CENTER FOR SPECIALTY PHARMACY EDUCATION

101

A CSPE Core Curriculum Series

ProCE

NASP
NATIONAL ASSOCIATION OF SPECIALTY PHARMACY

MS-101Pathogenisis: Diagnostic and Clinical Course Treatment Considerations in MS

Digital Guide Book

Multiple sclerosis (MS) affects an estimated 400,000 people in the U.S., with approximately 10,000 new cases reported every year. As a chronic and progressive neurologic disease that requires lifelong, dynamic treatment via costly, high-touch medications that also require special handling and storage, multiple sclerosis therapies are often delivered via specialty pharmacy programs.

The **NASP/CSPE MS Core Curriculum Series** is intended to increase specialty clinicians' knowledge of the evolving MS treatment paradigm and provide the necessary professional education to counsel patients and caregivers on the myriad therapeutic options, routes of administration, and behavioral/clinical/financial variables that must be considered alongside drug therapy choices when treating MS across care settings. As the first installment in the four-module NASP/CSPE MS Core Curriculum Series, this activity introduces MS pathology, epidemiology, and symptom management to specialty pharmacists and nurses

Learning Objectives

The target audience for this activity includes pharmacists and nurses caring for MS patients.
Upon completion of this activity, the participant will be able to:

- Describe the basic pathology, epidemiology and demographics of the MS population.
- Explain the diagnostic process for MS and the principles of the McDonald Criteria.
- List the four major clinical courses of MS, Relapsing Remitting MS (RRMS) and Secondary Progressive MS (SPMS).
- Explain the diagnostic category of Clinically Isolated Syndrome (CIS) and be aware of the high risk of MS in this setting.
- Review symptomatic issues that complicate MS and how best to manage them.

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About the Faculty

Joy Derwenskus, DO, MS

Dr. Derwenskus attended the University School of Osteopathic Medicine and Health Sciences in Des Moines, Iowa. Upon completion of medical school, she did her internship at Evanston Hospital in Chicago followed by neurology residency at Case Western Reserve University in Cleveland, Ohio. She then went to Mt Sinai in New York City for fellowship in MS where she was a Clinical Fellow of the National MS Society. During fellowship also completed a master's program in clinical research. In 2005 she joined the faculty at Northwestern University working in the Northwestern Comprehensive MS Program where she was promoted to associate professor of neurology. In 2015 she moved to Nashville, TN and joined Advanced Neurosciences Institute in Franklin. There she sees patients and participates in clinical trials. She also publishes, writes book chapters, presents at meetings, and speaks nationally about MS.

Heli Hunter, MSN, ACNP, MSCN

Heli Hunter received a Master's Degree in Nursing as Acute Care Nurse Practitioner at Vanderbilt University in 2000 and has over 20 years of nursing experience Multiple Sclerosis. She was an integral part in the establishment and development of Advanced Neurosciences Institute in Franklin, TN, and helped develop and direct a thriving multiple sclerosis clinical practice and research center. Currently she works at Schapiro MS Center in Golden Valley, MN, focusing in patient care and clinical research, while staying active in public and peer education. She has been certified as an MS Nurse since 2002 and has served as a past member of the Multiple Sclerosis Nurses International Certification Board. Heli is passionate and committed to sharing her knowledge and experience of MS with other health care professionals, and her goal is to enhance the role of nurses and advance practice providers in MS care.

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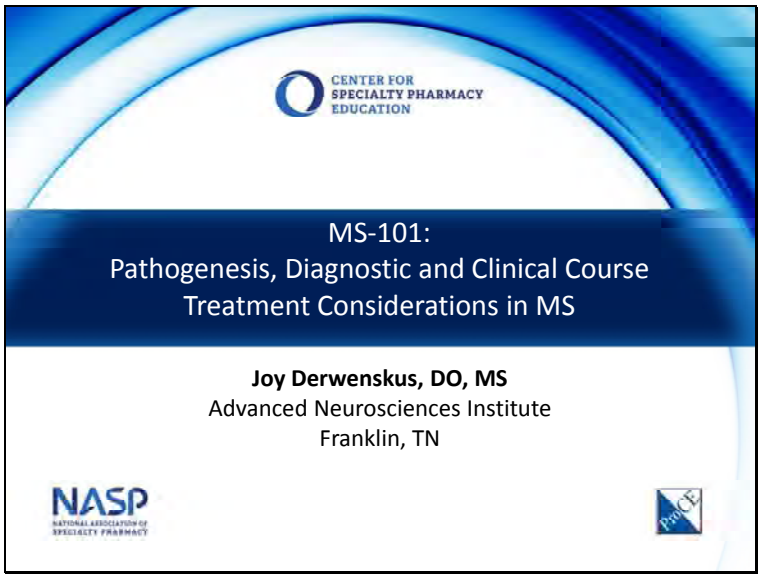
The NASP Education Committee felt the following information may be helpful as part of the MS Curriculum Series. This is published on the National MS Society's webpage - a highly recommended resource for MS information. www.nationalmssociety.org

What are the different types of MS?

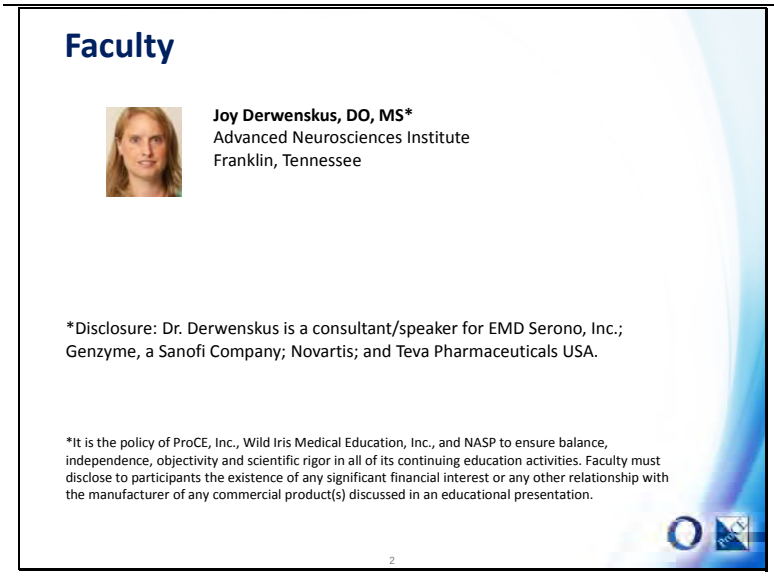
In an effort to develop a common language when discussing, evaluating, and treating MS, the Society conducted an international survey among scientists who specialize in MS research and patient care. Analysis of the responses resulted in the publication of four disease courses in 1996. In 2013, the International Advisory Committee on Clinical Trials of MS updated the disease course definitions based on advances in the understanding of the disease process in MS and in MRI technology:

- **Clinically Isolated Syndrome (CIS)**: a first episode of neurologic symptoms caused by inflammation and demyelination in the central nervous system that may or may not go on to become MS.
- **Relapsing-Remitting MS (RRMS):** a disease course characterized by clearly defined flare-ups (relapses) or episodes of acute worsening of neurologic function followed by remissions (with partial or complete recovery) during which no disease progression occurs. Frequency: Approximately 85% of people are diagnosed with RRMS.
- **Primary-Progressive MS (PPMS):** a disease course characterized by nearly continuous worsening from the onset of symptoms, with or without occasional relapses. The rate or progression varies over time, with occasional plateaus. Frequency: Approximately 15% of people are diagnosed with PPMS.
- **Secondary-Progressive MS (SPMS):** a disease course that follows after an initial RRMS course. Following an initial period of time with RRMS, the disease becomes more steadily progressive, with or without occasional relapses. Frequency: If left untreated, 50% of people with relapsing-remitting MS develop this form of the disease within about 10 years of initial diagnosis.

Source: http://www.nationalmssociety.org/About-the-Society/Press-Room/MS-the-Disease#section-11



Well, thank you for joining me today. Today, we're going to discuss MS-101, covering pathogenesis, diagnostic and clinical course treatment considerations in multiple sclerosis.



My name is Joy Derwenskus and I'm an MS specialist. I practice at Advanced Neurosciences Institute in Franklin, Tennessee. There are my disclosures. I've cared for MS patients and had an MS-specific practice for a little over ten years.

Learning Objectives

- Describe the basic pathology, epidemiology and demographics of the MS population.
- Explain the diagnostic process for MS and the principles of the McDonald Criteria.
- List the four major clinical courses of MS, in particular Relapsing Remitting MS (RRMS) and Secondary Progressive MS (SPMS)
- Explain the diagnostic category of Clinically Isolated Syndrome (CIS) and be aware of the high risk of MS in this setting.
- Review symptomatic issues that complicate MS and how best to manage them.

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The learning objectives for today. We'll describe the basic pathology, epidemiology and demographics of the MS population; explain the diagnostic process for MS and the principles of the McDonald criteria; list the four major clinical courses of MS, in particular relapsing-remitting MS and secondary progressive MS; explain the diagnostic category of clinically isolated syndrome, or CIS, and be aware of the high risk of MS in this setting; review the symptomatic issues that complicate MS and how best to manage them.

MS-101 Overview

- Background
- Epidemiology of Multiple Sclerosis (MS)
- Anatomy and Pathophysiology
- Clinical symptoms of MS
- Diagnosis utilizing the McDonald Criteria
- Disease course
- Clinically Isolated Syndrome (CIS)
- Symptoms of MS
- Symptomatic management

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The overview of the MS-101 talk: we'll cover some background and epidemiology of MS, including some anatomy and physiology. We'll talk about the clinical symptoms of MS, what makes one be suspicious for MS. How we diagnose MS, utilizing the McDonald criteria. We'll go over the disease course, including what's referred to as this clinically isolated syndrome, or CIS. Then, we'll end with talking about the symptoms of MS and the symptomatic management.

Background

- Multiple Sclerosis (MS) is a disease of the central nervous system (CNS).
- The underlying pathologic process is autoimmune in nature, which leads to myelin destruction.

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Some background information. MS is a disease of the central nervous system, the brain and spinal cord. The underlying pathologic process is autoimmune. The body starts attacking itself, and specifically attacking myelin, which leads to this breakdown of myelin.

Epidemiology of MS

- Age of onset usually 20-40
- Women outnumber men 3:1
- ~400,000+ affected in U.S.
- ~8,500–10,000 new cases yearly
- More common among those of Northern European descent
- Most common cause of disability in young adults

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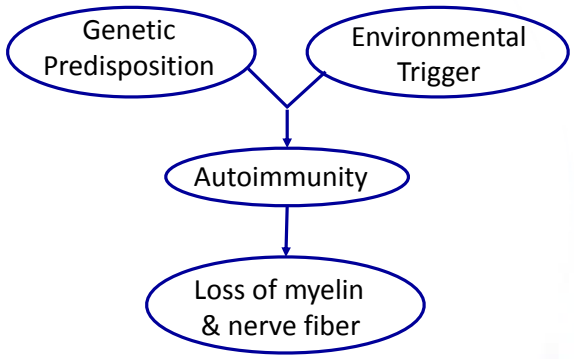
We say MS is a disease predominantly of young women. The typical age of onset is usually between the 20s and 40s, but that's not to say that people can't present younger, or even in pediatric populations; as well as at the other end of the spectrum. It presents a little older in age, but most commonly present in 20s to 40s. Women do outnumber men. Now, the ratio we would say is 3:1. It is more common among those of Northern European descent. And, it is the most common cause of disability in young adults.

