

A Closer Look at The Importance of Treating and Managing MS Relapses

featuring

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1. Brief Overview of Multiple Sclerosis

So, multiple sclerosis is an inflammatory disease of the central nervous system. It's a common cause of disability in young people and it can cause a variety of different neurological symptoms including things like vision loss, numbness, weakness, trouble with balance or trouble walking. And it's an important cause of these sorts of symptoms, particularly in people in the prime of their lives, ages 20, 30s, 40s are the peak age at which multiple sclerosis presents itself.

MS is a pretty common disease, especially in the modern world. In the United States we believe that around 250 or 300,000 people have MS. It's hard to estimate those numbers precisely but we say that roughly one in a thousand people has multiple sclerosis.

Multiple sclerosis is a complicated disease and it's very varied in the way that it can present, so there's not one single symptom that is the hallmark of multiple sclerosis. In fact, it can be many different types of neurological symptoms. But when a young person develops loss of vision or blurred vision in one eye, in particular, or weakness in the arms or legs, or a loss of feeling or numbness in tingling that occurs in a large part of the body like an entire side or an entire limb. Those things often raise the suspicion for multiple sclerosis and that ought to warrant a work-up by a primary medical doctor and by a neurologist.

I think that MS is a very varied disease and there are people who have MS who have basically no signs of it. MS can be mild, it can be well controlled. Other folks who have had MS have a much harder time with it and can accumulate a significant amount of disability. Some people who have multiple sclerosis are debilitated by it and may need a cane to walk or may need a wheelchair to get around. Often those sorts of symptoms develop gradually over time with multiple sclerosis and there are many medicines that have been designed to prevent those sorts of outcomes. But no two people with MS are exactly the same. Some folks will have very mild symptoms and other people will battle it every day, and that's an important thing for people with MS to understand that there's no one MS story. I think it's also important for doctors, neurologists, and general medical doctors who take care of people with MS to understand is that it's hard to predict what happens to an individual person. Everybody's story with MS is unique and medicine and care has to be personalized to each person.

2. What is an MS Relapse?

Multiple sclerosis can take a variety of different forms and the most common form of MS is called relapsing remitting MS. It's usually abbreviated RRMS. And what this means is the attacks of neurological symptoms or dysfunction happens as these relapses. MS is an unusual disease in the sense that it can have these relapses and remissions and the way those relapses are defined is very particular. So for one thing a relapse is one way of talking about a worsening of MS symptoms. Other terms for this are an MS exacerbation, or an MS attack, or an MS flare-up. These terms all basically mean the same thing but that can be confusing because it's being referred to in different ways.

But for the sake of our discussion today we're going to talk about MS relapses. An MS relapse is the emergence of new neurological symptoms or real significant worsening of previously stable neurological symptoms in someone with MS. When I say 'neurological symptoms' I mean the sorts of things that MS can cause like vision loss, blurred vision, double vision, numbness or tingling, weakness in the arms or legs, loss of balance. These individual neurological symptoms when they come on relatively acutely over a short period of time we consider to be a new MS relapse.

Now, relapses are defined as these symptoms happening for more than 24 hours at a time. This is important because folks with MS may have day-to-day little fluctuations. One day might be a little worse than the next or a little better than the next. But what we're looking for when we're thinking about an MS relapse are truly new onset of these symptoms lasting for more than a day. I say that also because people with MS, or people without MS, might have transient neurological symptoms, a little bit of tingling in a toe or a finger, or feeling that vision was a little bit off for a few minutes; floaters, for instance, in vision. Those things are not MS relapses, these are transient little changes. What we think about as a relapse is something that starts and lasts for at least a day and usually considerably longer.

3. Why do MS relapses occur?

When someone is having new symptoms that may be an MS relapse, the first question we try and figure out is if they're having a relapse and then if so, we figure out if we're going to treat it. Then we figure out why they are having it. So the first question is someone having a relapse requires an assessment in the office typically. One of the things that we have to think about and distinguish is between an MS relapse and something called a pseudo-relapse or a pseudo exacerbation. This is a worsening of other symptoms, a worsening of MS symptoms that often can come from things like being overheated or having a fever, or being under significant stress.

