at all, you've got, you know, more of the information is being passed that way than it's ever been in your poo

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Steve Patterson

to be honest with you.

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Clare

Yeah. So I had another question. So tracking back to the specific methods, your shedding the virus through your poo, through wastewater, does the virus degrade a lot? Is there a point where there's no return? You can't sort of sequence it anymore? How does that work?

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Steve Patterson

No, I mean, that's a really good point. I mean, it is it's one of the sort of real challenges of working, particularly with an RNA virus, is much less stable than DNA. So the RNA does degrade. We were getting wastewater that was sort of chilled as soon as it was collected. And then everything had to be sort of passed in a cold chain.

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Steve Patterson

We certainly noticed that the kind of methods worked in clinical samples. We had to adapt those because the RNA was getting more degraded. You know, we were using shorter little fragments that we were amplifying from the genome in order to counter that. And some of the other challenges as well are that, you know, as opposed to clinical data where it's a single genome that you're sequencing, this is kind of a soup of different people's contribution to that sample.

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Steve Patterson

And so, you know, some of the some of the work in that microbial genomics paper was about separating hundreds of those different contributions and trying to, you know, sort of do that bioinformatics pieces accurately as we can.

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Clare

Yeah, amazing. Okay, so COVID, it's still happening. I think this is still relevant to carry on with this wastewater monitoring to monitor it within the population. Where do you potentially see wastewater monitoring fitting in in the future? I suppose beyond COVID, if we ever get we have to get beyond that.

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Steve Patterson

So I mean, certainly COVID is going to be with us for a while. But, you know, the the big thing, obviously, is that vaccination and to some extent people's previous exposure means that that's much more controlled in hospital admissions are much less. It's still going to be with us and people are still going to get sick from it.

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Steve Patterson

And unfortunately, some people will die from it, as they do with flu and with other pathogens. You know, the continued threats from things like polio as well, I don't think actually be able to come up with a coordinated network and actually be able to use the one sample that's able to test for multiple pathogens and seeing how we can use that in a kind of UK wide basis.

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Steve Patterson

I mean, the government are going to they've got a biosecurity strategy and wastewater epidemiology may well form part of that over the next few years and there is some work being done to see what the potential of it is to to protect against various pathogens that that might be out there and provide that kind of public health information.

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Clare

I can really see this coming into its own when it comes to reduction in vaccinations and then monitoring the population for the rise again of those types of pathogens. Is that right? Would that work?

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Steve Patterson

You can always see how stretched the NHS is and if they're able to get information ahead of time as to when they're likely to see an influx of patients into the units or into the geriatric units with a with a pathogen, then that's that's got to be able to help them.

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Clare

Mm. Okay. And this is very much here to stay. Wastewater monitoring would be kind of a central part of public health reporting in the UK. Do you think for the foreseeable future?

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Steve Patterson

I hope so. I think the challenge that people themselves need to do is to kind of show the value of it, to show, you know, it's not enough just to be able to take the samples, generate the data. There has to be decisions that can be made as a result of that data. And I think to give the kind of confidence to the public health officials, it's about sort of validating that.

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Steve Patterson

It's about showing the value of that for them and that maybe the last bit of the journey that we need to do, we're getting there but we would still need to join the dots.

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Clare

So yeah, definitely, yeah, data is very valuable. It's about what you do with it that makes a difference. What kind of things would they be able to do? I'd appreciate this might be outside of your specialty.

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Steve Patterson

One of the is probably about modeling the pressures on the NHS. One of it might be about detecting local outbreaks of a particular pathogen and then deciding what kind of response that is to make. Is the pathogens spreading elsewhere, or is that kind of give information on whether there's a particular community that's being susceptible to a pathogen? So you talked about vaccine hesitancy there, kind of help identify particular communities where vaccine uptake is low.

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Steve Patterson

And I think it's always going to be in conjunction with other information on the ground that that's going there and part of a kind of coordinated suite of data.



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Clare

Yeah, Amazing. Oh, okay. I've got is there anything else you wanted to add or get across at all?

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Steve Patterson

No, I think that's fine. Yes. Yes. I think it's been yeah, quite fun.

00:13:00:20 - 00:13:25:18

Clare

That's been yeah, it's been really great. Thank you so much for your time. I really appreciate it. So wastewater monitoring was fundamental to understanding more about COVID as it gave scientists population level information on the viruses infecting our bodies. COVID may no longer be considered an emergent threat, but the benefits of monitoring wastewater are still being explored in other avenues.

