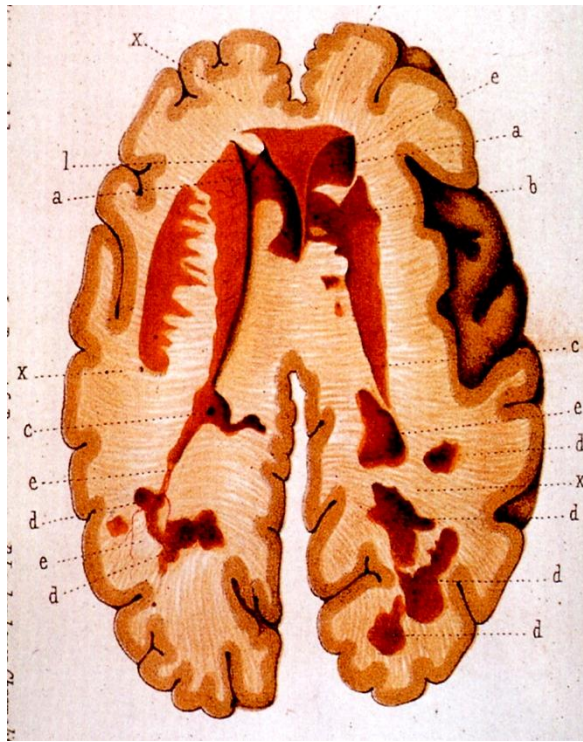


Update of Multiple Sclerosis (MS)

Dr. Motlabur Rahman
Associate Professor
Department of Medicine
Dhaka Medical College

19th Century Highlights



MS-related central nervous system pathology—Jean Cruveilhier, c 1841



Jean-Martin Charcot (1825–1893) described features of MS

What is Multiple Sclerosis (MS) ?

- MS is thought to be a disease of the immune system – perhaps autoimmune.
- The immune system attacks the myelin coating around the nerves in the central nervous system (CNS – brain, spinal cord, and optic nerves) and the nerve fibers themselves.
- Its name comes from the *scarring* caused by inflammatory attacks at *multiple* sites in the central nervous system.

What MS *Is Not*:

- **MS is not:**
 - Contagious
 - Directly inherited
 - Always severely disabling
 - Fatal—except in fairly rare instances

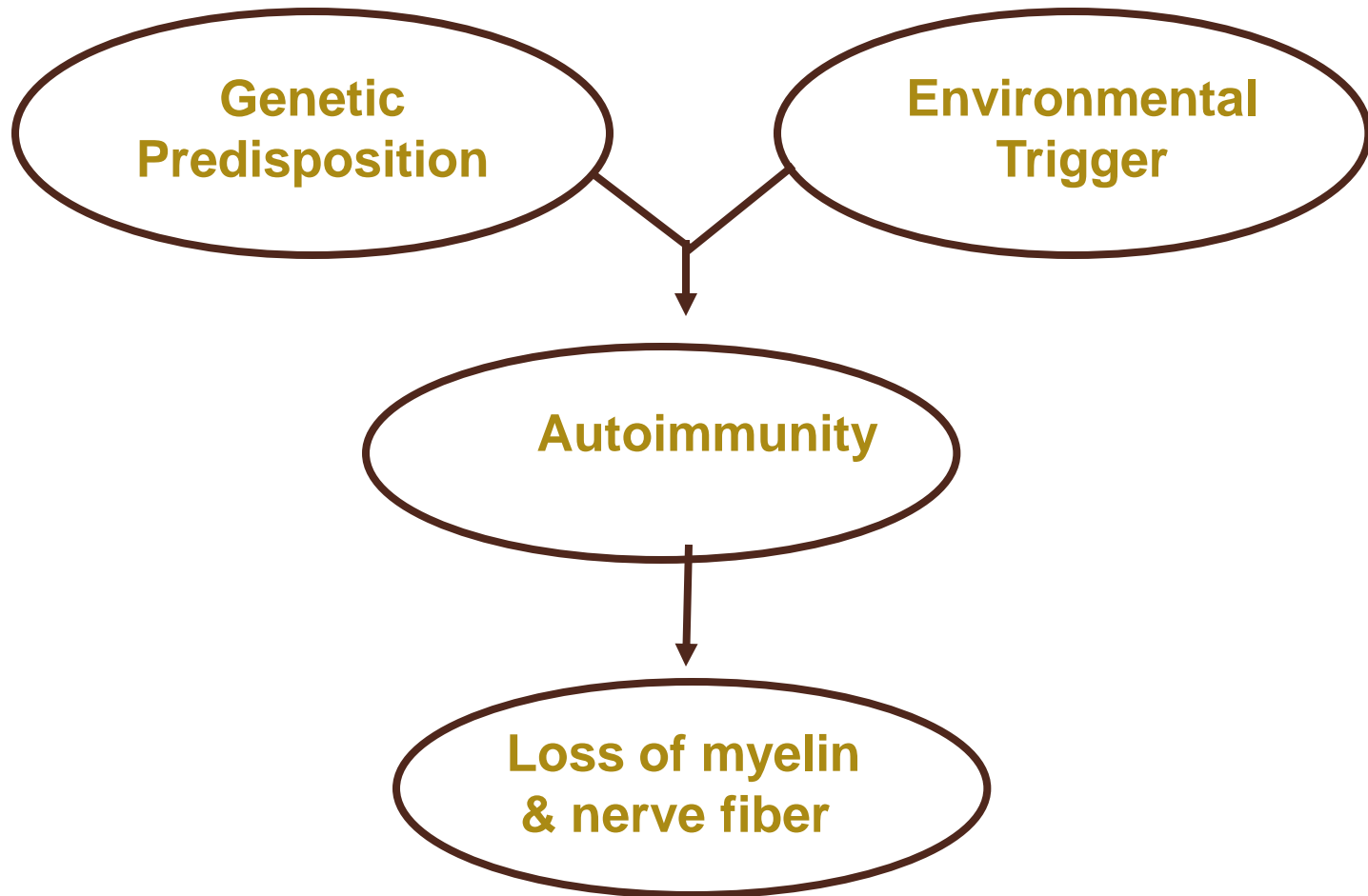
Who gets MS?

