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 common, but they're 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 immunodeficiencies 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 that long," the physician observed.

When a primary immune deficiency is suspected in a patient, it's 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, failure to thrive, persistent diarrhea, and *Pneumocystis carinii* infections are associated with defective cell-mediated immunity. Infections involving encapsulated organisms such as *Haemophilus influenzae* and *S. pneumoniae* suggest a B-cell or complement defect.

'Play the odds' when searching for immune deficiency: 75% of all primary immunodeficiencies are disorders of antibody production.

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.

"T-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 a level 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. ■

Think Stress Hyperglycemia in Nondiabetic Sepsis Patients

BY PATRICE WENDLING
Chicago Bureau

NICE, FRANCE — A new study suggests that stress hyperglycemia may be an important predictor of morbidity and mortality in nondiabetic patients with sepsis.

The study included 242 nondiabetic patients hospitalized with severe sepsis in three hospitals in southwestern Greece during a 1-year period. Hyperglycemia was defined as an admission or in-hospital fasting glucose level of 126 mg/dL or more, or a random blood glucose level of 200 mg/dL or more on two or more evaluations.

Stress hyperglycemia—a transient elevation of blood glucose levels due to various factors including stress, injury, and surgery—was present in 20% of the patients, Dr. Lydia Leonidou reported at the 16th European Congress on Clinical Microbiology and Infectious Diseases.

Moreover, a significantly higher percentage of septic patients who had stress hyperglycemia died, compared with patients who had normal glucose levels (43.4% vs. 13.2%).

Stress hyperglycemia was not related to a genetic predisposition to diabetes mellitus. Only 6% of hyperglycemic patients had a first-degree relative with diabetes, compared with 11% of normal glycemic patients, reported Dr. Leonidou and her colleagues at the University of Patras (Greece).

Sources of infection in all patients were: respiratory tract 42%, urinary tract 35%, intraabdominal 16%, central nervous system 3%, soft tissue 3%, and endocarditis 1%. Hyperglycemic patients were older than normal glycemic patients, but the difference was not statistically significant (73.4 vs. 65.7 years). There was no significant difference in gender, body mass index, C-reactive protein, blood cultures, and hospitalization days between groups. Hemoglobin A_{1c} levels were significantly higher among hyperglycemia patients (5.73% vs. 5.44%) but were within the normal range of 4-5.9%.

Patients with stress hyperglycemia had a significantly higher sepsis-related organ failure assessment (SOFA) score than patients with normal glycemia (mean 4.9 vs. 2.9). This finding left some in attendance to question whether stress hyperglycemia caused poor outcomes or was just another surrogate marker like SOFA scores. Lead author Dr. Charalambos Gogos responded, "We believe that hyperglycemia is not [just] a surrogate marker, but something you have to fight in your patients with good glycemic control." ■

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.

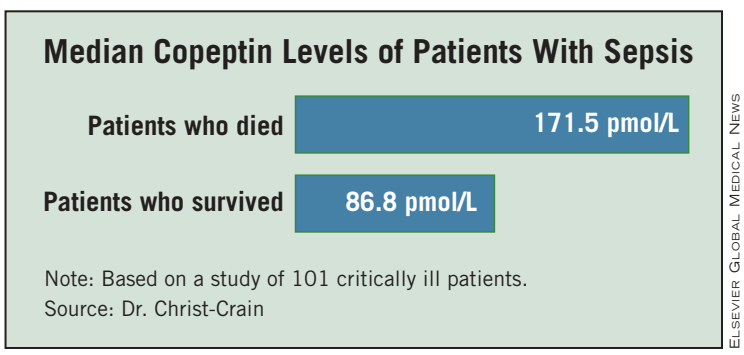
A team of researchers from the departments of endocrinology and internal medicine at University Hospital, Basel, Switzerland, led by Dr. Mirjam Christ-Crain, evaluated 101 consecutive critically ill patients over a 9-month period and compared their relative serum copeptin levels with those of 50 healthy 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 50 pmol/L, those with severe sepsis 73.6 pmol/L, and those with septic shock 171.5 pmol/L. In comparison, healthy controls 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 blood levels of 171.5 pmol/L, compared with 86.8 pmol/L among those who survived.



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Septicemia is the 10th leading cause of death in the United States, claiming 33,464 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." ■