

ASK KRIS



Kris McFalls has two adult sons with chronic diseases treated with IG and is also on IVIG therapy herself. Formerly a physical therapist assistant, Kris is an avid patient advocate and now works with NuFACTOR, a sponsor of *IG Living*. Kris is eager to find answers to your questions. Email them to editor@igliving.com. Your confidential information will not be used for any purpose but communicating with you about your questions.

Reader: What is the association between omega-3s (specifically EPA and DHA) for inflammatory disorders? Then, what is the proper dosage and how safe is it, particularly for those with weakened immune systems? It looks promising but scientists were unable to recommend a certain dose, length of time or brands.

Kris: Terry Harville, MD, PhD, medical director of three laboratories at the Departments of Pathology and Laboratory Services and Pediatrics at the University of Arkansas for Medical Sciences, answered this reader's question. Please note that the doses Dr. Harville mentions are not recommended for any specific individual. Patients should check with their healthcare providers to determine the proper dosage of any medication.

Dr. Harville: Specific studies are wanting. Studies performed a few years ago demonstrated that people with rheumatoid arthritis or osteoarthritis could reduce by one-half their dosage of NSAID (non-steroidal anti-inflammatory) medication when they were taking 5 or 6 grams of omega-3 fish oil each day. For example, a dose of 500 mg could be as effective at 250 mg each day when the patient is also taking 5 or 6 grams of omega-3 fish oil each day.

More recently, omega-3 fatty acids have been used to treat high serum triglyceride levels. The new brand name is Lovaza™ (formerly Omacor™). The dose is 4 g

per day in divided doses, for this FDA-approved prescriptive medication.

The benefit of omega-3 fatty acids is their anti-inflammatory potential. This has been applied to a variety of autoimmune conditions, with variable degrees of success. Nervous system conditions, autism, inflammatory bowel disease, arthritis disorders, cardiovascular diseases, etc., are among those where success is claimed.

Omega-3 fish oil typically comes in 1 g capsules. The dosing for an adult is typically approximately 6 g of omega-3 fish oil each day in divided dosing, e.g., 2 capsules three times a day or 3 capsules two times a day. Each capsule contains 1 g of fish oil (eicosapentaenoic acid, EPA, from approximately 180 mg to 465 mg and docosahexaenoic acid, DHA, from approximately 120 to 375 mg or approximately 300 mg to 840 mg total per capsule, depending on the brand). To achieve significant benefit, some suggest at least 3,000 mg of total omega-3s are required each day, especially for some of the more severe conditions. Therefore, a capsule with more EPA and DHA per capsule means that more omega-3s will be ingested with fewer capsules. It is suggested effects will be noticed in a minimum of two months (this is the case for triglyceride reduction), but six months or longer may be required for some conditions.

Since the fish oils can cause you to burp and develop a fishy taste in the mouth, and may result in stools that have a fishy odor, one should begin with one capsule per day, increasing over a week or two, or even longer, to better tolerate the full dosing.

Side effects may occur. As noted, the fishy odor and taste may cause problems in some people. It is recommended that people with known allergies to fish or soybean should not take the omega-3s. ➤

ASK KRIS

People interested in omega-3s should discuss this with their physicians before taking them. Bleeding may occur more readily, so people on Coumadin, heparin (Lovenox™) or aspirin should use omega-3s only under the guidance of their physicians. The typical dosing adds 6 g of fat to the daily diet, which is 10 percent or more of the recommended daily fat intake for an adult, therefore other fat intake should be reduced accordingly. The increase in fat in the diet may affect diabetes, so people with diabetes should discuss the use with their physicians.

There are no studies that I am aware of looking at the effects of omega-3 fatty acids on people with weakened immunity. A quick PubMed search of "omega-3 and immunodeficiency" reveals that 34 articles are available. Perusing the titles and abstracts reveals several in which positive impact is noted and none that would indicate contraindication for use in someone with immune problems. Again, however, patients should discuss the use of omega-3 fatty acids with their physicians.

When thinking about use of omega-3 fatty acid supplements, one could consider that this could be similar to the diet of someone from cold water latitudes on essentially a "fish only" diet. Indeed, some speculate that this may have been important to the health of early Norse explorers and their successful explorations and conquests.

Cyrus: I have been suffering with neuropathy for five or six years and I have read that IVIG is generally effective only in the first 18 months. Second, I do not know how effective the treatment is for patients with extensive nerve, joint and muscle pain. Third, I have heard that IVIG gives only temporary relief. And finally, IVIG contains the antibodies of 10,000 to 20,000 people and I am not sure what other side effects I could develop. Thank you for the information you are providing to me. You guys are really amazing and wonderful people.

