



**MULTIPLE SCLEROSIS
ASSOCIATION OF AMERICA**

presents

The Treatment and Management of MS Exacerbations

Live Webinar

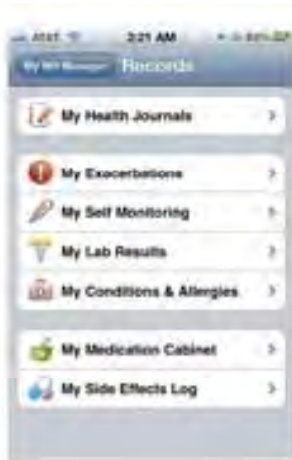
February 2, 2012 7 pm Eastern

Guest Presenter



**Ben Thrower M.D.
Andrew C. Carlos MS Institute
Shepherd Center**

This program is made possible through an unrestricted educational grant from Questcor Pharmaceuticals, Inc.



Providing Information . . .

- Toll-free bilingual Helpline (800) 532-7667
- Online response forum MSquestions@msassociation.org
- New mobile phone application *MY MS Manager™*

Finding Answers . . .

- Website: www.msassociation.org
- Publications, videos, webcasts
- S.E.A.R.C.H.™ initiative
- MRI Diagnostic and MRI Institute



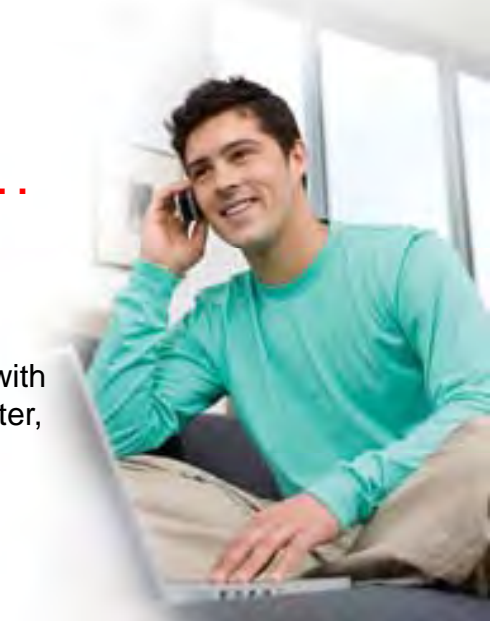
Programs and Services

Easing Daily Life . . .

- Equipment distribution
- Cooling program
- Barrier-free housing

Staying Connected . . .

- Public education & awareness events
- Social media presence with sites on Facebook, Twitter, YouTube
- Networking Program



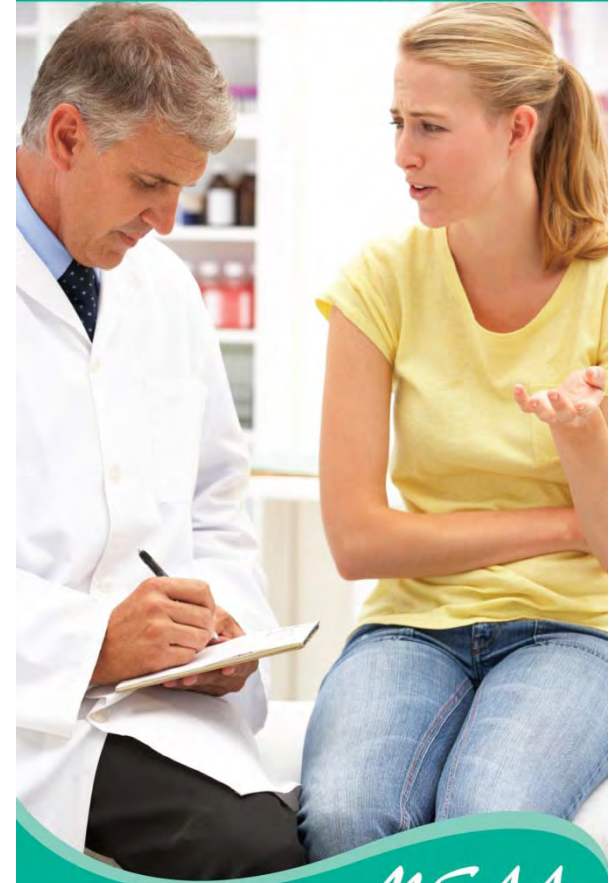
New MSAA Publication

As part of the educational grant from Questcor Pharmaceuticals, MSAA is pleased to offer a new a publication on this important topic, titled:

This eight panel brochure gives a concise and thorough explanation MS relapses and treatment options with important tips on treatment monitoring and follow up.

As with all publications from MSAA, this brochure is provided free of charge and is available by visiting our website, www.msassociation.org, or calling our toll-free number (800) 532-7667.

Understanding and Treating MS Relapses



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Participating in the Webinar

MSAA encourages you to actively participate in tonight's webinar by:

- Responding to the polling questions included in the program
- Submitting your email questions throughout the webinar by typing in the Chat box on the lower left side. We will address as many questions as time allows at the end.
- Completing a follow-up survey at the end of the program to help us improve future webinars and develop additional programs to meet your needs

If you are experiencing any technical problems with tonight's webinar, you can also use the Chat box feature to type in your issue. The online moderator will respond to your "chat" and work to correct the problem.

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Overview: Multiple Sclerosis

