Bread, Cheese, and Deadly Infections – Unfriendly and Untreatable Fungi

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SPEAKERS

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Maggie Fox 00:00

Hello and Welcome to One World, One Health with the latest ideas to improve the health of our planet and its people. I'm Maggie Fox. All of us here on planet Earth are facing problems such as pollution, climate change, and infectious diseases (old and new). All of these problems are connected. This podcast is brought to you by the One Health Trust with bite-sized insights into ways to help.

When people think about infectious diseases, we usually think about viruses and bacteria, maybe parasites like the ones that cause malaria. But there's another cause of infectious diseases — fungi (we're not talking about mushrooms or truffles). Fungal diseases, such as Aspergillus mucormycosis or black fungus disease, and a new pathogen called Candida Oris directly kill 1.3 million people a year and contribute to the deaths of 5 million more people according to the World Health Organization.

In this episode, we're chatting with someone who's trying to do something about it. Ana Alastruey Izquierdo works at the Mycology Reference Laboratory at the Instituto de Salud Carlos III in Madrid, Spain. She's also a member of the Global

Action for Fungal Infections (or GAFFI for short). She's tried to make people aware of how we're making an already bad problem worse with some of the ways we spray crops and with climate change. Anna, thank you so much for joining us.

Ana Alastruey-Izquierdo 01:29

Thank you, Maggie. I'm very happy to be here.

Maggie Fox 01:31

Can we run through some of the fungi that infect people and how do they get them?

Ana Alastruey-Izquierdo 01:36

Yeah, that's a very important question. There are 1.5 million species of fungi, but only a few of them can cause disease. They play a crucial role in breaking down organic material; they are important for food production; and they produce cheese and beer. So, everybody knows fungi (as we cannot live without fungi and the beer, bread, and cheese they produce). Nobody, right!

But the ones that are really pathogenic are the ones that I like (to keep an) eye on because that's where I do most of my research. There are only a few hundred, but they cause disease in humans, animals, and plants. The ones that are in humans are Candida Albicans and Aspergillus Fumigatus (most prevalent ones). But there are some others, such as Candida Auris, that have been causing major problems, such as the outbreaks in hospitals, that are very difficult to control over the last few years.

And also, there are some mucormycosis that were important during COVID. They caused a big problem in India. And the range of diseases that they can cause is also very variable. They can cause superficial infections, such as onychomycosis

(an infection in the nails which is very common and usually caused by fungi). They also cause vaginal candidiasis (which is also a prevalent condition among women) and severe diseases with high mortality rates.

Maggie Fox 03:13

And one of the most new and severe diseases is Candida Auris, which is spreading quickly, of late, in Europe. It's even closing hospitals in countries, such as Brazil. Can you talk a little bit more about Candida Auris.

Ana Alastruey-Izquierdo 03:26

I think it has been like a star — the star in the fungal world in the last year. It was just recently discovered in 2009. And we only knew it because it was isolated from an ear infection. But then suddenly, in 2015, or 2016, several outbreaks started to occur in different countries.

So, it was suddenly a nosocomial pathogen — a pathogen that was causing infections in the hospitals. It's now becoming a big problem, as you said. There are outbreaks in hospitals in Italy, Greece, Spain, the US, Brazil, and South Africa. So, it's a very interesting pathogen, especially because it's very resistant to the treatment.

Maggie Fox 04:13

You mentioned that it started out as an ear infection. How can an ear infection make people so sick that they might die?

Ana Alastruey-Izquierdo 04:20

That's something that we are still not very sure about (how that happened). But there is a theory that it could be because of global warming and all these environmental changes because as I said, there are 1.5 millions of fungal species, but only a few of them can cause disease. So, the process is that this species was around in the environment without really being a real pathogen, and then it caused an ear infection, which kind of is still superficial.

The reason these fungi cannot cause disease is that they are not able to grow at 37 degrees or lower body temperature. I think that with global warming, the fungi are adapting to grow in higher temperatures. And that's how this pathogen became human pathogen. But this is only theory (and it has never been true). However, what did happen was that it spread all over the world and started causing diseases in different parts of the world at the same time.

Maggie Fox 05:23

Who's vulnerable to these fungal infections? Do they infect healthy people or only those who have some kind of immune suppression?

Ana Alastruey-Izquierdo 05:31

Yeah, that's also a very interesting question. So, fungi are ubiquitous. They are all around you and everybody breathes these spores every day. And usually, the inhalation of spores is the main root of infection. However, most of us do not get sick. There is a group of fungi called endemic mycoses that are also able to cause disease in immuno-competent population — normal people with regular immune system.

They are restricted usually to certain rare geographical regions and are related more with specific environmental exposure like valley fever coccidioidomycosis, which is in the US, but, usually, most of the fungi are opportunistic infections. The people who are at risk of them are the immunocompromised people.

So, people with HIV and patients who are taking immune suppressors (such as transplant patients), and old people who have undergone chemotherapies and biological treatments. So, whenever your immune system is not in perfect shape, the fungi can attack and cause a disease. And of course, you can treat these fungi with drugs, but some of them are developing, what's known as, resistance to the antifungal drugs.

Maggie Fox 06:51

Some are also already naturally resistant to antifungal drugs that we use. How does that happen?

