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Clare Baker

Hello and welcome. I'm Claire and you're listening to Microbe talk, the podcast by the Microbiology Society. For this edition of the podcast, I'm delighted to be joined by Dr Tim Inglis from the University of Western Australia. Tim is editor in chief at the Society's Journal of Medical Microbiology, where he published his latest article, 'A Systematic Approach to Microbial Forensics'.

00:00:30:02 - 00:00:35:15

Clare Baker

Fantastic. Well, thank you very much for joining me on podcast. I'm very excited to speak to you too.

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Dr Tim Inglis

My pleasure.

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Clare Baker

Really. And my first question is always to be able to introduce yourself.

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Dr Tim Inglis

Yeah, well, I've I wear several hats, obviously, from the Microbe Biology Society point of view. I'm the editor in chief of the Journal of Medical Microbiology, which is a big responsibility, but a great position to be in. I'm a medical microbiologist based in Western Australia, and I do quite a bit of public health microbiology as part of my overall brief as a clinical academic.

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Dr Tim Inglis

I'm also with the University of Western Australia and I've got an interest in translational research with a particular focus on antimicrobial resistance, sepsis and emerging infectious diseases.

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Clare Baker

Amazing, amazing. And so we're here today to talk about your your paper. I mentioned to you before the call, I came across it and immediately went, oh, microbial forensic. That sounds really interesting. And what is my review of forensics? I said, Is this a good place to start?

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Dr Tim Inglis

Well, if you take a look at the words superficially, it sounds quite obvious. It started with microbiology. Yeah. And we get the fact that it's got to do with forensic stuff. And most people think they know what forensics is because they watch TV shows.

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Clare Baker

Yeah.

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Dr Tim Inglis

But the reality is that these days, a lot of forensic work done in laboratories is very procedural. It's highly repetitive, and it's an application of science to methods to the needs of legal processes. So maybe the easiest way to think of forensic microbiology is what the microbiology laboratory does to support legal processes, to provide evidence, to support an investigation, and that may be used for or against a particular process in the law courts.

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Dr Tim Inglis

Now, you notice that I'm talking about forensic microbiology, but it's not the same as microbial forensics. Yes. And let me just unpack that a little bit. Microbial forensics is is subtly different. It's a branch of forensic microbiology that deals with bioterrorism, the alleged use of bioweapons. So it's very much more at that higher level of government and government agencies.

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Dr Tim Inglis

So involve in probably national or international crime and possibly even offensive activity by states or non-state actors that have a very big agenda. So it's big picture stuff.

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Clare Baker

Yeah, Interesting. Interesting. And I hadn't quite made that adjustment before, but I suppose having spoken to you and also read the paper, it makes perfect sense because it's such a completely different methodologies mentioned. And would you be able to give us a bit more kind of background as to how those methodologies differ between microbial forensics and forensic microbiology?

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Dr Tim Inglis

I think the first thing to say is this Obviously there's quite a bit of an overlap because there will be a lot of processes that are common to the application of forensic science, to processes, to investigations that require a microbiologist to be involved. So if you're looking, for instance, at a case of assault or a case of that might be a capital crime like murder, there is a possibility that micro-organisms are a part of the evidence, the technical evidence presented in that to support an allegation that somebody is the culprit for that particular crime, because the organisms that were present and found at the scene of the crime have a match, for instance, as a

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Dr Tim Inglis

result of genotyping with organisms that have been obtained from the specimen that the alleged perpetrator may have provided during the investigation, or it may be something that links a series of events together. The key thing to understand in all of this is it is the application of the science of microbiology to an investigative process. And in my limited experience of forensic microbiology, gee, it would largely be a small part of the overall body of evidence presented to put together a prosecution.

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Dr Tim Inglis

So realizing that forensic investigation is only a part of that normally police investigation into a particular crime, which will involve interviews, will involve other forms of evidence. There may be signals, evidence, telephone transcripts, voice recordings that have been picked up off the Internet, a variety of other things. So microbiology is rarely a major part of forensic investigation, at least in my experience.

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Dr Tim Inglis

Now, microbial forensics is obviously a different matter entirely, because in this bigger picture stuff, whether it's something like bioterrorism or alleged use of biological weapons by somebody working on a national or international scale, then those things are major crimes. Absolutely. And the micro organism is right at the center of the process.

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Clare Baker

Yeah.

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Dr Tim Inglis

So the microbiology becomes crucial, but it's important we don't get too ahead of ourselves in this because as with all microbial forensics and wider forensic investigation, there are multiple forms of evidence that can be used to put a case together. So you've got you've got the human evidence, which would be the results of interviews, possibly by a national police force or by some sort of intelligence agent.

