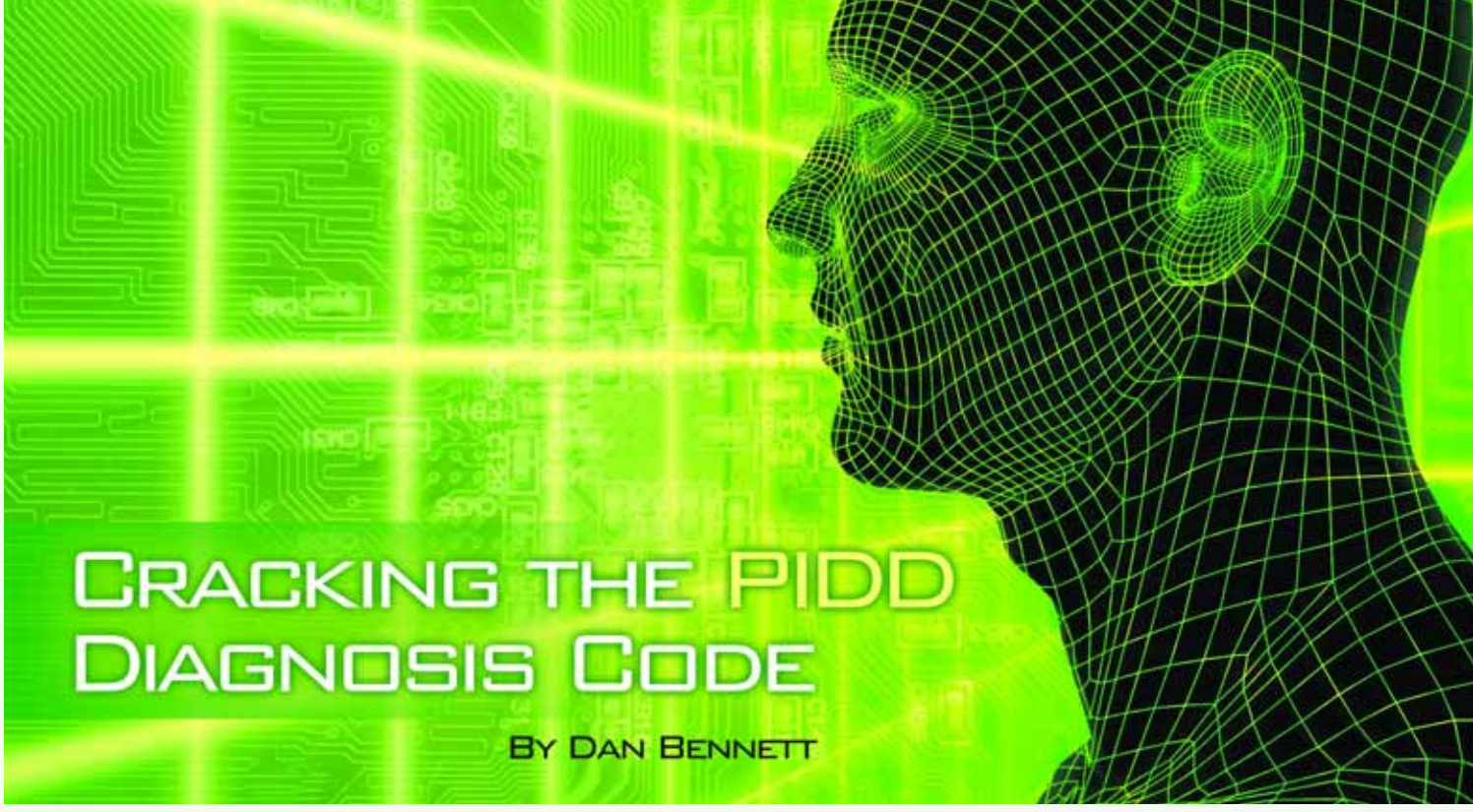


Cracking the PIDD Diagnosis Code

By Dan Bennett

Some medical diagnoses are easier to determine than others. Patients with primary immune deficiency diseases (PIDDs) know that a diagnosis is not always easy for their physicians. Many patients go several years and endure many tests before an accurate diagnosis arrives. Clearly, few things involving PIDD are obvious.

"This is a common story," said Steven Holland, a physician at the National Institute of Allergy and Infectious Diseases at the National Institutes of Health. "Like many things, florid cases are easy to identify, but subtle ones are hard. Also, the doctor—and the parent—are usually reluctant to think about the unusual, when the symptoms can also be due to usual things, such as a cough that can be a cold or pneumonia; a fever that can be a virus or an abscess. In my experience, the main challenges come for the families after the diagnosis. Most [PIDD] syndromes are relatively rare, and that means that the number of doctors and nurses who are familiar with them is small."

The result is often a delay in diagnosis and treatment. "These kids and adults are often stuck in emergency rooms or in new cities trying to get help on the one hand, and educate everyone around them on-the-fly about their disease," Holland said. "And if they get someone who is unaware of their own ignorance, the results can be devastating as well as frustrating."

Once a healthcare professional suspects PIDD, certain tests are suggested, but again, with PIDD those tests vary. "It all depends on the part of the immune system that is impaired," Holland said. "Usually I use the specific infections or syndromes—viral, bacterial, localized or disseminated—to decide which area to test, such as antibody, neutrophils or cell-mediated. There are standard evaluations that typically look at antibody defects first—the most common causes—and then go down a specific pathway after."