In this situation, old symptoms of MS can show themselves again as opposed to a new, brand new symptom happening. These pseudo exacerbations or these sort of fluctuations that can occur important to distinguish from true relapses so the presence of fever, the possibility of infection, the possibility of physical or metabolic stresses need to be thought about by the physicians or nurse practitioners that are taking of the patient; and that needs to be looked for. If someone is having a relapse then we think about treating that relapse and we'll talk about treatment of relapses shortly.

But if someone has a relapse, the final question is why? Why did that relapse happen? We know that our medicines are designed to prevent them, to make for fewer relapses and fewer lesions, and few symptoms over time; and we know that none of our medicines are perfect. But if someone is on medicine for MS, one of the disease-modifying therapies, we want to understand is that medicine working well enough for that person, is it preventing relapses enough?

And the first thing that we have to make sure is if the patient is taking the medicine. And one of the main reasons that someone might have breakthrough MS disease -- that is, a relapse despite the fact that they've been prescribed to take one of the disease modifying therapies -- is because they may not be taking it or they may not be taking it correctly, or they may not be taking it enough. And that's an important thing for us to figure out because number one, the medicine is only going to work if someone's taking it; and number two, we have a variety of medicines and we're very lucky that in the modern era we have many different therapies to try and prevent relapses. So if someone is not taking their medicine or not able to take it, it's important that we know that and think about whether the medicine is working and whether it's the right one for the right person.

4. Why should you be aware of MS relapses?

I think that awareness of relapses is very important for a number of reasons. Number one is most of our medicines for multiple sclerosis are designed to prevent relapses. They're designed to prevent these new attacks and that's important because not always does an attack or a relapse of MS resolve completely. So someone who's had let's say loss of vision from an MS relapse -- what we usually call optic neuritis -- that may cause a worsening of vision and a loss of visual clearness or acuity that can last for a period of time. Even when it recovers someone might not get all of their vision back. They could be left with some degree of residual visual loss after a relapse. So preventing relapses is important because we want to prevent these new events and we want to prevent the accumulation of symptoms or disability that they can leave behind.

So it's important that people know what a relapse is, for one thing, because this is what neurologists and MS specialists are trying to prevent and it's important that people know when they happen so that their neurologist and MS specialist can be aware of it and use that to help guide their therapy. Another major consideration about MS relapses and being aware of them is that MS relapses are treatable potentially, and so it's important that people with MS are able to distinguish between daily fluctuations or small worsening of symptoms as opposed to a true new acute relapse. They really do need to bring this to the attention of their neurologist, their MS specialist, or their doctor to consider whether it should be treated.

5. When should you call your doctor?

If someone with MS is having a new symptom or they're concerned, I tell my patients that I'd rather know about it than not know about it. And so I tell patients to have a relatively low threshold to give us a call if they're having new symptoms so that we can be aware of them.

In general, if someone is concerned that they could be having a relapse, they've developed new symptoms, or they're troubled by the possibility that old symptoms have suddenly returned it's best for their treating doctor, their neurologist, or their MS specialist to know about it. I would prefer to know about symptoms like this sooner than later.

We think of relapse as a new inflammatory attack of MS, a new episode where the immune system is attacking part of the nervous system. What causes these new symptoms is an area in the nervous system that's being damaged by acute inflammation, new inflammatory changes. So we want to know about that soon because our treatments for relapses are involved in trying to stop that immune system attack from happening, to try and quiet it down. The sooner we know that, the sooner we can bring someone in, assess them, and see if they need to be treated for their MS relapse.

It's important for us to be aware of MS relapses and see patients who are having them as quickly as possible so that we can assess them directly. When we see someone who may be having a relapse we go through a neurological exam. Most people who have MS are familiar with the types of things that the neurologists will do to look at them such as checking their vision, checking their pupils, making sure that their eyes are working properly, making sure that their eye movements are normal and that their sensation and strength in their face is normal. Making sure that the strength in the limbs are what they should be, and that the reflexes are normal. We'll look at things like ambulation and gait, and walking and balance to make sure that all these are functioning properly.