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Dr Tim Inglis

So there may be signals tracking, there may be various other aspects of technical evidence provided and in the case of microbial forensics, some of that evidence may be environmental data like wind direction and wind speed. If we're talking about something that has been distributed by an aerial route. And a good example of that would be the bird loss incident where anthrax spores were probably disseminated as a result of an accident at a factory.

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Dr Tim Inglis

And eventually it came to light that the the victims of that accidental dissemination were all within a plausible airborne plume of anthrax spores. So you see how you can use different pieces of information to put together a narrative. And that narrative obviously an extent possible.

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Clare Baker

Yeah.

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Dr Tim Inglis

But the tricky bit is how do you get to the point where you have got proof? Because there is a big difference between considering something as a plausible possibility.

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Clare Baker

Yes.

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Dr Tim Inglis

And establishing something as a matter of certainty. And the distance between those two points, those different levels of assurance that a particular series of events has happened, the way we think it happened is really right at the heart of microbial forensics supporting that investigate into a bioterrorism or bio weapon incident in a way that understands the strong connection between the biology and its consequences is really interesting.

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Clare Baker

Really interesting. And I imagine it's quite difficult to get microbiologists and scientists to approach a certainty and to give a level of certainty in what they're doing, because that's the essence of science, is it is not knowing so much and it's quiet.

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Dr Tim Inglis

Definitely. We like head job and as members of my team know that one of our mantras is that everything in the natural sciences is provisional and subject to modification in the light of further evidence. Whereas a court of law doesn't like uncertainty. Now, I guess we're not talking about engineering tolerances here. We're talking about logical processes which have multiple levels of complexity, which is what makes this a particularly big challenge for those who get involved in it.

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Dr Tim Inglis

And that's why working with a variety of people in various different organizations and gaining insights from people who've got different skill sets that fit into supporting these sorts of investigations, it's become increasingly clear that whilst will never reach 100% certainty in any

of these investigations, we can at least put together a pretty compelling narrative if we recognize that there are different contributors to the story.

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Clare Baker

Yes.

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Dr Tim Inglis

Each of which need to be listened to and understand how their pieces of the jigsaw puzzle fit together, which is why we've got a picture, a schematic diagram in the paper on the microbial forensic process. You only see this. It's very easy to. Yes, it even has color in it.

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Clare Baker

Yes.

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Dr Tim Inglis

And this emphasizes the fact that there are four main domains of scientific activity, if you will. Those four domains, the ones I'm most familiar with, are the clinical microbiology and the public health microbiology and the clinical microbiology of the disease syndromes and about what the clinical laboratory does to identify the the etiology, the cause, the microbial agent responsible for disease.

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Dr Tim Inglis

What is a process is that is sometimes very complicated but well-worn parts for those who work in clinical laboratories, including veterinary, clinical. Now, the public health component is perhaps a little bit more subtle because that's about case clusters. It's about population, and it's also about populations of microbes. And importantly, it includes not only descriptive epidemiology, but techniques that were well familiar with in microbiological sciences, molecular epidemiology, and the environmental microbiology that sometimes goes behind that.

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Dr Tim Inglis

Again, not suggesting that animal health is a key part of all of this, because many of the recognized bioweapon agents may also cause animal disease. Therefore, from a human point of view, yes, but the other parts of this process are ones that are a little bit more recherché because they are not used in day to day clinical practice by clinical microbiologists.

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Dr Tim Inglis

They're probably not the sort of things that public health officials give much thought to, but the mechanisms of microbial disease, that mechanistic approach where you really drill down into the relationship between different skills of biological organization, whether it's genes, transcription to proteins, cell biology, maybe tissue or organ system function. But the connection between all of these and things like processes, responsible for transmission and exposure in the case of alleged bioweapon use, delivery mechanisms and the use of an enhanced accelerators and adjuvants.

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Dr Tim Inglis

And then finally, there's what we all want to get towards what ever we think about the right or the wrongs of exposure and use of these agents. We all like to think about countermeasures. What are we going to do about it? Addressing the so what question do we only have barrier controls? Can we decontaminate environmental surfaces? What anti-microbial do we need to use?

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Dr Tim Inglis

Are there any vaccines? Now that is a process. And I think one of the important things that we've learned over recent years, particularly following the the white powder incidents in the wake of 911.

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Clare Baker

Yes.

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Dr Tim Inglis

Is that this is not something that you package as a single. We tick off all the boxes, we complete this process and hey presto, we've got an answer. It's actually and deliberately displayed here in the figure as a wheel and it rotates. It's an iterative process. So you go around once and you pick up some clues and you begin to understand that if you're a clinical microbiology, you need to talk to people in animal health and you need to talk to people who are really good at microbial genomes.

