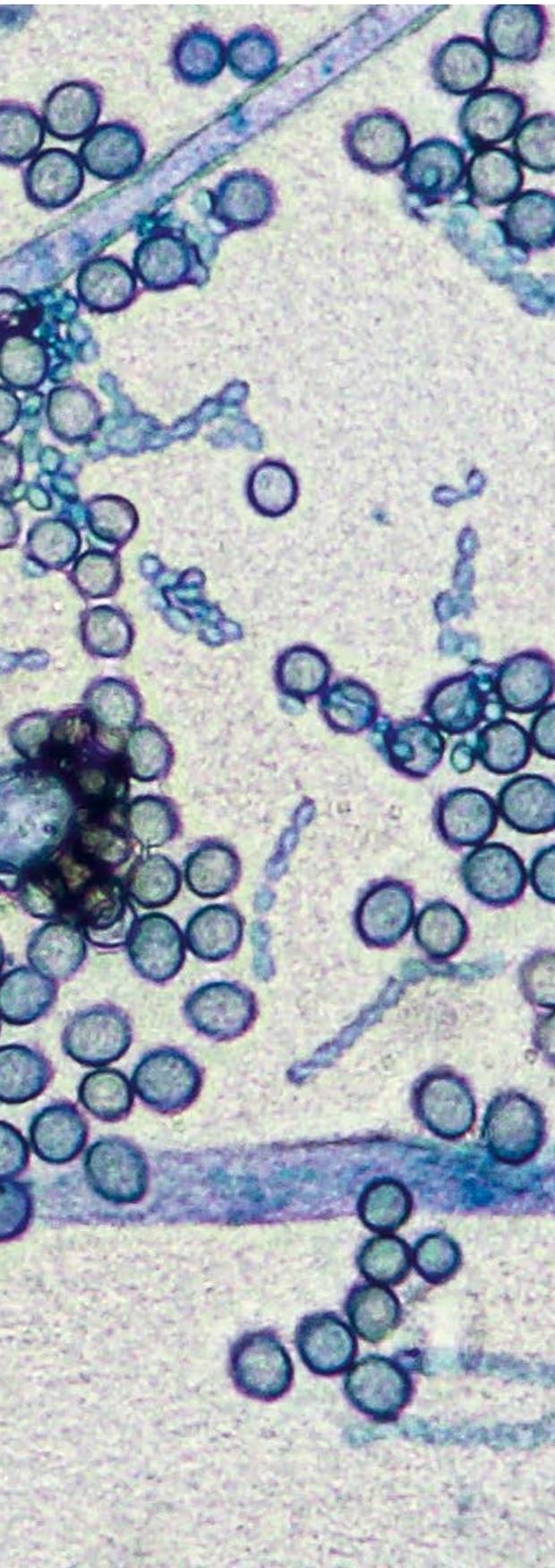


Underestimated and lethal!

Such are the fungal
invasive infections



←
Aspergillus sp.
 formed in
 rotten bread,
 dyed with blue
 lactophenol
 at 1%
 40x objective,
 10x ocular
 lens, 400x total
 magnification
 with imprinting
 technique.

In the kingdom of these germs, there are some six million species, but three of them particularly affect human health to the degree of becoming a threat for public health and a hard challenge for therapies that could save lives.

By Ximena Serrano Gil

Photos Carolina Firacative, Ximena Serrano.

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Fungi. This word, by and large, conditions the popular imagination to picture representations of wild or edible mushrooms, nasty injuries on the skin, nails and hair or allergies, but beyond that, there are some that may cause the host's death when invading the human body.

Yes, indeed, there are some fungal species that can trigger infections in the blood, brain, lungs, and other vital organs unless they are timely treated based on an adequate diagnosis. This has turned the invasive fungal diseases into underestimated and lethal enemies all over the world. Biologist and Medicine doctor [Carolina Firacative](#), professor at the School of Medicine and Health Sciences of Universidad del Rosario and member of [Studies in Translational Microbiology and Emerging Diseases Research Group \(MICROS\)](#), in the same institution, has investigated the risk factors of those who develop such illnesses to recognize the impact of fungi-related infections in human health.

The scenario gets complex if we take into account that both in the environment and in every millimeter of our skin and mucosa, an endless number of microorganisms cohabit; many times, they are disregarded when it comes to assess a patient. The fact is that, in general, when it comes to infections, we tend to think about bacteria or viruses rather than fungi; therefore, the patient will not respond to the treatment because they are, biologically, quite different microorganisms.