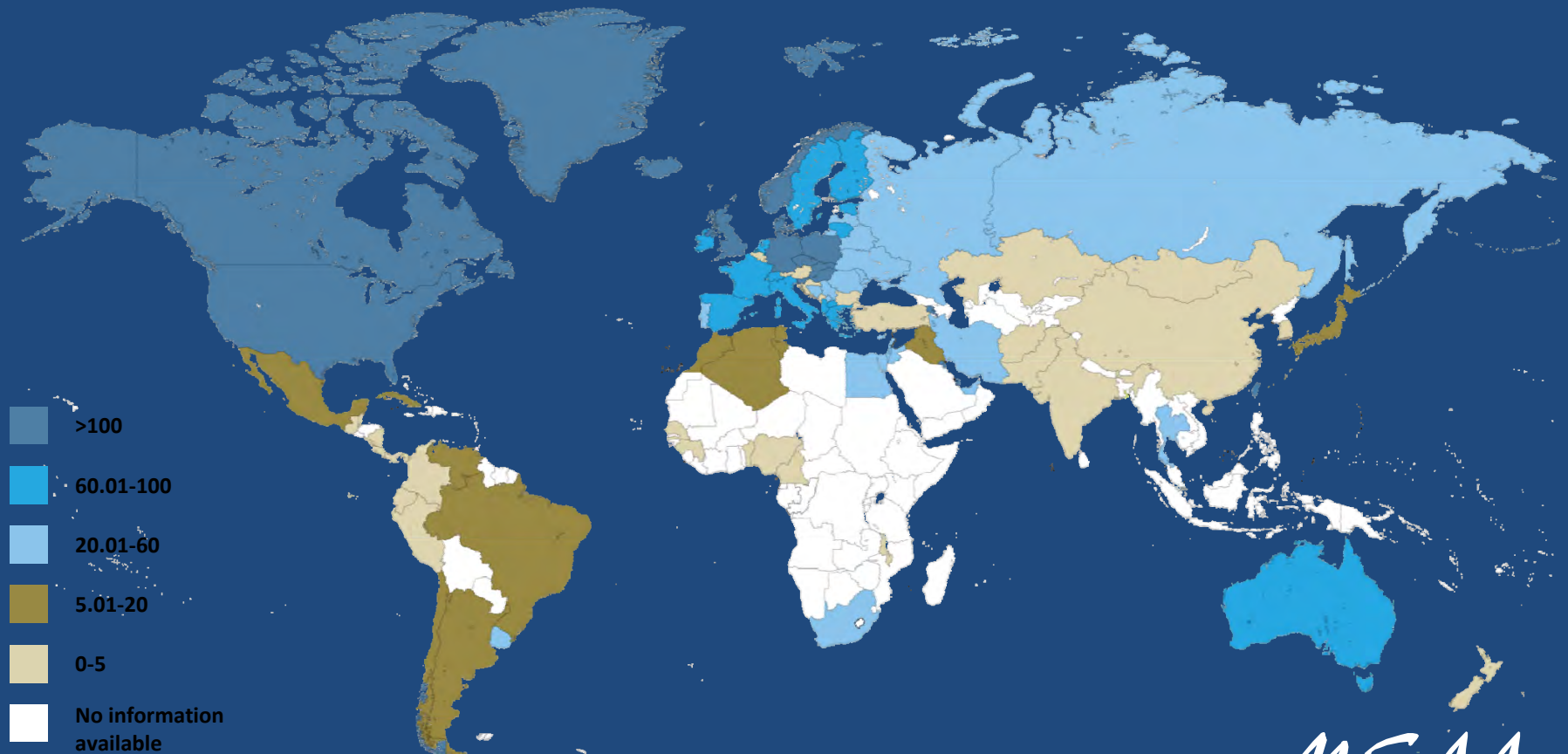
- ▶ A chronic, progressive, unpredictable disease of the brain and spinal cord
 - Caused by autoimmune attack directed at axons, the long projections of nerve cells that conduct electrical impulses
- ▶ Many neurologic symptoms are possible—motor, sensory, and cognitive functions can be affected
- ▶ Characterized by episodes of worsening symptoms known as *relapses*
 - Relapses resolve partially or completely over time
 - Disability can increase over patient's lifetime

Compston A, et al. *Lancet*.
2008;372:1502-1517.

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MS Is a Relatively Common Disorder in Developed Countries

Prevalence of MS per 100,000 People



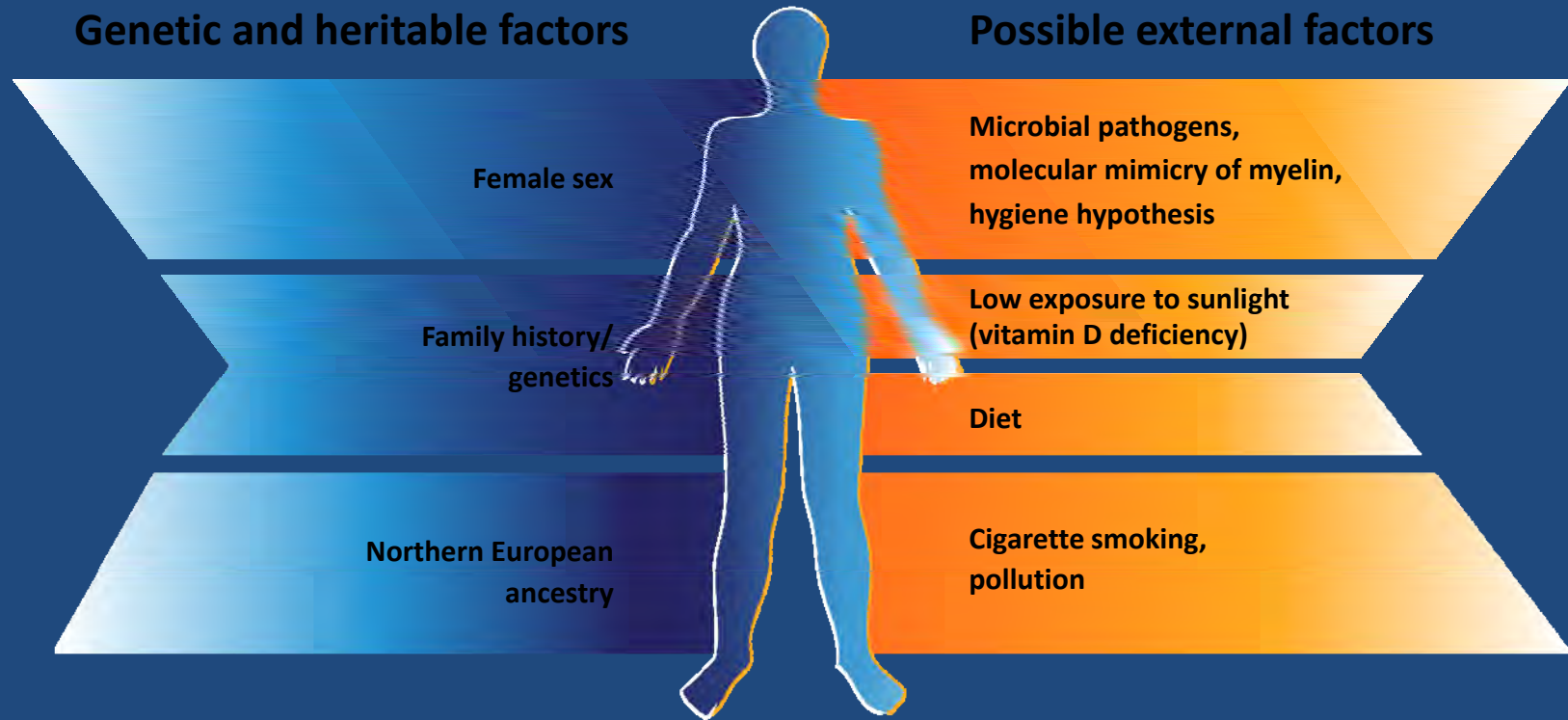
World Health Organization. 2008.