Ana Alastruey-Izquierdo 06:58

You see, everything is interesting in the fungal world. So, one of the biggest problems, when compared with bacteria, is that we have a very limited number of treatments or antifungals. So, when we say this is a multi-resistant fungus, we are talking about mainly three classes. It's not that we really need to invest more in having more treatments. But going back to your question and how this has really happened is that there are fungi that are intrinsically resistant.

There are some species that are resistant to all the treatments that we have now, such as Lomentospora prolificans, which is a rare disease, but whenever you get it, it is very difficult to treat, and mortality is very high. But there are some others. This is where we are more worried now because they're developing resistance and the numbers are rising worldwide now. They are developing resistance because of the pressure (it can be on one side from the clinical treatment).

So, these are sometimes patients that had very low treatments because they either have a chronic infection or they are prophylactically treated (because of the weak immune system). And this is very prolonged because the treatments are usually long-term. So, they can develop resistance because of long-term treatments in the clinic and because of the use of fungicides in agriculture (as fungi are mainly pathogenic to plants).

Maggie Fox 08:25

So, let's talk a bit more about the way crops and plant treatments affect these fungi. Can you talk about how they help them develop resistance to drugs that are used in people?

Ana Alastruey-Izquierdo 08:36

As I said, fungi are one of the major groups of pathogens that can affect plants. So, these antifungals are used to protect the crops and the flowers. We really need to treat them to be able to protect them and not get infected. So, the problem occurs when these antifungals (that are used in clinics) are also used in fungicides in agriculture. It has been demonstrated that the chemical class (of these antifungals), is more or less the same despite not being the same specific agent.

Moreover, the use of the same class in the environment and for treating the plants is putting pressure on this species and (as a result) they are developing resistance. So, as we were saying, fungi are all over the world and they are really living. They're ubiquitous. So, they are in the plants, the sea, and everywhere. But whenever you treat the field with fungicides, you are putting pressure on them and thus, they are developing secondary resistance (or resistance to the treatments that we use in clinics).

Maggie Fox 09:41

Why do we even do that? Why do we use the same chemical treatments on plants and crops as we use to treat people? How did that even happen?

Ana Alastruey-Izquierdo 09:48

This is a very good question. It seems stupid, right! It's like why you would ever do that. While there are differences between plants and pathogenic fungi and humans. They share fundamental characteristics, the antifungal cells are effective for both groups. And it's very difficult to develop new antifungals because fungi are vastly different than bacteria and viruses and are closer to us.

So, they are eukaryotic. They have a eukaryotic cell. And it's more difficult to develop to find targets that you can fight that are not toxic to us. Thus, there is a very limited number. That's why they have been used in fungicides.

Maggie Fox 10:35

It sounds to me like the people who develop these antifungal crop treatments weren't talking to scientists and physicians who treat fungal diseases in people.

Ana Alastruey-Izquierdo 10:50

Yeah, I think that we are making a difference now. So, it's true that one cannot ask agricultural people to not use fungicides because they also need something to treat the plants. But what we are now trying to open the discussion with them. We are, at least, trying to protect the new entities because we've seen this with azoles which are a group of antifungals that have been in use for more than 20 years in both clinics and for the environment.

But now there are new classes. Luckily, in the last year or so, there has been a development of new antifungals. And there are two new classes of antifungals that have been in clinical trials, and they are costing millions of dollars and also years of research that are still not licensed for use in the human environment. But the regulations for using fungicides in agriculture are not that big.

Also, it takes a very short time to develop a fungicide. So, the same chemical agents that are already used in the environment have been licensed for use in fungicides. The aim of this group of people, that has been trying to put together all these stakeholders, is to protect the new agents and I think now, as you said, it

seems stupid, but we are in different worlds. And sometimes you really need to talk to each other and it's sometimes not that easy.

Maggie Fox 12:18

The World Health Organization recently released a list of the priority fungal pathogens. Can you talk about how that's useful?

Ana Alastruey-Izquierdo 12:25

I am very happy that in the last October, the WHO released the first ever fungal priority pathogen list, in which we have prioritized the most important species (while taking into account this antifungal resistance problem, mortality, severity, and several other complications). We have detected several areas for action, meaning public health surveillance, research and development.

And I think it's important to convey and amplify the message that we need to develop new antifungals because they are very limited. But we also need to create better diagnostics because we still don't have a very good diagnostic for a fungal infection. Sometimes, or on many occasions, fungal infections are diagnosed late or even in autopsies (during post-mortem). Also, a fungal infection is usually suspected after a couple of rounds of antibiotics that are not responding.

So, they don't know what to do and then suddenly somebody comes up and says that maybe this is a fungal infection. So, we really need to improve the capacity; uncover and improve the knowledge; raise more awareness; and educate healthcare workers at all levels. I think this is very important because these infections don't have specific (things and) symptoms (and are thus, always suspected).

So, the list that the WHO has released has had an impact and many people are now paying attention to fungal infections. This is creating awareness (which is one

of our main priorities with initiatives like this podcast). It's a very fundamental task.

Maggie Fox 14:07

Anna, thank you so much for joining us.

Ana Alastruey-Izquierdo 14:10

Thank you.

Maggie Fox 14:11

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