What Causes MS?



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It's hard to believe we still don't know what causes MS. It is really thought that if you take someone, an individual who has a genetic predisposition, and then expose them to some environmental trigger, this is what leads to this autoimmune process and destruction of the myelin; and potentially the nerve fibers as well.

Etiology of Multiple Sclerosis

- Inflammatory disease of the Central Nervous System (CNS)
- Exact cause remains unknown
- Higher prevalence in more temperate latitudes
- Risk for disease is acquired by adolescence (~15 y/o) and maintained with migration to other latitudes
- Suggests environmental exposure may have a role in pathogenesis
- Vitamin D (sun exposure) may be protective against developing MS

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We refer to it as an inflammatory disease, again, of the central nervous system, and the exact cause remains unknown. It is more common and has a higher prevalence in the more temperate latitudes, so northern North America; Canada. The risk for disease is acquired by approximately age 15. What they say is that you assume whatever risk of where you've lived until the age of 15, and if you migrate after that to other latitudes, you maintain where you lived prior to adolescence.

Now, given this whole latitude difference, kind of leads to concern that, there must be some environmental exposure that plays a role in the pathogenesis. Mostly an area of big interest these days has been vitamin D. What don't people get as much of in the more northern latitudes in North America? Well, it's sun. There is some thought – and what do we get from sun? It's vitamin D. There's some thought that, really, vitamin D may be protective against developing MS. There's lots of studies looking at vitamin D levels and the association with increased risk for MS, and even more disease activity in patients who have MS.

Etiology of MS: Emerging Theories

- Possible infectious agents such as **Epstein-Barr Virus** (EBV), **Human Herpes Virus 6** (HHV6), **Chlamydia pneumoniae**, ***Mycobacterium avium* intracellulare infection (MAI),** etc. have been considered as possible triggers for MS:
  - EBV persists in B cells and MS patients may not be able to eliminate these cells as well[1]
  - EBV may induce a humoral response, and the antibodies may cross react with myelin basic protein (MBP)[2]

1. Fernandez-Menendez S et al. Epstein-Barr virus and multiple sclerosis: from evidence to therapeutic strategies. *J Neurol Sci* 2016 Feb 15;361:213-9. Epub 2016 Jan 6.
2. Mameli G et al. Serum BAFF levels, methypredsinolone therapy, Epstein-Barr virus and Mycobacterium avium subsp. paratuberculosis infection in multiple sclerosis patients. *Sci Rep* 2016 March 9;6:22401.

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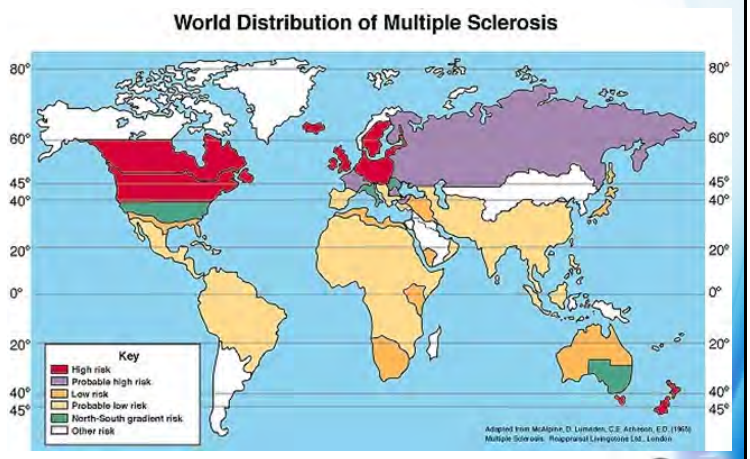
Now, what is this environmental trigger in terms of could there be some infection that's associated with that? This is an emerging topic right now; but all along they've thought, maybe there's something infectious. Various organisms have been considered over time, like EBV, or Epstein-Barr virus, which is a virus that causes mono; human herpes virus 6 (HHV-6) or chlamydia; mycobacterium avium. They've all been considered as possible triggers.

But I think the hot, as I call it, the hot virus right now is the EBV virus. And so, there are lots of studies looking at this. Some of the more recent ones looking at EBV actually persists in B cells, and MS patients maybe can't eliminate these cells as well; and that the EBV may induce a humoral response, and that these antibodies that are produced may cross-react with myelin basic protein, which then leads to this autoimmune process, attacking the myelin. But again, we don't really know at this time. I always say, no virus has stood the test of time but the EBV virus right now is kind of the hot virus.

Worldwide Prevalence of MS



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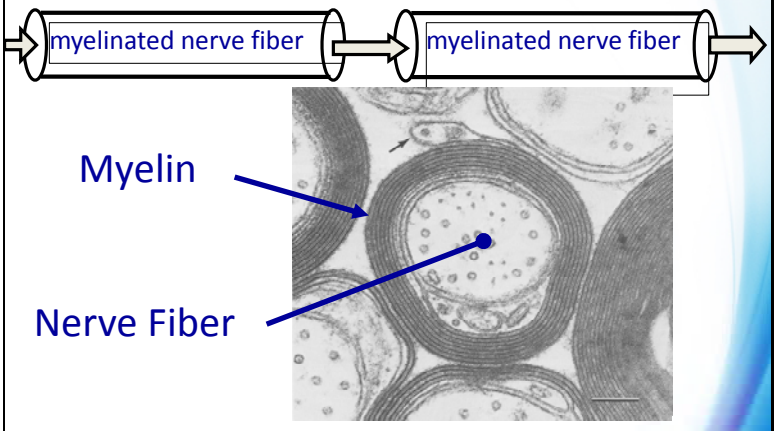
This is showing the worldwide prevalence of MS and what I was talking about; that the more northern temperate latitudes have a higher incidence of MS. Again, not to say it doesn't occur in other places, but much more common.

Normal Myelinated Axon



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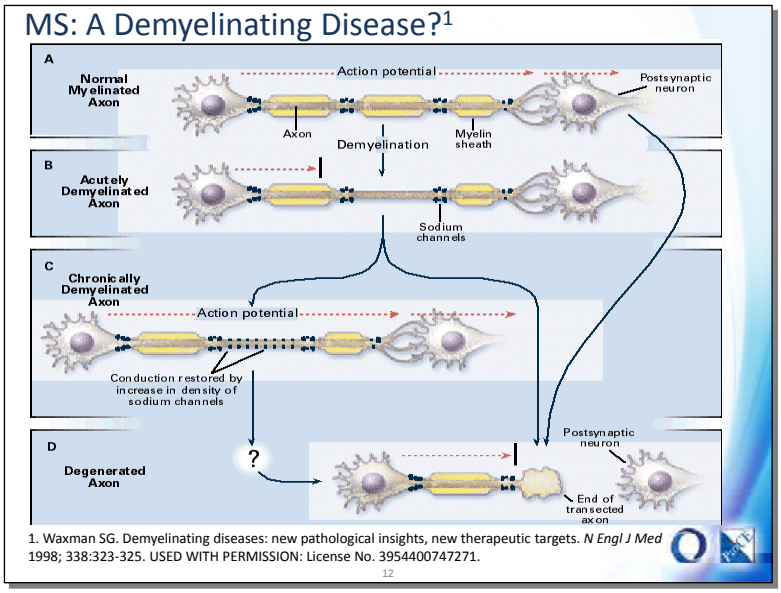
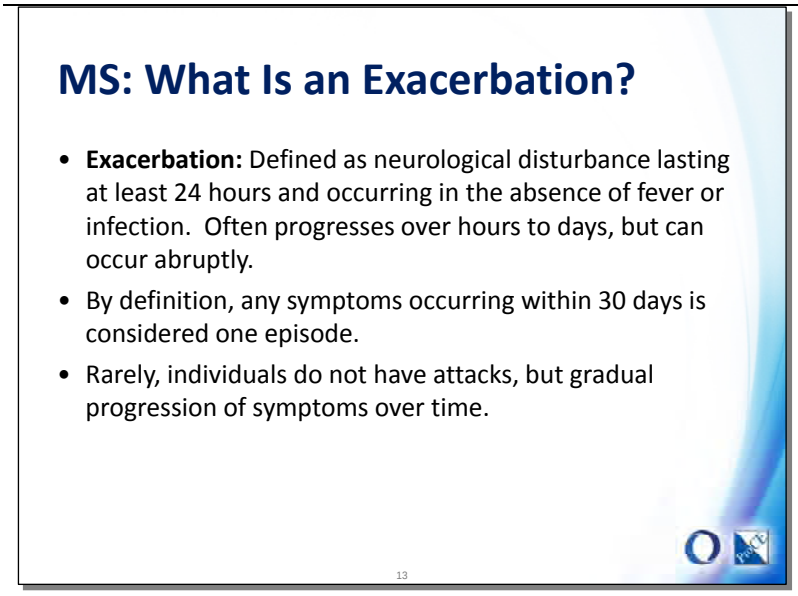
Looking at some pathology now. This is electron microscopy of a neuron and it's in cross-section here. You see the nerve fiber here in the center, and then around it are these layers of myelin. That's what it looks like microscopically.



This figure shows a normal myelinated nerve cells, or neuron. And you have the cell body and the axon here and these cells can be very long. In order for a message to travel very quickly, you have this myelin covering it. So, it's insulating the nerve cell, and the message travels very quickly, then, down actually, it jumps from node to node here, but the message can travel very quickly through this nerve cell so the signal can get through.

Now, what can happen is that, for some reason, if the body attacks itself and attacks this myelin, you get breakdown of the myelin, and the message is impaired getting through. It can't get through. Depending upon where that occurs will determine what type of symptoms one can have.

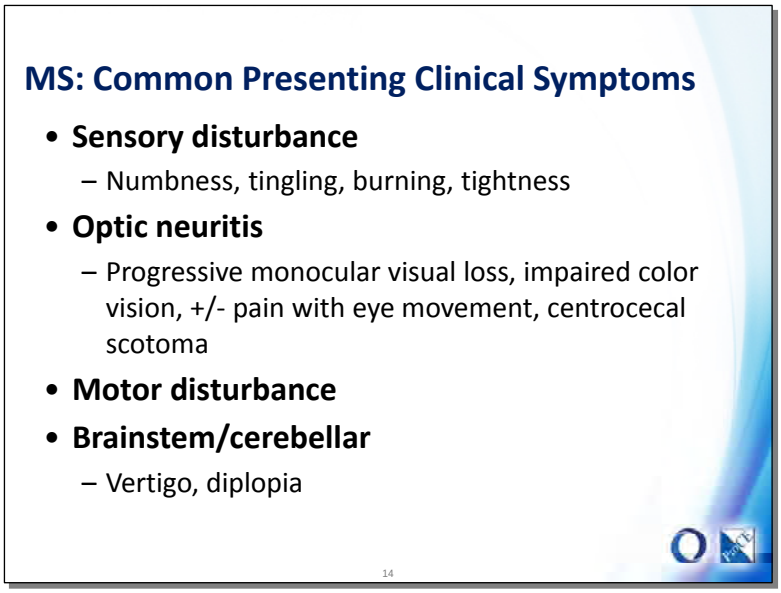
Then I want to jump down to this bottom view. Not only do we get demyelination here, where the myelin may be affected and be destroyed, but sometimes the nerve fiber itself can get broken down. We call it transected. We don't know what happens first. Is it just that the myelin is broken down, and that doesn't provide nutrients to the nerve fiber itself, and that's what leads to the destruction of the axon? Or, is it just that the axon gets destroyed, and that secondarily the myelin is impacted? But regardless, these are probably – this type of involvement, when you get this transection of the nerve fiber itself, probably a more destructive-type lesion. Later I'll show you some images on MRI, and what that might correspond with, and what we see on MRI.



