

# The Invisible Second Threat to Cancer Patients – Drug-Resistant Infections

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## SUMMARY KEYWORDS

Cancer patients, drug-resistant infections, antimicrobial resistance, chemotherapy, radiation therapy, infection control.

## SPEAKERS

Maggie Fox, Yehoda Martei, Speaker 2

**Maggie Fox** 00:00

Hello and welcome to One World, One Health, where we chat with people working to solve the biggest problems facing our world. I am Maggie Fox. This podcast is brought to you by the One Health Trust with bite-sized insights into ways to help address challenges, such as infectious diseases, climate change, and pollution. We take a One Health approach that recognizes that we are all in this together, and everything on this planet — the animals, plants, people, and the climate and environment — are all linked.

Cancer is a scary diagnosis, even though many cancers are now much easier to treat and cure, people still dread getting the diagnosis, and the treatment can be complex. And cancer often isn't even what kills a patient. The second leading killer of cancer patients is, in fact, an infection. More and more often, those infections are caused by drug-resistant organisms, which is known as antimicrobial resistance (AMR).

Although we know it happens more frequently, not many people are tracking just how often it does occur. One of those people is Dr. Yehoda Martei, an assistant professor of medicine at the hospital of the University of Pennsylvania. She and colleagues set out to see just how commonly these drug-resistant superbugs were affecting cancer patients compared to other people getting treated as outpatients.

They found that drug-resistant infections were three times more common in cancer patients than in other people getting outpatient treatment in the U.S.; for inpatients, people being treated in the hospital, it's about twice as often. We're chatting with Dr. Martei in this episode to talk about the problem, how it arises, and what can be done about it.

Yehoda, thanks so much for joining us.

**Yehoda Martei** 01:52

Thank you very much.

**Maggie Fox** 01:55

Why are cancer patients at such a higher risk of infection in general?

**Yehoda Martei** 02:01

So, there are multiple reasons why cancer patients are more prone to infections, some of them are related to the cancer itself, and some are related to the treatment that we give for the cancer to cure it or to manage it.

So, when we think about cancers that affect the body's immune function — to be able to produce immune cells to fight off infection. Diseases such as leukemia and lymphoma, which we call hematologic malignancies, impair the body's ability to do this. So, it makes cancer patients with these tumors more prone to infections. Additionally, therapies that we give to treat cancer can damage the bone marrow. Typically, we think about chemotherapy or radiation therapy, and these can damage the bone marrow, which makes specific cells that help fight bacterial infections. So, something that we call neutrophils can be very low in patients who are receiving chemotherapy, and when these are low, it also impairs the ability to be able to fight infection.

Another reason might be because cancer patients just undergo a lot of procedures, and so whether it's surgery, insertion of intravenous lines or urinary catheters, all of these, the introduction of foreign bodies impairs the body's ability to have a physical barrier against infection. Other side effects can also damage the gut lining and cause cancer patients to have a higher risk of having translocation of germs that can cause infection.

**Maggie Fox** 03:28

And then why would they have a higher risk of drug-resistant infection in particular?

**Yehoda Martei** 03:35

So, I think that the mere fact that cancer patients have a higher risk of infection in general, They do receive a lot of antibiotics, either for preventing infections or for treating infections, and the more antibiotics you get exposed to, and the longer duration of antibiotics that you have, there's higher the risk of developing infections.

There's also the fact that cancer patients tend to have more contact with the healthcare system, and so they end up having more frequent appointments in the outpatient setting, as well as admissions, either for treatment of their cancer or inpatient admissions for complications of their cancer. So, they do receive antibiotics during this period, which can then predispose them to having resistant organisms during subsequent admissions or subsequent contact with the healthcare system.

**Maggie Fox** 04:24

That's something we need to talk about, because, unfortunately, hospitals are supposed to be clean places. They've also become places where you can acquire these drug-resistant organisms. It's a place where they live and grow.

**Yehoda Martei** 04:35

Yeah, I think it's sort of a double-edged sword in that people who are sick get admitted to the hospital, and so I think resistance organisms are acquired.

So, one of the things that our data showed is that even though historically, we think about hospital systems as being at a higher risk for acquisition of drug-resistant organisms, data and The Lancet Oncology show that patients in the outpatient setting, so patients who are just attending the clinic or being treated in the outpatient setting also have an increased risk of being exposed to resistant organisms.

