

PI and Allergies

Differentiating between infections and allergies in PI patients is the only way to ensure proper treatment.



By Jim Trageser

HAVING A PRIMARY immunodeficiency disease (PI) and allergies can seem illogical since PI is caused by a weakened or compromised immune system whereas allergies are the result of an overactive immune system. But, according to Roger Kobayashi, MD, an allergist-immunologist in Omaha, Neb., the seeming contradiction is based on an outdated understanding of what constitutes a compromised immune system. “The old concept that all these immune abnormalities were separate has been reanalyzed and changed,” he explained. Rather than referring to an immune deficiency, Dr. Kobayashi says he prefers the term “immune dysregulation.”

“In the old days, it was thought that if your immune system did not react to bacteria, cancer or other agents, you had an ‘immune deficiency,’” says Dr. Kobayashi. “If your immune system made a mistake and attacked things that were ordinarily harmless — peanuts, cat dander or pollen — that would be called ‘allergy.’ If your immune system made a mistake and went after itself, it would be called ‘autoimmune

disease.’ If it turned on inappropriately or did not turn off when it was supposed to, it would be called ‘autoinflammation.’ It was thought that all four of these things were separate and different — but nothing could be further from the truth. If you have part of the immune system that coordinates the immune response, but it doesn’t function correctly, then you can visualize how the control mechanism would create problems in one or all four of the immune abnormalities.”

Dr. Kobayashi offers the following illustration of what happens when the immune system’s controlling mechanism malfunctions: “If your dog is normal — happy and healthy — when you come home from work, the dog gets all excited, wags its tail, jumps on you, licks your face and everything is fine. If a crook comes in, the dog gets all excited, starts barking and might bite that individual. If the mailman goes by, the dog might bark for a little while, and when the mailman leaves, the dog stops barking. If your kids or relatives come by, and the dog knows them, the dog will not do anything.

Now, imagine your dog gets hit on the head. Same dog. You come home, the dog gets angry and bites you. That's autoimmune disease (lupus, rheumatoid arthritis). Ordinarily, your immune system would not attack itself, but something is wrong. All of a sudden, a criminal or burglar comes into your house. The dog doesn't do anything! That's immune deficiency as we know it. What happens if your kids come home? Instead of being happy, the dog bites them, too! That's allergy; it's attacking things that are normally harmless. What happens if the dog continues to bark and go nuts after the mailman leaves? Autoinflammation. How can you have immune deficiency and allergies at the same time? You go back to the central controlling mechanism and how it can manifest in different ways."

Understanding PI and Allergies

PIs are a group of more than 350 rare, chronic disorders caused when there is a shortage or improper functioning of one or more of the five major classes of antibodies in the human immune system.¹ These classes are immunoglobulin G (IgG), the most common, which protects against bacteria and viruses in the circulatory system; IgA, which coats the intestines and other mucous membranes; IgM, the primary antibody released by the body to fight infection; IgE, used to fight parasites, and also associated with allergic reactions; and IgD, which is the least understood, but is found in trace amounts in the bloodstream.²

When the immune system is working properly, the body recognizes a hostile invader such as a virus, bacteria or fungus is attacking it and produces the appropriate antibodies to isolate and remove or kill the invader. A healthy immune system will even help protect against dangerous developments in the body such as cancer cells.

An allergic reaction occurs when the body's immune system reacts inappropriately to the presence of a benign substance such as pollen, animal dander, mold, etc., by producing and releasing IgE antibodies, which stimulate cells in the body to release certain chemicals (histamines) as if the host was under attack. These histamines result in nasal congestion, runny nose, itchy skin or hives.³

Diagnosing an Allergy in a PI Patient

According to Dr. Kobayashi, correctly diagnosing an allergy in PI patients can be a challenge even for experienced physicians because PI patients are more prone to infection, and allergic reactions manifest similarly to symptoms of infection.

Tips for Preventing Allergies

Food Allergies

Get in the habit of reading ingredient labels, with no exceptions. Never assume you know what's in a food package. If you enjoy dining out, visit www.foodallergy.org and fill out a "chef card" that you can present to your server when ordering. Harvard Medical School suggests writing down your emergency action plan to follow in case you accidentally ingest something you're allergic to — and to carry it all times.⁶ In cases of severe food allergies, either have the entire family on the same restrictions or invest in separate cooking and eating utensils to prevent accidental contamination.

