

# PI: The Road to Diagnosis & Treatment

By Abbie Cornett



Despite the uptick in diagnoses of primary immunodeficiency diseases, a lack of awareness about them persists, even among physicians, so locating an immunologist is crucial for proper diagnosis and treatment.

“THE ROAD LESS traveled is frequently the more difficult path” is an adage that is particularly true for individuals with a primary immunodeficiency disease (PI), whose path to a correct diagnosis and treatment often takes years. And, while the delay in diagnosis has been significantly decreased today, taking between five and seven years, this isn’t true for all. Some PI patients still aren’t correctly diagnosed for more than a decade,<sup>1</sup> leading to lifelong physical, mental and financial complications for patients and their families.

Delayed diagnosis can be caused by many factors. In the past, PI was considered primarily a childhood disease, so it wasn’t suspected in adults.<sup>2</sup> Yet, even though today it is recognized PI can also develop in adults, many healthcare practitioners are unfamiliar with the disease and its symptoms, so it is often overlooked. What’s more, symptoms can manifest in different ways, many of which are mistaken for more common conditions such as sinus and ear infections, pneumonia and gastric problems. Left undiagnosed, these recurrent infections can lead to chronic lung disease.<sup>3</sup>

### How Rare Is PI?

PI is a term used to describe more than 300 disorders related to the dysfunction of the immune system. While PIs are considered rare, they are not nearly as uncommon as once thought. Because of increased awareness and improved diagnostic tools, more people are being diagnosed than in the past. A 2005 survey by the Immune Deficiency Foundation (IDF) estimated there were 250,000 people in the United States diagnosed with a PI.<sup>4</sup>

### Getting Diagnosed with a PI

Specific warning signs (symptoms) are indicative of PI, and they differ between adults and children (Table 1). When these symptoms present, many patients are unaware or unsure when they should see an immunologist. According to Terry O. Harville, MD, PhD, medical director in the special immunology laboratory at the University of Arkansas for Medical Sciences, an immunologist should be consulted as soon as an immune disorder is suspected, most importantly to prevent long-term complications.

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Immunologists are specially trained in diagnosing and managing problems related to the immune system. In the U.S., becoming an immunologist requires at least an additional

**Table 1. 10 Warning Signs of Primary Immunodeficiency<sup>14</sup>**

Children	Adults
1. Four or more new ear infections within one year.	1. Two or more new ear infections within one year.
2. Two or more serious sinus infections within one year.	2. Two or more new sinus infections within one year, in the absence of allergy.
3. Two or more months on antibiotics with little effect.	3. One pneumonia per year for more than one year.
4. Two or more pneumonias within one year.	4. Chronic diarrhea with weight loss.
5. Failure of an infant to gain weight or grow normally.	5. Recurrent viral infections (colds, herpes, warts, condyloma).
6. Recurrent, deep skin or organ abscesses.	6. Recurrent need for intravenous antibiotics to clear infections.
7. Persistent thrush in mouth or fungal infection on skin.	7. Recurrent, deep abscesses of the skin or internal organs.
8. Need for intravenous antibiotics to clear infections.	8. Persistent thrush or fungal infection on skin or elsewhere.
9. Two or more deep-seated infections, including septicemia.	9. Infection with normally harmless tuberculosis-like bacteria.
10. A family history of primary immunodeficiency disease.	10. A family history of primary immunodeficiency disease.



nine years of training beyond a bachelor's degree. After obtaining a medical degree, physicians undergo three years of training in internal medicine or pediatrics and must pass the exam of either the American Board of Internal Medicine or the American Board of Pediatrics. To become an immunologist, a two-year fellowship in an allergy/immunology training program is required. They then must pass the certifying examination of the American Board of Allergy and Immunology (AAAAI). Immunologists who have the FAAAAI designation in addition to MD have met many of the highest standards in the field.<sup>6</sup>

The first step in finding an immunologist is to get a referral from a primary care physician.

Due to this extensive training, immunologists know which tests need to be performed to determine if patients have adequate levels of immunoglobulins (antibodies that immune cells make to fight off bacteria, viruses and other harmful invaders), and whether those immunoglobulins are responding appropriately. The most common tests include a quantitative immunoglobulin panel, antibody titer assays, basic B and T cell flow cytometry panel and lymphocyte proliferation assays.<sup>5</sup> These tests combined with a physical examination and a medical and family history provide the

information possible for immunologists to correctly diagnose a PI and select the best course of treatment.

