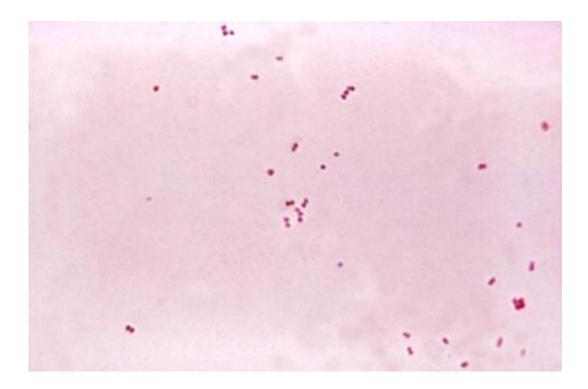


Is it brain infection or cancer? A new rapid test could hold the answer

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Gram stain of meningococci from a culture showing Gram negative (pink) bacteria, often in pairs. Credit: public domain

When patients present with neurologic symptoms such as severe headaches or seizures, the symptoms could suggest anything from infection, cancer, or an autoimmune disease of the brain or spinal cord, leaving physicians scrambling to find the cause in a short amount of time. The differences in diagnosis can mean having mere hours to act or being able to take days or weeks to devise a treatment plan. Now,



researchers at Jefferson (Philadelphia University + Thomas Jefferson University) have developed a test that could rapidly parse out infections of the brain from other diseases. The diagnostic could prove particularly useful in infants and young children.

"We have many tests for making diagnoses, but the ones that conclusively indicate infection can often take more time than we'd like, especially in cases of childhood meningitis or encephalitis," said Mark Curtis, MD, Ph.D., Associate Professor of Pathology, Anatomy and Cell Biology, who also works as a hospital pathologist. "Once confirmed with additional research, our test could provide a first, rapid and less invasive way to look at what's happening in the brain and guide treatment or further testing."

The results were published in the journal PLOS ONE on October 31st.

Rather than testing for the presence of bacteria or virus, the researchers looked at the first tell-tale signs of infection: the cytokines produced by the patient's immune system in response to pathogens and other injury processes. "Cytokines are an alarm system in the body," said Dr. Curtis. "Infectious agents activate a multi-pronged inflammatory response, a key component of which is the release of different combinations of cytokines tailored to combat pathogens. Changes in <u>cytokine</u> levels of cerebrospinal fluid offer a very early measurable sign of infection."

Dr. Curtis and colleagues decided to see if they could detect patterns within the cytokines that might differentiate infections from other brain diseases or disorders. In the retrospective analysis, the investigators looked at samples collected from 43 patients who had received spinal taps during their hospital stays. The researchers then tested the <u>cerebral</u> <u>spinal fluid</u> (CSF) for the presence of 41 different cytokines and noticed that patients with confirmed infection of the central nervous system had a different cytokine fingerprint from those confirmed as having tumors



or autoimmune disease. This suggested the test could be used to tell the conditions apart.

Additionally, within the patients identified with central nervous system infections, the CSF cytokine fingerprint was different in cases of viral infection compared to those with non-viral pathogens, such as bacteria or fungi.

"With only a small amount of spinal fluid needed, CSF cytokine analysis could be used as one of the first diagnostic tests to rapidly triage serious central nervous system disorders and guide immediate intervention," said first author, Danielle Fortuna, MD, an Assistant Professor, in the Department of Pathology and Laboratory Medicine, at the Hospital of the University of Pennsylvania.

Worldwide, meningitis and encephalitis affect more than four million adults and children each year. "Infants and <u>young children</u> have an especially high risk of meningitis and encephalitis and the related, often serious sequelae," said Dr. Curtis. "Being able to rapidly identify a central nervous system disorder as infectious can be crucial in rapid response."

"In addition, the test could distinguish viral from non-<u>viral infections</u>, a distinction that could spare a child with a viral <u>infection</u> from an unnecessary course of antibiotics, and tailor the care toward antiviral and supportive measures as needed," said Dr. Curtis. "Moving forward, our goal is to formally validate our findings with a larger sample size that includes both adults and children for future use in the clinical arena."

More information: Danielle Fortuna, D Craig Hooper, Amity L Roberts, Larry A Harshyne, Michelle Nagurney, Mark T Curtis, "Potential role of CSF cytokine profiles in discriminating infectious from non-infectious CNS disorders," *PLOS ONE* (2018).



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