Available at:

www.msif.org/en/about_msif/what_we_d_o/atlas_of_ms. Accessed May 2, 2011.

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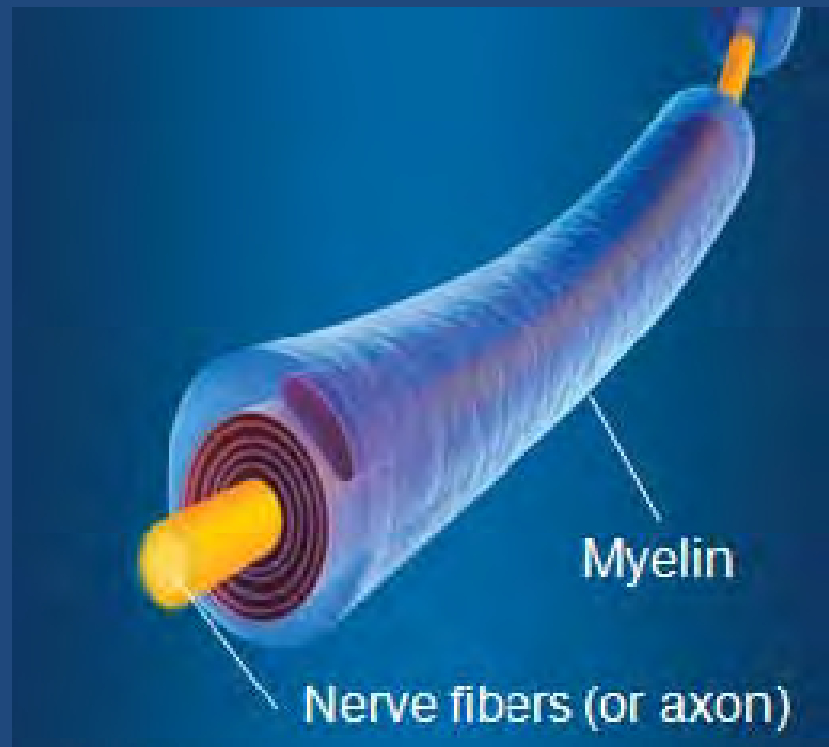
Hereditary and External Factors Contribute to MS



Compston A, et al. *Lancet*.
2008;372:1502-1517.

Electrical Signals Are Conducted Along Axons

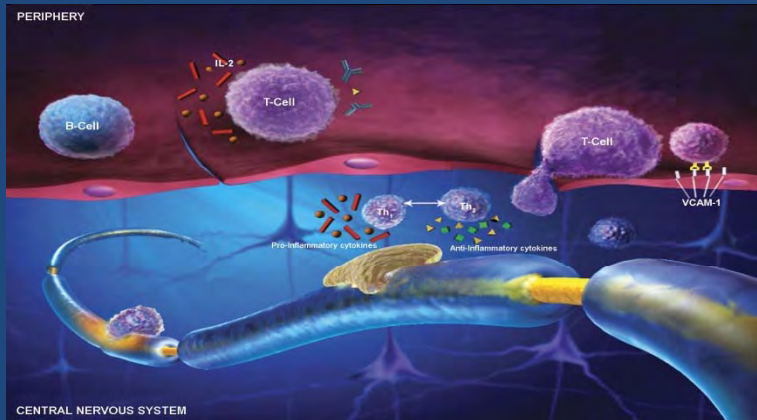
- Myelin coating makes rapid signaling possible



Compston A, et al. *Lancet*.
2008;372:1502-1517.