### Finding an Immunologist

Finding an immunologist is often easier said than done. As of 2015, there were only 4,630 immunologists actively practicing in the U.S.,<sup>7</sup> which is just a 7.1 percent increase since 2010.<sup>8</sup> And, a report released in February 2017 by the Association of American Medical Colleges states the numbers of new primary care physicians and other medical specialists are not keeping pace with the healthcare demands of a growing and aging population. Specifically, it projects shortfalls in non-primary care specialties will range between 33,500 and 61,800 by 2030.<sup>9</sup>

Locating an immunologist can be even more difficult for patients who live near no major medical centers or in rural areas, necessitating travel hours away or even to different states for treatment. Patients in rural areas also face greater challenges in treatment. According to Dr. Harville, the secret to long-distance treatment success is communication between the patient and all parties providing care. It's imperative the immunologist be notified as soon as the patient becomes ill to enable working with either their primary care physician or emergency room doctor to coordinate care.

The first step in finding an immunologist is to get a referral from a primary care physician. In fact, depending on the patient's type of insurance, a referral may be mandatory. Without a referral, many insurance plans will not pay for the visit, requiring patients to pay out of pocket. Before scheduling an appointment, patients should examine their policy's explanation of benefits to be sure their visit is covered.

When trying to find an immunologist without a referral, patients have a number of helpful resources available.

Organizations such as the Jeffrey Modell Foundation, Immune Deficiency Foundation (IDF), Clinical Immunology Society and Wellness.com have drop-down menus on their websites that display immunologists by ZIP code (Table 2). Another option for patients is to contact patient support groups in their area for a recommendation.

## Understanding Treatment Options

PIs are usually treated with immune globulin (IG) replacement therapy,<sup>10</sup> which can be administered either intravenously (IVIG) or subcutaneously (SCIG). The differences between the two administrations include where therapy is given, how often treatment is required and severity of side effects.

IVIG administered through a vein or port in the hospital, clinic or home is typically given every three to four weeks. While IVIG is well-tolerated by most patients, medications may be required to help manage side effects,<sup>11</sup> which can range from mild to severe and can include headache, nausea, chills and backaches. In rare instances, patients can experience life-threatening side effects such as aseptic meningitis, renal dysfunction, thrombolytic events (clotting) and anaphylaxis.<sup>12</sup>

SCIG, on the other hand, is administered in smaller volumes infused under the skin using small needles and an infusion pump.<sup>13</sup> Treatment is more frequent, typically once a week, which helps patients maintain more consistent antibody levels, and eliminates the issue of low trough levels that can occur with IVIG as infusion time nears. Side effects of SCIG are also reduced and, in some cases, eliminated so

the need for pre- and postmedication is reduced. The most common side effect is local irritation (redness, swelling, itching, blanching) at the needle sites.

SCIG may be the best option for patients who live far from their immunologist. An immunologist can give therapeutic orders for a home healthcare agency to administer the SCIG for patients or train patients to infuse it themselves.

However, receiving care at home gets more complicated if SCIG is not an option. Patients receiving IVIG at home need to be monitored by a healthcare professional trained to administer IVIG and knowledgeable about the potential adverse reactions that can occur.

In addition to treatment with IVIG or SCIG, an immunologist may prescribe prophylactic medications such as antibiotics, steroids and others.

## A Difficult But Not Impossible Road to Diagnosis

Today, with advances in treatment, communication and home healthcare, the road to treatment, while still difficult, is easier than it has ever been. The key is knowing when and how to seek an immunologist. Then, with the correct diagnosis and treatment, most patients can lead happy and productive lives. ■

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**Table 2. Sources for Locating an Immunologist**

**Immune Deficiency Foundation:**

[primaryimmune.org/about](http://primaryimmune.org/about)

**Clinical Immunology Society:**

[clinimmsoc.org/CIS/Find-an-Immunologist.htm](http://clinimmsoc.org/CIS/Find-an-Immunologist.htm)

**Jeffrey Modell Foundation:**

[jmfworld.com/information-booth/find-an-expert](http://jmfworld.com/information-booth/find-an-expert)

**Wellness.com:**

[www.wellness.com/find/immunologist](http://www.wellness.com/find/immunologist)