What's an exacerbation? We consider an exacerbation a neurologic disturbance lasting at least 24 hours; occurs in the absence of fever or infection. Typically, what happens is that people will get symptoms that will slowly progress over hours to days. It is, however, possible that someone can get symptoms that come on much more acutely, that even could be concerning at times for something like a stroke. But usually, symptoms will slowly worsen over hours to days. We would consider that an exacerbation or a relapse. We use these terms interchangeably.

By definition, any symptoms that occur within a 30-day period of time is considered one episode, and if you have onset of symptoms and then two weeks later you get something else happening, that's still all considered part of one relapse, or one exacerbation.

Rarely, there's a form of MS where people don't have attacks. They just have slow worsening of symptoms over time; and we'll talk about that.



What are some of the common presenting symptoms that people will have with MS, the clinical symptoms? Well, probably the first two are the most common, and that's sensory disturbance; whether that's numbness or tingling; burning; tightness sensation. People sometimes will describe where they might have a little numbness in their toes; and then a day or two later that numbness has gone up to their knees; and then a few more days later then it's up to the waist, and, they describe that it feels like they have a tight belt around them. That's all a very typical presentation for involvement of the spinal cord, actually, something that we would refer to as transverse myelitis. You need to have a characteristic pattern of this, which makes you be suspicious that it's something demyelinating.

Sensory disturbance is very common; also is something called optic neuritis. Optic neuritis is just inflammation of the optic nerve. And what people will present with is, they have progressive, usually monocular, so, in one eye, vision loss, which kind of worsens over time. Pretty common that they will have pain with eye movement. They may notice that colors are off in that eye. Like, if they're looking at stoplights or stop signs, the red seems more orange. They sometimes describe where they have a patch, like, a scotoma. So, it's a centrocecal scotoma, where there's a patch that they say they can't see through; it looks like they're looking through a veil of some sort, or a screen. That's also a very common presenting symptom with MS.

You can also have motor disturbance, weakness, whether that's half an arm and a leg, or both legs. You could have brainstem or cerebellar involvement that can lead to vertigo, which is the abnormal sense of movement, whether that's spinning, or feeling like you're on a ship, or diplopia, double vision.

Symptoms at Onset of MS[1]

Symptom Type(s)	Percentage (%)
Sensory changes in arm/legs	33
Unilateral visual loss	16
Polysymptomatic	14
Slowly progressive motor deficit	9
Diplopia	7
Acute motor deficit	5
Others (bladder, cognitive, pain, etc.)	16

1. Diagnosis of multiple sclerosis. Paty DW, Noseworthy JH, Ebers GC. In: Paty DW, Ebers GC, eds. *Multiple sclerosis*. Contemporary Neurology Series, FA Davis, 1998.

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Now, if you look at a breakdown, and this is from a Canadian group, of what do people present with at onset of MS, so, as I was mentioning before, probably the most common thing are sensory changes, followed by vision loss, unilateral vision loss. Sometimes people present with what we call polysymptomatic. Maybe they have vision problems as well as some sensory. They have more than one symptom going on at one time. Then you can see motor deficits, that diplopia; here's this more acute motor deficit. Like I said, these would be situations that sometimes, maybe they'd even present to an ER acutely, thinking they're having a stroke. Again, not very common, but can occur.

Then these others, which they've lumped together here. But, rarely, people can present with just cognitive changes alone; or just bladder changes alone; or I've seen just sexual dysfunction. Not as common, but you are lumping those together here.

Classic Definition of MS:

Lesions of the central nervous system with dissemination in space and time

Caveat: No better explanation is currently available.

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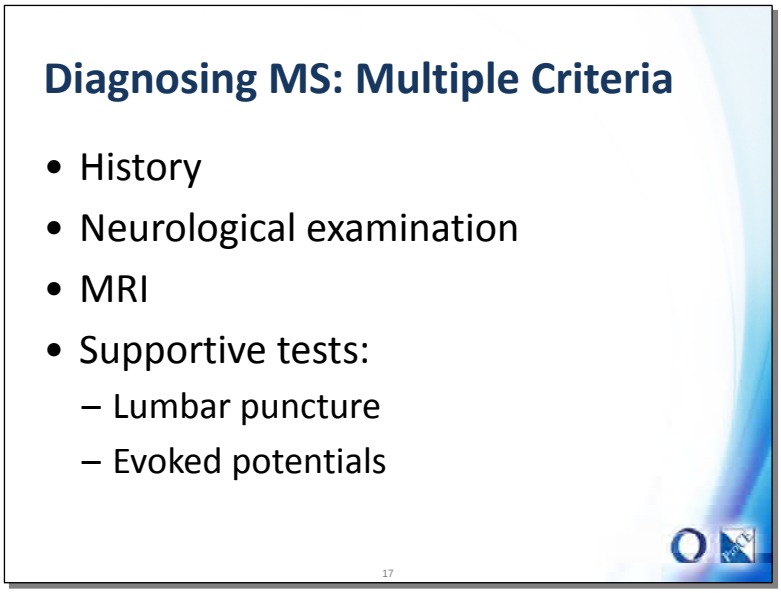
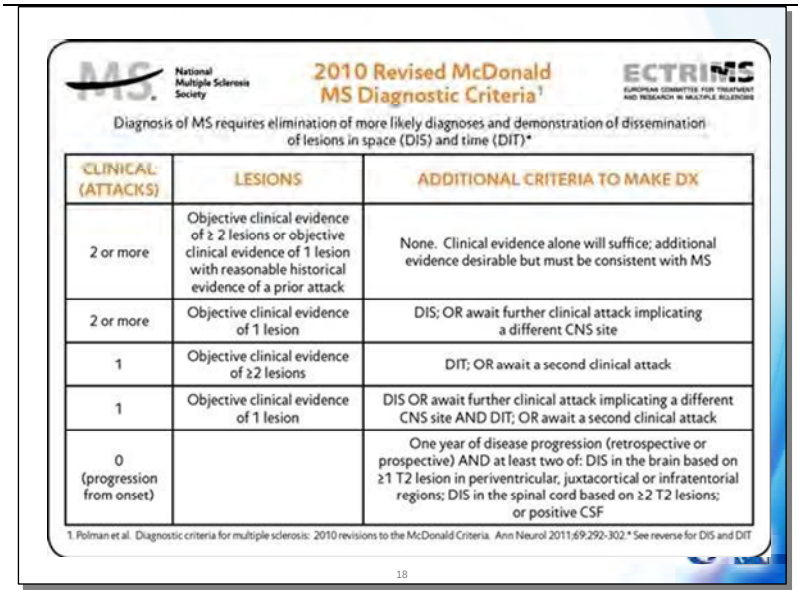
The classic definition of MS is that you get lesions of the central nervous system, and you have to have, or fulfill, dissemination in space and dissemination in time. Meaning that you have involvement of different parts of the nervous system, and spread out over time. So, more than that 30-day interval that I was talking about. Now, the caveat always to making a diagnosis of MS is that there's no other better explanation for that.



Now, when we're making the diagnosis, probably just like all of medicine, the most important things are the history and the exam. You know, getting the story from them. What have your symptoms been? How did the symptoms come on, and what parts of the nervous system do you think were involved, based upon what their symptoms were? Then, obviously, performing a comprehensive neurologic examination; and if you find, abnormalities on that, that would be consistent with what their presenting symptoms were. The history and exam are probably the most important things. Nowadays, MRI also has been very helpful in terms of diagnosing MS. Those are probably the three main things that we do, is history, exam and MRI.

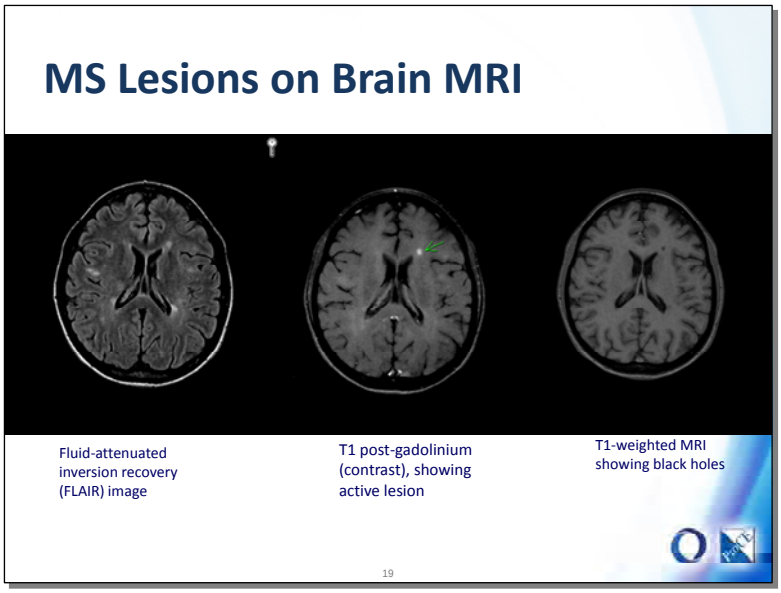
Now, in some cases we can do some other supportive tests as well. These tests may or may not be done. I think neurologists all have kind of differing thoughts about doing these tests. I think in some cases people do these tests on every patient that they're working up for MS. In other cases, maybe they're doing it for concern there's something else potentially going on. If we want to look at the spinal fluid, we can do a spinal tap, looking at the routine things like, the protein, and the cell count. But also, we can look for these proteins that are called oligo clonal bands in the spinal fluid. If they are unique bands, more than what you see in the blood that would be supportive of a diagnosis of MS, as well as something called an IgG index.

Then, you can do evoked potentials. There are different types of evoked potentials: visual evoked potentials, somatosensory evoked potentials, and brainstem auditory evoked potentials. But those are tests, again, if abnormal, would support that diagnosis. Potentially, if you have a patient, let's say, they presented with something maybe in the spinal cord. If you did a test that showed abnormality with the visual evoked potentials, meaning that the optic nerves are involved, even though they've never had any visual symptoms, support dissemination in space as well.



This is what's referred to as the McDonald criteria for diagnosing MS. It has been revised several times now, but this top portion shows if someone has two or more clinical attacks, and if you find you have abnormalities on their examination supporting those attacks, really, you don't have to do any further kind of testing. That's kind of the old diagnosis, where we would have to wait for somebody to have two clinical events. But what these McDonald criteria did is actually took somebody who presented with a single episode, and enabled us to take MRI, and any change on MRI, to make a diagnosis of MS. We're able to diagnose MS earlier. Again, we take somebody with a single event, and then utilize MRI to kind of confirm that dissemination in time.

