Interpreting Serology Tricky in Epstein-Barr Mono

Clinical judgment should come first in evaluating suspected cases of EBV mononucleosis in children.

BY ROBERT FINN
San Francisco Bureau

PORTLAND, ORE. — It's easy to misinterpret the results of serology tests for Epstein-Barr virus, so these results should not substitute for clinical judgment in suspected cases of Epstein-Barr mononucleosis in children, Sarah S. Long, M.D., said at a conference sponsored by the North Pacific Pediatric Society.

"You do laboratory tests to confirm your clinical suspicion, not to go fishing," said Dr. Long of Drexel University, Philadelphia. "If you apply [these tests] to populations that are at low pretest probability of having the disease, most of your results will be false positives."

And in the specific case of Epstein-Barr virus (EBV), some of the serology results will remain positive for the rest of the patient's life, long after the clinical syndrome has resolved.

Although some patients believe that they have a chronic EBV infection, often it's because they test positive for these antibodies, and the physician can provide reassurance that the antibodies are an indication of a resolved, not a chronic, infection.

Serology is not always necessary when clinical signs and symptoms are strongly suggestive of EBV mononucleosis, Dr. Long said.

"If you have a 16-year-old with exudative pharyngitis, you get a CBC and you've got 30% atypical lymphocytosis, don't go any further," she said.

"He's got EBV mononucleosis and you're home free and can predict the rest of it. You don't need a heterophile [antibody test], you don't ever want to follow up if that test ever becomes negative, and you don't need specific serology."

On the other hand, one shouldn't turn a blind eye to the hemoglobin, neutrophil, and platelet counts. Patients with thrombocytopenia or neutropenia in addition to lymphocytosis may have leukemia.

Of the four serology tests, the Epstein-Barr nuclear antigen (EBNA) test can be the most misleading.

The virus expresses nuclear antigen only when it becomes latent, and following that, the patient will be EBNA positive for the rest of his or her life, Dr. Long said.

Therefore, a positive EBNA means that the patient does not currently have EBV mononucleosis.

The way to remember this, Dr. Long suggested, is to think of the acronym EBNA as standing for "Epstein-Barr not applicable."

In a patient with acute EBV mononucleosis, the heterophile antibody test will be positive, as will tests for IgM viral capsid antigen (VCA) and IgG VCA. EBNA will be negative. When the mononucleosis is on its way toward resolution, the heterophile antibody and the IgM VCA may be positive or negative. IgG VCA will be positive (and will remain so for life), but EBNA still will be negative.

Finally, once the mononucleosis has resolved, heterophile antibody and IgM VCA will both be negative, while IgG VCA and EBNA will both be positive. ■

Evaluating EBV Infection Based on Serology Results

Status of Infection	Heterophile Antibody	IgM VCA	IgG VCA	Epstein-Barr Nuclear Antigen
Acute	+	+	+	–
Nearly Resolved	+/–	+/–	+	–
Resolved	–	–	+	+

Source: Dr. Long

RotaTeq Efficacy Endures Through Expiration Date

BY ALICIA AULT
Contributing Writer

WASHINGTON — Merck's experimental RotaTeq vaccine was effective against moderate and severe rotavirus at the end of its shelf life, which appears to be 18 months, lead investigator Umesh Parashar, M.D., reported at the National Immunization Conference sponsored by the Centers for Disease Control and Prevention.

A new vaccine is eagerly anticipated, because rotavirus causes 440,000 deaths and leads to 2.1 million inpatient visits in children under age 5 worldwide each year, said Dr. Parashar of the National Center for Infectious Diseases at the Centers for Disease Control and Prevention (CDC). Rotavirus causes 5% of deaths in children under age 5 worldwide. In the United States, there are few deaths—only 20-60 per year—but there are 200,000-272,000 emergency department visits and 400,000 outpatient visits because of rotavirus annually.

Stan Block, M.D., a pediatrician in private practice in Bardstown, Ky., presented the RotaTeq data on behalf of trial sites in the United States and Finland.

RotaTeq is a pentavalent oral vaccine, aiming to provide protection against the G1, G2, G3, G4, and P1 strains.