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Clare

This method could prove useful to scientists who want to understand more about antimicrobial resistance. Antimicrobial resistance or AMR, is global health risk and is often referred to as the silent pandemic. Microbes are becoming increasingly resistant to antimicrobial drugs that were previously effective against them, making it more and more difficult to treat infections. Understanding the spread of AMR is fundamental to scientists being able to tackle it.

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Clare

I spoke to Dr. Anne Leonard to find out more about this and her work on monitoring the spread of AMR in our natural environments. Just a quick note to the listener, we recorded this podcast over Zoom Call, so apologies for any deviations in the quality of the audio.

00:14:10:11 - 00:14:20:22

Anne Leonard

My name is Dr. Anne Leonard and I'm an environmental microbiologist, environmental epidemiologist at the University of Exeter, and I work on antimicrobial resistance in the environment.

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Clare

So I think we'll start with talking about sort of AMR monitoring AMR in wastewater. And then I'd really be interested in going into your research specifically about antimicrobial resistance in waterways, which sounds quite scary. So we'll start with the AMR monitoring. So I think you mentioned that you'd recently done a review of this, this kind of monitoring and research.

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Clare

Yeah, I mean, like how does it work, I suppose is the first question!

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Anne Leonard

Well, when you say wastewater monitoring... We in this country collect our sewage, then we treat it, then we discharge it. Say wastewater may also affect the treated effluent that wastewater treatment plants discharge to the environment. Treatment of sewage doesn't produce a sterile effluent. It contains large numbers of microorganisms, including antibiotic resistant bacteria. But once sewage goes through that wastewater treatment process, the resistome, or the collection of resistance genes and mobile genetic elements changes.

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Anne Leonard

And it probably doesn't tell you after treatment what it did tell you before treatment, about the human population, but it may indicate the types of resistance genes that might be introduced to the environment that receive this effluent from human sources. And this effluent is discharged to surface waters so into streams, Rivers the see antimicrobial resistance released to the environment doesn't necessarily die off completely or delete to negligible levels.

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Anne Leonard

There's potentially important but underappreciated route by which antimicrobial resistance and sewage and wastewater is transmitted back to humans. If, for example, people come into contact with antimicrobial resistance in the environment.

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Clare

Wow. Okay. So it's like a two-fold problem, isn't it? Is that there's not it's not just antimicrobial resistance genes in bacteria in the wastewater, and then our beaches and seas and stuff. It's also that the antibiotics themselves can then perpetuate that. So it could potentially grow.?

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Anne Leonard

When you take a dose of antibiotic, some of it is absorbed, some of that kind of undergoes chemical modification in the body and becomes inactive. But some of those residues remain active and they're able to exert a selective pressure on bacteria in the gut or or in the environment that the increase in the relative proportion of antibiotic resistant bacteria.

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Clare

Gosh, yeah. I mean, I think about like tackling antimicrobial resistance. I think about things like; not giving antibiotics to people who've got viruses; not overprescribing. But then in my head I'm like, well, of course people need antibiotics when they're really sick. So if those, you know, antimicrobials make their way into the water systems from a hospital, for example, whereas I'm sure loads is getting discharged, I suppose it yeah, massively exacerbates the problem.

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Anne Leonard

Absolutely, antibiotic resistance, antimicrobial resistance is it's presents a unique challenge in that it can proliferate in the environment outside of humans like bacteria are ancient and have evolved mechanisms of surviving in complex microbial communities, which doesn't involve surviving in the presence of compounds that other microorganisms produced. to outcompete other organisms for resources.

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Clare

Mmm. So you mentioned a little bit that just to go back a little bit, this idea of using methods with samples of wastewater to look into what genes are present in sort of microbial populations from samples of wastewater, etc., but kind of I suppose in a broad sense, how do those methods work?

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Anne Leonard

So when we're thinking about antimicrobial resistance, we're not just interested in species that make humans sick. Because bacteria can spread their genes horizontally we might want to take a broader perspective on antimicrobial resistance in complex microbial communities, and we can use methods such as metagenomic sequencing, which takes all the DNA from a microbial community and then analyse that DNA identity of different antibiotic resistance genes based on the sequence of nucleotides.

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Anne Leonard

in those are extracted DNA molecules. The mechanisms for resistance are encoded genetically. So bacteria that are.. this is why antibiotic bacteria undergo a selective pressure to be resistant because it confers an evolutionary advantage to resist the action of antimicrobials, antibiotics, that they can then pass on to their offspring.