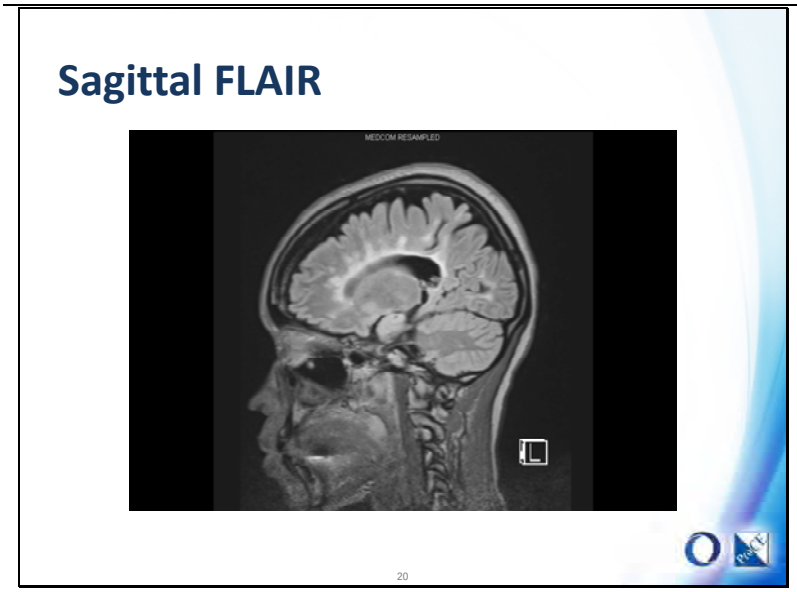
Then this bottom one is showing where you've not had any clinical attacks, and there's this rare form of MS that's referred to as primary progressive MS, and this gives the diagnostic criteria for that, to fulfill dissemination in space and dissemination in time.



Here are some MRI pictures showing some typical lesions that we see in MS. These are all what we call axial images. This first one is a FLAIR MRI here. What FLAIR sequences do is, they make the CSF dark and the ventricles become dark, and so we can see lesions right up next to the ventricles very well. It's very common that people in MS will get lesions right next to the ventricles. This is a FLAIR sequence.

The next one is what's called a T1 post-gad sequence. This is when we're giving the gadolinium or the contrast dye. What you can see is that this lesion here is really, these other spots, you don't really see on here but this one, shows up very bright on this scan. So, this is an active lesion. We say it enhances with gadolinium. We know that's a newer lesion with active inflammation. That lesion is probably anywhere from about four to six weeks active, so we know that that's a newer spot. This other spot that's out here, you can say it's older, older than four to six weeks old. That's all you can say about that; but that there's indication of both new and older disease.

Then this last MRI sequence here is what's called a plain T1, without the gadolinium. Now, what you can see here is that this active lesion is dark on this one. We refer to that as a black hole. You can see black holes acutely when you have active inflammation. But over time, if that black hole persists on a follow-up scan, that probably is a more destructive-type lesion, what I was showing before, in that picture where the axon was destroyed, or transected. This probably refers to these more destructive-type lesions like that, if it persists.



This is a sagittal FLAIR sequence. When we look at MRIs in MS patients, we like to look at what's referred to as a sagittal view. You can see that's the nose, and the back of the head, and a slice down the center here, of the brain. You can see these white spots, all kind of perpendicular here to this lateral ventricle. We refer to these as Dawson's fingers. These are very characteristic lesions with MS. You see those, that's usually what we're going to be dealing with. That's a very common appearance of MS on MRI.

Typical MS Disease Course

- 85% of patients present with relapsing remitting MS (RRMS)
- Within 10-15 years, 50% of patients will develop secondary progressive MS (SPMS), which is associated with significant disability
- Over years there is often progression of disability (EDSS - expanded disability status scale). There is some data to support baseline disease burden, and early change in MRI predicts disability.

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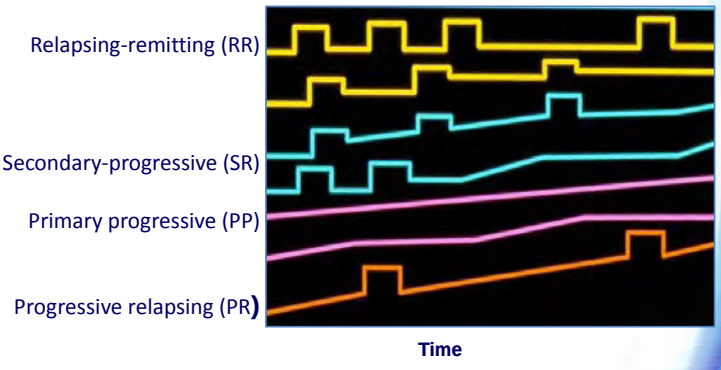
What's the typical disease course in MS? Well, most patients, about 85% of patients will present with the relapsing-remitting form of MS. These are the patients that have attacks or symptoms, these exacerbations or relapses, and then get better.

Now, if you follow people over time, and if you look at natural history studies, within 10, 15, 20 years, about half of these patients will transition into a more progressive form of MS that we refer to as secondary progressive MS, which is associated with more disability – with significant disability. Now, regardless, MS over time, often will progress and we if we're looking at disability, there's a scale that we use. It's referred to as the EDSS—the expanded disability status scale. It's a scale that's between zero and ten, zero being completely normal; ten is death. The lower scores of the scale are often determined by abnormalities on the neurologic exam.

The scale's really been criticized because it is really geared towards people who are ambulatory and heavily weighted for ambulation. If you take somebody, for instance, who walks with a cane, they're automatically a 6.0. If they walk with a walker, they're a 6.5. If they're in a wheelchair, they're a 7.0. It's been a criticized scale, but nonetheless is the scale that we use to follow patients. Then, we have data that has shown if you look at baseline disease burden on MRI, or even change early in the disease course, will predict disability. People with higher burden of disease at onset will have greater disability, and the same holds true if you have more change over time early on, for disability.

Clinical Patterns of MS[1]



1. Adapted from Lublin et al. Defining the clinical course of multiple sclerosis: results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis. *Neurology*. 1996;46:907-911.

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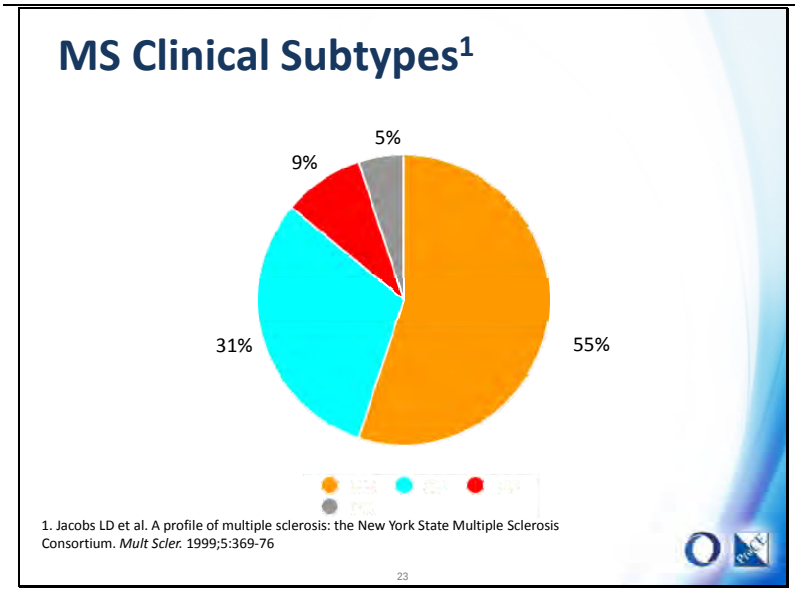
Here are the clinical patterns of MS. The top two yellow ones are what's referred to as relapsing-remitting. You can see somebody coming along, and then they have a relapse; then they stabilize; and then they get better. Then, they go along till they have another relapse. That's relapsing-remitting.

This one is also relapsing-remitting, but you can see if you have a relapse is that you don't always make a complete recovery. This person, for instance, didn't get all the way back to their baseline. They actually had some leftover symptoms, some residual symptoms from a relapse. Then they went on, had another relapse, and they made an incomplete recovery. You can see, you can accumulate disability over time just by having relapses, and therefore we like to try to lessen the risk for having relapses if possible. This is relapsing-remitting MS.

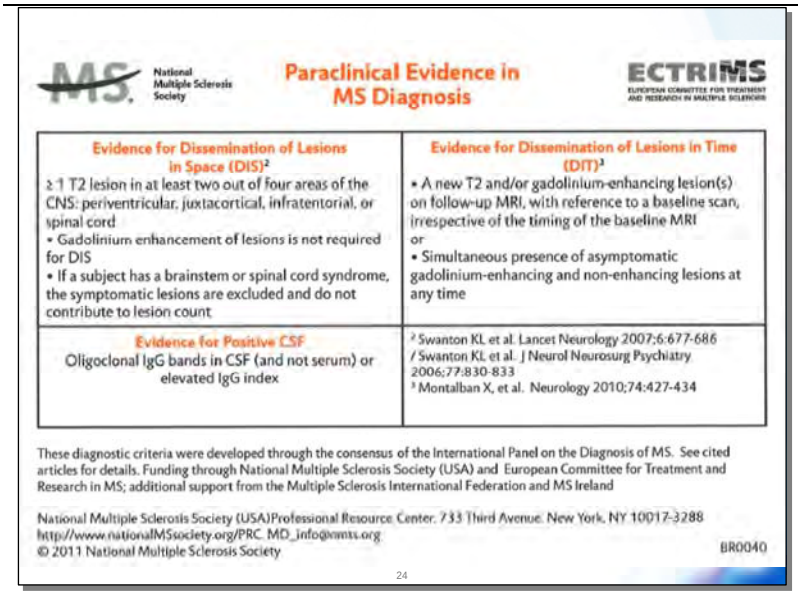
Then, this is the course I was talking about referred to as secondary-progressive. You have a patient having a relapse; but then in between the relapse they slowly are worsening their baseline. Usually, walking and strength. Then they can have another relapse, and they can slowly worsen. Then you can see, on this line, they stabilize, but then they slowly worsen. You get to the point where, in some of these patients with secondary progressive disease, they may no longer have relapses; they just have this slow progression.

Then the rarer form of MS is what's called primary progressive MS, and that's where people just have this slow progression, no relapses, and no acute symptoms. This type of MS, as I say, like all disease, is very unpredictable. Sometimes these people can plateau out for a period of time, then they can slowly worsen again, and they can plateau out. That's what we refer to as primary progressive.

Then there's even a rarer form of MS referred to as progressive relapsing, where there's slow progression over time, and you think maybe they're going to have primary progressive MS, and then they go on to have a relapse. All of these forms, wherever there's relapses, will be considered a relapsing form of MS. We would treat it as that, as a relapsing form of MS.

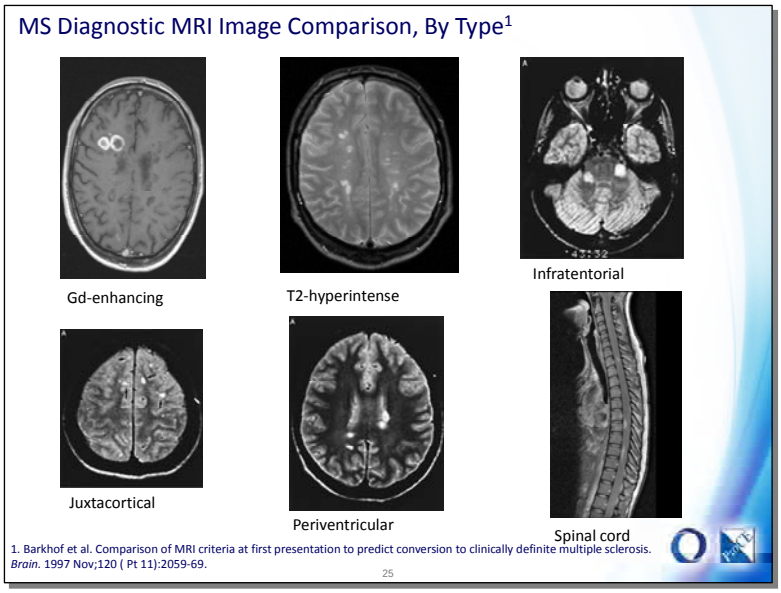


If you look at the breakdown of the clinical subtypes in a population, this is from the state of New York consortium, they looked at in their database. You can see that the vast majority of people here are going to be in relapsing-remitting MS, and then 31% in secondary progressive; 9% primary progressive; 5% of this progressive relapsing.



