

**NATIONAL MULTIPLE SCLEROSIS SOCIETY
MS LEARN ONLINE INTERNET PROGRAM
MANAGING THE SIDE EFFECTS OF DISEASE MODIFYING AGENTS**

>>Welcome, and thank you for joining the National Multiple Sclerosis Society's MS Learn On Line Internet program. I am Rick Turner your host and medical correspondent. The management of multiple sclerosis has been substantially advanced by the availability of the disease modifying agents. Today in our third of four webcasts we will specifically speak to the side effects of these agents. We welcome back Dr. Fred D. Lublin to help us sort through some of these issues. Dr. Lublin is a Saunders Family Professor of Neurology at Corrine Goldsmith Dickenson Center for multiple sclerosis at Mt. Sinai Medical Center in New York.

Thank you again for being with us Dr. Lublin.

>>**Dr. Lublin:** Nice to be here.

>>**Rick Turner:** We have lots of questions from listeners regarding side effects, and as we go through these questions some of them may be more appropriately addressed by a nurse. To begin Doctor, give us a general overview of the side effects that are typical in each of the disease modifying agents.

>>**Dr. Lublin:** With the interferons the major side effect is what is called a flu-like syndrome because it makes you feel like you have influenza. That is characterized by fever, chills, muscle aches and a generally crummy feeling. Not everyone gets this and in most patients it resolves fairly rapidly over weeks to months. In a small percentage of patients it continues throughout the course of their treatment. It could be treated with nonsteroidal anti-inflammatory agents or Tylenol and frequently our nurses will advice patients to pretreat with one of those agents and then follow up over the next 24 hours with periodic supplements of anti-inflammatory agents.

The other side effect of all of the subcutaneously injected agents, that is, those that are injected under the skin such as Betaseron, Rebif and glatiramer acetate is some irritation and burning at the injection sites. You may get some red spots. Very rarely with interferon one can get necrosis, that is, breakdown of the skin at the injection site but that is uncommon. In addition, with the interferons one has to monitor both blood counts and liver function because rarely there may be alterations in those bodily functions that need to be followed and if they occur one might have to alter the dose or change the medication.

>>**Rick Turner:** How about the typical side effects of Copaxone?

>>**Dr. Lublin:** Other than the skin irritation, the only other significant side effect of Copaxone is an uncommon reaction called the systemic reaction that occurs immediately after an injection is given and it is characterized by flushing, tightness in the chest and/or throat, palpitations and sometimes chest pain. It can feel quite uncomfortable but it lasts seconds to minutes and although we do not know what causes it nothing serious has ever come of it.

>>**Rick Turner:** We have a question for you coming all the way from Italy. Ada asks how one knows if they have developed antibodies to their treatment? She also says, "I understand that once the antibodies are developed the patient cannot use any of the interferons."

>>**Dr. Lublin:** Antibodies can occur to interferon and you, as an individual, probably could not tell that you had them. The concern about antibodies is that in some patients with high levels of antibody the effectiveness of the interferon may be reduced. The only way to know that it is there is if the drug stops working. That is a very difficult determination to make. There is an assay blood test that could be done to determine if someone has antibodies but one does not usually do this unless you are specifically suspicious the antibodies may be there. Once you have antibodies to any of the interferons then the antibodies will effect all interferon. However, there is reason to believe that over time the antibodies will go away.

>>**Rick Turner:** How common an occurrence is that?

>>**Dr. Lublin:** It depends on the type of interferon used and so the occurrence could be anywhere from 5% to 30% but it is hard to know what that means clinically for individuals.

>>**Rick Turner:** How often do blood levels need to be taken to check for liver problems when taking interferons Doctor?

>>**Dr. Lublin:** This is very important. One cannot start taking interferon and then just forget about it. One needs to monitor liver function and blood counts periodically. We recommend for our patients every three months and in fact we check a little more frequently than that right after they start the therapy. It needs to be followed and needs to be followed as long as they are on the medications. Even

after a couple of years if they have had no problem they still need to get periodic blood tests.

>>**Rick Turner:** Our next listener, Barbara, ask why after receiving an Avonex injection is she becoming immobile to the point where standing up to do anything is difficult?