When an MS relapse causes new symptoms, we can usually see them on this neurological exam, and that's why we're so meticulous about it. When we find signs and symptoms of a new attack and particularly if that relapse is causing some problem for a patient -- difficulty walking, difficulty working, difficulty seeing, some true challenge, some impairment of their quality of life and their function -- those are the relapses that we are apt to try and treat and try and treat promptly.

6. How does your doctor test for an MS relapse?

So for an MS relapse what we assess is a clinical assessment. It's really based on the history and the description of the symptoms, which is why it's so important that people with MS are aware of their symptoms and cognizant of them, and able to describe them to us in some detail. It's based on our neurological exam. It's based on what we find clinically in the room. There are tests that can help, so MRI is the most useful test to find additional information to confirm that a relapse is happening.

MRI, of course, is our way of taking a picture of the brain and the spinal cord, the central nervous system, and what we look for on MRI in the setting of a possible relapse are new lesions, new areas where the immune system has attacked, caused an area of inflammation or swelling. We can see that on an MRI. So often times it's a way of adding information for us to see how bad a relapse is or how many new lesions are there. But it's not necessary to judge whether someone is having a relapse, not in every case. That judgment is really made clinically.

7. Why treat an MS relapse?

The goals of treating an MS relapse, if it occurs, are to try and make it resolve as quickly as possible. So our principles of treating an MS relapse are to try and make those symptoms go away, to try and quiet them down. And so the sooner we do that, the sooner we can think about treating a relapse, the quicker we're likely to be able to bring about its resolution. One of the challenges of treating relapses is that the natural history of an MS relapse is to get better on its own, but often times we don't want to wait for that to just happen. We want to help that process along so that someone with MS will get their vision back quicker, get their walking back quicker, get their feeling back quicker and not wait.

What we don't know for sure is whether treating an acute relapse actually makes it recover better than it would have without treatment. That's actually very difficult to study, and it's almost impossible to do a study of that because we would never want to deprive treatment for anybody that ought to have it, so we may never have the full answer to that question. But our standard of care is to recognize an acute relapse, and offer one of the approved medicines to treat it, to bring about its faster recovery.

When a MS relapse occurs it can affect someone's functioning at home, it can affect their abilities at work; it can affect their quality of life; so relapses are not trivial in that regard. Sometimes even what is a mild relapse can impair someone's abilities. You know, for instance, a graphic designer who has optic neuritis, she may not lose a great deal of visual clarity but if she loses her ability to see color -- which is common with optic neuritis -- that could impair her work life in a way that somebody else might not notice because it's so important to her. And similarly, someone who uses their hands in a very fine-tuned way, a pianist or a surgeon, if they have a mild MS attack where they have clumsiness in their hand, that's something that someone else might not notice but for them it could be a huge problem for their abilities to perform their job, for their abilities to maintain their standard of living. And so treating those, and doing that in a personalized way where you take into account who is the person, what do they need to be able to do, and what is the MS relapse limiting for them, is very important in deciding when to treat.

8. How do you treat an MS relapse?

There are a number of different strategies that we can use to treat an MS relapse, but the principle is the same, and that is you recognize that a new attack of inflammation is happening in someone's central nervous system and we want to quiet that inflammation down. And so our medicines, our treatments for relapses, are anti-inflammatory strategies. We want to quiet the immune system down, the immune system which is attacking a person's myelin, attacking the brain or spinal cord, or optic nerve. We want to stop that from happening and do so as quickly as possible.

So our treatments are anti-inflammatory treatments, and the mainstay treatments are steroids or a hormone called ACTH, which is like a steroid. The steroids that are used for multiple sclerosis are anti-inflammatory steroids, and they're given in high doses for a short period of time. We call this "pulse steroids." So this is not the same as chronic, long-term steroid use; and again, the steroids are not to prevent relapses in the future. They are to treat the relapse that's happening now.

So the standard way steroids are given for an MS relapse is three to five days of intravenous (or IV steroids) and the dose is usually 1,000 milligrams of steroid a day, for three to five days. Now, this is a high dose. For something like asthma or arthritis someone might take five or ten milligrams of steroids. For something that's acute like back pain where someone takes steroids for a few days, it's often 60 or 50 milligrams of steroids. This is a thousand milligrams of steroids. It's a much higher dose intended to really quiet down the inflammation that's happening somewhere in the nervous system but it's only given for a few days and then it is stopped.