Now, this is back to the McDonald criteria, and looking at what's needed on MRI to fulfill dissemination in space and time. I don't think it's important to know exactly, where these lesions have to be; and how many you need to have. But the point is, there's four regions that you have to have or that you can consider. Periventricular, right next to the ventricle. Juxtacortical, further on the brain, right next to the cortex. Infratentorial would be brainstem or cerebellum, or the spinal cord. The point is, you don't need a lot of lesions. You just need one or more lesion in two of the four regions. You just really only need two lesions, but if they have a characteristic appearance, and in those locations, then they can fulfill dissemination in space.

Then, to get dissemination in time on MRI, you need to have a new lesion form, whether it's active or not. A new T2 or a gadolinium-enhancing lesion on any follow-up scan fulfills dissemination in time. If you have somebody who had an initial event, whether that's, optic neuritis, and then they have an MRI that looks characteristic and meets these criteria for dissemination in space, and then they have a repeat scan and they have a new lesion, that would be – without anything clinical going on, that would still be enough to call them relapsing-remitting MS.



This is showing some of these MRI locations. Here again, is a gadolinium-enhancing lesion, so, these active lesions. These are these T2 lesions that you see on MRI. These are infratentorial. These are very characteristic-looking locations for kind of these infratentorial lesions in MS. So, juxtacortical, you get these smaller lesions further out, next to the cortex of the brain, definitely occur in MS. Then, the more typical kind of periventricular lesions.

Then, this picture, showing the spinal cord lesions. Here's a lesion in the spinal cord. Here's another one. This is the spinal cord coming down, that's dark. But these kind of white areas in the cord, here, and here, and here—are abnormal, and consistent with lesions in the spinal cord that would be more characteristic for a demyelinating process, something like MS.

Clinically Isolated Syndrome (CIS) Definition

- Initial clinical event consistent with demyelinating disease with symptoms lasting at least 24 hours
  - ie., Optic neuritis, transverse myelitis

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Clinically isolated syndrome. I've mentioned it already. It's an initial clinical event that's consistent with demyelinating disease. You have to, again, have symptoms that last for at least 24 hours, and it can be anything. It depends upon again, what part of the nervous system's involved. If it's the eye, it would be optic neuritis. If it's in the spinal cord, it would be transverse myelitis.

Importance of Brain MRI in Patients with CIS

- Predictive for risk of developing MS
- Brain lesions can be a clinically silent characteristic of demyelinating disease which increase the risk for developing MS.
- However, even those with a normal brain MRI at the time of the initial neurological event/demyelinating episode are at increased risk for developing MS.

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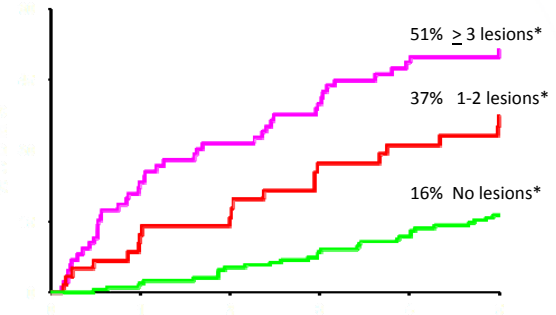
If somebody presents with an initial event, that you're concerned, could this be something like MS, the most important thing to do is the brain MRI, and see what that looks like. Because that is what would predict their risk for going on to develop MS. If you have somebody who presented with optic neuritis and they have brain lesions that looked characteristic for demyelinating disease, they are definitely at increased risk for developing MS.

Now, that being said, even people who, if they present with an episode, whether, again, if it's optic neuritis or transverse myelitis, and even they have a normal brain MRI, they are still at risk for developing MS.

Presence of MRI Lesions Predict Development of MS[1]



ONTT: Optic Neuritis Treatment Trial
*Number of lesions present at baseline
1. Optic Neuritis Study Group. The 5-year risk of MS after optic neuritis. Experience of the optic neuritis treatment trial. *Neurology 1997;49(5):1404-13*

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This is an older study, but this is the Optic Neuritis Treatment Trial. Its patients that had optic neuritis were enrolled in this trial, and this is their five-year follow-up—their five-year risk of MS after optic neuritis. What you can see is that, obviously, the more lesions you have, you're at a greater risk of developing MS. But even if you didn't have any lesions on that baseline MRI after optic neuritis, at five years, 16% of those had gone on to develop MS.

Is It MS or CIS?

- This distinction is often confusing for patients
- Disease course is variable and unpredictable. Transition to MS can occur in months to years.
- CIS is a term for someone with a characteristic demyelinating episode and a brain MRI that does not fulfill diagnostic criteria
- **MS diagnosis is made when there is either a change on MRI over time or another clinical event**

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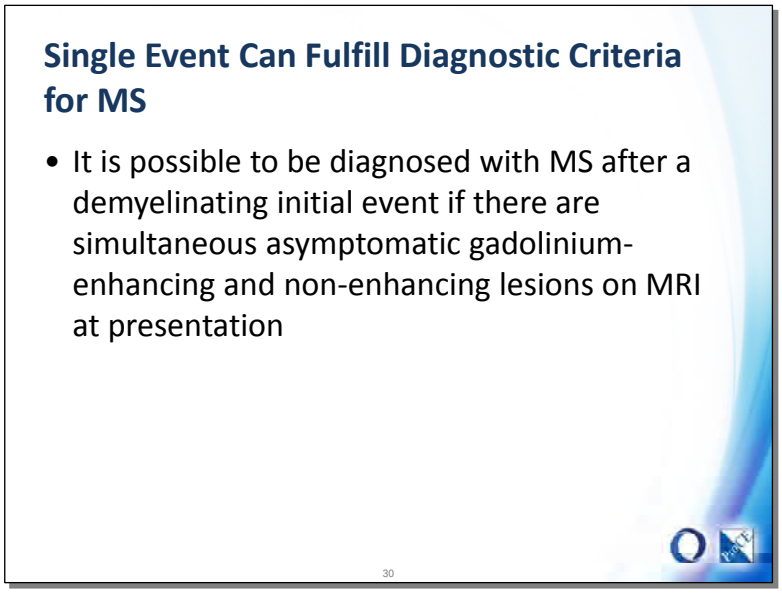
I always think that sometimes the semantics of this gets confusing for people, and for patients. Do I have MS or not? What's the CIS? I think this distinction is often confusing for people. But I think, basically, CIS is a term that we use for someone who has had a characteristic demyelinating episode, and a brain MRI that does not fulfill diagnostic criteria to be called MS.

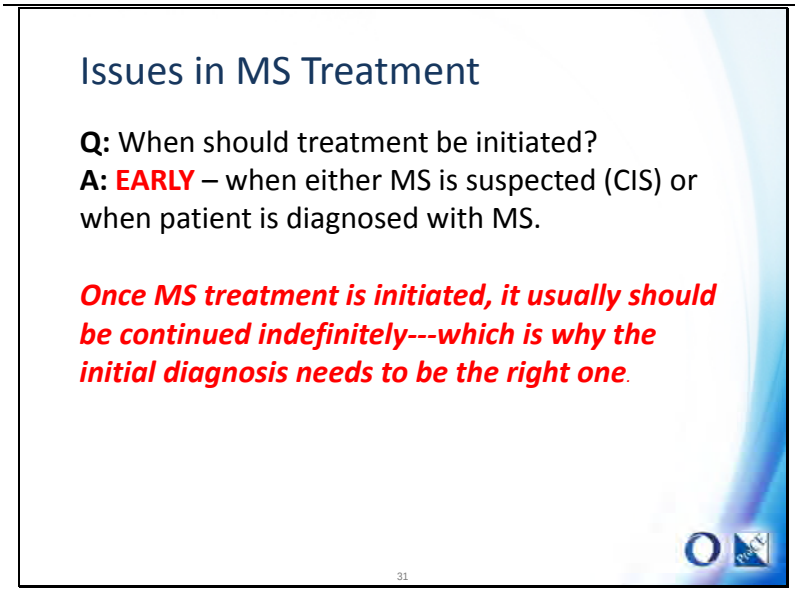
Now, when somebody transitions to MS is determined by, if they have either another clinical event or we follow them pretty closely with MRI, doing interval MRIs over a period of time; and if they develop change on their MRI over time they then would be diagnosed with MS.

Now, this disease course and this transition to MS is variable and unpredictable. I mean, there are

people who could present with an optic neuritis and do fine for years; and there are other people who can present with an episode and have a change on MRI on a three-month follow-up scan, or a six-month follow-up scan. So, it's quite variable and unpredictable. The whole disease is, which is why we really are good about wanting to get people on treatment.



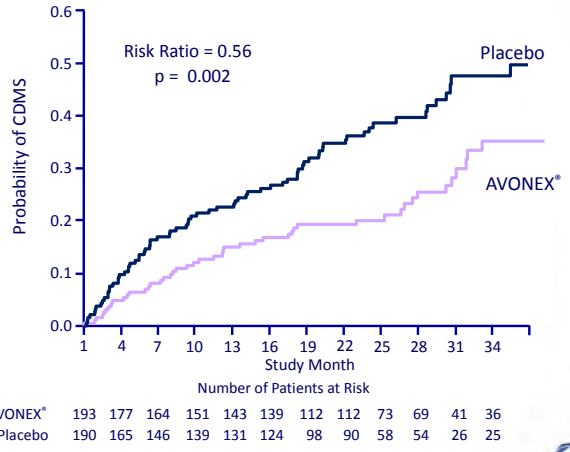
Now, it is possible, with the most recent revisions to the diagnostic criteria – to the McDonald criteria, that after a single event somebody can be diagnosed with MS; one event, one MRI, and be diagnosed. If you have somebody who has an initial demyelinating event, and if you look at their brain MRI and you see lesions that are active and lesions that are not active – so, new lesions or enhancing lesions that are asymptomatic, meaning, they presented with optic neuritis, so it should be the optic nerve involved, but yet you see an enhancing lesion in the brain MRI as well as some older lesions that are not enhancing on the brain MRI, that's actually enough. If you meet the dissemination in space and time, that's enough to fulfill diagnosis. So, a single episode, single brain MRI, you can call somebody relapsing-remitting MS. The great thing about the McDonald criteria, is that by utilizing MRI we are able to make an earlier diagnosis for patients.



When do we treat? When should we treat a patient? And I guess I would just answer that it should be early, as soon as we're suspicious that this is MS. So, whether it's at CIS, or when they, have the official diagnosis; but, as soon as we're suspicious this is MS, and we don't have another explanation for it, we should put somebody on treatment.

Really, once we get somebody on treatment, it's always the question, well, how long are we going to have to stay on this? Usually, the thought would be that we would continue that indefinitely. That's why we need to be pretty convinced at the onset, before we put somebody on treatment, that's what we're dealing with.

CHAMPS Study: First CIS-Specific Trial IFNβ-1a (AVONEX®) Reduced CDMS by 44%[1]



Number of Patients at Risk

AVONEX®	193	177	164	151	143	139	112	112	73	69	41	36
Placebo	190	165	146	139	131	124	98	90	58	54	26	25

1. Galetta SL. The controlled high risk Avonex multiple sclerosis trial (CHAMPS Study). *J Neuroophthalmol*. 2001 Dec;21(4):292-5.