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Dr Tim Inglis

And then you come back around and then you go back again because what you're looking for is those specific features that differentiate the event that you're investigating from what would be normal for that microbial toxin. So all the different things in the clinical presentation or the laboratory features of the organism are the differences in the way that cases and case clusters have occurred.

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Dr Tim Inglis

The epidemic curve might be different. The fact that there may have been no animal cases before human cases is something that's so analysis, which would be all all of those sorts of things that set alarm bells ringing because what you're doing is you're developing testing and then refining a working hypothesis. So again, gets back to your earlier point and a very important point about science being conditional and provisional and a process that lacks that 100% certainty that the locals are looking for before they can do prosecution.

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Dr Tim Inglis

So a key touchpoint in microbial forensics is it is not principally about apportioning blame that is down to law enforcement agencies and other official organizations that have responsibility for these things, because that requires those interviews. It requires the the technical and the signals evidence that will support a case. This is more about understanding the microbial processes in a way that makes sense to biomedical scientists who are used to working through a series of tests and processes that are familiar to most of us to establish the connection between a microbe and a disease.

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Clare Baker

Yeah, I suppose the more you have, the more information you have from as broad is an area as possible, the more you have in your arsenal to be able to approach like what you said. A the you



mentioned like a plausible story, a nice thought process. Yeah. Well, you had the more evidence you have, the closer you can get to it.

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Dr Tim Inglis

But that's exactly right. And as you go through that process, you realize increasingly what is missing from the narrative that is developing. So if we recognize the importance of taking an iterative and a collaborative approach to this, the more you listen to those colleagues that bring other skillsets to the table, the more you recognize that there is a big difference between the standards of evidence that are going to be compelling in a court of law and the standards of evidence that might be necessary to initiate treatment in a patient with an individual incident instance of that particular disease.

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Dr Tim Inglis

And in legal terms, they talk about the difference between sufficient and necessary evidence. We may have sufficient evidence that a particular microbe has been responsible for the case. Cluster of disease X in a particular population, but we may not have the necessary evidence to establish responsibility or what's referred to as agency for an organization or an individual. So this is not primarily about criminal blame, it's about etiological attribution.

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Clare Baker

Interest. Stay interesting. Yeah. This type of paper in Journal of Medical Microbiology is not something I've come across before. It's quite a different type of paper. And so I was actually interested to maybe take a little bit of a left hand and ask you what sort of inspired you to write this paper? What kind of led you to it?

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Dr Tim Inglis

Well, we've been working within this space and I individually have been working on it for the last 20 years as a public health microbiologist with biosecurity responsibilities and biosecurity, for the most part, is about dealing with the worst bioterrorism, all which is Mother Nature. And so I had a longstanding involvement and interest in emerging infectious diseases in working at how to cope with the latest and greatest threat.

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Dr Tim Inglis

And at the rate that we burn through new organisms at the moment, there's plenty to keep me from getting bored. So that's been very interesting. But obviously in 2001 we had problems concerning anthrax that went round the world and I got heavily involved in dealing with the white powder incidents in Western Australia at the time in my capacity as public health microbiology.

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Clare Baker

Sorry to interrupt. Would you be able to explain what ISIS incidents are? Yeah. And just as.

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Dr Tim Inglis

What was happening at that time was we got a lot of people doing copycat stuff, putting white powder into envelopes and mailing them to people that they didn't like. Mm. And as time went by, they got more and more sophisticated in these hoax activities and it absorbed a huge amount of time for public health microbiologists in most of the developed world.

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Dr Tim Inglis

Now, only a fraction of those white powder incidents involve any bacillus anthracis spores and obviously the majority of those in the US. So we didn't get to deal with any live anthrax here in Western Australia. I'm very happy to report we spent a lot of time going through that. Yeah, Do we do we deal with this envelope containing a white powder as if it's a real and credible threat?

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Dr Tim Inglis

Or do we just incinerate it and move on to the next task? And that exercise is a lot of people well be on public health and public microbiology services in 2001 so that that was a bit of a trigger to get involved in these sorts of things and have to be able to cope with them as time went on.

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Dr Tim Inglis

But those sorts of skills are now part of standard operating procedures for clinical and public health laboratories all around the world. And fortunately, we've got to the point where relationships with different first responder agencies are now so good that only a tiny trickle of

specimens come through because importantly, in many jurisdictions, even putting together a credible hoax that claims to be anthrax is itself a crime with some pretty hefty penalties in some jurisdictions.

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Dr Tim Inglis

So it's kind of warm people off. That is good investigation. We can usually track down who's been responsible and then they've they've got a case that they they have to answer to with evidence to support a potential prosecution. So this is a good example of forensic microbiology. It's not necessarily bioterrorism. It's certainly not alleged bioweapon use, but it is something that messes with people and causes a huge amount of inconvenience.