The steroids that are given for three to five days, usually intravenously are effective at bringing about the resolution of symptoms of an MS relapse. But it can take some days for that to happen, so I always talk to patients about what they can expect from the steroids in terms of how quickly will they work, and the answer is usually over days to a couple of weeks the relapse should be quieted down. But it does vary from person-to-person and from relapse-to-relapse.

And steroids given at these doses do have a set of side effects that we always have to counsel our patients about. So number one, this is usually intravenously, so typically our patients will get hooked-up to an IV once a day for three to five days. That can sometimes be done at home and have a nurse come out to the house, and set someone up at home to do this in the home. Sometimes it can be done in an infusion center or at an MS Center, so someone may have to come every day for three to five days for an hour or two and get their dose of steroids and then they can go about their day. And in the case of a severe relapse, or someone who has a considerable amount of disability, who maybe can't function at home while they're having a relapse sometimes, will make the decision to bring someone into the hospital and give them the steroids for a few days during a hospitalization.

Now, the steroids have a set of side effects that go along with them. Number one, patients can often experience an unpleasant metallic taste in their mouth when they're getting steroids at this high of a dose, so that's important to tell people. Number two, steroids even for a few days can cause people to retain some salt and water, so they might gain a few pounds of water for a few days. I tell my patients that they'll pee it out over the days that follow but people can be concerned about gaining water weight for a few days. It can sometimes make acne pop-up again, so folks who haven't had acne since they were in their teenage years might have it again, and they might flush and be a bit red in the face for the days that they're getting the steroids. That too is pretty transient, goes away. Steroids at these sorts of high doses can cause upset stomach and there's a risk for ulcers with doses of steroids like this. So we typically counsel our patients to take an antacid or a stomach medicine during the days that they're receiving the steroid course to try and make that symptom better.

Additionally, steroids can sometimes "rev people up" a lot. They can give people extra energy. This can be fine for some folks and I've had patients that wake-up at four o'clock in the morning while they're getting their steroids and go around and clean their house or their apartment and have a lot of extra energy. But sometimes it can actually keep people up at night. It can "rev them up" a little bit too much, and so at times some medicine to help people sleep or relax might be useful during the days that someone is getting courses of steroids. So I typically tell people to eat a low salt diet for the days that they're getting steroids to not eat terribly spicy or stomach upsetting foods.

{I tell patients] to try and get some extra potassium in their diet, because the same way that steroids can cause people to retain salt and water they can also lose a little potassium. Some bananas are a good dietary source of potassium. [People might want to] take an over-the-counter stomach remedy to prevent upset stomach, and to consider the need for something to help them sleep at night.

Now, there are medical conditions that can make steroid treatment more complicated. So, for instance, someone who has multiple sclerosis and diabetes, that needs to be managed very carefully because steroids, even given for a few days, can cause [blood] sugars to go very high. So sometimes folks with diabetes might need to be in the hospital setting while they're getting steroids, so that their blood sugars can be checked, so that they can receive insulin if they need it, and to keep that from becoming a problem. And similarly, someone who's had very high personal energy levels or almost mania on steroids on the past, they might benefit from being in the hospital for a few days to observe them and make sure that that doesn't occur again. In general, there's a risk and benefit to every treatment, and there's a risk and benefit to treatment with steroids. I'm emphasizing the side effects so that people know about them. But, in general, steroid treatment is brief, it's a few days long, it's well tolerated and it can be effective at bringing about the faster resolution of a MS relapse.

I try to explain to everybody when we're considering steroids what it will entail. One of the misconceptions is that these are the same type of steroids as body builder steroids. This is a totally different type of steroid. These are an anti-inflammatory steroid. Not the body building type.

Many people are concerned with the long-term consequences of steroids and those are much less the issue for the short pulses of steroids. And if we're doing our work with the disease modifying therapies, and someone's only having one relapse every three years or every five years, these short doses of steroids for such infrequent doses don't bring about the long-term consequences that people think about of steroid use.