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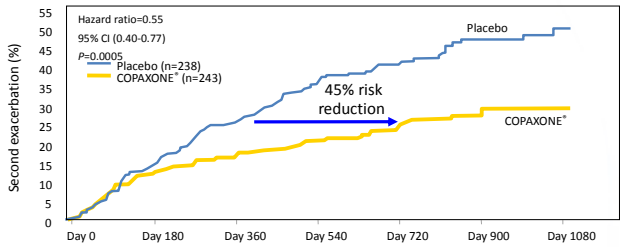
I just put in here two slides of some studies that were done in CIS. I put this one called the CHAMPS trial. It's with interferon beta-1a that's given intramuscular once a week, or otherwise called, Avonex. This was the very first study that was done in clinically isolated syndrome. Basically, they took people who had their initial event and started them on treatment right away. What it showed is that it could reduce or slow conversion to MS. So, it was of benefit.

PreCISe Study: COPAXONE® (glatiramer acetate injection) significantly delayed the second clinical event[1]

Primary endpoint: Time to second clinical event



- COPAXONE® significantly delayed the second clinical event by more than a year (386 days)

1. Comi G et al. Effect of glatiramer acetate on conversion to clinically definite multiple sclerosis in patients with clinically isolated syndrome (PreCISe study): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2009 Oct 31;374(9700):1503-11.

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This is the PreCISe trial, which used glatiramer acetate, which also showed the same thing: that we can delay the time to the second event by treating them earlier. Since then, there's been other CIS studies done as well, but I just included these two. We have clinical trial data saying we can treat people after their initial demyelinating event, even if they maybe haven't fulfilled the diagnostic criteria for MS. We can delay the time to when they are diagnosed with MS.

Natural History of MS[1]

As MS progresses from the **subclinical phase** to the **monosymptomatic**, **relapsing-remitting**, and **secondary progressive phases**, the following phenomena occur:

- Brain volume **decreases**
- Accumulated MRI lesion burden **increases**
- Cognitive dysfunction **increases**
- Level of disability **increases**

1. Hartung HP et al. Mitoxantrone in progressive multiple sclerosis: a placebo-controlled, double-blind, randomised, multicentre trial. *Lancet* 2002;360:2018-2025.

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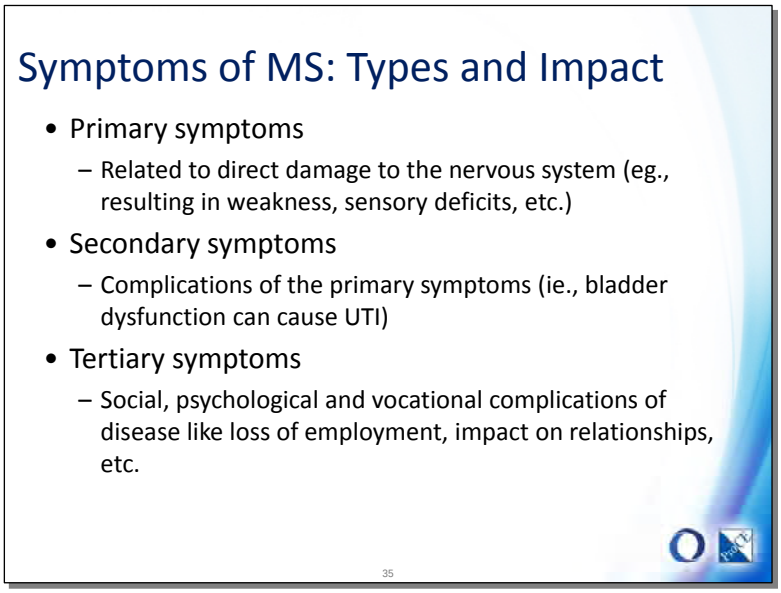
The natural history of MS progresses. It talks here about this subclinical phase. There are some people that get scanned for a variety of reasons. If they got in a car accident, and they maybe had a CAT scan that showed some abnormality, and then they went and had an MRI. There are people that can be picked up sub-clinically, even before their first episode, and they can have disease activity.

But then people can go on and have their first clinical event, so they'll be mono-symptomatic, and then progress into this relapsing-remitting course where they're having these relapses and getting better, and then slowly maybe transition into this secondary progressive phase. But as were going through this over the years, what will happen is that they accumulate lesions on brain MRI. The brain volume shrinks over time; the brain volume decreases.

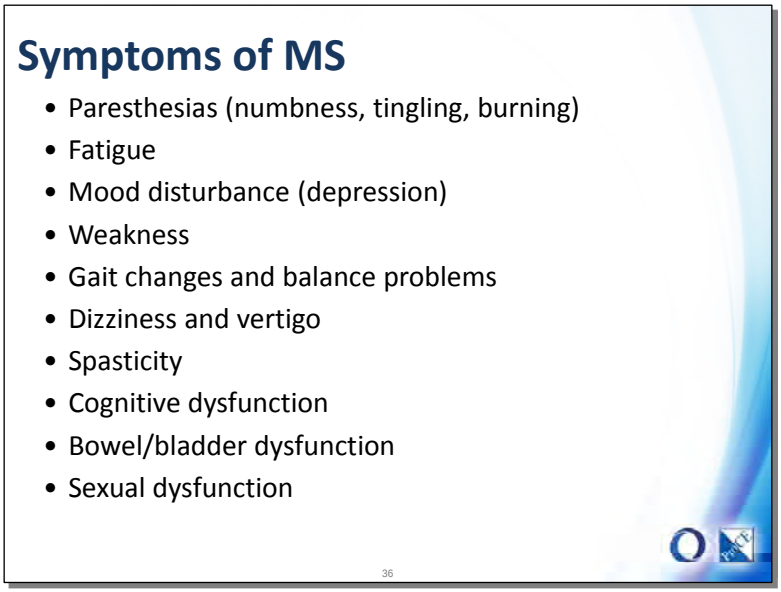
They can have increasing disability over time, and their cognitive dysfunction also increases.



The symptoms of MS, types and impact. There's primary, secondary, tertiary symptoms with MS. The primary symptoms are those symptoms that are related to direct damage to the nervous system. Whether that's the weakness, or the sensory deficits, due to the underlying neurologic disease.

Then there are secondary symptoms, which are complications of the primary symptoms. For instance, if somebody has bladder dysfunction, the bladder's not working, they can't empty their bladder well, they're set up for getting a urinary tract infection. The UTI's a secondary symptom.

Tertiary symptoms are the social, psychological and vocational complications of disease, such as, like, loss of employment; the impact it has on relationships; and so on.

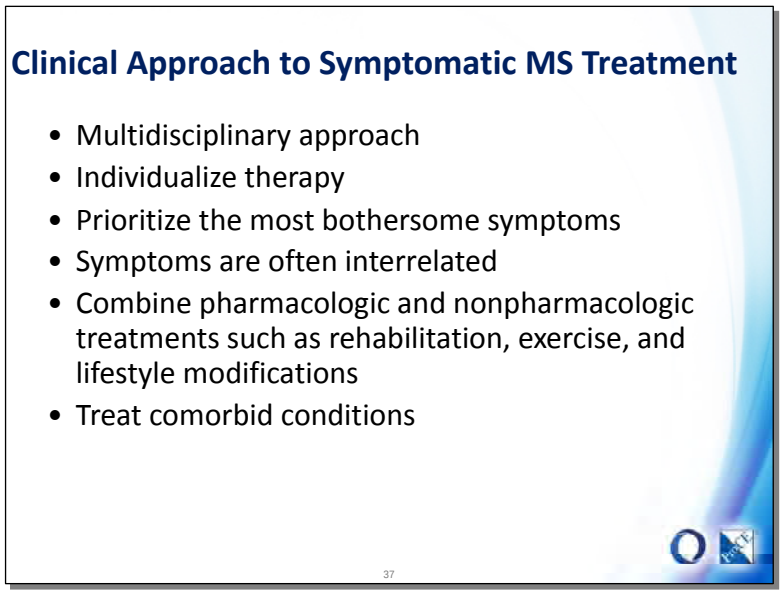


Now we're going to talk a little bit about the symptoms of MS. My talk, MS-101, is talking about the symptoms. We're not really going to talk about the disease-modifying therapies. That will be discussed in the MS-102. So, stay tuned for that.

Symptoms of MS: there's a lot of symptoms. That doesn't mean a patient has to have all of these symptoms. But again, probably common symptoms are paresthesias, numbness; tingling; burning. Fatigue is very common. Feeling lassitude which often is worse in the heat.

Mood disturbance, like depression, is very common in MS. And I always tell people, it's not a woe is me, I have this disease; it's related immunologically, pathologically to what's going on in the brain.

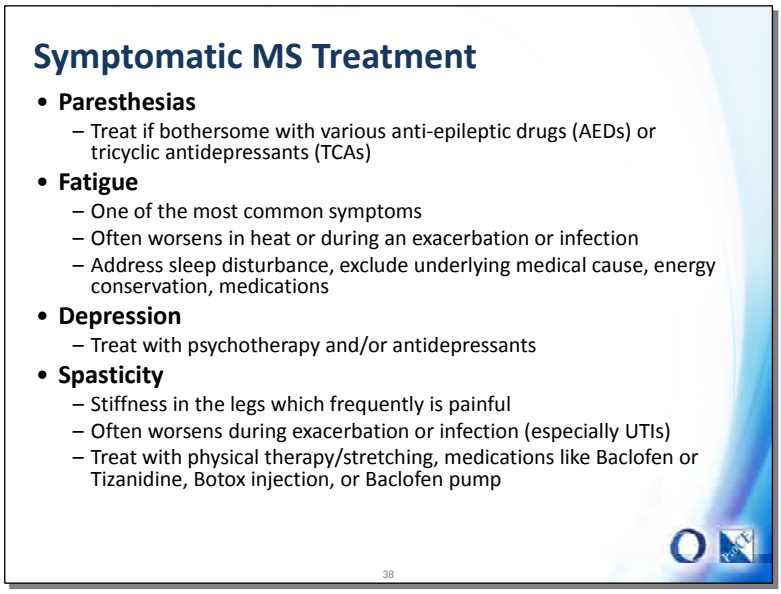
Weakness. Gait changes. Balance problems, so, dizziness; vertigo. Spasticity or stiffness, where their legs can spasm out, or when they stiffen out; or when they walk, their legs are really stiff. People often say, "I walk like I'm Frankenstein," but that's due to spasticity or stiffness. Cognitive dysfunction, is another very common problem with MS. Fortunately, usually it's mild, but nonetheless it's there, and can impact your overall function, quality of life, ability to work, and so on. Bowel and bladder dysfunction. And sexual dysfunction.



How do we approach symptomatic MS treatment? Well, I think it's very important it's a multidisciplinary approach. You have to individualize therapy. Again, lots of people will have symptoms; doesn't mean they will, and every patient is completely different. What one person experiences, the other person is completely different from what another MS patient may experience.

I think, also, that not all symptoms have to be treated. I think just if it's bothering the patient; impacting their function, quality of life. People may have multiple symptoms, but it's important to ask them, okay, so, we're going to deal with one of these things now. What's the most bothersome symptom? Then, prioritize that one. Sometimes it can be hard to sort out, because the symptoms are often interrelated. I think big ones for that are mood, cognition and fatigue; I mean, those really are interrelated. Trying to talk to patients and delve into what's really the underlying problem, what we're going to focus on to treat, is very important.