Myelin Is Damaged During Course of MS

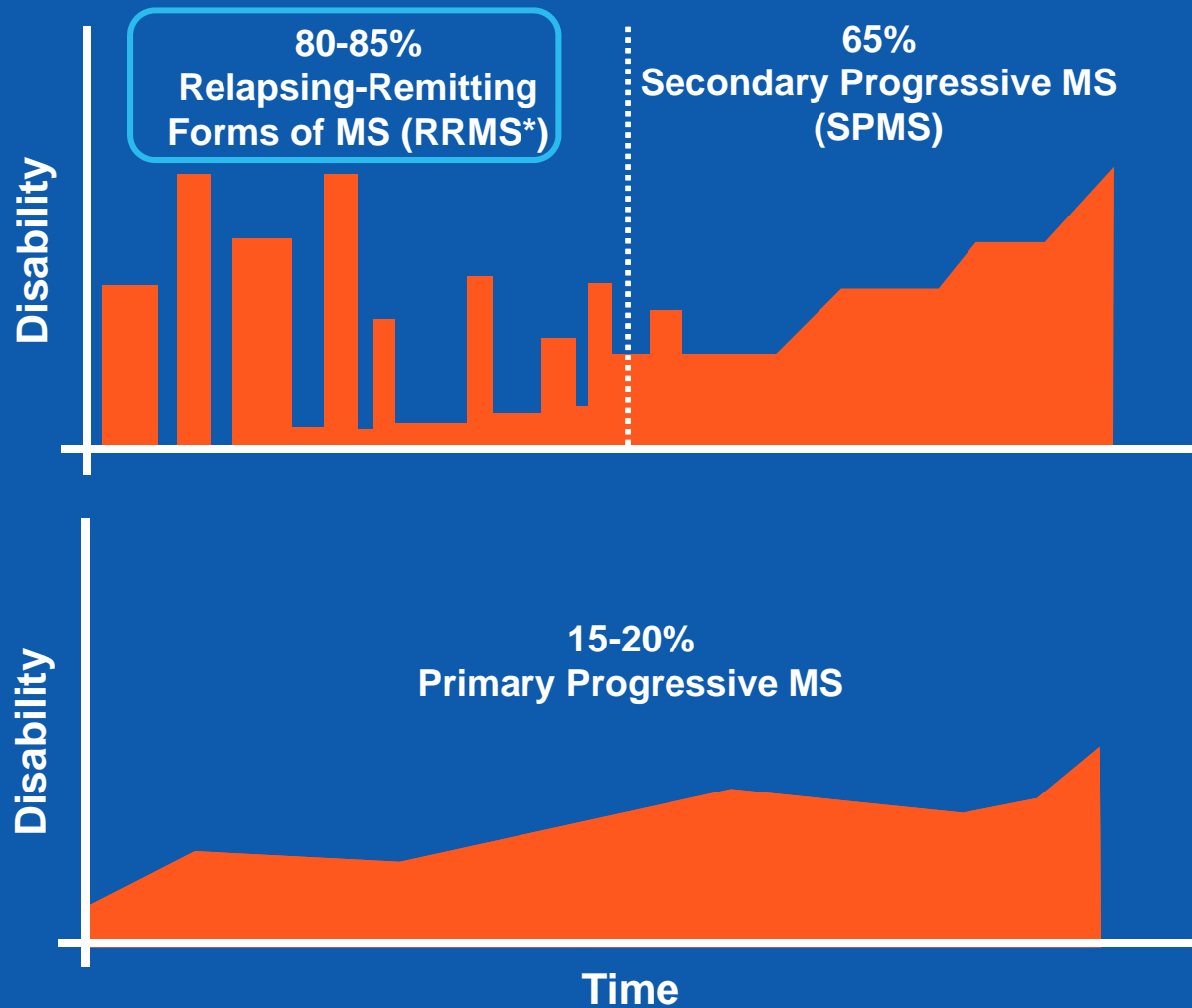
- ▶ Immune cells cross into the CNS and attack myelin



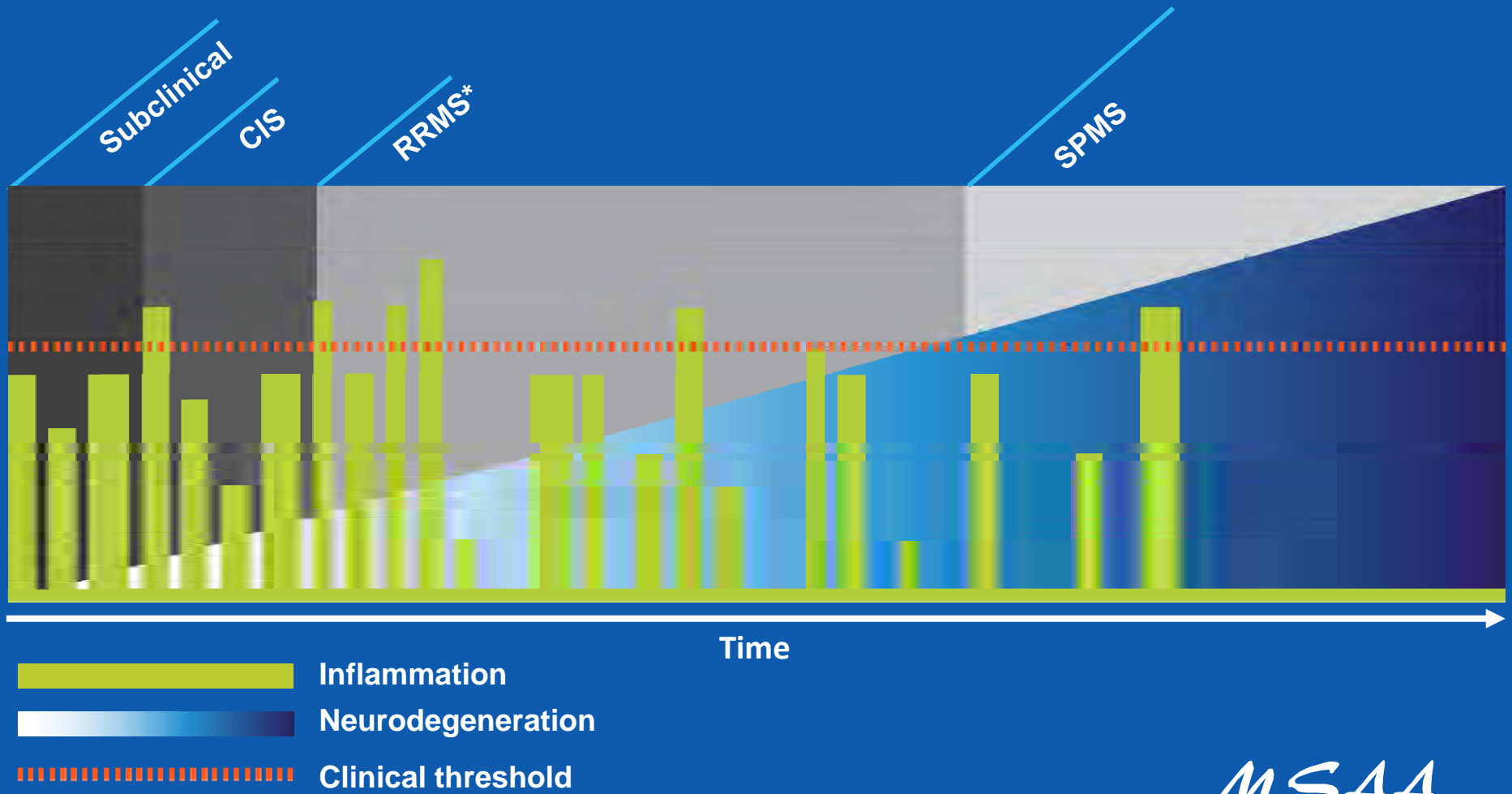
- ▶ Axons with damaged myelin cannot conduct electrical signals

Compston A, et al. *Lancet*.
2008;372:1502-1517.