Before the testing, there are the clues. The Jeffrey Modell Foundation publishes the 10 Warning Signs of PIDD (see the tear-off attachment). The Immune Deficiency Foundation (www.primaryimmune.org) quotes a recent survey showing that only 12 percent of patients with a primary immune deficiency disease were initially diagnosed before age 1. Though the majority were diagnosed before reaching age 12, approximately 43 percent were not diagnosed until they reached adulthood. "Half of all persons with PIDD are not diagnosed until they are adolescents or older," the survey concludes. "One problem for early diagnosis is that the vast majority of patients have no family history of immune deficiency disease." Complications emerge from the lack of diagnosis. "The majority of patients suffered two or more hospitalizations before diagnosis," the survey states. "The majority experienced ear infections, bronchitis and pneumonias before diagnosis. Treatment significantly reduces the burden of disease."

IDF also provides clinical guidelines to physicians to help them recognize symptoms. According to an IDF publication, "The Clinical Presentation of the Primary Immunodeficiency Diseases (Physician's Primer)," "[a]lthough the initial description of patients with primary immunodeficiency diseases focused on their increased susceptibility to infection, these patients may also present with a variety of other clinical manifestations." The publication emphasizes that, "in some

patients, the noninfectious manifestations, such as autoimmune disease and/or gastrointestinal disease, may be the predominant clinical expression of their underlying immunodeficiency."

The primer goes on to explain that an increased susceptibility to infection is the hallmark of primary immune deficiency diseases. "In most patients, this is manifested by recurrent infections. Often, individual infections are not more severe than those that occur in a normal host. Rather, the striking clinical feature is the recurring and/or chronic nature of the infections. Typically, the infections do not occur only in a single anatomic site, but usually involve multiple organs or multiple sites within the same organ."

Heather Montgomery experienced symptoms as a young child, but it took several years for a proper diagnosis. She chronicled her experiences in a recent essay.

"When I was 18 months old, I was hospitalized with flu-like symptoms and a high fever," Montgomery wrote. "Over the next four weeks, my condition got worse with each day. My platelet count and white blood counts went way down and I was put into isolation. The doctors were doing tests every day, looking for some disease that caused my illness."

Troubled with a variety of ailments, Montgomery was kept away from other people, given antibiotics and placed on a special diet. This was her treatment for the next several years. "Back then, the medical community did not look for immune deficiencies in girls," Montgomery wrote. "Therefore, I was tested for leukemia, lymphoma and other forms of cancer. I was also tested for different types of lung diseases."

Finally, a diagnosis of agammaglobulinanemia emerged. Later, complications with insurance and much-needed medical equipment became commonplace for Montgomery. Numerous medical ailments have followed, but Montgomery has pressed on with support from others. "I'm sure anyone who has had to deal with a rare illness knows how hard it is to deal with all of the complications that come from it," she wrote. "I have been fortunate enough to have supportive friends and family members."

Charlotte Cunningham-Rundles, a pediatric immunologist at Mount Sinai Medical Center, says delays in diagnosis are common. "The data says that there can be a long lag time, four to eight years in some cases," Cunningham-Rundles stated. "Adults can look pretty well and still be immune deficient. Also, for adults, specialty care is divided up a lot, and maybe the overall theme is not being appreciated." Among the most common tests, she said, are complete blood count (CBC), immune globulins and antibody tests.

For Lisa Russo, a long break in symptoms meant a delayed diagnosis. She was ill as an infant, but her childhood and early adulthood were mostly free of symptoms, with the exception of the common cold. Two years ago, at 42, Russo developed bronchitis that wouldn't clear up. "Within two days off of the antibiotics, I was getting sick again," Russo said. "My physician has a friend who is an immunologist at Princeton, and after consultation they started testing my immune system. Now I've been on IVIG therapy for eight months, and the results have been amazing—no bronchitis since then."

Mike Blaese, medical director of the Immune Deficiency Foundation, noted internists and family-practice physicians spend little time in immunology training related specifically to these diseases during medical school, so they often don't consider more advanced illness that a specialist might suspect. One of the main challenges, Blaese says, is perception. With so few people, relatively speaking, diagnosed with PIDD, physicians perhaps tend to look past the possibility. Adding to the complexity is the fact there are more than 100 diseases under the PIDD umbrella. "What the IDF has been doing for 25 years is helping get the information out to healthcare professionals," Blaese said. "There have been all sorts of publications and clinical care guidelines. With the work IDF has done, and with the work of the Jeffrey Modell Foundation and other organizations, there has been a real improvement in information awareness regarding these subjects."

That wave of information is also intended for patients, with the parents of young patients a primary target of the ongoing campaign. "If nobody raises the suspicion, often the diagnosis will not happen," Blaese said. "If parents suspect such a problem and can somehow get referred to one of the websites dedicated to these diseases, then they should make a printout, take it to the doctor and ask the question: 'Is it possible my child has this?'"

Many parents can certainly relate to the frustration in achieving a diagnosis.

Marlo Wright's daughter, Chelsea, began getting high fevers starting at 8 months old, along with double ear infections. Nine years, 14 surgeries, three near-death situations and 59 doctors later, a specialist in Ohio diagnosed primary immune deficiency. "There were always these what-ifs, but never a clear diagnosis," said Wright, who lives in the Los Angeles area. "When I look back now, I can't count the number of times I was called overreactive."

Last year, Wright went to a NICE Day event in Carlsbad, Calif., and was connected to the experts at UCLA, where the now 12-year-old Chelsea was diagnosed with common variable immune deficiency, lupus and juvenile rheumatoid arthritis. Chelsea now receives subcutaneous immune globulin treatment once a week. "I couldn't be happier with the care she has now," Wright said. "My advice to others is to never stop talking on behalf of your child, never stop asking questions. You are your child's advocate." ◪

Please see companion article, "Quest for the Elusive Diagnosis" on Page 27.