I also think it's important that people understand that the dose of steroids, while very high is only given for a short period of time. One of the misconceptions about treatment of relapses is that if it's a mild relapse you can just take a little bit of oral steroids, a little bit of steroid pills and that'll do just as well; and that's really not how we practice. It's really a decision if a relapse needs to be treated or not, as the treatment is full. The treatment is the high-dose steroids given for a few days. But lower doses of oral steroids really have no place in the treatment of relapses anymore, and that's based on studies that were done in the '90s that have really changed the way we approach MS relapse treatment.

9. Are there other treatment options available?

So I think most relapses do recover and I definitely think that treating a relapse, for instance, with high-dose intravenous steroids brings about a faster recovery. I hesitate to tell people with MS relapses exactly what to expect. I follow it day-by-day and I'll often have someone come back in a couple of weeks after we've treated a relapse to make sure that it really has recovered and that those symptoms have faded out considerably. If someone has had an MS relapse and we've treated them with steroids and they have not recovered the function that we expect them to, we have a couple of options there too. I mentioned that in addition to steroids

there's another approved medicine for MS relapses. This is ACTH, and it's prescribed as Acthar Gel.

This is a self-injection of a hormone that is similar to a steroid in that it induces the body to make its own steroid, and it also works in a couple of other anti-inflammatory ways in the body. And this is often used as a second line medicine if steroids haven't been fully effective. It can sometimes also be used in place of steroids if someone has had one of those poor side effects or difficult consequences of steroids in the past and if there's reason to think maybe steroids aren't the best thing to do for this person again.

So if someone has either not responded fully to steroids in terms of their recovery, or they've had significant side effects or what we say contra-indications, reasons to avoid steroids, Acthar is another strategy that we can use to try and further bring about resolution of one of these attacks. Acthar has a similar side effect profile to steroid. Some studies have shown that it may be somewhat better tolerated. It is a more expensive medicine than steroids. Steroids are actually relatively in-expensive. Acthar is more expensive and so that risk and benefit has to be thought about also in terms of whether to use it.

We have a third option to treat relapses that have not recovered sufficiently, particularly severe relapses that require a hospitalization, and that's something called plasmapheresis or plasma exchange. This is a technique where this is done in the hospital. This is a technique where someone who's having an MS relapse is basically hooked-up to a machine not unlike a dialysis machine. Instead of doing what the kidneys do like a dialysis machine, this actually takes the inflammatory proteins out of the blood, and it's done every other day for about two weeks, so it's a real hospitalization where every other day this plasmapheresis gets performed and it slowly takes all of the inflammatory proteins out of the blood. This is an attempt to try and quiet down that inflammation that's causing these MS symptoms.

Plasma exchange is a more complicated procedure. It's only used for serious relapses that have failed to respond to one of those two other treatments. And it is not without its risks. It requires 10 days to two weeks in the hospital. It requires being hooked up to this machine and big intravenous lines, or IV lines, connect it. So this is not a trivial procedure but it is a next step for someone who's had a severe relapse that hasn't responded.

10. What are reasonable expectations for relapse recovery?

Different relapses take a different amount of time to recover, and some certainly much quicker than others. We typically tell our patients that the recovery is fastest at the beginning but they can continue to get some recovery and some function back perhaps even for months. But I usually say about a month after we've done a course of treatment for a relapse is a useful time point to think about how good a recovery have we been able to get. So around a month afterwards is when I try and at the very least to speak to my patients about it, and hopefully see them so we can assess them, go through their neurological exam again, look at all of those functions and make sure we've gotten them back and see where we are.

I think the other point worth making about follow-up after a relapse is to consider if some degree of disability has been left behind. Does that change someone's new state of affairs for them after this relapse? And sometimes that can help to inform the decision about whether the disease modifying therapy is working because the goal is to prevent relapses, to prevent

disability, and to keep people well. If someone has had a severe relapse that has left them with some residual disability, we may be more apt to think about changing that disease modifying therapy, changing strategy moving forward.

