Staged Diagnostic Testing Proposed for Encephalitis

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ASPEN, COLO. — Dr. Mark J. Abzug has proposed a three-staged diagnostic approach to testing a child ill with encephalitis.

Encephalitis has an extraordinary number of possible causes for which an ever-increasing number of tests are available, he said at a conference on pediatric infectious diseases sponsored by Children's Hospital, Denver.

Under the banner of broad differential diagnoses, he listed more than 100 viruses; more than a dozen bacteria; parasites; fungi; parameningeal focus, autoimmune conditions, metabolic disorders; toxins; drugs; malignancy; and hemorrhage.

Even with extensive investigation, the etiology is elusive, according to Dr. Abzug, a professor of pediatrics at the University of Colorado, Denver.

Studies find a cause in only 25%–65% of cases.

The staged approach begins with first-line testing for the most likely causes, using CSF PCR testing for herpes simplex virus and enterovirus.

"Encephalitis is one of the most frustrating, if not the most frustrating, infectious disease consults," Dr. Abzug commented.

"Here is a child who was well, usually up to a day or two before. By the time you see the child, he or she may now be neurologically devastated," he said.

Few therapeutics are available, he added, and the damage is often irreversible in children who survive.

With so many possible causes and such poor results, Dr. Abzug offered his proposal, presented as "arguable," as an answer to a fundamental question for clinicians: Where do you start?

A reasonable approach begins with patient history, he said. It often provides more valuable information than diagnostic tests.

Dr. Abzug urged clinicians to ask about respiratory and gastrointestinal symptoms, vaccinations, family exposures to infectious diseases, recent travel, animal and insect exposures, consumption of unpasteurized dairy products, recreational activities such as spelunking and hiking, and pica/geophagia.

Seasonal outbreaks and diseases prevalent in the community also should be considered, he said.

Physical examination is not very helpful, as the findings do not usually point to a specific etiology, according to Dr. Abzug.

Focality, in particular, is almost always—although not uniformly—present in herpes simplex infections, but also can suggest other diseases.

"All that is focal is not herpes simplex disease."

His staged approach begins with first-line testing for the most likely causes. Dr. Abzug recommended cerebrospinal fluid (CSF) polymerase chain reaction (PCR) testing for herpes simplex virus and enterovirus.

The former accounts for 10%-20% of cases in the United States, the latter for up to 80% of encephalitis cases in which etiology is proved, he said.

Another 8%-10% of encephalitis cases with proven etiology are attributed to influenza virus.

In enterovirus season, do a viral culture or PCR of throat and rectal specimens, Dr. Abzug said.

During respiratory season, do a nasal wash with direct fluorescent antibody/viral culture testing for influenza, adenovirus, and other known respiratory viruses.

First-line testing also should include evaluation of symptomatic body sites and, if suggested clinically or by epidemiologic history, tests for exposure-related pathogens requiring specific treatments, such as tuberculosis.

In immunocompromised patients, do a CSF test for cryptococcal antigen and CSF PCR for varicella zoster, cytomegalovirus, Epstein-Barr virus, and (possibly) human herpesvirus 6. Always save CSF and serum, he said.

If this does not produce a diagnosis, Dr. Abzug proposed engaging in a second line of testing.

This would include Epstein-Barr serology; *Mycoplasma pneumoniae* CSF and throat PCR; testing for animal-related pathogens for which there have been relevant exposures; and tests for vector-borne pathogens, such as West Nile virus and other arborviruses, and for Lyme disease, if the epidemiology suggests possible exposures.

As a third line, Dr. Abzug recommended tests for miscellaneous pathogens if they fit the clinical context, such as parvovirus PCR and serology; human immunodeficiency virus PCR and serology; and tests for other specific exposure-related pathogens.

He also said to look for parasitic disease in the presence of a subacute course and/or eosinophilia in a child presenting with encephalitis.

"You can spend lots and lots of money, and not find anything," Dr. Abzug said, warning that no etiology will be identified in many cases.

In response to an audience question, he said he would start acyclovir treatment early on, and would continue it until herpes is ruled out or an alternate diagnosis is reached.

"Starting acyclovir until you know [the right diagnosis] is the right thing to do because the sooner you start therapy for herpes encephalitis, the better your outcome" if it turns out to be the culprit, Dr. Abzug emphasized. ■