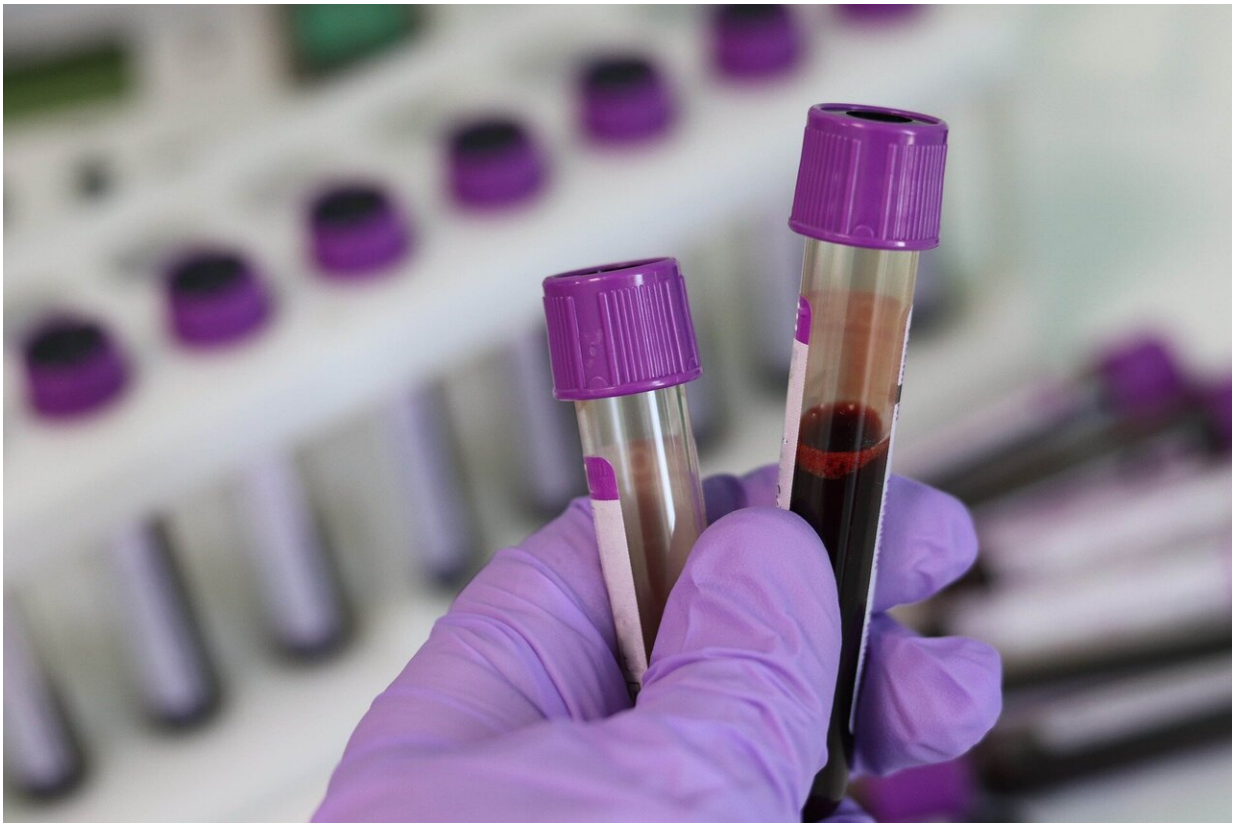


# New DNA test beats others at hunting down germs that inflame the brain, study finds

June 17 2019, by Cathie Anderson

---



Credit: CC0 Public Domain

Right now, neurologists don't have one test that can identify multiple causes of inflammatory neurological diseases such as encephalitis and meningitis. But UC San Francisco researchers say their new DNA test

hunted down more of these pathogens than any conventional test did in a newly released study.

Inflammatory neurological diseases are rare, costly to treat, difficult to diagnose and life-threatening.

The pioneering test developed by neurological researchers at UCSF is moving doctors closer to providing patients and their loved ones with the answers they seek. The test uses gene sequencing to identify more causes of these mysterious ailments than any conventional test now being used, according to study released late last week in the *New England Journal of Medicine*.

Conventional tests look for pathogens one at a time, so that means physicians essentially have to know what they're looking for to choose the right test to perform, UCSF researchers said. Without knowing the cause of these ailments, they said, it's impossible to know what treatments to employ.

"Patients with infectious and noninfectious encephalitis can be clinically indistinguishable from one another," said Dr. Michael Wilson, associate professor of neurology at UCSF and the co-first author of the paper, along with study coordinator Hannah Sample. "Having a broad-based test that either rules in [infection](#) or rules out infection can really aid these cases that are in gray areas between infection and not."