From 2002 to 2004, 1,310 healthy infants aged 6-12 weeks were assigned to receive three doses of RotaTeq (at the end of shelf life) or placebo. The doses were given 4-10 weeks apart. Children with a gastrointestinal disorder, recent surgery, or acute fever or who had taken steroids within 2 weeks of the trial were excluded. RotaTeq could be given simultaneously with other vaccines, said Dr. Block.

Children were monitored for acute gastroenteritis through one rotavirus season.

There were 69 cases of rotavirus, for an overall efficacy of 72.5%. For severe acute gastroenteritis, the vaccine was 100% effective, and for both moderate and severe gastroenteritis, it was 76.3% effective, said Dr. Block.

The vaccine also appeared to be very safe. There were five potential cases of intussusception (all were in the placebo group), but all were negatively adjudicated by an independent safety monitoring board, Dr. Block said.

Children who received RotaTeq did have a statistically significant increase in temperature after the first dose, compared with placebo—13.4% of RotaTeq vaccinees, compared with 8.8% of placebo recipients. However, there was no increase in rates of fever after the second or third dose, he said. Only one child was documented to have a rotavirus vaccine strain a few days after the first dose of vaccine.

Merck is continuing a larger, 70,000-patient safety study. Preliminary results were presented at the CDC's Advisory Committee on Immunization Practices meeting in February, said Penny Heaton, director of clinical research at Merck.

So far, there have been 12 cases of intussusception in the RotaTeq group and 15 in the placebo group, she said. ■

Immunizations in High-Risk Adults: What Really Happens in Primary Care

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — Using ancillary staff to obtain patient immunization and medication histories before the patient sees the physician could go a long way toward improving immunization rates among high-risk adults, Linda Hill, M.D., said at the National Immunization Conference sponsored by the Centers for Disease Control and Prevention.

Despite long-standing recommendations for annual influenza vaccine and one-time pneumococcal vaccination for adults aged 18-49 with chronic lung, cardiovascular, metabolic, and immunosuppressive conditions, overall coverage levels are only 20% for influenza vaccine and 8% for Pneumovax. Rates are just slightly better for diabetic patients, at 27% and 15%.

The Healthy People 2010 goal is 60% for both vaccines, said Dr. Hill of the department of preventive and family medicine at the University of California, San Diego.

In an effort to determine what types of preventive health issues are addressed during a typical office visit, Dr. Hill and her associates audiotaped 37 visits of patients aged 20-50 years old with chronic conditions.

Patients were seen at three community health centers and one private practice between September 2003 and January 2005.

The average visit lasted about 13 minutes. About 5 minutes were spent taking the patient's history, half a minute on providing generic health information, another 1-2 minutes on evaluations such as explaining test results, and about a half minute on the physical exam. Only fractions of minutes each were spent offering health recommendations, such as "you should get more exercise"; discussing preventive services other than immunizations, such as mammograms; and discussing and/or planning immunizations.

Of the 24 visits in which immunizations were discussed, the discussion took a little over a minute. But when immunizations were discussed and the patient actually got a shot, less than half a minute was spent on the discussion. And during those 24 visits, no other preventive health issues were discussed, noted Dr. Hill, who is also associate director of the Center for Behavioral Epidemiology and Community Health at San Diego State University.

Of interest, on average more than half of the visit (8 of the 13 minutes) was spent discussing the history, mostly the patient's medications.

Although this isn't surprising, the actual discussion tended to be more about trying to figure out what the patient was taking and in what dose than about assessing the appropriateness of the dose or explaining to the patient what it was for.

Previous data have shown that, more than any patient characteristic, physician advice is the greatest predictor of receipt of immunizations. Moreover, physician immunization advice is more likely to occur when the physician to staff ratio is at least 1:4 and when the time spent with the physician is at least half of the total visit time.

It would make sense to have ancillary staff members obtain and document immunization and medication histories prior to seeing the physician, thereby leaving the physician more time for more complex decisions and for talking with the patient about important preventive health measures such as immunization, Dr. Hill said. ■