Understanding primary immunodeficiency

A healthy human body has an elaborate system in place to rid itself of infectious microorganisms as well as to protect against future infections. So, when we're afflicted with a common illness, such as a cold, flu, sinus infection, or ear infection, we expect to recover fully after a somewhat predictable period of discomfort—the time it usually takes for the body's immune system to conquer the infection.

But in people who are either born with or acquire an impaired immune system due to a hereditary or genetic defect—a condition known as primary immunodeficiency, or PI—the body is unable to fight off invading microbes efficiently, which results in recurrent infections (e.g., ear infections, sinusitis, bronchitis, or pneumonia), infections that don't improve with treatment, or unusually severe infections.

"There are over 150 different types of primary immunodeficiency, but the condition is highly under-recognized both among patients and doctors," explains allergist/immunologist Dr. Binod Thakur. "People are either born with PI or they acquire it when, at some point, their body stops making antibodies. Fortunately, most forms are very rare, especially the severe ones. The acquired forms are more prevalent, and most are related to an antibody or immunoglobulin deficiency."

Dr. Thakur also points out that primary immunodeficiency and secondary immunodeficiency are distinct from one another. People with secondary immunodeficiency develop immune problems, as the name implies, secondary to another identified medical problem or a particular treatment for a medical problem, such as HIV/AIDS, diabetes, long-term corticosteroid treatment, or chemotherapy for cancer or leukemia.

Experiencing two or more of the following warning signs justifies speaking with a doctor about the possible presence of an underlying primary immunodeficiency:

*Eight or more new ear infections within one year
*Two or more serious sinus infections within one year
*Two or more months on antibiotics with little effect
*Two or more pneumonias within one year
*Failure of an infant to gain weight or grow normally
*Recurrent, deep skin or organ abscesses
*Persistent thrush in the mouth or elsewhere on the skin after age one
*Need for intravenous antibiotics to clear infections
*Two or more deep-seated infections
*A family history of primary immunodeficiency.

Broadly speaking, PI stems from a problem either with the cellular or humoral components of the immune system. For example, if the neutrophils or macrophages—types of white blood cell that support immune defense by "eating" bacteria—are either diminished or impaired, bacterial infection can result. Also, the diminished number or improper function of lymphocytes, another form of white blood cell, can lead to different types of fungal, viral, or chronic infections.

PI stemming from the humoral component can be categorized into at least two types: those related to the complement system (various proteins that assist, or "complement," the antibodies) and those related to the antibodies themselves.

Immune problems related to the complement system are quite rare and can lead to infections such as meningitis and respiratory infections. Problems with the antibodies are much more common and can be classified into several different subtypes. Two of the more prevalent forms (among the acquired types) are common variable immunodeficiency, in which multiple immunoglobulin classes are affected, or selective

immunoglobulin deficiency, in which the immune system is able to fight off certain bacteria but not others.

In treating PI, certain basic principles apply to all cases. “If you get an infection, you need prompt treatment with appropriate antibiotics. And, since you can’t effectively fight off infection, it’s important to take preventive measures to avoid exposure to contagious people. I also highly recommend—especially if you have an immune problem stemming from the humoral component—that you make sure your vaccination status is kept up to date. Maintaining general good health and a positive attitude is helpful, as well,” Dr. Thakur comments.

He goes on to caution that live vaccines are contraindicated for those with a severe form of PI or cellular PI. These individuals can, for instance, receive a flu or polio shot with killed vaccine, but receiving the oral form of these vaccines with a live (albeit weakened) virus would be disastrous.

Beyond the basic treatment principles, there are also specific treatments for certain immune-system defects. For example, people with severe antibody deficiency leading to chronic or recurrent infection may benefit from immunoglobulin replacement via intravenous or subcutaneous infusion. “This treatment doesn’t cure the condition permanently. It requires ongoing replacement, every four to eight weeks for the long term, and for most people, this is lifelong. However, it is very effective and has saved many lives of those who would otherwise have died,” says Dr. Thakur.

Another specific treatment is the use of biological agents—or immuno-modulators—in patients with phagocytic defects. Some severe PI cases can also be treated with bone marrow transplant. “Work is also being done on genetic modification for certain severe immunodeficiencies, which involves correcting the defective gene and replacing it in the patient,” Dr. Thakur adds.

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