Dust and Pollen Allergies

Dust-proof your home! Use HEPA (high efficiency particulate arrestance) filters on both your furnace/air conditioner and vacuum cleaner. Consider replacing carpeting with tile or hardwood flooring, and swapping out window blinds for curtains (which should be laundered monthly) or shades. Obviously, dusting and vacuuming weekly is a must. Keep windows closed, and use the air conditioner to reduce the amount of dust and other allergens entering your home. Enclose mattresses and pillows in an allergen-impermeable cover. Wash all bedding weekly in hot water, and pillows once a month. Try to avoid wool blankets. Keep dogs and cats out of the bedroom of anyone with a dust allergy. Finally, depending on where you live and the climate, consider installing a dehumidifier to keep the inside humidity below 50 percent (this helps cut down on the number of dust mites, which can contribute to a dust allergy).

Insect Allergies

The American Academy of Allergy, Asthma and Immunology cautions that insect repellants do not typically work against the stinging insects that cause most allergic reactions: wasps, yellow jackets, hornets, honeybees and fire ants.⁷ Avoiding areas where these insects are known to be is the best defense. Wear shoes and socks when outside, rather than open sandals. Wear long-sleeve shirts and full-length pants when outdoors, and avoid bright-colored clothing. Don't use sweet-smelling perfumes, colognes, deodorants or hair sprays, as these can attract insects. Keep food covered at all times when eating outdoors, and do not drink from a soda can as insects will fly or crawl inside seeking the sugar. Consider venom immunotherapy to decrease the severity of future reactions.

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Immune Globulin Subcutaneous
(Human) 20% Liquid

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CIDP

Chronic Inflammatory
Demyelinating Polyneuropathy
IN ADULTS



Important Safety Information

WARNING: Thrombosis (blood clots) can occur with immune globulin products, including Hizentra. Risk factors can include: advanced age, prolonged immobilization, a history of blood clotting or hyperviscosity (blood thickness), use of estrogens, installed vascular catheters, and cardiovascular risk factors.

If you are at high risk of blood clots, your doctor will prescribe Hizentra at the minimum dose and infusion rate practicable and will monitor for signs of clotting events and hyperviscosity. Always drink sufficient fluids before infusing Hizentra.

See your doctor for a full explanation, and the full prescribing information for complete boxed warning.

Hizentra is a prescription medicine used to treat:

- Primary immune deficiency (PI) in patients 2 years and older
- Chronic inflammatory demyelinating polyneuropathy (CIDP) in adults

Treatment with Hizentra might not be possible if your doctor determines you have hyperprolinemia (too much proline in the blood), or are IgA-deficient

with antibodies to IgA and a history of hypersensitivity. Tell your doctor if you have previously had a severe allergic reaction (including anaphylaxis) to the administration of human immune globulin. Tell your doctor right away or go to the emergency room if you have hives, trouble breathing, wheezing, dizziness, or fainting. These could be signs of a bad allergic reaction.

Inform your doctor of any medications you are taking, as well as any medical conditions you may have had, especially if you have a history of diseases related to the heart or blood vessels, or have been immobile for some time. Inform your physician if you are pregnant or nursing, or plan to become pregnant.

Infuse Hizentra under your skin *only*; do not inject into a blood vessel.

Self-administer Hizentra only after having been taught to do so by your doctor or other healthcare professional, and having received dosing instructions for treating your condition.

Immediately report to your physician any of the following symptoms, which could be signs of serious adverse reactions to Hizentra:

#1 Ig Prescribed for PI¹

Are you a person with PI who takes Hizentra?
Do you care for someone who does?