That is why hundreds of thousands of people across the world, particularly those immunocompromised, suffering from cancer, HIV, transplants, and COVID-19, among other base conditions, are attacked each year by microorganisms like [Candida albicans](#), [Aspergillus fumigatus](#), and [Cryptococcus neoformans](#), the most common fungal species responsible for invasive pathologies in humans.

The review made by Firacative, under the title [Invasive Fungal Disease in Humans: Are we Aware of the Real Impact?](#), published in [Memórias do Instituto Oswaldo Cruz](#), linked the risk factors and the most common base conditions to develop a fungal disease. From the epidemiological perspective, the three most frequent and highest risk infections are **candidiasis**, produced by yeasts of the genus *Candida*; **aspergillosis**, caused by the *Aspergillus* fungus; and **cryptococcosis**, generated by the *Cryptococcus*.

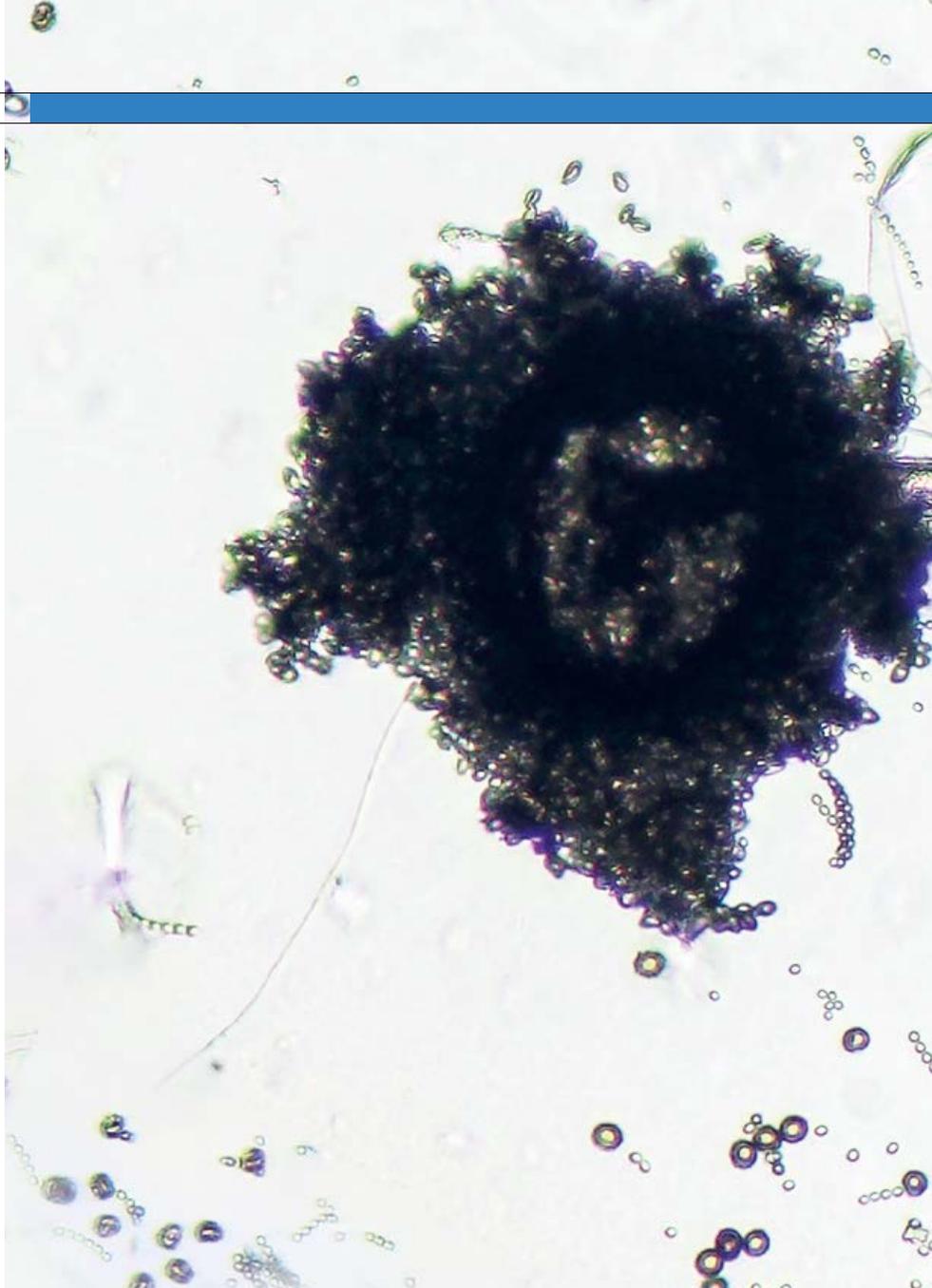
The frequency in which people face these germs is very high, as we practically live surrounded by them. “*Candida* lives with us. If we take a sample of our inner cheeks, we will find it there, as well as in the intestine,” the researcher states. Likewise, these microorganisms can survive for long hours on a diversity of surfaces like bathroom curtains, computer screens, stereoscopes, or public transportation handrails, “but if there is a balance with other microorganisms like bacteria, or a stable immune system is maintained, the disease will not develop,” Firacative adds.