MS Has a Variable Clinical Course



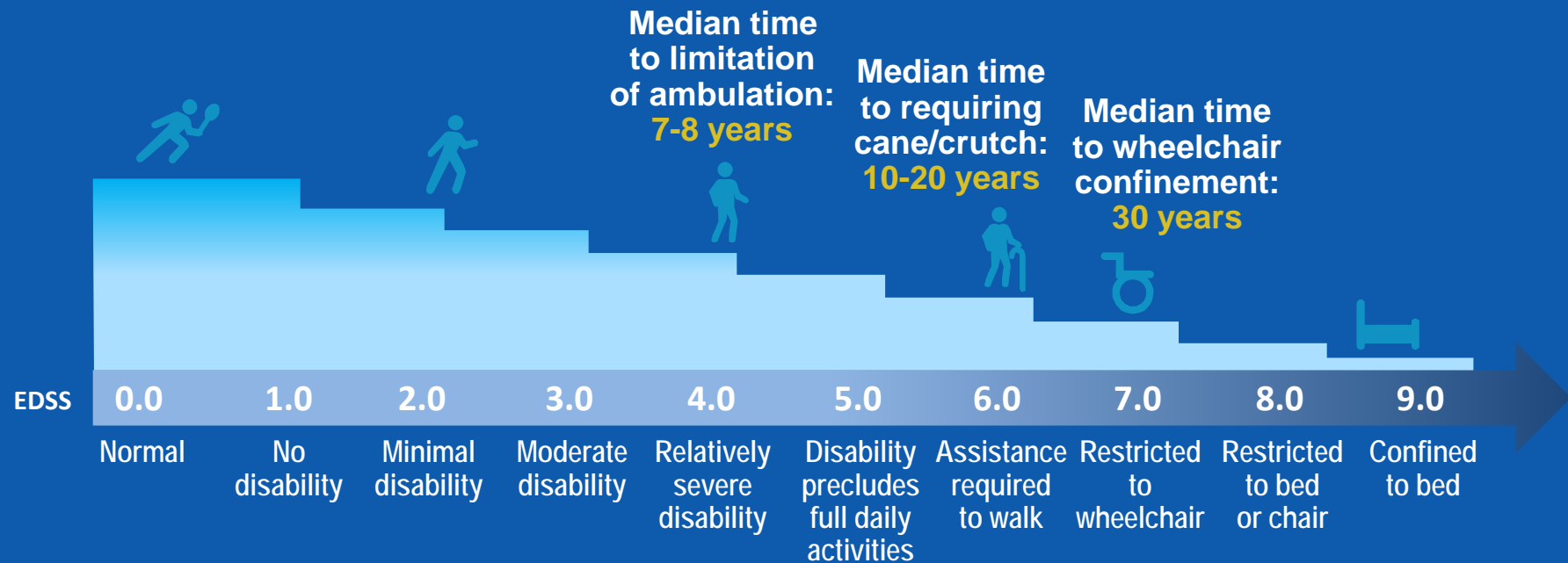
Relapsing Forms of MS: Inflammation Gives Way to Neurodegeneration



CIS, clinically isolated syndrome.

Compston A, et al. *Lancet*. 2008;372:1502-1517.

Untreated MS Is Associated With Progressive Disability

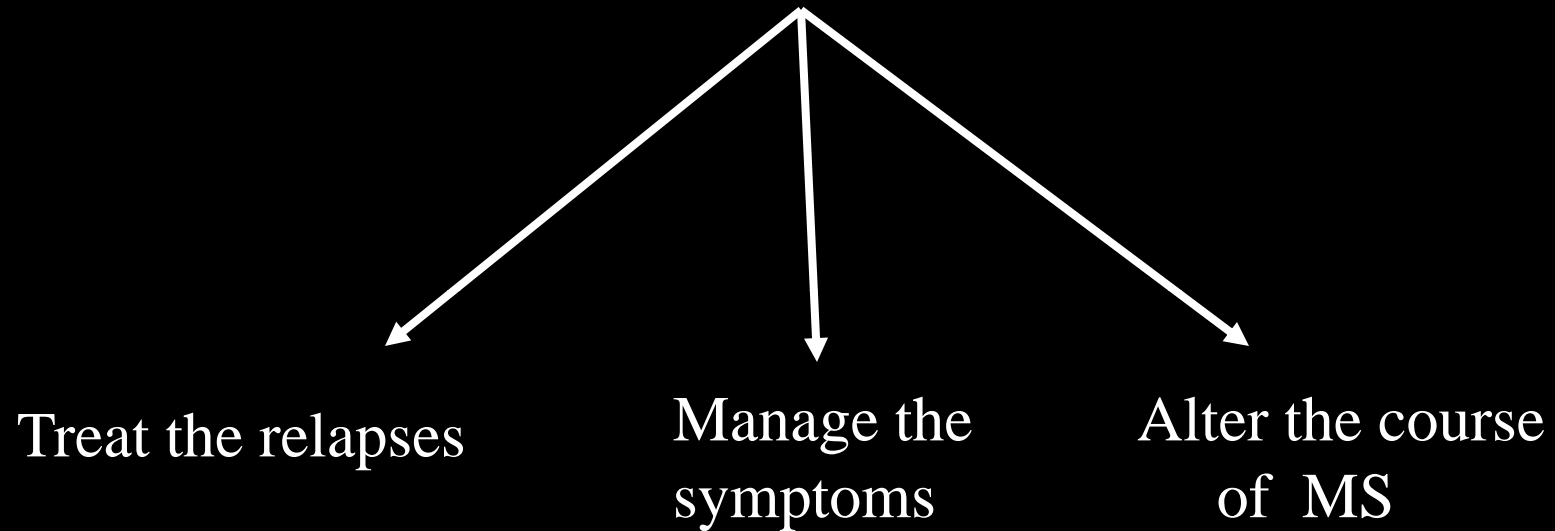


EDSS, Expanded Disability Status Scale.

Amato MP, et al. *Mult Scler.* 1999;5:216-219.

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Medical Management of MS



What is an MS Exacerbation?

