

Combo therapy helps knock out fungal meningitis

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Study found 2-drug treatment reduced death risk from cryptococcal meningitis by 40 percent.

(HealthDay)— A drug regimen containing two powerful antifungal medicines—amphotericin B and flucytosine—reduced the risk of dying from cryptococcal meningitis by 40 percent compared to treatment with amphotericin B alone, according to new research.

The study also found that those who survived the illness were less likely to be disabled if they received treatment that included flucytosine.

"Combination antifungal therapy with amphotericin and flucytosine for HIV-associated [cryptococcal meningitis](#) significantly reduces the risk of dying from this disease," said the study's lead author, Dr. Jeremy Day, head of the CNS-HIV Infections Group for the Wellcome Trust Major

Overseas Program in Vietnam.

"This combination could save 250,000 deaths across Africa and Asia each year. The key to achieving this will be improving access to the [antifungal agent](#) flucytosine," said Day, also a research lecturer at the University of Oxford.

Flucytosine is more than 50 years old and off patent, according to Day. The drug has few manufacturers, and it isn't licensed for use in many of the countries where the burden from this disease is highest, he said. Where it is available, the limited supply often drives the cost higher, Day noted.

"We hope the results of this study will help drive increased and affordable access to both amphotericin and flucytosine," he said.

Infectious disease specialist Dr. Bruce Hirsch, an attending physician at North Shore University Hospital in Manhasset, N.Y., said that in the United States, "the use of these medicines, amphotericin and flucytosine, is the usual standard of care for this [dangerous infection](#), and is followed by long-term treatment with fluconazole [another antifungal]."

But, Hirsch noted that this [infection](#) is unusual to see in the United States.

That's definitely not the case in the rest of the world. There are about 1 million cases of cryptococcal meningitis worldwide each year, and 625,000 deaths associated with those infections, according to study background information.

Meningitis is an infection of the meninges, the protective membranes that cover the brain and the spinal cord. Meningitis can be caused by bacteria, viruses and fungi, according to the U.S. Centers for Disease

Control and Prevention. Cryptococcal meningitis is caused by the fungus *Cryptococcus*. There are 30 strains of *Cryptococcus*, and one that often causes disease is *Cryptococcus neoformans*.

"Most of us have been exposed to *Cryptococcus neoformans*. It is ubiquitous in the environment, associated with trees, bird guano and soil. Infection is thought to occur from the inhalation of spores," Day said.

People can be infected for years without knowing it, according to Day. But, if someone who's infected has weakened immunity, the infection can then start to wreak havoc. Common ways people become immune-suppressed are through an [HIV infection](#), taking immune-suppressing medications for organ transplantation, or taking immune-system altering medications for chronic inflammatory diseases, Day explained.

The current study included 299 people with cryptococcal meningitis who were randomly assigned to one of three treatment regimens: amphotericin B alone for four weeks; amphotericin B plus flucytosine for two weeks; or amphotericin B plus fluconazole for two weeks. People in the second and third groups were also given eight weeks of follow-up therapy with fluconazole.

The investigators found that [combination therapy](#) with amphotericin B and flucytosine resulted in a 40 percent lower risk of death compared to amphotericin therapy alone. Combination therapy with [fluconazole](#) didn't appear to affect survival rates, according to the study.

The combination therapy with flucytosine also resulted in lower levels of *Cryptococcus* in the spinal fluid, according to the study.

Side effects were similar in all three treatment regimens. Possible side effects are anemia, low levels of potassium, low white blood cell counts and additional infections, the study authors noted.

"This study is the first ever to demonstrate that a combination of antifungal drugs can significantly reduce the risk of death from this disease," Day pointed out.

The reason for the success of this particular combination is that it quickly kills *Cryptococcus*, according to the author of an accompanying editorial, Dr. John Perfect, of Duke University Medical Center in Durham, N.C. "In cryptococcal meningitis, the principle is set: the rapid killing of yeasts at the site of infection translates into a better outcome," he wrote.

"Long-term success in the treatment of cryptococcal [meningitis](#) depends on how well we kill yeasts with the initial treatment regimen," Perfect added.

The study, which was funded by the Wellcome Trust and the British Infection Society, is published in the April 4 issue of the *New England Journal of Medicine*.

More information: To learn more about *Cryptococcus*, visit the [U.S. Centers for Disease Control and Prevention](#).

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