So, I think as much as hospitals play a role in this, I think there's also just the broad recognition that AMR is becoming more prevalent even in the community and outpatient setting.

**Maggie Fox** 05:22

Now you've done a lot of your work in the U.S. Do you have any idea about what's going on in the rest of the world?

**Yehoda Martei** 05:30

I do! So, part of my work that is not AMR-related is actually looking at cancer outcomes in low-resource settings, and I do a lot of my work in Sub-Saharan Africa. Currently work in Botswana, which is in southern Africa. So, even though this work is based in the U.S., I think what we can infer based on just the prevalence of AMR in low-resource settings is that it's likely to be much worse in lower-resource settings.

So, I do see patients in Botswana, for instance, where patients are not only diagnosed with cancer, but also have a high risk or a high prevalence of human immunodeficiency virus (HIV). When patients present with infections, the type of infections that they can acquire is a combination of risk factors related to their cancer immunosuppression, but then they're also their HIV immunosuppression.

So, I think it's a bit more complicated to treat cancer patients in low-resource settings. I think based on multiple factors like poor infection control, so sanitation, access to clean water, and also lack of vaccination, poor access to diagnostics and antimicrobial medicines. I think we are likely to see more higher risk of AMR in cancer patients compared to a data and if you thinking broadly about what this data means in terms of extrapolating to low resource settings, I think it's most likely that resistance is much worse than we reported in our data, in the U.S.

**Maggie Fox 06:57**

So, you're not just a numbers person; you are also directly treating patients. So, cancer is really hard to fight all on its own, without adding this extra burden for patients and the care team. Tell us what this means. What have you seen?

**Yehoda Martei 07:15**

I do think it's really challenging to treat cancer patients with infection, and I think it's challenging for the care team, as well as for the patients and their families. So, in terms of our ability to deliver high-quality care, having an infection disrupts care significantly. So, a patient who is infected has to have adequate infection control before you can administer chemotherapy, because you can make them significantly worse by administering therapy while they still have an infection. So, we've definitely had cases here in the U.S. and also in Botswana that illustrate this.

I think maybe the differences are really in the care team and availability of specialists to guide their treatment. But patients who have multiple infections with resistant organisms have a higher risk of being admitted to the intensive care unit. They end up having a prolonged stay, and in most cases, you hold your cancer therapies, and it's distressing for families, you know, because cancer is a big diagnosis, and you're ready to get treated and "fight this," and then you end up encountering an infection, and it seems like the team isn't doing anything for your cancer, but what infection does is really sort of pull the brakes on how well you can administer cancer treatment, and so it causes several delays and treatment. In a few cases, it can be fatal, especially in low-resource settings, where access to antibiotics in some cases might not even be guaranteed.

**Maggie Fox 08:40**

I mean, it's obviously fatal. It's the second leading cause of death for cancer patients, so it's got to be the worst somebody could be cured of their cancer, but the darn infection comes in and kills them.

**Yehoda Martei 08:53**

Absolutely! I think that is one of the reasons why I think there needs to be a wider recognition of the global health crisis within the oncology community. I think we've been very siloed in medicine and thinking about subspecialty focus, and so AMR sort of falls within the realm of infectious disease doctors.

I think, given the fact that our patients are at risk for AMR, for fatal complications from this, and the fact that a lot of the therapies that we give are predicated on having adequate infection control, this should be sort of a policy education issue that's highly prioritized within the oncology community, and I don't think there's a lack of recognition of AMR. We send cultures all the time. Do we know what this data looks like on an individual patient's level? I think there's just a lack of global acknowledgement that there is a crisis that significantly impacts our population, and we should really be involved in how we come up with solutions to address this.

**Maggie Fox** 09:55

Now, some of the newer cancer treatments — the way they're described to the public is that they rev up the immune system to fight cancer. Is this the sort of thing that could help cancer patients fight off infections as well?

**Yehoda Martei** 10:11

That's a bit of a complicated question. It's a logical progression of thought, but it's complicated in that although the immune system is "revved up," I think it's logical to think that some infections might have better control because of a more heightened immune system, but increasingly, even patients who get immunotherapy get it in combination with other immunosuppressive regimens. So, you'd still get immunotherapy, but at some point, during your treatment course, you might receive just standard chemotherapy or radiation therapy, so I think there are still combinations of treatment that predispose you to infection risk.