With *Cryptococcus* and *Aspergillus* something similar happens: “They are not in our bodies, but they are in the environment. In general, *Cryptococcus* is found where there are doves or other birds and their faeces. *Aspergillus*, which can circulate in heating systems and air-conditioning equipment, resides in trees, vegetable material (foliage, flowers or bark), and on the ground.

“We are constantly inhaling infectious particles and that doesn’t cause big problems, but it can be so if the person suffers from some kind of immunosuppression or a serious underlying disease,” the expert explains. The concern is valid because although humans are naturally resistant to most invasive fungal illnesses and disease severity depends on the host’s immune response. A study published in 2017 in the [Journal of Fungi](#) points out that invasive aspergillosis affects over 300,000 patients per year, out of almost 10 million at risk.

An underestimated record

According to the study [Prevalencia mundial y multinacional de enfermedades fúngicas: precisión de la estimación](#), it is estimated that on a global scale, 1.5 million people die annually due to these diseases, a similar figure to deaths by tuberculosis and three times higher than the mortality rate due to malaria. From this standpoint, fungal diseases constitute an emerging problem worldwide.



↑
Photomicrograph of *Aspergillus* sp. conidiophores and conidia, one of the most common fungal pathogens causing invasive disease in humans. Lactophenol blue stain. 400X Magnification.

However, most of them are not taken into account when it comes to routine hospital attention since keeping a record of them at public health institutions is not mandatory, so, there is no reliable information as to its local, regional, or cross-border prevalence.

“We can say that in Colombia, at large, the record is underappreciated and data is scarce,” Firacative affirms. Faced with this scenario, clinicians Carlos Álvarez Moreno, Jorge Cortés, and David W. Denning, from the Faculty of Medicine of Universidad Nacional, from the Clínica Universitaria Colombia and from Manchester University, respectively, [published, in 2017, a study on the burden of fungal infections in Colombia](#). The results reveal that they found roughly 755,000 cases of these infections, out of which close to 600,000 corresponded to candidiasis and 130,000 to aspergillosis. Those findings allowed them to



Carolina Firacative, professor at the Escuela de Medicina y Ciencias de la Salud (School of Medicine and Health Sciences) of the Universidad del Rosario, has researched other factors having an incidence in the complexity of these affections, such as the susceptibility of those pathogens to anti-fungal medicine.

conclude that fungal infections account for an important burden of disease for the Colombian population, as it affects approximately 1.5 per cent of the population.

In addition to her work mentioned above, researcher Firacative has studied other factors having an impact on the complexity of these maladies, such as the susceptibility of these pathogens to anti-fungal medicine. “We analyzed whether the drugs we have today can be good or useful for the treatment. We also analyzed what types of patients are mostly affected by these fungi; why some of them are affected while others are not. Similarly, from an environmental approach, we examined where these fungi proliferate, and found cases where a hospital located near a wood area favors the fungi to enter through the air-conditioning ducts and infect a patient. Thus, we could track down the fungus, the patient, and its environment thoroughly, because this is multifactorial,” the academic puts in context.

What is a fungal disease?

Also known as mycosis, it is caused by a great variety of fungi which live both in the environment and in the microbiota (range of microorganisms living in the body). It becomes invasive when it brings about progressive infections in internal organs, which end up being lethal if not timely diagnosed and treated.