- Also known as relapse, flare or attack¹
- Sudden worsening of one or more MS symptoms that had been previously stable for over a month¹
- Appearance of new MS symptom(s) that last for over 24 hours¹
- Exacerbations can last anywhere from days to weeks but may also last for months¹

1. National MS Society Website. <http://www.nationalmssociety.org/about-multiple-sclerosis/what-we-know-about-ms/treatments/exacerbations/index.aspx>. Accessed April 18, 2011

Importance of Treating MS Relapses

- Studies have shown MS relapses can have a long term effect on disability^{1,2}
- MS relapses can affect a patient's Quality of Life (QOL) ³⁻⁵

Challenges Associated With QoL Changes During a Relapse ⁵
Relapse symptoms
Side effects associated with relapse-related medications
Loss of income resulting from inability to work
Costs associated with care
Strains on the coping mechanisms of patients and their families
Social isolation
MS-related fatigue

1. Leary SM, et al. *Postgrad Med J*. 2005;81(955):302-308.

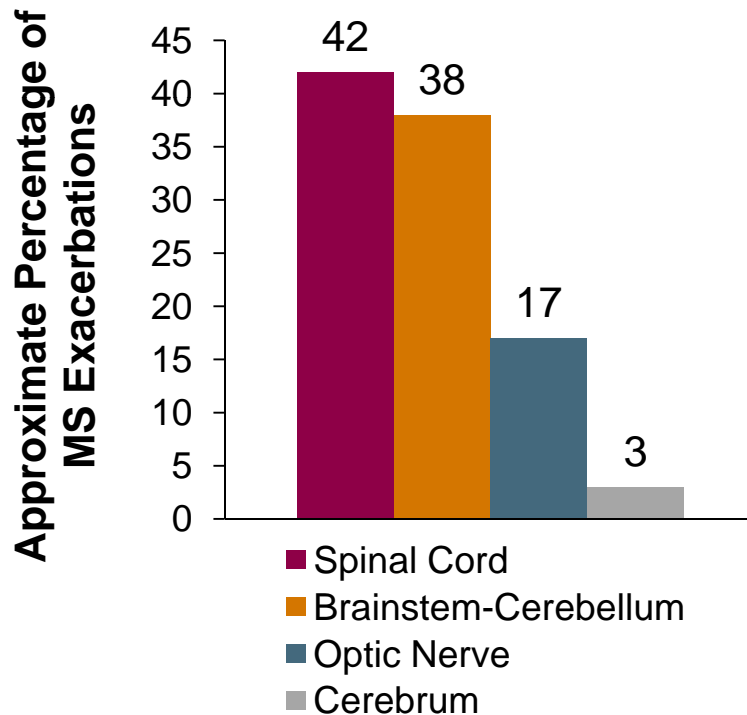
2. Lublin FD, et al. *Neurology*. 2003;61(11):1528-1532.

3. Patterson MB and Foliart R. *Gen Hosp Psychiatry*. 1985; 7(3): 234-238

4. Murray TJ. *Neurol Clin*. 1995; 13(1): 197-223

5. Halper J. *J Neurol Sci*. 2007;256(suppl 1):S34-S38.

MS Relapses Are Caused by Inflammation in the CNS



Spinal Cord
Weakness or numbness Loss of muscle function (especially in the lower torso) Difficulty going to the bathroom
Brainstem and Cerebellum
Walking (gait), balance, and coordination problems Dizziness Uncontrollable shaking (tremors or muscle spasms)
Optic Nerve
Changes in your ability to see
Cerebrum
Problems with memory and attention Seizure
Other
Fatigue Pain

Compston A and Coles A. *Lancet*. 2008;372(9648):1502-1517.

Rosner LJ and Ross S. In: *Multiple Sclerosis: New Hope and Practical Advice for People With MS and Their Families*. 2008.

<http://www.nationalmssociety.org/about-multiple-sclerosis/what-we-know-about-ms/treatments/exacerbations/index.aspx>. Accessed April 18, 2011.

A Decrease in Quality of Life Accompanied an Increase in EDSS

Decline in SF-36 Scores of MS Patients Compared to the General Population

	Physical Function	Role-Physical	Social Function
MS patients with EDSS 3.0-6.0	-58%	-74%	-31%
MS patients with EDSS \geq 6.5	-90%	-83%	-43%

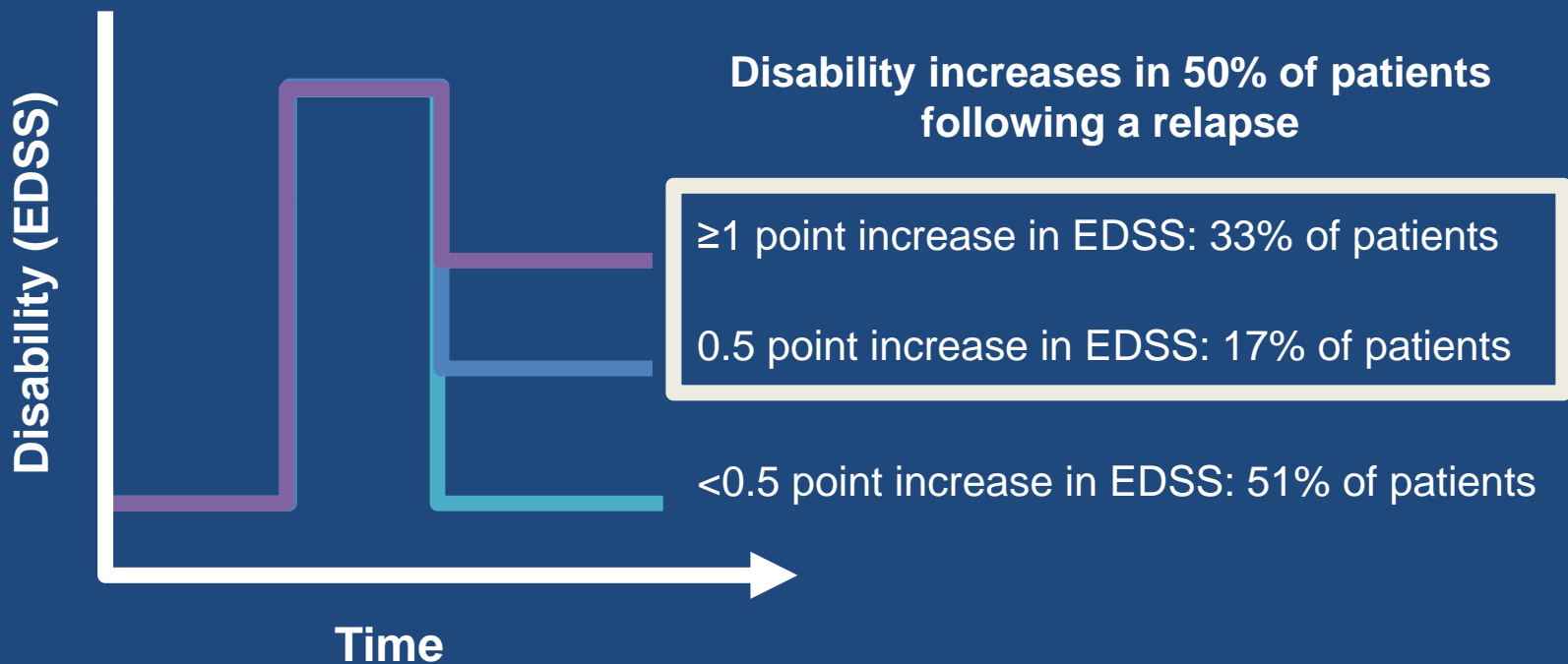
- Functional scores decreased significantly with disease progression in patients with MS
- Functional scores for severely affected MS patients were considerably lower than those for the general population