As far as treatment, we often will combine pharmacologic and non-pharmacologic treatments. And I'm a big proponent of rehabilitation; exercise; lifestyle modifications. All these things are very, very important. I think it's important to not forget that MS patients can get other things wrong with them. If they do, those must be treated, those other comorbid conditions, such as thyroid disease. They can get hypothyroidism and that can contribute to their fatigue as well. So, we can't discount that.



Now, we're going to go through some of the symptoms individually and talk briefly about their treatments. The first one is paresthesias. Again, this numbness; tingling; burning. Again, if bothersome, there are medications we can try. I always tell patients, it's kind of a trial and error. We see, we try things, and we push up the dose, and see how they respond to it. But various seizure medications are used, anti-epileptic drugs, or tricyclic antidepressants, we will use for this tingling, burning pain that people can experience.

Fatigue, again, is a very big one. Often worse in the heat, but also can be worse when people are having an exacerbation or if they're sick with any kind of infection. I can't emphasize enough that we have to always make sure we're not just chalking everything up to MS; that people can have other problems.

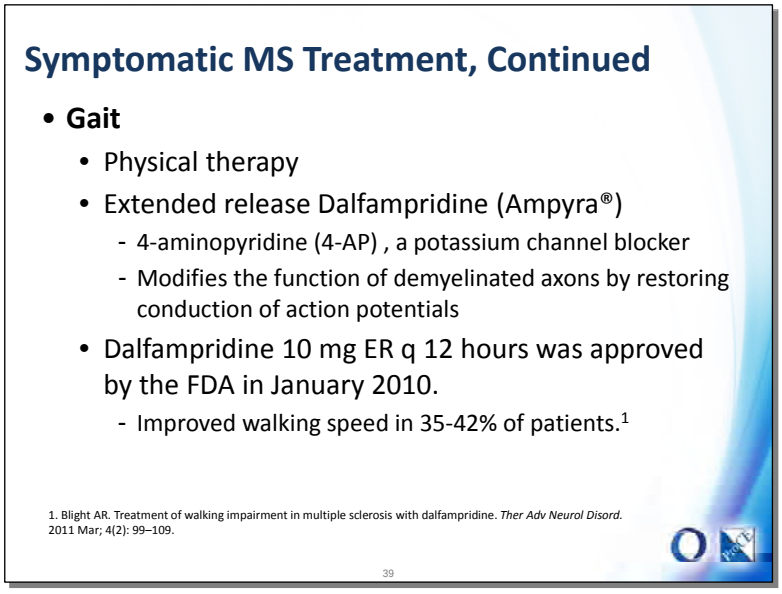
Many people with MS can have sleep problems. So, how are you sleeping at night? Well, if you're having issues, well, why are you having issues? Well, maybe it's their bladder; or maybe it's their spasticity; or maybe they have restless legs syndrome, or maybe they have sleep apnea. If you don't look for these things, you're not going to find that. Again, excluding other underlying medical causes, whether that's hypothyroidism, or anemia, or B12 deficiency. But then I think involving therapy, talking about both physical and occupational therapy and about energy

conservation. And sometimes we have medications that we can try for fatigue.

But I think, also, making sure that their mood is okay. Because if it's their mood that maybe is contributing, maybe you need to treat their mood, and see if they get more energy in that respect. Depression is a very, again, common symptom with MS. I always tell people, no one ever wants to admit that they're depressed, but it's such a common problem. For some people, maybe just psychotherapy will be enough. For others, really, you have to think about putting them on antidepressants. If it improves their overall function, quality of life, and gives them more energy, I think that impacts them.

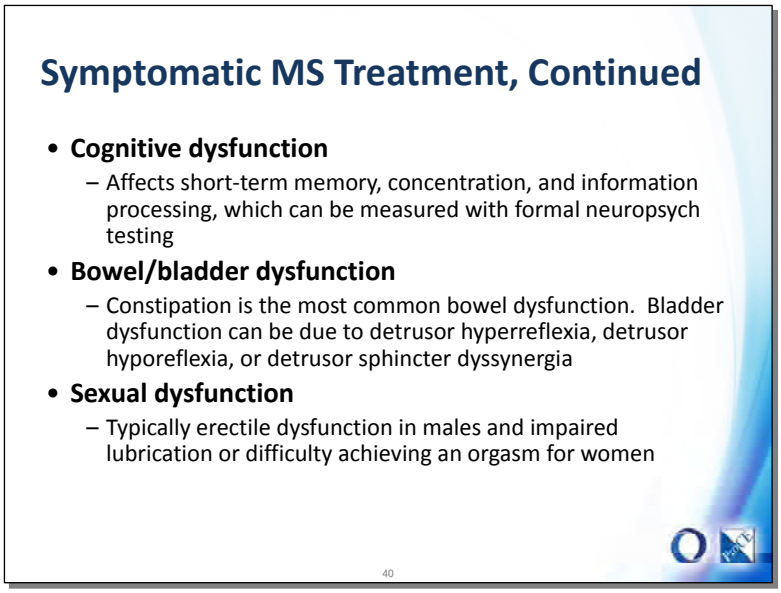
Spasticity, that's the stiffness I was talking about. Frequently it's painful. It's often worse at night. People say, I do okay, but at night it really bothers me, and I can't sleep. It also worsens with an exacerbation or an infection. I think when patients call and they say my spasticity's worse, the first thing I think of is that, well, we've got to make sure is it UTI? How's your bladder? And even check them. Because sometimes they may not be symptomatic from their bladder, but they may still have a UTI. So, important to kind of think about.

Then, how do we treat spasticity? Physical therapy/stretching is probably the first line that I would do, the first thing I would try. We do have other medications that we can use, like baclofen or tizanidine. Rarely, we can do Botox as well, depending upon where the spasticity is or what muscle groups are involved, as well as potentially, rarely, a baclofen pump.



Gait issues with MS is also not uncommon. I think, first and foremost, I would probably go to physical therapy. I encourage patients to get involved with physical therapy and exercise, trying to be active. But there is a symptomatic medication that's been approved for MS patients, called dalfampridine, which is a form of pyridine, a potassium channel blocker that basically enables messages to get through where there's areas of demyelination. It's a medication that you take every 12 hours.

You know, I tell patients, the unfortunate thing is, it works for about 35 to 42% of people in the clinical trials. It improved their walking speed. We measure how fast they walk, what's called the timed 25-foot walk. But if people respond, it really can impact them. For some people it helps with their endurance and strength as well. So, at least something to think about if one is having some gait issues.



Cognitive dysfunction. Again, a common one; usually affects more short-term memory, their concentration. People say, I just don't process as well. I can't multitask like I used to be able to do. The unfortunate thing is that, from a bedside perspective, when we're evaluating a patient, it's hard to assess that. In order to really have that done properly, patients have to be referred for neuropsychological testing, which I think is important to do to have a baseline, especially if they're having some cognitive issues, and especially if it's impacting their work. Important to have that information. The neuropsychologist can provide some compensatory strategies for a patient.

Bowel and bladder dysfunction. As far as bowels, usually constipation is the most common problem with bowels. Bladder, probably the most common problem is that urgent bladder, where they really have to rush to the bathroom, and they may not make it there in time. But they can also have an issue where the bladder doesn't empty well. It sometimes requires them to catheterize as well. But there's medications that we can try, and depending upon what the symptoms are, I may refer them to urology so they can do testing of the bladder, and test the post-void residual and so on.

Then, sexual dysfunction. For males it's usually erectile dysfunction; for women, it's impaired lubrication or difficulty achieving an orgasm. Sexual dysfunction is also common in MS, but no one ever talks about it. Usually patients don't want to talk about it. But it is another symptom that really can impact their quality of life and their relationships, so it's something that needs to be addressed, and I really try to ask about it. Especially at first visits, I will definitely cover that to really focus on and to address the symptoms if it's impacting them.

Now, we're going to be handing things over to Heli Hunter. She's an MS nurse practitioner who's going to discuss MS symptom management and patient education from the nursing point of view.

Faculty

Heli Hunter, MSN, ACNP, MSCN
Schapiro Center for Multiple Sclerosis
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*Disclosure: Ms. Hunter is a consultant/speaker for Mallinckrodt Pharmaceuticals; Genzyme, a Sanofi Company; Novartis; and Teva Pharmaceuticals USA.

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In her presentation, Dr. Derwenskus covered the first four objectives. I will now discuss the role of the MS nurse, and some MS symptom management issues. I am a nurse and I have worked many years with MS patients as an advanced practice provider. I have assessed, treated and counseled numerous patients, but my favorite part is to take a patient history and to listen to their MS story.

Learning Objectives

- Describe the basic pathology, epidemiology and demographics of the MS population.
- Explain the diagnostic process for MS and the principles of the McDonald Criteria.
- List the four major clinical courses of MS, in particular Relapsing Remitting MS (RRMS) and Secondary Progressive MS (SPMS)
- Explain the diagnostic category of Clinically Isolated Syndrome (CIS) and be aware of the high risk of MS in this setting.
- **Review symptomatic issues that complicate MS and how best to manage them.**

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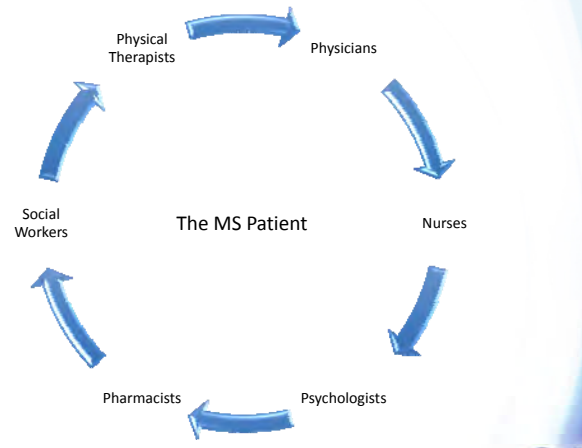
I will review the role of the MS nurse first, and then discuss symptom management issues.

Teamwork



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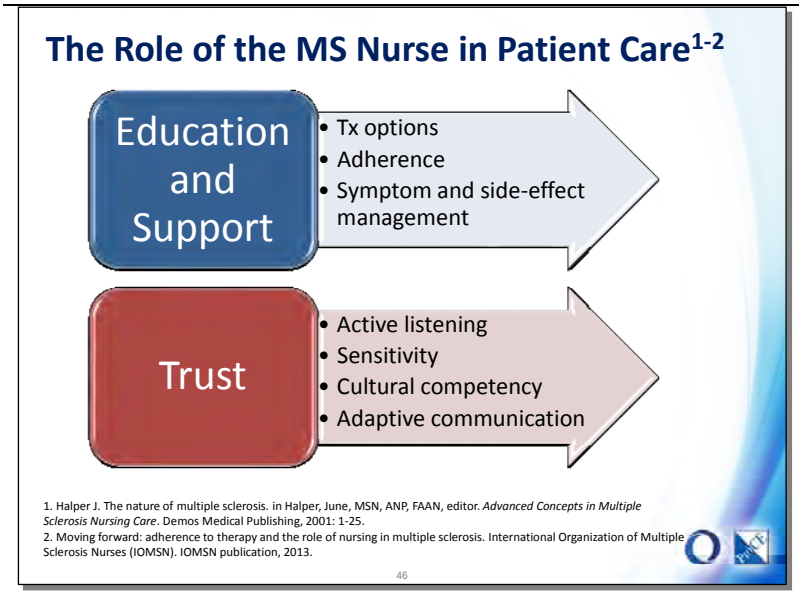
An MS nurse works in tandem with other MS specialists in health disciplines, including physical therapists, social workers, psychologists, and with specialty pharmacists.