Infections cause less than half of most meningitis and encephalitis cases, UCSF researchers said. The rest result mostly from autoimmune system reactions.

The last thing doctors want to do is suppress the immune system of a patient with an infection because the consequences could be harmful, Wilson and other researchers explained. Yet that's precisely what is

needed for a patient with an autoimmune disease.

To prevent delays and errors, Wilson, Dr. Charles Chiu and other UCSF researchers came up with a test they call mNGS, short for metagenomic next-generation sequencing. It identifies the pathogens found in a patient's [cerebrospinal fluid](#) by sequencing the genes of invading viruses, fungi, bacteria or other organisms.

Chiu said their team was "frankly surprised" to discover that a significant proportion of the diagnosed infections—13 of 58, or 22.4% - were detected only by the mNGS test, despite exhaustive and comprehensive testing done in hospitals offering highly specialized neurological care.

"This highlighted the usefulness, and perhaps the necessity, of introducing new diagnostic technologies into the clinic to enable more timely and accurate diagnoses that will hopefully lower health care costs, decrease lengths of stay, and ultimately save lives," said Chiu, also director of the UCSF-Abbott Viral Diagnostics and Discovery Center.

U.S. hospitals don't see that many cases of these neurological diseases. In 2006, only 24 out of every 100,000 U.S. citizens were hospitalized for meningitis, Chiu said, and for encephalitis, that rate was about 7 out of 100,000.

Despite the small number of people hospitalized with encephalitis, Chiu said, the cost of their treatment is \$2 billion.

To find the types of challenging neurological cases needed for this study, UCSF received cerebrospinal fluid samples from 482 patients at eight medical centers. The adults and children were being treated as far away as Children's National Medical Center and as close as UC Davis Medical Center. Of the 482 patients, 204 completed the study.

In 57 cases, tests showed that an infection was causing the patients' symptoms, the UCSF said, and the mNGS test successfully identified 32 infections in 31 patients. It not only confirmed 19 cases of infection detected in conventional tests but also found 13 pathogens that other tests had missed, including a case of the St. Louis encephalitis virus that had not been seen in California since 1986.

The UCSF researchers acknowledged that their new test is no silver bullet. Although it found more infectious causes than any other test, it failed to detect 26 infections caught by conventional tests. West Nile virus proved tricky because the virus comes and goes from cerebral fluid, they said, so it might not have been present when a spinal tap was done.

They also noted that the DNA of other pathogens may not be present in the spinal fluid, and other infections had been found in places such as a brain abscess or antibodies.

Of the remaining 147 patients completing the study, 46 had neurological inflammations caused by autoimmune diseases or other non-infectious disorders, Chiu said, and he and other researchers never found the cause of inflammation for 101 of the patients.

"The fact that 50% of these patients continued to lack a diagnosis despite all testing, including mNGS, underscores the challenges," Chiu said. "It is likely that some of these patients did have infections but remained undiagnosed, as in the case of West Nile virus infection mentioned previously, or had an as-yet undescribed autoimmune disease."

He and his team are trying to develop a way to use algorithms or statistical modeling that can potentially discriminate between bacterial infection, viral infection, and autoimmune disease, he said, and that

process may shed some light on the undiagnosed cases.

The UCSF researchers also are planning to expand the mNGS testing to look for different diseases and to other types of body fluids, such as looking at blood plasma to diagnose infectious cases of sepsis or looking at respiratory fluid to diagnose pneumonia. They also want to try other types of sequencing platforms that can yield results in six hours rather than the 90 hours required for mNGS results.

Chiu said that the diagnoses of all 58 infections were made while all patients were living, but not all of the patients' lives could be saved. The 30-day mortality rate for patients in the study was 11.3 percent.

"Some of the infections that were identified are not treatable because there isn't an effective drug for the infection," Chiu said. "An example is a fatal case of St. Louis encephalitis virus infection that was diagnosed using the mNGS test in an elderly immunocompromised patient from California."

So, will patients with encephalitis or meningitis be getting the mNGS test in California hospitals soon?

"The test is currently costly," Chiu said, "and only large reference laboratories or clinical laboratories at large medical centers such as UCSF have the resources and expertise to run it. It will likely not be available to other hospitals until the test is miniaturized ... or until the costs of sequencing decrease sufficiently to make the test cost-effective for hospital laboratories."

©2019 The Sacramento Bee (Sacramento, Calif.)

Distributed by Tribune Content Agency, LLC.

Citation: New DNA test beats others at hunting down germs that inflame the brain, study finds

(2019, June 17) retrieved 9 April 2024 from <https://medicalxpress.com/news/2019-06-dna-germs-inflame-brain.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.