EDSS 3.0 = moderate disability, in which the patient is able to perform normal everyday activities without assistance.

EDSS 6.0 = assistance needed to walk 100 m and rest breaks needed after walking short distances and performing physical tasks

EDSS 6.5 = constant assistance needed to walk 20 m without resting

Relapses Lead to a Lasting, Stepwise Accrual of Disability



To Treat or Not?

- Most studies have shown that recovery from a relapse is the same with or without steroid therapy.
- Treatment does lead to quicker recovery.

Available MS Relapse Treatment Options

- IV Steroids¹
 - Brand name: Solu-Medrol[®] (methylprednisolone)
- Adrenocorticotrophic hormone (or ACTH)¹
 - Brand name: Acthar[®] (repository corticotropin injection)
- Low- and high-dose oral corticosteroids¹
 - Brand name: Deltasone[®] (prednisone) and others
- Other treatment options
 - Plasmapheresis or plasma exchange¹
 - May be considered for the 10% of very severe relapses that do not respond adequately to standard steroid treatment

1. National MS Society Website. <http://www.nationalmssociety.org/about-multiple-sclerosis/what-we-know-about-ms/treatments/exacerbations/index.aspx>

Steroids for Relapses

- Solumedrol (methylprednisolone) – usually given at a dose of 1 gm/day for 3 to 5 days. Prednisone tapers are optional.
- Some studies have shown equal efficacy and tolerability for an oral equivalent of prednisone (1250 mg/day).

Steroids: IV vs. Oral

- High dose oral prednisone (500mg – 1250 mg/day for 3 -5 days) is equally efficacious to IVMP 1 gm/day for 3 -5 days.
- High dose oral steroids show equal bioavailability to IVMP.
- No difference in gastric tolerance.

1) Barnes D, et al. *Lancet*. 1997 Mar 29; 349(9056): 902-6.

2) Alam SM, et al. *J Neurol Neurosurg Psychiatry*. 1993; 56: 1219-20.

3) Metz LM, et al. *Neurology*. 1999; 53: 2093-2096.

Steroid Side Effects

- Tremendous variability from person to person.
- Mood changes, anxiety → agitation → psychosis.
- Increased BP, serum glucose, stomach acid.
- Hypokalemia.

“I get a little agitated on
steroids.”



A Role for Rehabilitation

- Relapses were managed with IVMP 1 gm/day x 3 days alone or with comprehensive rehabilitation.
- The rehab group performed better at 1 and 3 months on measures of disability and quality of life (p values ranged from , 0.01 to 0.03).

The Walton Centre for Neurology and Neurosurgery, Liverpool, UK. *J Neurol Neurosurg Psychiatry*. 2003 Sep; 74(9): 1225-30.

Alternative Relapse Rx

- IVIG may be used for those intolerant to steroids or for relapses resistant to steroids, .4gm/kg QD for 5 days.
- Plasma exchange.
- Acthar gel (ACTH) 80 units subq daily for 5 days.

Plasma Exchange

- Plasma exchange in IVMP refractory demyelinating events (N = 22)
- 12 had RRMS and 10 had other inflammatory demyelinating conditions
- Cross over design: sham vs. plasma exchange

Weinshenker BG. *J Clin Apher.* 2001; 16(1): 39-42.

Plasma Exchange

- 42% of PE patients had moderate or greater improvement over two weeks vs. 6% of sham patients
- 3 sham failures improved when crossed over to PE

Weinshenker BG. *J Clin Apher.* 2001; 16(1): 39-42

IVIIG for Steroid Resistant ON

- 47 MS subjects with optic neuritis.
- 20/400 vision or worse after IVMP.
- Symptoms for 2 to 3 months.
- Randomized to IVIG 0.4 gm/kg daily x 5 days, then 0.4 gm/kg Q 4 weeks x 5 months or more IVMP.

IVIg for Steroid Resistant ON

- 18/23 IVIg subjects reached 20/30 vision or better.
- 3/24 of the steroid group reached 20/30 vision or better.

What is Acthar?