**Maggie Fox** 10:47

Well, it's kind of tailored to cancer, right? You're training the immune cells to recognize cancer, not to recognize an infection, right?

**Yehoda Martei** 10:54

Exactly. So, it's modulated in that it's trained specifically to detect or rev up the immune system towards cancer. You know, sometimes when you rev up the immune system, you also cause the immune system to attack the patient's organs, or there's a side effect of the therapy. So, patients might develop inflammation of the liver or gut or lung toxicity that might then require steroids to suppress the immune system, which increases the risk. It's just a lot more complicated, but a good thought in terms of revving up the immune system. I think that there are opportunities for research into thinking about how the immune system itself can help fight infections specifically. But cancer immunotherapy might not be sort of a natural remedy for AMR.

**Maggie Fox** 11:40

You know that very few people have done the kind of surveillance that you're doing. Why not?

**Yehoda Martei** 11:46

So, I have asked myself that as well! I'm an oncologist, and so I don't think about AMR surveillance as my primary research focus. I think what's unique about the study was the partnership that came together, and then also access to this database that has samples from cancer patients and non-cancer patients from multiple institutions around the U.S. I think that was one of the huge trends of this study.

I do believe that there are smaller studies out there that are institution-based. So, a lot of institutions, or almost all institutions, have electronic medical record systems, and so this data has been fed into systems all the time.

So, I think on a hospital-based level, this data can be generated. This analysis should be frequently generated to assess regional trends or hospital trends in resistance. But I think being able to do this sort of multi-institutional, national scale study is unique, and the challenges might be in sort of how the data is collected and whether there are common metrics that can be synthesized across different institutions as organically as it is in this database that we used.

**Maggie Fox** 12:54

So, what are some of the solutions there might be? Is it just having more and better drugs? Is it keeping patients away from any potential sources of infection or multiple diseases?

**Yehoda Martei** 13:05

Multiple things, and I think you hit on some of the important ones, I think there's really a need for good infection control, then simple things like hand hygiene and isolation protocols — they're really great in academic institutions, but not available in all community practices.

I think there's also a need for really good antimicrobial stewardship. So, when we prescribe antibiotics, we start with sometimes empiric antibiotics, which means you make a good guess of what the bug might respond to, but then within 48 hours, you have culture data.

So, these are samples, either blood or urine, that you take to the lab. So, we should really be quick to tailor our antibiotics based on what this data tells us. If it's resistant, we change our antibiotics. If our antibiotics are too broad and we can narrow them down, we should de-escalate. And so, having antimicrobial stewardship in place is important.

I think that the outpatient setting is where there is also a need to really focus on diagnostic stewardship. We do prescribe easily within the outpatient setting, but calling patients to follow up when their culture data comes back, and figuring out whether you need to change the antibiotic regimen, is important. I think also educating patients on the duration of antibiotics and why they're being prescribed is important.

Sometimes you start taking antibiotics that are supposed to be taken for seven days, and the patient feels great after three days, and they start emphasizing the importance of the duration. The increased risk of our resistance to misuse or improper use is important for patients to know as well. You touched on one thing, which is sort of the research component. I think there is a huge need to develop a research pipeline for antibiotics. And an example, like in which I frame this, is thinking about the cancer drug pipeline. I think there are more than 1000 new drugs in the cancer research and development pipeline, and this is compared to just, you know, less than 100 for antibiotics.

And when you think about the global health crisis of AMR resistance, this is wholly inadequate and unmatched to the potential threat of AMR. And so, I think there's a need for investments in that. And it also requires multi-stakeholder partnerships to make these investments in this kind of research, because it's high risk as well. I think, as oncologists, AMR should be a problem that we prioritize, because we

treat our patients holistically, and so this is not just an infectious disease problem. It's our problem because our patients get infected.

**Maggie Fox** 15:30

Yehoda, thank you so much for taking the time to chat with us.

**Yehoda Martei** 15:33

Thank you so much for having me. It was great chatting with you. Thank you,

**Maggie Fox** 15:39

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