- Usually diagnosed between 20 and 50 yrs
 - **Occasionally diagnosed in young children and older adults**
- More common in women than men (2-3:1)
- Most common in those of Northern European ancestry
 - **More common in Caucasians than African Americans; rare among Asians**
- More common in temperate areas (further from the equator)

What causes MS?

- The most important factors to consider include:
geography, age, environmental influences, and genetics.
- Some others believe that --
Reduced vitamin D level may affect.
- Viruses may trigger for MS –
measles, herpes virus (HHV-6),
rubella, Epstein-Barr virus.

What Causes MS?



What is the genetic factor?

- **The risk of getting MS is approximately:**
 - 1/750 for the general population (0.1%)
 - 1/40 for person with a close relative with MS (3%)
 - 1/4 for an identical twin (25%)
- **20% of people with MS have a blood relative with MS**

The risk is higher in any family in which there are several family members with the disease (aka multiplex families)

What is the prognosis?

- **One hallmark of MS is its *unpredictability*.**
 - Approximately 1/3 will have a very mild course
 - Approximately 1/3 will have a moderate course
 - Approximately 1/3 will become more disabled
- **Certain characteristics predict a better outcome:**
 - Female
 - Onset before age 35
 - Sensory symptoms
 - Monofocal rather than multifocal episodes
 - Complete recovery following a relapse

What happens in MS?

“Activated” T cells...

...cross the blood-brain barrier...

...launch attack on myelin & nerve fibers...

...to obstruct nerve signals.



What happens to myelin and nerve fibers?



What are *possible* symptoms?

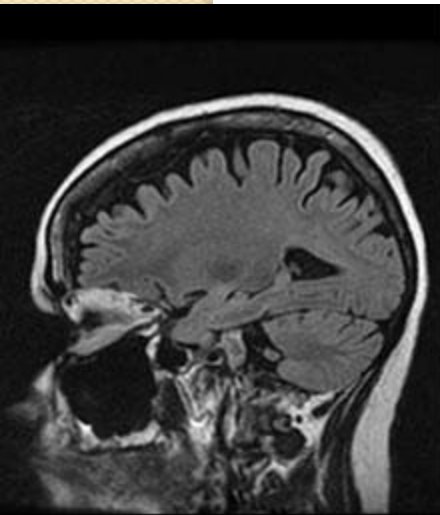
MS symptoms vary between individuals and are unpredictable