11. What about pregnancy and MS relapses?

One of the important things about taking care of people with MS is that many of them are young women, women of child-bearing age and potential, and so we have to think about how pregnancy fits in when deciding on treatment and when thinking about relapses. First of all, pregnancy is a somewhat protected time for people with MS. There's a lower risk of relapses during pregnancy than there is not during pregnancy. The reason for this is basically that during pregnancy a woman's immune system has to be quieted down a bit so that she can carry the fetus and the immune system doesn't attack, doesn't attack this fetus even though it's not entirely her. So the immune system is under control and told to be a little bit quieter during pregnancy, and for folks with auto-immune disease like MS that often leads to an improvement or a lower risk of relapses during pregnancy. Most of our MS disease-modifying therapies aren't used during pregnancy, but pregnancy itself serves that purpose. It helps to prevent relapses to an extent. The postpartum period, after a woman delivers, is a somewhat riskier time for MS relapses. Just as the relapse rate goes down during pregnancy, there's an increased risk after she delivers and the immune system is revving itself back up again and getting back to normal, so that postpartum few months is a somewhat more vulnerable time. Certainly not every woman with MS who delivers a baby is going to have a relapse, but I definitely tell my patients to be aware of that, to be mindful of it, and certainly to communicate with us in the postpartum period if she's having any new neurologic symptoms that could be a relapse.

I also tell my patients who are pregnant or considering getting pregnant that steroids are used during pregnancy. We have perhaps a higher threshold to treat someone with steroids during pregnancy, just because the less medicine the better during a pregnancy. But steroids are approved for use in pregnancy, particularly in the third trimester; and if a relapse occurs to let us know and for us to consider the use of steroids even though she's pregnant. I think that's an important point because some people with MS think that because they're not taking their disease modifying therapies during pregnancy, they can't take any other therapies, they can't take any other medicines, and that isn't true. So steroids can be used. We do that in conjunction with a woman's OB GYN so that we're all on the same page. But our hands aren't tied during pregnancy if a relapse were to occur.

12. What is a good plan for managing MS relapses?

MS relapses happen unpredictably and so I think it is hard for people with MS to know when they're going to happen and to plan ahead for them. One thing that some folks with MS will do is if they disclose to their employer that they have multiple sclerosis, they may want to let them know that in the event of a relapse they may have to miss work or they may have to be out of work or need accommodations. They may need to work from home for some period of time while the relapse is ongoing or while the relapse is being treated. Some patients of mine have filed FMLA paperwork in advance which allows them family medical leave in the event that relapse could occur that might take them out of their workplace for a period of time.

In general, I tell my patients to focus on the fact that whatever the relapse is we are going to address it and so I try to have them focus on the plan, focus on the fact that we're going to bring them in, we will assess them with our neurological exam, we'll consider the need for MRIs, we will consider the need for relapse treatment, and that there's a plan and a response in place if a relapse occurs. I think that's an important thing to focus on instead of the unpredictability, is to focus on the fact that there's a predictable response that their doctors will have for them.

13. What does the future hold for MS treatment advances?

So relapses happen in very different frequencies for different people, and there are folks with MS who have had one relapse in ten years and there are other people with MS who had multiple relapses even in a year or two. On average when we look at how we treat MS today people have far fewer relapses now than they did 15 or 20 years ago. In the old days we used to think of one relapse a year being normal, though there is no one "normal" for people with MS. But our modern clinical trials --how we assess whether our disease-modifying medicines are working -- bring that relapse rate down to one in every three years or one in every five years. There have even been clinical trials where the relapse rates have been more like one in every ten years, and that's a wonderful thing for people with MS, though it's not possible for everyone. But it's important that we try to get the relapse rates down that low or lower moving forward, and I think that our new generation of medicines has the potential to do that.

You know, I think multiple sclerosis is a tough condition and I think it's tough for anybody who gets diagnosed with it. But I think if one has to have multiple sclerosis, this is the best time in human history to have to deal with it, because we have so much at our disposal that we can do for people who have MS. And I encourage people with MS to seek care and to seek a neurologist or seek an MS specialist who knows about the current advancements and the current treatments that we have. Because if you have to have multiple sclerosis and you have it now, let's use all of the modern abilities that we have and all of the advancements that have happened in the last 20 years for everyone's benefit. Nobody should have to be without that.