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Clare

Okay. Yeah. Yeah. So you're aware of the kind of patterns of genes present in these species and you're able to kind of look for those within a microbial community?

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Anne Leonard

Yeah. With antibiotic resistance, we're talking about thousands of different antibiotic resistant genes. If you just take a sample of sewage and plate out onto agar perhaps as little as 1% of all microorganisms can be grown agar on a in a lab. So you've really taken a very, very narrow perspective on the very large problem that is antibiotic resistance. And if you take a an approach such as Metagenomic sequencing, which aims to capture information about all the different resistance genes and the complex microbial community, out of that culture instead, that can tell you a great deal more about the resistance genes harbored by that community of microorganisms.

00:20:09:16 - 00:20:32:14

Clare

Yeah. Yeah. Makes sense. Makes sense. Okay, so we got this really complex method of how we're monitoring antimicrobial resistance and how we can do it on this sort of large, larger scale, basically through wastewater, because it's this amalgamation of lots of people in lots of areas and this kind of stuff. What, what can we do? Like what can scientists do with it?

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Clare

What does that information mean?

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Anne Leonard

Well, there's some evidence emerging that data about antimicrobial resistance in wastewater correlates with data on local, regional clinical infections. But wastewater monitoring for antimicrobial resistance is still quite a new field. And there's a lot we don't know about how the resistome changes between fecal elimination and the point of sampling wastewater from wastewater monitoring so sewer systems and sewage itself.

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Anne Leonard

These are really complex matrices. You know, the presence of some substances in sewage and chemicals that can inhibit some of the assays we use to detect antimicrobial resistance. But others, like I talked about antibiotic residues they might promote and increase antibiotic resistance in the sewer system itself. And then on top of that, things like blockages, spills, biofilms very flow through the system, that it is a complex system to try and navigate and try and interpret the outputs of antimicrobial resistance analysis.

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Anne Leonard

It's potentially an incredibly promising tool and exciting area of research.

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Clare

Yeah, yeah, definitely. Who'd had thought that working with sewage and wastewater would be so interesting? So the the role that wastewater plays in proliferation of antimicrobial resistance. So there's antimicrobial resistant microbes in the wastewater that is being treated, but these kind of genes, these traits still survive and then they're pumped into the sea where we are then bathing surfing, doing all of our fun activities when the weather's a bit nicer.

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Clare

How dangerous is that to people?

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Anne Leonard

It's really important question to ask. The natural surface waters are reservoirs of diverse antibiotic resistant bacteria they receive, like you just said, wastewater effluent from wastewater treatment plants as well as untreated sewage spills, which contribute additional antibiotic resistant bacteria along with those antibiotic residues that I was talking about. and they are often environments that people like you rightly pointed out, enjoy recreational activities that bring people in to direct contact with waterborne antimicrobial resistance.

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Anne Leonard

And through my research, we've we've demonstrated the presence of sewage associated antimicrobial resistance in coastal bathing waters. And in addition, an association between human recreational exposure to bathing waters and fecal colonization by these bacteria. In that study, for example, we we recruited surfers who we know swallow a lot of seawater when they go surfing in coastal bathing waters.

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Anne Leonard

And we asked them to send us a fecal swab, which collected a small amount of their gut microbiome, their fecal microbiome, which we then tested for the presence of these same antimicrobial bacteria and we compared them to the swaps sent to us by people who don't go in the water. And we found that

surfers were about three times as likely to have to treat important antibiotic resistant bacteria in the fecal microbiome compared to people who don't go in the water.

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Anne Leonard

So what does that actually mean for human health in the spread of antimicrobial resistance? Like colonization is an initial step in the pathway between exposure and infection and people who are colonized by antibiotic resistant bacteria could go on to develop infections that fail to respond to antibiotic treatment. If, for example, the resistance genes and the colonizing bacteria, the kind of invading bacteria transfer to a transient pathogen in the gut environment, or onto the resident microbiome. Or potentially the gut bacteria infect other sites of the body, for example, the gut microbiome is a source of infection for bloodstream and urinary tract infections.

