Expert Details Hepatitis B Tests' Clinical Value

The serologic markers of the B virus help distinguish infection with it from other hepatitis virus infections.

BY SHERRY BOSCHERT
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SAN FRANCISCO — Tests for hepatitis B surface antigen, surface antibody, core antibody, and type "e" antigen each play an important role in diagnosing infection and level of infectivity, Dr. Tina Q. Tan said at the annual meeting of the American Academy of Pediatrics.

These serologic markers of the hepatitis B virus help distinguish infection with this virus from other hepatitis virus infections, all of which cause nonspecific signs, symptoms, and laboratory findings, said Dr. Tan of Northwestern University, Chicago.

Hepatitis B prodrome can cause fever; malaise; headache; myalgia; nausea or vomiting; and right upper-quadrant pain. Jaundice or hepatomegaly may be seen, but more than 50% of infections are asymptomatic.

A positive hepatitis B surface antigen (HBsAg) test almost always indicates that the patient is either acutely or chronically infected, she said. Very rare cases have been false positives. A positive hepatitis B surface antibody (HBsAb) test indicates that the patient is immune to the hepatitis B virus or to infection with the virus, either because of vaccination or because the patient gained immunity by recovering from an acute infection.

A positive hepatitis B core antibody (HBcAb) test means different things, depending on the type of antibody. A patient who is IgM positive has recently been infected with the hepatitis B virus. Positivity to IgG antibody could indicate a past infection or a chronic infection with hepatitis B virus. In rare cases, patients who have been vaccinated against hepatitis B will have false-positive HBcAb IgG results.

Knowing what each of these tests represents leads to a relatively simple three-step process for initial interpretation of the hepatitis B panel of tests, Dr. Tan suggested:

1. If the HBsAg is negative and the HBsAb is positive, then the patient is immune to hepatitis B, either through natural infection or through vaccination.

2. If the HBsAg is positive and the HBsAb is negative, then the patient has either acute or chronic hepatitis B infection.

3. If both the HBsAg and HBsAb are negative and the HBcAb is positive, this could be a false-positive result, or the patient is either chronically infected or recovering from acute infection, or the patient may be immune to hepatitis B but the HBsAb level is too low to be detected, Dr. Tan said.

A fourth serologic test, for hepatitis B "e" antigen (HBeAg), is a marker of infectiousness. People with HBeAg have very high concentrations of hepatitis B viral DNA in their bodies and are at very high risk of transmitting the infection to others.

These serologic marker tests may need to be repeated over time to serially assess the patient's status, she said. A chronic carrier of active hepatitis B who is HBeAg positive, for example, should be followed with HBeAg tests until a negative result suggests that the level of infectiousness has dropped.

Patients who are being followed or treated for acute hepatitis B infection should get repeated marker tests to look for hepatitis B surface antigens to appear, which would indicate that they've recovered from the infection. If HBsAg tests remain negative for more than 6 months, the patient is a chronic carrier of the virus. "This is what you're trying to prevent," she said.

An estimated 78,000 new hepatitis B infections are diagnosed each year in the United States. Approximately 5,000 people each year die prematurely from chronic liver disease caused by chronic hepatitis B infection.

The childhood risk for an acute infection to become a chronic infection falls from a high of about 95% of babies who are infected at birth to about 10% of children who are infected with hepatitis B at age 5 years.

The risk for perinatal transmission of hepatitis B infection ranges from about 20% if the mother is HBsAg positive to as much as 90% if the mother also is HBeAg positive.

Use of hepatitis B vaccine and hepatitis B immune globulin can prevent perinatal transmission in about 95% of cases. ■

Hepatitis B Panel Interpretations

HbsAg	HBsAb	HBcAb	Interpretation
–	–	–	Susceptible to hepatitis B
–	+	+	Immune because of natural infection
–	+	–	Immune because of hepatitis B vaccination
+	–	+ (IgM)	Acutely infected
+	–	+ (IgG)	Chronically infected
–	–	+	Recovering from acute infection; or false-positive HBcA result; or chronic infection; or immune but HBsAb level too low to detect

Notes: HBsAg is hepatitis B surface antigen. HBsAb is hepatitis B surface antibody. HBcAb is hepatitis B core antibody.
Source: Dr. Tan

ELSEVIER GLOBAL MEDICAL NEWS

New Meningococcal Vaccine Immunogenic, Tolerated in Infants

BY MARY ANN MOON
Contributing Writer

A new tetravalent meningococcal vaccine proved to be immunogenic and well tolerated in infants in a phase II study, investigators reported in JAMA.