Kris: On a personal note, we know it is true that IVIG contains antibodies from thousands of people and it can cause reactions, but it is those antibodies that give the

relief patients need from their symptoms. In the case of my kids, it is the antibodies from thousands of people that give my boys protection from infections. I posed your questions to Dr. Todd Levine of Phoenix Neurological Associates.

Dr. Levine: The questions you ask are concerning the timing of IVIG initiation and how it might affect a disease that has been present for a long time. Finding an effective therapy is easier the earlier you start. However, if the nerve disease is caused by the immune system and if the disease is active, then IVIG will be effective at any time in your disease. In addition, if the neuropathy is progressive, then taking no therapy will surely result in continued worsening.

The IVIG is only effective as long as the antibodies are in your system, so, generally, from four to six weeks. However, the effects for most people are very long-lived, as long as you receive treatment every four to six weeks. Many physicians will try to transition you over to other immunomodulatory therapies once they know you have responded to IVIG.

Finally, IVIG is a human blood product and that might have some risks, but there are countless systems in place to be sure that no communicable diseases are passed through IVIG therapy.

So, in summary, if you opt for no therapy, things may worsen. The only way to know if IVIG will work is to try, but both you and your physician need to weigh the risks of the therapy against the potential benefits.

Denise: My son will be turning 18 soon and is currently covered under CHAMPUS Tricare (his father is retired military). Since this is a pre-existing condition and my son will continue to need IVIG, will he still be covered even if he's no longer attending school or will I have to find a different insurance carrier?

Kris: I did some Internet research and found the information below on the Tricare website.
www.mytricare.com/internet/tric/tri/tricare.nsf/EXT/TRCRBscs_Elgbly_1?OpenDocument&SC=TRICAREBasics~Eligibility

The Tricare programs are available to family members of active duty military service members and to military retirees and their dependents. These dependents include:

- Spouses
- Unmarried children under age 21
- Unmarried children under age 23 who are full-time students
- Stepchildren adopted by the sponsor

Those who are eligible must be listed in the Defense Department's worldwide, computerized database, the Defense Enrollment Eligibility Reporting System. The following are not eligible for Tricare benefits:

- Parents and parents-in-law of active duty service members or retirees
- People who are eligible for health benefits under CHAMPVA (Civilian Health and Medical Program of the Department of Veterans Affairs)
- People age 65 or older who are eligible for Medicare can receive Tricare For Life benefits.

You can also phone Tricare at:

Northern states: 877-874-2273

Southern states: 800-403-3950

Western states: 888-874-9378

Susan: Is testing for trough levels necessary for management of IG dosage? I am managed based on number of infections, how I feel, etc. Many other PIDD patients are managed by trough levels.

Kris: This question comes up often and it has been my experience that doctors vary a great deal on the response. I posed this question to Dr. Harville.

Dr. Harville: This is a great question. In the past, when lower dosing of IVIG or even IMIG (intramuscular immune globulin) was being used, it was important to know the trough value (serum IgG level) prior to the next dose, to help determine if the dose being given was sufficient and the interval of dosing was correct. With the lower dosing given at that time, patients were somewhat more likely to have some breakthrough infections, and the trough values

could be used to justify greater or more frequent dosing.

With further availability of IVIG during the past few years, and further studies, it has become apparent that a higher trough value is associated with fewer infections and complications, especially long-term problems with respiratory diseases. Therefore, many physicians like to see the trough IgG level to near-normal (i.e., approximately 1,000 mg/dL), rather than greater than 400 mg/dL, as was common in the distant past.

How often should trough levels be measured? Perhaps once or twice a year for someone who is stable and infection free. Perhaps more frequently in growing children. In an adult who is infection free, after it is known that the trough is sufficiently high, further determinations may not be needed—assuming that the adult is hypogammaglobulinemic (i.e., IgG < 400 mg/dL) due to his or her immunodeficiency and trough determinations could be used to demonstrate achievement of better levels. For patients with dysgammaglobulinemia (i.e., initially normal, near-normal or even high IgG levels), trough measurements may not have much validity.

There is an important reason to measure trough values in younger children. Some young children will have delayed maturation of immunity and may have low IgG and IgA values for their age, with recurrent infections and poor recall antibody responses to immunization challenges. As these children grow, they may overcome the maturation delay and actually develop normal levels of IgG and IgA, as well as IgM. Therefore, following trough values and IgA levels in the younger child may reveal this process and actually allow for the discontinuation of IVIG therapy.