The infection may begin by inhaling infectious particles from the surroundings or by direct inoculation. However, fungi must meet four criteria to unleash an invasive disease in the human being:

- Being able to grow at or above mammalian body temperature.
- Getting to the internal tissue by penetrating or evading host barriers.
- Lysing tissues and absorbing their components.
- Having the ability to evade host immune defenses.

One of the threats leading to a fungi infection happens when a person is admitted in the hospital or in intensive care units (ICU). It is the case of *Candida* which, although it normally remains in the skin, it may enter the blood when the needle of a syringe goes through the skin or through the use of intracranial or intravascular devices. For that reason, it is so important to take all the necessary measures in patients undergoing surgeries with this kind of hospital supplies.

The article written by the professor details that *Candida albicans* and other species of *Candida* have the ability to form biofilms in permanent bladder catheters, in cardiac valves, in particular prosthesis, and even in different tissues of the patient. The [biofilms](#) are a group of microorganisms that stick to all surfaces, helping to develop a high tolerance to antimicrobial medicine, and therefore, they lead to resisting the antifungal active principles.

At this point, it is worth mentioning that the lengthy or indiscriminate consumption of antibiotics suppresses and destabilizes the growth of beneficial bacteria, which enable a balance in the body. That situation contributes to strengthen the resistance of fungus to pharmacological treatments that may fight

them off. When these therapies do not represent any competition facing those good bacteria any more, a greater colonization is generated and may remain longer in the patient.

And now, climate change...

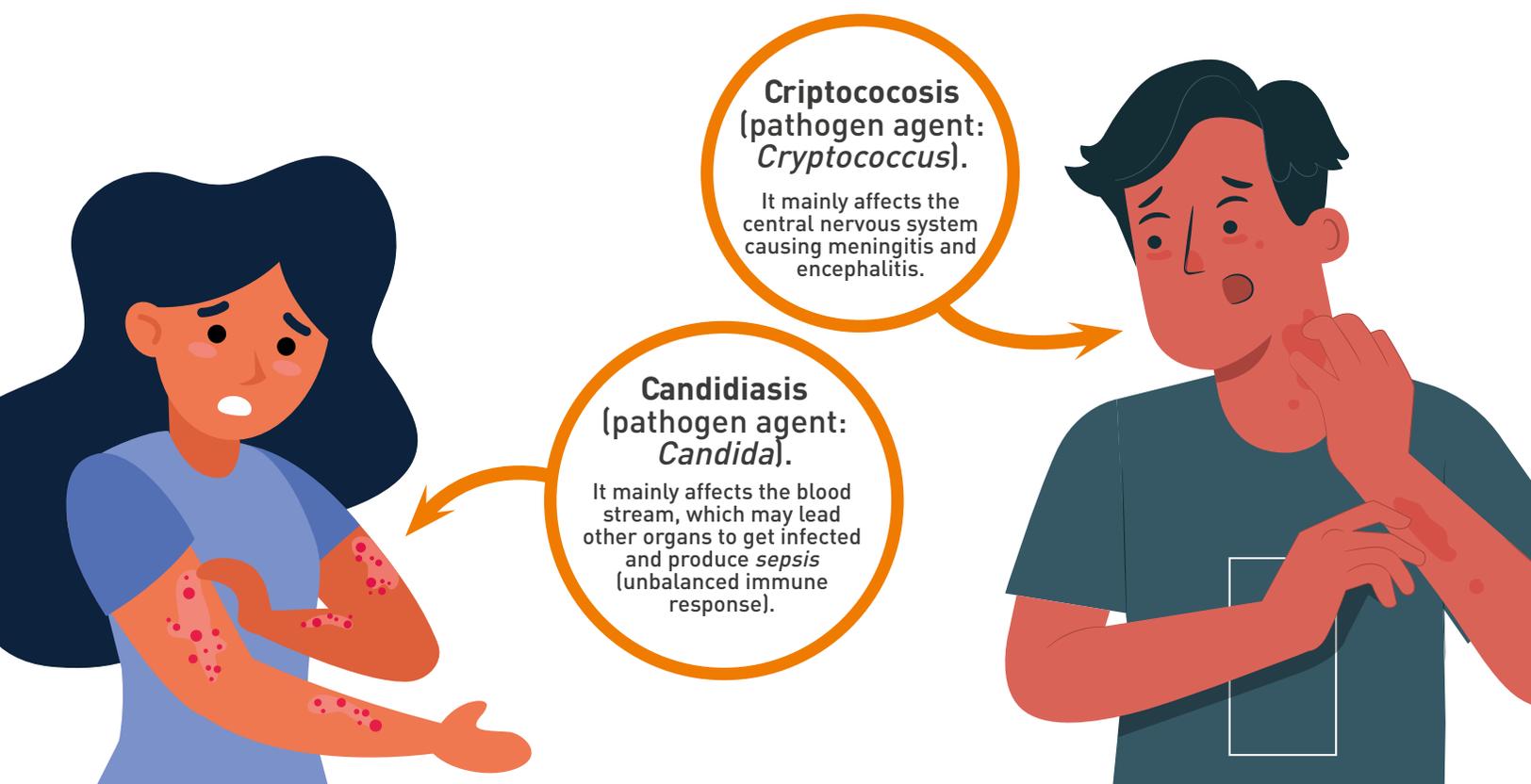
Additionally to what has been explained, yet another antagonist steps into this chain of invisible universes threatening public health: climate change. The disruption of climate conditions may have an influence in spreading fungi and in the likelihood of infecting more hosts.

