Tests Spot 90% of Primary Immunodeficiencies

Patients with recurrent infections can be screened for an immune deficiency by using two blood tests.

By Bruce Jancin
Denver Bureau

Keystone, Colo. — Two screening lab tests—a CBC and quantitative immunoglobulins—are sufficient to diagnose more than 90% of all patients with primary immune deficiencies, Dr. Erwin W. Gelfand said at a meeting sponsored by the National Jewish Medical and Research Center.

When should a nonimmunologist become suspicious that a patient has an underlying immunodeficiency?

“When you think of it—and you should always be thinking of it in a patient with recurrent infection. Immune deficiencies are not rare, but not rare, either,” said Dr. Gelfand, chairman of pediatrics at the center, as well as professor and vice chairman of pediatrics and professor of immunology at the University of Colorado, Denver.

For example, selective IgA deficiency is present in 1 in 400-700 individuals, most of whom have no idea they have an immunodeficiency disorder.

“If you go to an allergy clinic or inflammatory bowel disease clinic or rheumatology clinic, the prevalence of IgA deficiency is much higher,” Dr. Gelfand said.

Recurrent infection is by far the most common symptom of primary immunodeficiency. But differentiating recurrent infections in the setting of normal immune function from those associated with an underlying immunodeficiency is often clinically difficult. These days infections in patients with a primary immunodeficiency are usually mild. Affected patients present with otitis media, sinusitis, and low-grade pneumonia, not the osteomyelitis, mastoiditis, recurrent consolidating pneumonias, and other severe infections emphasized in older textbooks.

“Also, the age at which patients present with primary immunodeficiency has changed drastically in recent decades. When I grew up in this field, all the patients presented in the first 2-3 years of life. It was amazing. Now, for every kid I see with a primary immune deficiency—particularly antibody deficiencies—under 5 years of age, I see two or three adults. And we’re not just talking about adults in their 30s or 40s, but even in their 60s who present with a genetic disease. It can take a long time,” the physician observed.

When a primary immune deficiency is suspected in a patient, it is often helpful to consider the patient’s history and symptoms in terms of the four components of specific host resistance: antibody, complement, phagocytic cells, and cell-mediated immunity.

Specific infections can often be matched to specific immune defects. For example, deep-seated Staphylococcus aureus infections suggest a phagocytic cell defect. Recurrent viral and fungal infections in failure to thrive, persistent diarrhea, and Pneumocystis carinii infections are associated with defective cell-mediated immunity. Infections involving encapsulated organisms, such as Hemophilus influenzae and S. pneumoniae suggest a B-cell or complement defect.

Dr. Gelfand urged physicians to “play the odds” when searching for immune deficiency.

“Seventy-five percent of all primary immunodeficiencies are disorders of antibody production,” he said.

Cell deficiencies are present in infancy because they’re incompatible with survival. Complement defects are rare, and phagocytic cell defects are also pretty rare,” according to the immunologist.

Most primary antibody deficiencies feature both low serum IgG and low-to-absent IgA levels. Dr. Gelfand considers an IgG level below 200 mg/dL in a child less than 1 year old of potential concern. Ditto to below 300 mg/dL in a 1- to 2-year-old and less than 300-400 mg/dL in anybody older.

Primary immune deficiencies are far more common in males because many culprit genes are located on the X chromosome. A history of atopic disease greatly reduces the odds that an immune deficiency is present.

Evaluation for possible immunodeficiency in a patient with recurrent infections is one circumstance where family history is of little value. It’s been important to me on maybe one occasion in 1,000 patients,” Dr. Gelfand recalled. “A 16-year-old came in and said, ‘My brother has X-linked agammaglobulinemia.’ That was very helpful. But most of the time it’s very difficult to tell anything from the family history,” he noted.

Medicinal News

New Test for Identifying Sepsis Outlined by Swiss Researcher

By Jonathan Gardner
Contributing Writer

Glasgow, Scotland—Swiss researchers have identified a hormonal precursor that may make it easier for physicians to identify patients suffering from sepsis, according to a study presented at the 8th European Congress of Endocrinology.

The substance is copeptin, a precursor to vasopressin, which is produced when the body undergoes stress such as septic shock. Vasopressin is unstable and has a short half-life, making it difficult to use to identify patients suffering from sepsis. Copeptin, on the other hand, is more stable and is derived from the same precursor molecule.

A team of researchers from the departments of endocrinology and internal medicine at University Hospital Basel, Switzerland, led by Dr. Mirjam Christ-Crain, evaluated 101 consecutively critically ill patients over a 9-month period and compared their relative serum copeptin levels with those of 50 healthy controls.

Copeptin levels were measured at admission, day 2, and hospital discharge or death. Copeptin levels were identified in the blood using a test that will soon be available commercially from the German medical equipment manufacturer Brahms.

Of the 101 critically ill patients, 53 had sepsis, severe sepsis, or septic shock; 48 had systemic inflammatory response syndrome (SIRS). At admission, patients with SIRS had a median copeptin level of 27.6 pmol/L of blood, those with sepsis 30 pmol/L, those with severe sepsis 71.6 pmol/L, and those with septic shock 171.5 pmol/L. In comparison, healthy control patients had a median copeptin level of 5 pmol/L, Dr. Christ-Crain said.

Patients with sepsis, severe sepsis, or septic shock who died had median copeptin levels of 171.5 pmol/L, compared with 86.8 pmol/L among those who survived.

Septicemia is the 10th leading cause of death in the United States, claiming 73,464 lives in 2004, according to the Centers for Disease Control and Prevention.

“Copeptin is a novel tool to assess the prognosis of sepsis,” Dr. Christ-Crain said. “It might help to guide the resource allocation of hospital care to those patients especially in need for intensive surveillance.”