Therefore, monitoring the health of the patient is necessary, including the extent of infections, but trough values also appear to be important, especially for maintaining sufficient IgG levels to help prevent long-term problems in patients with hypogammaglobulinemia. ➤

ASK KRIS

Jennifer: I have a few questions:

1. Do PIDD patients tend to have a lot of depression at times?
2. Does immune globulin tend to make people retain water easily? I seem to do so every month, and I do watch my salt intake a lot. Crazy body!
3. In what other ways can immune globulin make the body react negatively?

I am feeling frustrated with a body that doesn't always cooperate. I do like the SubQ every week, and having it on my own schedule. That is one good thing!

Kris: I asked immunologist Dr. Richard Schiff, global medical director for Baxter Healthcare, to address your questions. I want to thank you for bringing up the issue of depression. I hear about this frequently, but too few patients are comfortable discussing it with their physicians. This information will certainly help other readers.

Dr. Schiff: I don't know of any specific studies of depression in PIDD patients, although surveys do indicate a fairly high rate. This is true for most chronic illnesses, but I don't necessarily think it is specific to immune deficiency. However, infection and autoimmune diseases do alter cytokine profiles and can make people feel tired or depressed. Situational depression responds to the usual medications. Otherwise, it is worth a close look for subclinical infection and autoimmune disease to be sure they are not contributing.

I don't know of any studies that show that immune globulin causes water retention. Gammagard S/D has a lot of salt and can transiently cause fluid retention, but it should only last for a few hours. It should be less apparent for SubQ because less is given at a time. Water retention suggests hormonal imbalance.

The last question is too nonspecific to be answered. If a patient has an infection, the IVIG can react with the germs and cause a reaction—fever, chills, fatigue, etc.—similar to having the flu. These symptoms often improve as trough levels rise and infections are better controlled. SubQ dosing should help but not if absorption is not as good. It is worth checking levels and again, looking for signs of occult infection (e.g., sinusitis).

Kris: Please remember, before making any changes to your treatment, you should always seek the advice of your personal physician.

Jennifer responds: I don't think the depression is product-related, but I do know that I haven't been getting enough uninterrupted sleep for so long that it is putting my body under stress! So I try to take naps. ... You are really a godsend in my life right now! It is hard to talk to people who don't have a clue about how life is for you. They just give you the sympathy thing, but no understanding. Or they make you feel like you are totally germ-loaded and will get them sick! Are we really that contagious to others?

Kris: First of all, always ask for a copy of your blood work, and keep a binder with copies of any lab work you've had done. Then you and your doctor can notice any trends, and, if one day something does show up in the abnormal category that has been slowly moving that way, you are not taken by surprise and can talk with your physician regarding any concerns you may have. Also, if you have copies of all your lab work, you always have what you need if you see a new doctor.

As far as being contagious, my kids' physicians tell me others are far more dangerous to us than we are to them. I just don't think well-meaning people know what to do or say at times. It's a matter of educating them and understanding our own limits. The most important coping mechanism I have found is to have a sense of humor. There is no better medicine than laughter and a good friend.

Last, interrupted sleep over time can increase stress and be an indicator of depression. Try doing a Google search, and you'll find a lot of information on this topic.

Andy: I have checked into international health insurance companies for a long-term stay out of the country. So far, the only company that indicates it will cover me will probably cost nearly \$6,000 per year. This isn't entirely out of the question, but I would then face the problem of not having had any coverage in the United States for one year, so, when I return, I will have lost my pre-existing condition status.

Kris: I asked a reimbursement advocate with a national patient organization if your international insurance would be considered “credible coverage.” Credible coverage protects you, upon your return to the United States, from being categorized as having a lapse of coverage, which would require your going through pre-existing clauses. The reimbursement advocate’s response follows:

Response: Many insurance companies based in the United States offer international insurance. As long as the coverage Andy has found for an international plan is with a reputable, U.S.-based company that documents in writing that the plan is considered “credible coverage,” he should be fine. However, I would be very leery of any insurance company that I never heard of, and Andy should forget about the discount health plans that have recently gained some popularity. These plans are not considered credible coverage.

Suzanne: I’m trying to find out the side effects, if any, of IVIG.

Kris: This is a common question, so we try to address it as often as possible. Another reader recently asked specifically about infusion rate-related reactions, so I’ve asked my friend who is a pharmacist and IVIG expert to respond to both readers.

Response: Every patient is an individual when it comes to side effects to IVIG. Some patients can tolerate all brands of IVIG while others may only tolerate one or two. Most side effects occur with the first dose of IVIG, and for that reason first doses should always be given under a controlled setting. The rate of administration of IVIG can also be critical to reducing or eliminating side effects.