>>**Dr. Lublin:** Sometimes after an injection of interferon one can get a fever and fever is known to worsen the symptoms of multiple sclerosis. It does not alter the underlying disease. It just makes the symptoms that are there worse. I would be suspicious if she was getting fevers from the interferon and, therefore, probably would benefit from treatment with an antiinflammatory like Tylenol or ibuprofen or something of that sort.

>>**Rick Turner:** The next question says, "I have been on Betaseron for five years. The only place the injection does not sting is in my stomach. Needless to say I have not been very compliant about changing sites. I am very good about not getting near a spot that is tender or red. I have lately been developing lumps under the skin from previous shots sites. So, the questions are: what can I use on other sites to reduce the stinging and do I need to make my doctor aware of these lumps."

>> **Ms. Morgante:** Hi Rick. My name is Linda Morgante and I am a registered nurse at the Corrine Goldsmith Dickinson Center for MS at Mt. Sinai Hospital in Manhattan and Dr. Lublin has asked me to address some of the next questions.

The first question regarding ways to reduce the stinging and using other sites for injection is an important question. With some of the products that we are using, stinging after the medicine is injected is fairly common. Although Betaseron is stored at room temperature and should be warm enough at the time of injection I often recommend people hold the syringe in their hand for at least 10 minutes to bring it to body temperature because it is actually body temperature that helps reduce the stinging at the injection sites.

As far as the lumps go, I think it is important to make your doctor or nurse aware of the lumps because sometimes there are ways to reduce the lumps by using some topical creams. I think the most important issue is the site rotation. With Betaseron there is a small incidence of necrosis at the site of the injection which can be bothersome and really the only way to prevent necrosis is to rotate the sites. There are ways to create new areas on the body where subcutaneous fat is so it is

important to go over these issues with your doctor or your nurse and to look for areas in the body where you can pinch an inch or two, and depending on the fatty area adjusting your auto injector to a different depth sometimes helps reduce lumps and stinging and just using more sites. Rotating the sites is the key.

>>**Rick Turner:** The next question asks how can I bring ease to the divots in my thighs from old injections?

>>**Ms. Morgante:** The divits that are created by several of the subcutaneous products happen probably because some people are just prone to that happening. It is actually called lipoatrophy. The subcutaneous tissue actually gets hardened and then from the outside it looks indented. Unfortunately those areas never do resolve. You will have to use areas around your divits or other areas on your body. Again, asking your doctor or your nurse to go over sites with you to look at how much subcutaneous tissue you have is very important. Again, the best way to prevent divots or lipoatrophy is to be meticulous about rotating your sites. I know people sometimes say the best site is my buttock but it is not good enough to just use one or two sites. You really do need to use all of the sites to help prevent the divits.

>>**Rick Turner:** Nancy in Pennsylvania writes, “I have been taking Avonex for three-and-a-half years for relapsing-remitting MS. A few months ago I was diagnosed with rheumatoid arthritis. My antihistone level, she writes, was slightly elevated which makes my rheumatologist think that the arthritis may be Avonex induced. My neurologist disagrees. Have there been documented cases of interferon-induced rheumatoid arthritis in MS patients?”

>>**Dr. Lublin:** I am unaware of any cases of rheumatoid arthritis induced by interferon.

>>**Rick Turner:** On listener recently had a frightening reaction. Sandy says, “I have been using Copaxone daily for a year and a half. Last month I had one of those terrible reactions where I felt that I could not breath, my heart was racing, then at about 15 minutes my color was back to normal and I was fine. The help line has wonderful nurses but does not give much in the way of answers on why this happens and whether there are any long-term consequences. I was hoping you might shed some light on that.”

>>**Dr. Lublin:** We do not know why this reaction occurs. We think it may be because the medication gets directly into a vein, an occasional subcutaneous injection. We do not know of any long-term consequences of it. Individuals can

have it anywhere along the course of their treatment with Copaxone and we are not too concerned about it.

>>**Rick Turner:** An E-mail from Judy reads, “I have been taking Copaxone for five years. I never had a problem in the past but for about the last month or so either during the injection or immediately thereafter I am not only getting redness at the injection site but have started to develop welts and much pain. This pain lasts for a minute or two but the redness and the welts last a couple of days or more. I am starting to hate these daily shots now and never had a problem before this.”

