Deadly fungus became resistant to all existing drugs in 3 unlinked US patients

Enlarge / A strain of *Candida auris* cultured in a petri dish at the CDC.

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A deadly fungal pathogen developed the ability to resist all existing antifungal drugs on three separate occasions in the United States, according to a new report.

The fungus, *Candida auris*, was already classified as an "urgent threat" by the Centers for Disease Control and Prevention. But the emergence of so-called "pan-resistant" strains raises additional concern, according to the report's authors, who are infectious disease specialists at the CDC and the New York State Department of Health. They published their findings Thursday in the CDC's publication Morbidity and Mortality Weekly Report.

C. auris was first identified in 2009 in Japan and has since popped up in nearly 40 countries. (It arrived in the US by 2013, and New York City, Chicago, and New Jersey have been hit the hardest.) The insidious germ is known for creeping around healthcare facilities and infecting vulnerable patients, causing invasive infections marked by nondescript fever and

chills.

Somewhere between 30 percent and 60 percent of patients die from the infection. (Determining the exact fatality rate is tricky because the fungus often preys upon patients already suffering from life-threatening conditions.)

Part of what makes *C. auris* strains so dangerous is that they seem to develop resistance to antifungal drugs relatively easily. Only three classes of antifungal drugs are used to treat *C. auris* infections: triazole, polyene, and echinocandins classes. And many strains are already resistant to one or two of those.

A survey of strains found in New York discovered that over 99 percent could withstand triazole drugs, while over 60 percent were resistant to polyene drugs. So far, resistance to echinocandins has been rare in the US and, as such, that class has been the standard first-line treatment.

But, in the new MMWR report, the infectious-disease researchers describe just how easily that can change.

Fortified fungi

Surveillance of strains collected in the latter half of 2019 turned up three patients with pan-resistant *C. auris*, the report says. The patients were all in different medical facilities and had no contact or connection with each other.

In all three cases, the patients' *C. auris* infections started out with strains that were susceptible to echinocandins, and each was treated for prolonged periods with an echinocandin drug. After months on the drugs, subsequent testing showed that their once drug-susceptible infections had developed resistance to all classes of drugs available.

Two of the patients died within weeks of investigators isolating their pan-resistant strains in 2019. Both had

multiple underlying health conditions, were dependent on ventilators, and were colonized by multi-drug resistant bacteria. Thus, “the role of *C. auris* in their deaths is unclear,” the infectious disease researchers report.

After those two patients were identified, investigators looked back at older samples from other patients. That’s when they found the third case of pan-resistant *C. auris*, which was in a rectal swab taken from a patient in 2017. In that case, the antifungal treatment had cleared the patient’s initial drug-susceptible infection. But subsequent monitoring found the pan-resistant strain colonizing the patient, i.e., skulking around the patient’s body without causing an infection. The patient died 10 months after the pan-resistant strain was isolated.

The researchers report that:

> *Although extensive investigations failed to document transmission of pan-resistant isolates from the three patients to other patients or the environment, the emergence of pan-resistance is concerning. The occurrence of these cases underscores the public health importance of surveillance for C. auris, the need for prudent antifungal prescribing, and the importance of conducting susceptibility testing on all clinical isolates, including serial isolates from individual patients, especially those treated with echinocandin medications.*

Tenacious foe

This isn’t the first time that pan-resistant *C. auris* has been identified, the researchers note. Countries where *C. auris* arrived before reaching the United States have already reported increased resistance to echinocandin and their own pan-resistant strains.

Still, in an email to Ars, the New York State Department of Health added that “we cannot predict if pan resistance will develop again” here. The agency added that the measures outlined by the researchers in the MMRW report can “reduce the likelihood of development of pan resistance in the future.”

In addition to trying to keep the menacing microbe from becoming more resistant, researchers are also working on trying to scrub it out of healthcare facilities where it poses the most threat—which is extremely difficult. Recent studies suggest that copious amounts of fungal cells can drip from infected or colonized patients, drenching their surroundings in infectious, drug-resistant germs. On plastic surfaces, those fungal cells can form steely clumps that can survive for weeks. Rigorous bleaching and disinfection measures can sometimes fail to kill off lurking fungi.

In the event that pan-resistant *C. auris* does show up again in the US, there may be some treatment options, the New York health department says. Infectious-disease specialists should be called in and can make recommendations on a case-by-case basis. They might consider removing potentially contaminated medical devices or draining areas such as abscesses that might harbor *C. auris*. They could also try combination therapies or turn to experimental antifungal medications in development.

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