Voice2Voice®

Voice2Voice gives you an opportunity to connect with others who have been in your shoes. Dealing with PI can be challenge, and knowing someone who truly understands what you're going through can mean a lot.*

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Sign up at Hizentra.com/V2V

You may also call **1-877-355-IGIQ (4447)** Monday–Friday, 8 AM to 8 PM ET

- Reduced urination, sudden weight gain, or swelling in your legs (possible signs of a kidney problem).
- Pain and/or swelling or discoloration of an arm or leg, unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, or numbness/weakness on one side of the body (possible signs of a blood clot).
- Bad headache with nausea; vomiting; stiff neck; fever; and sensitivity to light (possible signs of meningitis).
- Brown or red urine; rapid heart rate; yellowing of the skin or eyes; chest pains or breathing trouble; fever over 100°F (possible symptoms of other conditions that require prompt treatment).

Hizentra is made from human blood. The risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent and its variant (vCJD), cannot be completely eliminated.

The most common side effects in the clinical trials for Hizentra include redness, swelling, itching, and/or bruising at the infusion site; headache; chest, joint or back pain; diarrhea; tiredness; cough; rash; itching; fever, nausea, and vomiting. These are not the only side effects possible. Tell your doctor about any side effect that bothers you or does not go away.

Before receiving any vaccine, tell immunizing physician if you have had recent therapy with Hizentra, as effectiveness of the vaccine could be compromised.

Please see brief summary of full prescribing information for Hizentra on adjacent page. For full prescribing information, including boxed warning and patient product information, please visit Hizentra.com.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

*Voice2Voice advocates are not healthcare providers or medical experts. For medical questions, please contact your physician. Voice2Voice advocates are compensated by CSL Behring LLC for their time and/or expenses.



Can IgIQ help you?

If you answer YES to any of these questions, call **1-877-355-IGIQ (4447)** Monday–Friday, 8 AM to 8 PM ET.

<p>Have you had a lapse in your insurance coverage?</p>	<p>Are you unable to afford Hizentra?</p>	<p>Would you like to connect with other Hizentra patients?</p>	<p>Do you need help paying for Hizentra?</p>	<p>Are you unable to afford Hizentra infusion supplies?</p>
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HIZENTRA®, Immune Globulin Subcutaneous (Human), 20% Liquid
Initial U.S. Approval: 2010

BRIEF SUMMARY OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use HIZENTRA safely and effectively. See full prescribing information for HIZENTRA.

WARNING: THROMBOSIS

See full prescribing information for complete boxed warning.

- **Thrombosis may occur with immune globulin products, including HIZENTRA. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors.**
- **For patients at risk of thrombosis, administer HIZENTRA at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.**

-----INDICATIONS AND USAGE-----

HIZENTRA is indicated for:
 *Treatment of primary immunodeficiency (PI) in adults and pediatric patients 2 years and older.
 * Maintenance therapy in adults with chronic inflammatory demyelinating polyneuropathy (CIDP) to prevent relapse of neuromuscular disability and impairment.
 -Limitation of Use: Maintenance therapy in CIDP has been systematically studied for 6 months and for a further 12 months in a follow-up study. Continued maintenance beyond these periods should be individualized based on patient response and need for continued therapy.

For subcutaneous infusion only.

-----DOSAGE FORMS AND STRENGTHS-----

0.2 g per mL (20%) protein solution for subcutaneous injection

-----CONTRAINDICATIONS-----

- Anaphylactic or severe systemic reaction to human immune globulin or components of HIZENTRA, such as polysorbate 80
- Hyperprolinemia (type I or II) (HIZENTRA contains the stabilizer L-proline)
- IgA-deficient patients with antibodies against IgA and a history of hypersensitivity

-----WARNINGS AND PRECAUTIONS-----

- IgA-deficient patients with anti-IgA antibodies are at greater risk of severe hypersensitivity and anaphylactic reactions.
- Thrombosis may occur following treatment with immune globulin products, including HIZENTRA.
- Aseptic meningitis syndrome has been reported with IGIV or IGSC, including HIZENTRA treatment.
- Monitor renal function, including blood urea nitrogen, serum creatinine, and urine output in patients at risk of acute renal failure.
- Monitor for clinical signs and symptoms of hemolysis.
- Monitor for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI])
- HIZENTRA is made from human plasma and may contain infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

-----ADVERSE REACTIONS-----

The most common adverse reactions observed in ≥5% of study subjects were local infusion site reactions, headache, diarrhea, fatigue, back pain, nausea, pain in extremity, cough, upper respiratory tract infection, rash, pruritus, vomiting, abdominal pain (upper), migraine, arthralgia, pain, fall and nasopharyngitis.