Patients' reaction to MS diagnosis may be a shock, or it may be a relief. Often, MS patients are young, in their 20s and 30s. They're making plans for college or a career, or they may be starting a family. MS may become a life-altering event; but, for most times, MS is a mild disease, allowing people to live active and productive lives. More often, though, patients spend an average of four years from symptom onset until MS diagnosis. These patients may be relieved to hear that there is a reason and explanation to perhaps vague symptoms, and that it is not their imagination. These patients are relieved to hear there is an explanation to their symptoms, and they have hope for improvement with treatment.



The role of the MS nurse in patient care is very important. Nurses educate and support the patient and their family members about MS symptoms. Nurses discuss MS treatment options and help patients make choices. Nurses address treatment adherence issues by asking if the patient is taking medication as directed, assessing and asking about side effects, and whether patient is missing doses. Nurses assist with symptom and side effect management of the patient's medications.

The nurse/patient relationship in MS begins with establishing a trusting relationship with the patient. This happens with active listening, listening to the patient's problems and concerns, and answering questions. The nurse adapts the patient education methods based on patient's needs/personality, in a sensitive manner, while being mindful of the patient's cultural preference. The nurse continuously adapts their communication style based on the individual patient's education level and experience.

MS Symptom Management: Bladder Issues[1-3]

Detrusor hyperreflexia

- Frequency, urgency, and urge incontinence
- Most common bladder symptom in MS
- Spontaneous bladder contractions, even with small urine volumes
- Common treatment:
  - **Anticholinergics** (can cause dry mouth, sedation, can worsen MS-related constipation)
- Offer counseling:
  - **Frequent bathroom breaks** and **manage water intake**

Detrusor hyporeflexia

- Urinary retention → Loss of bladder tone (incontinence)
- Treatment
  - Self-catheterization
- Additional complications
  - Urinary-tract or kidney infections
- Education
  - **Self-catheterization** and **UTI symptom recognition**

1. Moving forward: adherence to therapy and the role of nursing in multiple sclerosis. International Organization of Multiple Sclerosis Nurses (IOMSN). IOMSN publication, 2013.
2. The role of the MS nurse in relapse assessment and management. *MS Couns Pts* Winter 2016; 11:1; 4-13.
3. Frenette J et al. Symptom management. In :Halper, June, MSN, ANP, FAAN, editor. *Advanced Concepts in Multiple Sclerosis Nursing Care*. Demos Medical Publishing, 2001. 175-212.

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Next, I will talk about MS symptoms, starting with the bladder. The most common bladder problem in MS is called detrusor hyperreflexia. In this, a patient frequently experiences bladder urgency and frequency, sometimes with leaking. The bladder spontaneously contracts as it fills, even with small volumes. The bladder fills up quickly, and when it fails to store urine, bladder leaks.

The treatment for this often includes anticholinergic medications, which often cause dry mouth, daytime sedation, and may worsen MS-related constipation. The nurse may therefore counsel patients to try frequent bathroom breaks, at least every two hours and on schedule; also, to manage water intake rather than take medications. I advise my patients to drink at least two quarts of water a day, and drink water every hour rather than sipping throughout the day.

A less common but more serious MS bladder symptom causes urinary retention and loss of bladder tone, or detrusor hyporeflexia. The bladder fails to empty until its flow overflows, causing incontinence. This condition usually requires self-catheterization. Patients often experience frequent bladder infections. The nurse can train patients on self-catheterization, and also to recognize symptoms of the bladder infection.

MS Symptom Management: Bladder Issues (continued)

Detrusor-sphincter-dyssynergia

- Combination condition – both fails to store **and** fails to empty
- Hesitancy, incomplete emptying, and weak urine stream, ***combined with leaking/incontinence***
- **Management:**
  - Refer to urologist
- **Patient education:**
  - Avoid bladder irritants
  - Increase water intake
  - Increase urine acidity
  - Caution patients NOT to dehydrate/withhold fluids (**increases UTIs** and **worsens MS-related constipation**)

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The third condition is a combination of the two previous. In this, the bladder both fails to store and fails to empty urine. This is caused by detrusor sphincter dyssynergia. These patients can experience hesitancy, incomplete emptying, and a weak urine stream, combined with leaking and incontinence.

It is best to have a urologist manage this condition, but the MS nurse can assess symptoms and instruct patients in proper bladder care. This includes avoiding bladder irritants such as caffeine; increase water intake; and increase urine acidity with dietary supplements such as vitamin C or cranberry. This discourages bacterial growth in the urine. Sometimes MS patients with these bladder issues may try to manage it by withholding liquids, but this in turn may increase the chance of a bladder infection, and also may worsen constipation.

MS Symptom Management: Bowel Issues[1-2]

Constipation

1. Moving forward: adherence to therapy and the role of nursing in multiple sclerosis. International Organization of Multiple Sclerosis Nurses (IOMSN). IOMSN publication, 2013.
2. Frenette J et al. Symptom management. In :Halper, June, MSN, ANP, FAAN, editor. *Advanced Concepts in Multiple Sclerosis Nursing Care.* Demos Medical Publishing, 2001. 175-212.

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Constipation is a fairly common symptom in MS, and it fluctuates with severity. It may be worsened or caused by MS symptom medications, MS-related weak abdominal muscles, or MS-related immobility. The nurse may help manage constipation by first assessing the patient's dietary and fluid intake. She will counsel the patient on benefits of high-fiber foods; adequate fluid intake; benefits of regular exercise, such as walking; and also, side effects of MS symptom medications that may cause or worsen constipation. Several treatments over the counter are available for constipation, and these include bulk laxatives such as Metamucil or Citrucel; also, stool softeners and stimulants.

MS Symptom Management: Fatigue[1-2]

- Often late in the day
- May be worsened by exertion or heat
- "Lack of energy"
  "sense of lassitude"
  "mental fogginess"
- Heaviness in limbs/difficulty moving
- Patients frequently require more sleep

Priority

- **Nocturia**
- **Pain**
- **Restless legs**
- **Spasticity**

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The last symptom I will speak about is also the most common. Fatigue occurs in about 90% of MS patients. It often starts later in the day, in the afternoon or in the evening, and it may be worsened by exertion or heat. Often, MS patients experience a lack of energy, a sense of lassitude, or they complain of mental fogginess. MS-related fatigue may also present as heaviness in limbs or difficulty moving around. Frequently, I have found that MS patients require more sleep than they did prior to a diagnosis. If there are other factors contributing to the fatigue, such as nocturia, pain, restless legs or spasticity, these should be addressed first.

Fighting MS-Related Fatigue

- Good sleep hygiene
- Regular exercise
- Pacing daily activities
- Addressing side effects

Stimulants may be used to treat MS-related fatigue, but they **can cause insomnia**

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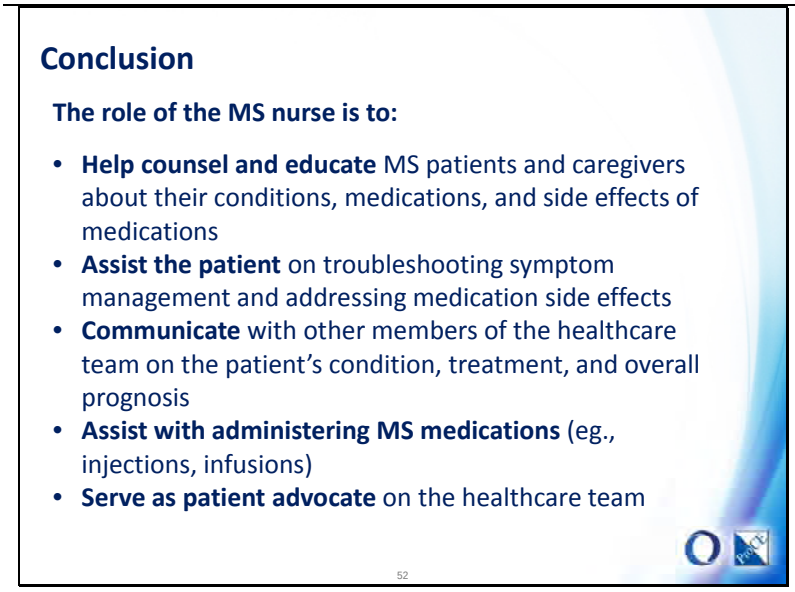
The nurse can instruct the patient to fight MS-related fatigue by using good sleep hygiene practices, regular exercise, pacing daily activities to reduce overexertion, and doing tasks that require concentration early in the day when they are more rested. Nurses can also address fatigue worsening and side effects of MS symptom medications. Many stimulants are available to treat MS-related fatigue, but they can worsen insomnia.



In conclusion, the role of the MS nurse is to help counsel and educate MS patients and their caregivers and families about their condition, their symptoms and their meaning, medications, medication side effects, and titration schedules. Nurses assist the patient on troubleshooting their symptoms and addressing medication side effects. Nurses also communicate with other members of the healthcare team regarding a patient's treatment responses, condition, and about their overall prognosis. Nurses assist with administering MS medications, either injectables or infusions. It is also important for the nurse to act as a patient advocate in the healthcare team and in the community.

I thank you for your attention, and I hope this was a helpful presentation.

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Post-Test

1. **Multiple sclerosis is a disease that predominantly affects young women.**
   a. True
   b. False
2. **MS is an autoimmune disease which primarily affects which of the following major organ system (s)?**
   a. Central nervous system and parasympathetic nervous system
   b. Central nervous system only
   c. Peripheral nervous system only
   d. Autonomic nervous system and spinal cord
3. **What agent may be protective against the development of MS?**
   a. Epstein Barr virus (EBV)
   b. human herpes virus 6 (HHV6)
   c. *Chlamydia pneumonia*
   d. vitamin D
4. **The most common form of MS diagnosed at initial patient presentation is:**
   a. relapsing remitting multiple sclerosis (RRMS)
   b. secondary progressive multiple sclerosis (SPMS)
   c. primary progressive multiple sclerosis (PPMS)
   d. progressive relapsing multiple sclerosis (PRMS)
5. **Why was MRI incorporated into the McDonald diagnostic criteria for MS?**
   a. To improve early diagnosis/detection rates of MS
   b. To provide additional diagnostic criteria to consider in a complex disease state
   c. To reduce false positives
   d. Both A and B
6. **The best predictor for going on to develop MS after an initial demyelinating event is abnormal:**
   a. brain MRI
   b. spinal cord MRI
   c. CSF
   d. evoked potentials
   e. blood test
7. **Some common symptoms of MS include:**
   a. numbness/tingling
   b. fatigue
   c. weakness
   d. cognitive changes
   e. all of the above
8. **Which of the following is an example of secondary and tertiary symptoms in multiple sclerosis?**
   a. Urinary tract infections and decreased ability to maintain employment
   b. Visual disturbances and fatigue
   c. Spasticity and gait problems
   d. Brain lesions
9. **Which of the following does NOT describe components of the MS nurse's role in patient care?**
   a. Discussing the meaning of patient's symptoms
   b. Educating patient about the side effects of medications
   c. Assessing for changes in the patient's condition
   d. Questioning patients about their lifestyle choices
10. **Which of the following is the symptom most commonly reported by MS patients?**
    a. Difficulty with emptying the bladder
    b. Feeling tired without a good reason (i.e., fatigue)
    c. Worsening constipation due to lack of treatment options
    d. Feeling more energized after a shopping trip