The tetravalent meningococcal vaccine that is currently licensed in the United States is recommended for all 11- to 18-year-olds, but was found to be poorly immunogenic in infants so is not licensed for use in children under age 2 years.

Because infants are the age group at highest risk for meningococcal disease, a new vaccine was developed and tested in an open-label, randomized controlled trial involving 421 infants in England and Canada.

The new vaccine—MenACWY—covers serogroups A, C, W-135, and Y. It was developed by Novartis Vaccines and Diagnostics, which funded this phase II study.

Two different primary three-dose schedules were evaluated: a single dose at 2, 3, and 4 months of age, and a single dose at 2, 4, and 6 months of age.

A two-dose schedule (a single dose at 2 and 4 months) also was assessed.

This was to examine the new vaccine's safety and efficacy when given according to the different routine immunization schedules in different countries, said Dr. Matthew D. Snape of the Oxford Vaccine Group, University of Oxford (England), and his associates.

A subset of infants also received a booster dose at 12 months of age, since some waning in antibody titers was expected, as has been observed after immunization against serogroup C alone. Another subset of subjects received a reduced dose of the vaccine at 12 months as a probe for immunologic memory.

One month after the immunization series was complete, 92% of the infants who had received the 2-, 3-, and 4-month schedule showed human complement serum bactericidal antibody (hSBA) titers of 1:4 or better against all four serogroups, which is considered protective.

Similar results were obtained with the 2-, 4-, and 6-month schedule, except that the proportion of infants with protective hSBA titers against serogroup A was lower, at 81%, Dr. Snape and his associates said (JAMA 2008; 299:173-84).

The infants who received MenACWY only at 2 and 4 months had less of a response. About 80% showed hSBA titers of 1:4 or better for serogroups C, W-135, and Y, and the response for serogroup A was 60%.

All serogroups showed a waning in antibody titers by 12 months of age. The subjects who received a booster at this time showed a 'reassuring' increase in titers.

All serogroups, particularly serogroup A, showed a waning in antibody titers by 12 months of age. The subjects who received a booster at this time showed a "reassuring" increase in titers, suggesting that a booster dose of MenACWY may be required to provide sustained protection, the investigators said.

Results in the subjects who received an immune challenge at 12 months suggested that the new vaccine did induce immunologic memory, they added.

The new vaccine did not appear to affect the immunogenicity of other routine vaccines given concomitantly, including vaccines against hepatitis B, diphtheria, tetanus, and *Haemophilus influenzae* type b.

There were 66 adverse events reported during the study period, but only 2 were thought to be potentially related to the study vaccine. Both resolved spontaneously.

The first was a brief episode of idiopathic thrombocytopenic purpura after the booster dose, which occurred in a child who had had a viral-like illness with oral ulcers and rash 2 weeks previously.

The second was an episode of supraventricular tachycardia, and it was found that this child had a history of the arrhythmias and had been enrolled in violation of the study's exclusion criteria.

The most important limitation in this study was that the number of subjects was "too small to draw firm conclusions regarding the safety of this vaccine, and therefore further studies will be required," Dr. Snape and his associates noted.

Nevertheless, in an editorial comment accompanying this report, Dr. Lee H. Harrison of the infectious diseases epidemiology research unit of the University of Pittsburgh, said the study "represents a substantial advance in the vaccine prevention of meningococcal disease."

It is not yet known whether the new vaccine prevents pharyngeal carriage of meningococcal organisms, "a major public health benefit" that has been noted in other conjugate vaccines such as those against pneumococcal disease and *Haemophilus influenzae* type b, Dr. Harrison said (JAMA 2008;299:217-9).

Given that the MenACWY vaccine "behaves immunologically like a conjugate vaccine," it would be expected to prevent pharyngeal carriage, which would in turn prevent transmission among the unimmunized population and thus promote herd immunity. ■