As doctor Firacative explains, “temperatures are higher and higher and fungi have already started to adapt to these new conditions. One of the abilities enabling a fungus to cause a disease is that it may survive an external average temperature of 40°C. This means that the average human body temperature of 37° C will not be an obstacle for it.”

Definitively, microorganisms have been skillfully adapting to climate change and have achieved a surprising evolution for that purpose.

Firacative indicates that many fungi are pathogens of key plants for agricultural activity, like tomato, potato, the banana tree, and a large number of flower crops that did not use to cause infections, but now they do. The tool to control them has been the application of fungicides. “These chemical products are similar, in their molecular composition and structure, to those taken by patients,” the expert warns. “If we take in such pathogens from an environment already exposed to agricultural drugs, that fungus may already be resistant to medicine.”

Fungi around us



Such question is reinforced in the publication [One Health: Fungal Pathogens of Humans, Animals and Plants](#), which explains that “the use of the same types of antifungal medicine in crop plants and in human beings generates an indirect selection pressure that increases the risk of developing strains resistant to the drugs used in antifungal therapy.”

These infections are never transmitted by intake; the problem arises when the infectious particles are cast over the crops, as the contact with the chemical products means that they will already present considerable levels of resistance; so, that drug will not be effective when the doctor treats the patient.

Fungal infections must also be considered

Although Carolina Firacative’s work contributes with findings and knowledge that feed the epidemiological global databases, the researcher highlights that beyond that effort, her role

Fungal diseases are an emerging issue worldwide. However, most of them are not taken into account when it comes to routine hospital attention as keeping a record of them at public health institutions is not mandatory.

Aspergilosis (pathogen agent: *Aspergillus*).

It mainly affects lungs and causes some masses damaging the pulmonary function. The greater infection risk is run by patients under chemotherapy and connected to mechanical ventilation.



Prevention Measures

It is common to see prevention campaigns for viral or bacterial diseases, but not for those stemming from fungi. The following is a list of recommendations made by researcher Carolina Firacative, for a public health campaign:

- Do not take vegetable material to a hospital (flowers, fruit and not even plants in pots).
- Carry out a correct maintenance service to air-conditioning and heating systems.
- Control mold on walls, furniture, etc.
- Promote the frequent wash of hands among health care staff.

as teacher is to tell students that they should not think only of bacteria and virus as infection sources; they have to keep fungi in mind as well since in transplant patients, in serious medical condition, or in terminal stage, only the main condition is taken into account, and other possibilities are not considered, such as complications of their health derived from fungi, resulting in less recorded cases than what really occur.

“To me, the most important thing is to raise awareness among health care staff that their patients can be attacked by these infections, which must be timely identified, or otherwise the mortality rate increases,” the professor emphasizes.

In some way, medical advances also contribute to increase the number of people exposed to these risk factors, as in past years, maybe only 1 transplant per week was performed, and now, 20 are practiced. Other indicators that have gone up over time are the number of cancer patients and HIV positive cases (5,000 new cases annually in Colombia, according to the surveys by the Ministry of Health and Social Protection).

Based on all these reasons, the researcher insists on the importance of effective and truthful communication “among colleagues, infectologists, clinical laboratories, and nursing staff, as this best practice increases the speed of an adequate diagnosis, and therefore, it may help the patient to survive.” ■