The good news is that most patients do not experience significant side effects to IVIG treatment. The most common side effects seen during an IVIG infusion are headaches and hypotension (low blood pressure), although hypertension (high blood pressure) can also occur. These reactions can be immediately managed

by slowing the infusion rate. In fact, these side effects usually help determine how fast an individual patient can be infused with each particular brand of IVIG.

Flu-like symptoms and malaise can also occur after an IVIG infusion. These can usually be treated by administering acetaminophen, aspirin or non-steroidal anti-inflammatory agents prior to and after each infusion. Some patients develop a tolerance to these side effects over time. If the side effects do continue to be a problem, a slower infusion of IVIG might resolve them or the patient can be switched to another brand of IVIG.

Rashes can occur with IVIG and are usually seen during the infusion, although sometimes they occur after an infusion. Rashes are treated with antihistamines or a corticosteroid, which can be added if the rash is more severe. If prophylactic treatment with antihistamines does not prevent recurrence of rashes, the patient can be switched to another brand of IVIG.

Severe post-infusion headaches, similar to migraine headaches, are an annoying side effect of IVIG infusion. Such headaches are considered to be aseptic meningitis and do not respond well to medications given either before or after an infusion. Some clinicians have experienced positive results with medications used to prevent and treat migraine headaches, although there is little confirmation of this in the published literature. Administering the immune globulin subcutaneously has been shown to benefit patients who experience these headaches or another brand of IVIG can be tried. A third option is to administer the IVIG infusion over a long period—12 to 24 hours—using an ambulatory infusion pump.

More serious side effects are less frequent and most commonly occur with the first infusion of IVIG or after switching to a different brand of IVIG. One of these less frequent side effects is a violent shaking syndrome similar to that seen with patients who are administered Amphotericin B. Another side effect is a severe back and leg pain syndrome that patients describe as excruciating. Treatment for both of these syndromes involves the administration of intravenous antihistamines, steroids and narcotic analgesics. When treated ➤

ASK KRIS

quickly, these side effects can be easily managed, and, in some cases, the infusion of IVIG can be resumed. Patients can be premedicated prior to subsequent infusions or switched to another brand of IVIG. Interestingly, patients do develop a tolerance to these side effects rather quickly and in many cases it is not necessary to switch brands of IVIG, although switching brands is most often done to ease the patients' concerns.

Anaphylactic reactions, also infrequent, can occur with IVIG infusions. An anaphylactic reaction typically starts with a patient complaining of tightness in the chest or throat and an increase in blood pressure. Unlike a true anaphylactic reaction, the progression of symptoms is much slower and can be managed prior to symptoms becoming more serious. Treatment with intravenous antihistamines and steroids can usually resolve this in a matter of minutes, and, in some cases, the infusion of IVIG can be resumed.

Two side effects to IVIG are considered extremely serious: renal complications and thromboembolic events. In the case of renal complications, most of the reported cases were with IVIG products that contained sucrose. Only one product containing sucrose is currently available in the United States (CSL Behring's Carimune® NF). Additionally, most of the patients who experienced renal complications had risk factors, such as advanced age, diabetes or prior renal problems. In the case of thromboembolic events, the specific IVIG risk factor is not clear, although sodium content may play a role. Again, patients who had risk factors for thromboembolic events, such as coronary artery disease,

prior strokes or prior blood clots, were most at risk. A slow infusion rate or avoidance of high-risk IVIG products in these high-risk patients is warranted.

Subcutaneous immune globulin administration is safer in these patient populations.

Rhonda: How is chronic inflammatory demyelinating polyneuropathy (CIDP) diagnosed? Is there a test that results in a definitive diagnosis? Can a definitive diagnosis be made without a nerve biopsy?

Kris: I again prevailed on Dr. Levine, and he provided the following answer.

Dr. Levine: CIDP is a very difficult diagnosis to make. There are certain research criteria for the diagnosis that are highly specific, but may miss many patients who have the disease.

In general, the most helpful tests are the nerve conduction studies. These tests can make the diagnosis without the need for the nerve biopsy or spinal fluid analysis. In some cases, however, the nerve conduction studies may not be definitive, and, therefore, a nerve biopsy or spinal tap can be performed to help support or refute the diagnosis.

In some cases, even with all of this testing, the question may still be whether or not a patient has CIDP. In these cases, if the symptoms are severe enough, a neurologist may choose to try to treat a patient with IVIG or steroids for a few months to see if there is improvement. ■

Have questions about living comfortably with your IG therapy?
Send them to editor@igliving.com or visit Ask Kris at www.igliving.com.