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Dr Tim Inglis

So, yeah, that that got me interested in this field. And since then, many of the skills that we developed then were applied to non bioterrorism, non bioweapon applications. But, you know, I'd just like to point out the other angle on this is I've spent quite a lot of time doing tropical microbiology because in Australia we've got a tropical north and we've got some interesting diseases there, including a disease called melioidosis, which I've done quite a bit of work on over the years because we have had the occasional small cluster.

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Dr Tim Inglis

We've spent time using our skills to investigate and that might not be a something of particular consequence outside of Australia if this is a problem here. But it is an organism on the on the bioweapons list. So there is the theoretical possibility that people might is the cause of this infection as a bioweapon if, if they were really clever and worked out how they could do that.

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Dr Tim Inglis

Personal opinion is essentially a pretty poor bioweapon. But that's another issue.

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Clare Baker

Amazing. Okay, I suppose you kind of slowly approached it and then Andrew yourself back. You talk about covered in your paper and I suppose how much do you think the investigations

around COVID has positively or negatively impacted the way in which microbiologists can carry out these types of investigations?

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Dr Tim Inglis

Sure. The the process that I developed for microbial forensic investigations and she goes back to as early as 2007, a paper that I published in JAMA Microbe that put together a kind of a hypothetical approach to establishing causality. And that has been used since then for a variety of emerging infectious disease applications. So it was perfectly natural that I should apply that as I did and published in JAMA on it at the beginning of the COVID pandemic.

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Dr Tim Inglis

It was an obvious next step when we got to the point that things were easing off and people were starting to ask questions, really searching questions about its origins that I should review using the method that that we've published previously in General Micro to assess the credibility of the deliberate release hypothesis. And that's exactly what I've done here, really to illustrate how this approach can be applied.

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Dr Tim Inglis

So it's not so much a matter of that. This is or this isn't a deliberate release. This is an illustration of how you put these four different major categories into action and what conclusion you reach. Now, it doesn't reach a different conclusion from what the major investigations that have been launched so far have arrived at, which is, as we all well know, inconclusive.

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Dr Tim Inglis

What it does usefully do is illustrate the point that if you take a systematic, multidisciplinary approach to your microbial forensic investigation, you can come up with a series of competing and mutually exclusive hypotheses for origin and causality. And importantly, the process will highlight the unanswered questions and some of those unanswered questions are in the text of the papers.

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Dr Tim Inglis

People can see there are some things we'll probably never get an answer to, but these are unanswered questions that you need answers to. If you're going to establish a credible case for a deliberate release.

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Clare Baker

Interesting. And kind of on that point as well, have there been methodologies developed whilst investigating cases that have positively impacted microbial forensics? Have there been developments in the way that we look at COVID leaned on microbial forensics at all?

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Dr Tim Inglis

I'm not aware of the details because I don't claim to have any any international connections that can tell me about the the secret stuff that goes on behind the scenes, because clearly it became a very political hot potato as and I think we're all aware, but I think we all saw even during the early days of the pandemic, the the insights that were getting very quickly by use of of genomic technology.

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Dr Tim Inglis

So the gene sequencing that was put into action very, very early on for tracking the development evolution of the viral genome as it moved from wave to way since understanding causality down at a granular RNA sequence level was I mean, it was fascinating to see it happen in real time, but it was it was also brutal because we were the victims of the consequences.

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Dr Tim Inglis

And the the thing that's a little bit more subtle that the the genomic experts do do a lot of bioinformatics have been have not put much emphasis on is what was done in the field of data science because the machine learning the modeling that was done to understand infection dynamics has provided vast additional insights that give us a lot of confidence in seeing the flows and the movements and the development of some clusters and secondary outbreaks and those sorts of things.

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Dr Tim Inglis

So if you extrapolate back, this swings the balance very much in favor of an accident is released. But again, it's sufficient, but it's not necessary evidence if you're looking for agency doesn't address that question.

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Clare Baker

This has been fabulous. I'm realizing that we are closely reading to that. Well, we've run over time, too, but thank you so much. Yeah. Thank you so much for your time today. This has been fascinating. So I'll put the link of the paper in the description. I think everyone should read it. Do you have Twitter or website or anything you want people to follow?

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Dr Tim Inglis

Yes, there is. We've obviously got the university website. There are a variety of other places that we can put things up, but particularly at the university and the things we will do. A bit of promotion are on this list.

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Clare Baker

Thank you so much.

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Dr Tim Inglis

Great, Excellent. Well, thanks for that.

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Clare Baker

Thanks again to Tim for joining me in such a fascinating examination of microbial forensics. If you'd like to read Tim's article in the *Journal of Medical Microbiology*, you can find the link in the description. If you liked this episode, please leave a like or a follow wherever you're listening.