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Anne Leonard

Another outcome is that these colonized individuals actually lose that colonization status over time. There's no continued selection pressure for bacteria to maintain that resistance, they might end up losing it. I suppose. Another consequence of gut colonization by antimicrobial resistance is, is the potential spread to other people, either through direct contact or via the environment. And, and these transmission pathways, dynamics, risks and consequences are quite poorly characterized, particularly for environmental antimicrobial resistance transmission.

00:25:14:16 - 00:25:24:06

Clare

We Yeah, yeah, definitely. That makes sense. Is there kind of so unseen is that it's so unseen and you know like...

00:25:24:09 - 00:25:24:13

Anne Leonard

The silent pandemic.

00:25:24:24 - 00:25:45:23

Clare

Yeah yeah. And I think a lot of people, definitely myself, think about anti-microbial resistance and you think about things like MRSA, where like, you know, for a fact that they're in hospital and they're really sick because of an antimicrobial resistant bacteria. So that's quite like worrying as well that this could all be affecting people without us even really knowing about it.

00:25:45:23 - 00:25:57:21

Clare

If there's these kind of anti-microbial resistant sort of qualities in a gut microbiome, how might that affect long term health of the public who use those bathing waters?

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Anne Leonard

In terms of long term health? We're not really we're not really sure. Eventually, someone who is vulnerable to infection comes into contact or is becomes colonized and becomes ill, with one of these resistant bacteria. And and they go into hospital and it's very difficult. They may need to use some of our last resort antibiotics which we're running out of in terms of a development pipeline, longer hospital stays, more invasive treatments and yeah it's a recognized problem

00:26:39:18 - 00:27:03:24

Clare

Yeah yeah, I that's that's why, again, we're focusing on it. It's just one of these things that I suppose in the wake of COVID... I suppose with COVID, you knew what it – well towards the end - you knew what it was. You kind of could map the spread. And with this antimicrobial resistance it's everywhere and most likely getting worse as we go, which is quite scary.

00:27:03:24 - 00:27:43:16

Anne Leonard

Yeah, I think that is I mean, there are obviously some similarities with COVID in that we think our current understanding is that COVID, sorry SARS-COV-2, originated in a zoonotic or an animal reservoir, and then kind of species hopped into humans and likewise with antimicrobial resistance genes. We we know there are specific examples of clinically important antibiotic resistant strains emerging on in animal reservoirs and in the environment that have mobilized into it or being transferred into human pathogens and then spread amongst humans.



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Anne Leonard

But with SARS-CoV-2, we were really only looking at one viral pathogen that was predominantly spread human to human. Antimicrobial resistance presents that much greater a challenge because it spreads from between humans, animals, the environment. We're talking about thousands of genes and millions of microorganisms.

00:28:09:02 - 00:28:30:02

Clare

Yeah gosh, It's not just spreading on the lateral plane, it's also kind of like 3D. Well, gosh, yeah, I'm, I suppose just my last question, so I want to make sure I get across. Relating back to your study and you mentioned it very briefly. Do you know much about how these sort of serious sewage leaks affects the like the data?

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Clare

The problem is it's something that we is it just another thing that we have to worry about, about these sewage leaks?

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Anne Leonard

I think it makes sense that the the leaking of untreated sewage into the environment would contribute to the problem of antimicrobial resistance in the environment. Untreated human sewage can enter the environment, through sewage missed connections especially - and and as well when there's very heavy rainfall we have in this country what's called combined sewer overflows, which means that the wastewater from your toilets gets combined with wastewater, stormwater.

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Anne Leonard

when it rains, they will go into the same pipes. So when it rains heavily, the volume of that stormwater plus wastewater can exceed the capacity of the systems, and there's an emergency spill to the environment, which prevents it from that untreated sewage coming back up into the streets, in people's homes, which would itself present rather large public health risk.

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Anne Leonard

And and so yeah, we do we do get spills. I think there was an article published in The Guardian today that said raw sewage spilled into English rivers 825 times per day last year. And although we don't know the volumes of sewage being spilled, it's his frequency of spills that is concerning in terms of what it could mean for the development and spread of environmental antimicrobial resistance and the health of people who come into contact with these environments.

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Clare

Yeah, I mean, it's mind boggling, but I suppose it's amazing that there is research happening like yours at the moment which is able to get as much information as possible. And you know, information is power and the fact that we have this kind of underlying backbone of information means that we're best positioned to be able to tackle AMR in the future.

00:30:29:16 - 00:30:41:13

Clare

Thank you very much for your time. Thank you for listening to Microbe talk. If you like this episode, please leave a comment wherever you are listening.