To report SUSPECTED ADVERSE REACTIONS, contact CSL Behring Pharmacovigilance at 1-866-915-6958 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-----DRUG INTERACTIONS-----

The passive transfer of antibodies may interfere with the response to live virus vaccines, and lead to misinterpretation of the results of serological testing.

Based on March 2018 revision

In fact, an allergy is sometimes suspected as the underlying cause of repeated infections in individuals who have not yet been correctly diagnosed with PI.

With so many different PIs and thousands of otherwise harmless substances causing allergies, making a correct diagnosis is oftentimes a difficult task. In children, physicians need to be vigilant in assessing each infectious episode since even those with healthy immune systems tend to contract an infection, on average, once a month.

“Some babies have characteristic features either at birth or shortly thereafter, which lets the doctor suspect they might have an immunological syndrome,” says Dr. Kobayashi. “Babies get sick all the time. They get colds. But, some babies may get serious infections [such as] blood poisoning, meningitis or severe infections of the gut or skin, and that will make the doctors look [at PI as the cause].” The problem, though, he says, is once children are given antibiotics, they get better. So, most doctors don’t think of PI.

Because allergies are far more common than PIs (about 10 percent of the population has at least one allergy), physicians are trained to consider testing for allergies whenever a child has recurring symptoms, says Dr. Kobayashi. But, if parents suspect something else is going on, they have to advocate for their child. If the doctor is testing for allergies, parents may suggest the doctor also test for PI.

What should be emphasized, says Dr. Kobayashi, is these diseases don’t always occur in isolation; they can occur in combination. It’s important for physicians to recognize that if a child is sick more often than others, an allergy or PI should be considered. But, if a child has a serious infection, they must consider an immune deficiency.

Dr. Kobayashi suggests parents become familiar with the Jeffrey Modell Foundation’s (JMF) 10 warning signs of PI:

- Four or more new ear infections in a year;
- Two or more sinus infections in a year;
- Two or more months on antibiotics with little improvement;
- Two or more cases of pneumonia in a year;
- Failure of an infant to gain weight or attain normal growth;
- Recurrent deep skin or organ abscesses;
- Persistent fungal infection (thrush);
- Need for intravenous antibiotics to treat infections;
- Two or more deep-seated infections, including septicemia; and
- A family history of PI.

If a child has two or more of these warning signs, JMF says it is time for parents to ask their physician to test their child for a PI.⁴

Adults also need to be aware of changes in their health. Common variable immune deficiency (the most prevalent form of PI) generally manifests in adulthood, often in a person’s 20s or 30s. Symptoms are typical of any PI: frequent infections in the ears, respiratory system and sinuses.

Adult PI patients with repeated symptoms of infection should be insistent with their doctor that allergies also be looked at as a possible cause.

Tendencies and Trends with PI and Allergies

Some PIs are associated with an increased susceptibility to allergies, and others are associated with specific allergies. For instance, the Immune Deficiency Foundation (IDF) points out that patients with hyper-IgE syndromes tend to develop more allergies than other PI patients.⁵ And, Dr. Kobayashi explains that patients with an IgA deficiency are more susceptible to food allergies.

IDF suggests working with a physician who specializes in PI if an allergy is suspected so a testing regimen specific to that patient can be put in place.

Living with PI and Allergies

Other than watching carefully for interactions caused by prescription drugs that treat PI and allergies, PI patients will generally approach allergy prevention and treatment the same as anyone else. Of course, the best way to treat allergies is to avoid allergens. In serious cases, allergies can lead to a life-threatening condition known as anaphylaxis, in which swelling can block the throat and blood pressure can drop dangerously low. If anaphylaxis is possible, patients should carry their epinephrine injector at all times.

PI patients need to be vigilant about their health so infections can be treated quickly. Dealing with allergies is just as important so symptoms can be quickly diagnosed and addressed, and allergies can be differentiated from infections. ■

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