>>**Ms. Morgante:** Rick, I will go ahead and answer this question. It is unusual and disheartening to be on medicines for so long and then all of a sudden to develop side effects and site reactions. Unfortunately, you are not alone. This happens to many people. Again, having a frank discussion with your doctor or nurse about how to handle these is so important because your technique may not be quite right so reviewing your technique again is always helpful. Even though you are an expert in five years maybe you are just doing something a little differently than you were in the beginning so just a review of your technique is important. Again, rotating your sites. Sometimes the redness and welts are helped by applying a topical hydrocortisone cream. During the allergy season when histamine levels are very high some people who are more allergic tend to have these lasting welts and I do know that sometimes oral medications like Zyrtec or Claritin can help reduce the evidence of these welts happening. Again, it is just having that frank discussion, showing your doctor or nurse your skin, going over your technique, going over your rotation schedule, taking a look at your auto injector, looking at the depth you are using, maybe adjusting the depth for different places on the body, that often helps, you do not use the same depth necessarily for every single injection site, and maybe for that time you might need some oral medication to help out as well as some topical creams.

>>**Rick Turner:** Is there anything being studied for site reactions such as a topical that would greatly reduce the reaction time and inflammation?

>>**Ms. Mogante:** Well, you know the area of injection reactions has been under study, particularly by nurses in the field of MS, since we first saw Betaseron come to market. It was actually a study that demonstrated that the auto injector was the key to helping reduce injection site reactions with that medication and helped the following medications when they came to market develop the same kind of system using an auto injector to administer the medicine. Auto injectors do seem to be a help in reducing inflammation. It is important to look at your settings and make

sure that your auto injector settings are right for the amount of subcutaneous fat you have and the areas of the body that you are using. Some women have very small arms and do not need the needle to go in so deep in their arms. That is an important part of care when it comes to reducing inflammation and reaction time. Also, the skin. Making sure the skin is clean. I do not think it is always necessary to rub the skin with alcohol. People do not wait for alcohol to dry which is another important part if you are using alcohol. If you have just showered and your skin is clean there is no need to use alcohol before your injection. Avoiding ice in my practice has been a big help to patients who are having lots of redness and inflammation. Rather than icing the area we just try using nothing and that seems to help. I think there are some small studies looking at whether or not using just a warm soak after the injection is helpful to reducing some of the site reactions. Each individual is different and each person reacts differently so some techniques work better for some people than they do for other people. It is very individually tailored and it is important to find the best protocol for your skin.

>>**Rick Turner:** Dee would like to know if there are any statistics to show whether or not persons changing to Avonex premixed formula have had more or, I guess, fewer side effects. Doctor?

>>**Dr. Lublin:** I do not know if there are any statistics. We anecdotally had patients complain to us of a return of interferon like side effects like the flu-like syndrome after switching to the premix formula but it wore out just like we saw with those originally treated.

>>**Rick Turner:** Audry wants to know if Avonex causes thyroid gland problems. If a person develops thyroid problems should they stop using Avonex?

>>**Dr. Lublin:** There is some information that suggests there may be induction of thyroid problems with individuals who take interferon. It is still a little controversial but the issue is there. However, the thyroid problem can be treated relatively easily so we do not recommend that they stop using interferon, whether the Avonex or any of these others for that reason. Also, there is an increased incidence of thyroid problems in individuals with multiple sclerosis whether they are treated or not.

>>**Rick Turner:** Dr. Fred Lublin thanks very much for helping us to sort through some of the side effects people are experiencing.

>>**Rick Turner:** The National MS Society is proud to be a source of information for you about multiple sclerosis. Our comments are based on professional advice, published experience, and expert opinion, but do not represent individual therapeutic recommendation or prescription. For specific information and advice consult a qualified physician. If you have a question that was not addressed, please E-mail us at mslearnonline@nmss.org. If you would like more information on multiple sclerosis, click on the resources link on your screen or call the chapter nearest you for an answer to your question. You can reach your chapter by calling 1-800-FIGHTMS. That is 1-800-344-4867. You may also want to check the National MS Society's web site where you will find more information about today's topic and a menu of other web casts available to participate in.

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Please join us for our next web cast where we will continue our discussion on treatment ???? for multiple sclerosis.

For the National Multiple Sclerosis Society I am Rick Turner wishing you health and happiness.