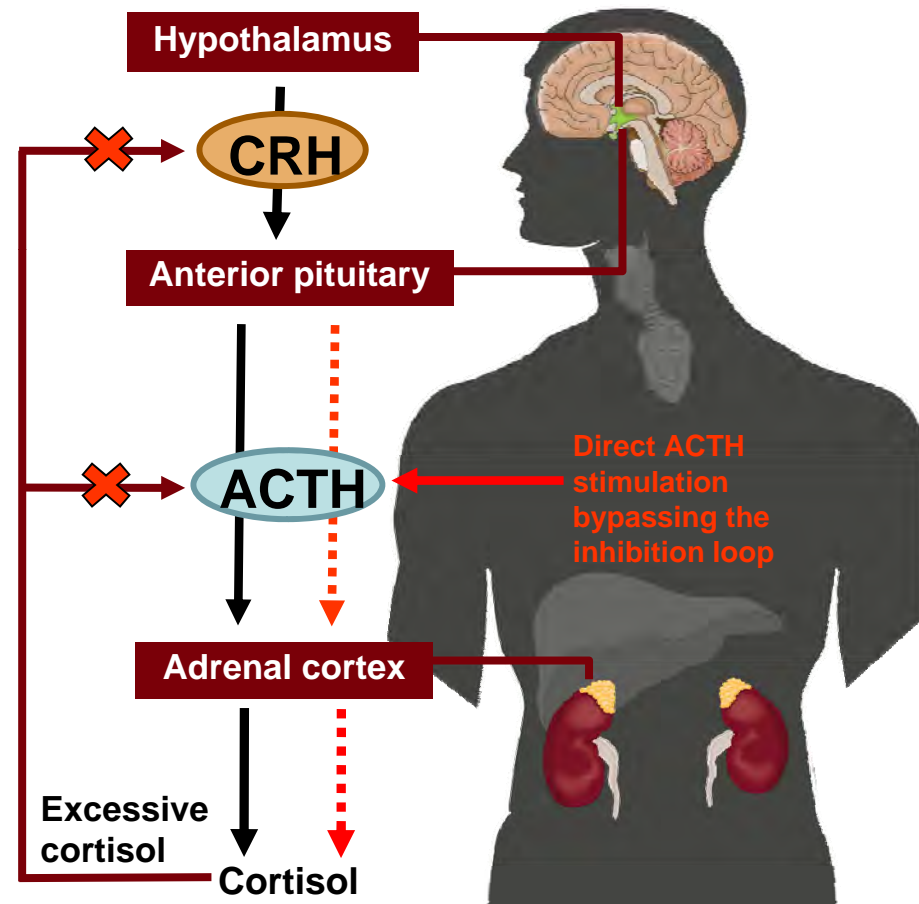
- H.P. Acthar® Gel or Acthar
- Prescription medication
- Contains the hormone adrenocorticotropin (a-DRE-no-cor-ti-co-tro-pin) also known as ACTH
- Available as 5-mL multidose vial
- Can be administered by self-injection
 - Subcutaneous (beneath the skin)
 - Intramuscular (into the muscle)
- Your doctor will determine your appropriate dose



Refer to the full prescribing information for H.P. Acthar Gel for a complete list of Adverse Events, precautions, and warnings. H.P. Acthar Gel [package insert]. Questcor Pharmaceuticals, Inc.; 2010.

How does Acthar Work?

- Acthar helps the body reduce inflammation in ways different than steroids:
 - Helps your body produce natural steroid hormones
 - Cortisol
 - Corticosterone
 - Aldosterone
 - Other hormones
 - Works in concert with your natural immune system to help suppress the relapse



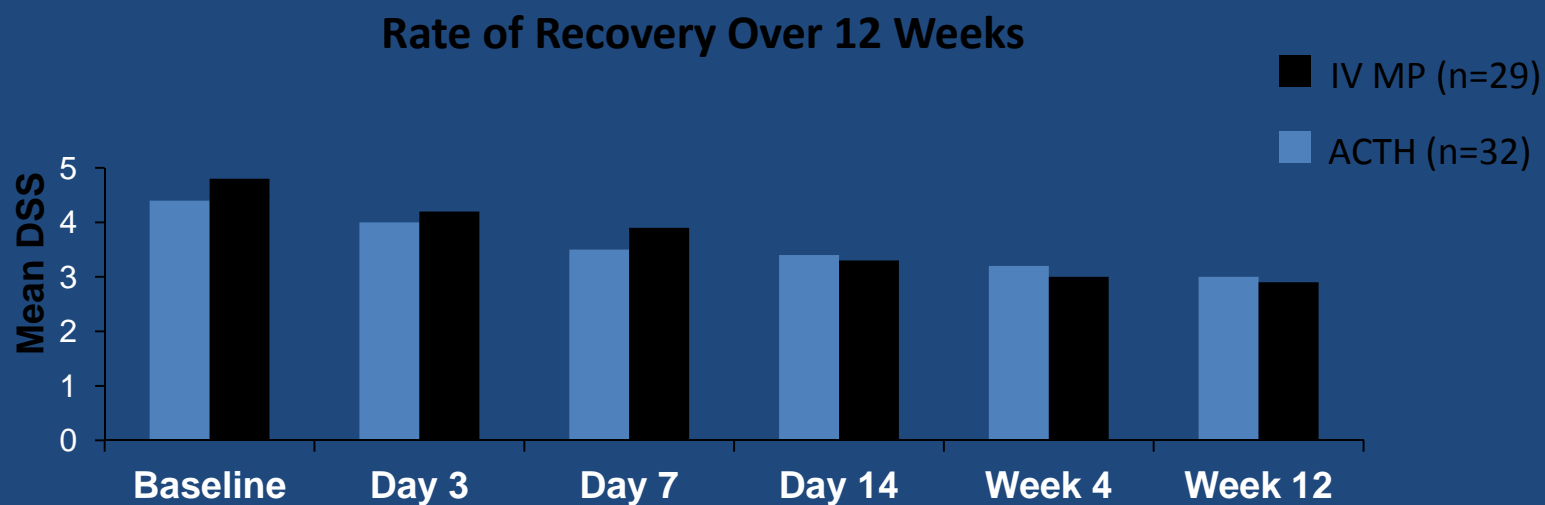
Refer to the full prescribing information for H.P. Acthar Gel for a complete list of AEs, precautions, and warnings.

Abbreviations: CRH, corticotropin-releasing hormone; AMP, adenosine monophosphate.

1. H.P. Acthar Gel [package insert]. Questcor Pharmaceuticals, Inc.; 2010.

Diagram adapted from: Gums JG and Tovar JM. In: *Pharmacotherapy: A Pathophysiologic Approach*. 2005:1396.

No Difference in Effectiveness Shown Between ACTH and IV Steroids



Safety

2 patients withdrew from the study because of AEs (1 who received ACTH and 1 who received MP)

Thank You For Your Attention

Questions?



Thank You

This concludes MSAA's Webinar:
The Treatment and Management of MS Exacerbations

This webinar will be available soon on MSAA's website: www.msassociation.org

MSAA would like to thank Dr. Ben Thrower for his time and expertise in presenting on this important topic and our program sponsor
Questcor Pharmaceuticals, Inc.

Thank you for participating in MSAA's webinar.