- Fatigue (most common)
- Decreased visual acuity, diplopia
- Bladder and/or bowel dysfunction
- Sexual dysfunction
- Paresthesias (tingling, numbness, burning)
- Emotional disturbances (depression, mood swings)
- Cognitive difficulties (memory, attention, processing)
- Pain (neurogenic)
- Heat sensitivity
- Spasticity
- Gait, balance, and coordination problems
- Speech/swallowing problems
- Tremor

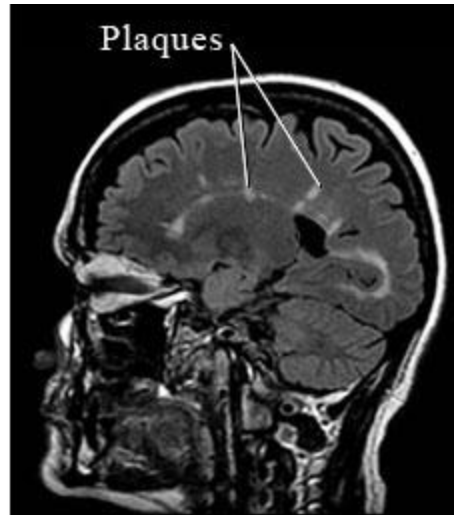
How is MS diagnosed?

- **MS is a clinical diagnosis:**
 - *History*
 - *Physical examination*
 - Laboratory tests
- **Requires dissemination in time and space:**
 - Space: Evidence of scarring (plaques) in at least two separate areas of the CNS (space)
 - Time: Evidence that the plaques occurred at different points in time

What tests may be used to help confirm the diagnosis?



Healthy brain



Brain with damage (lesions or plaques) caused by MS

- Magnetic resonance imaging (MRI)
- Visual evoked potentials (VEP)
- Auditory evoked potential
- CSF study



Making the Differential Diagnosis

Infection (Lyme, syphilis, PML, HTLV-1)

Degenerative spinal disease

Motor neuron disease

Metabolic (B12 deficiency, familial diseases)

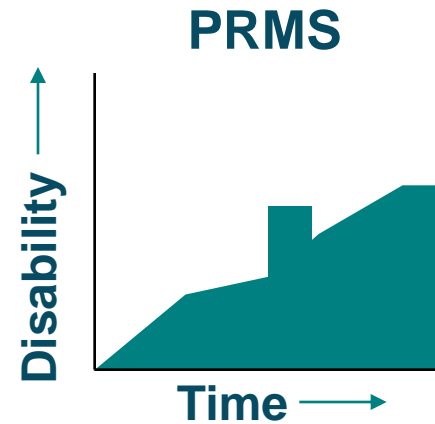
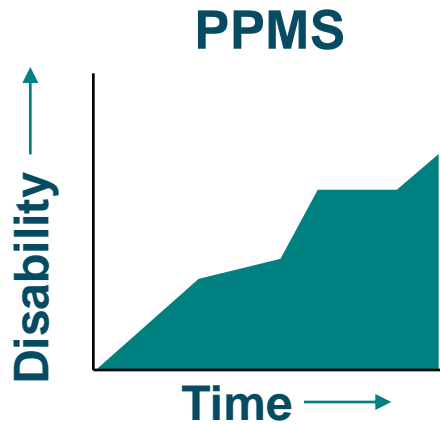
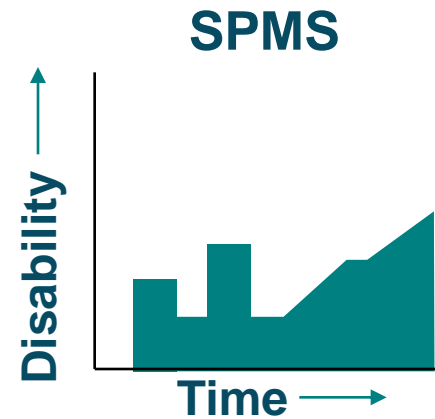
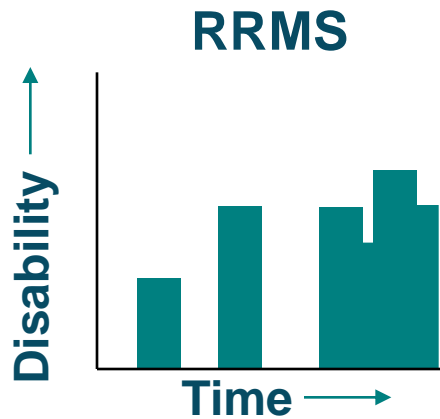
CNS Lymphoma

Inflammatory (SLE, Sjogren's, vasculitis, sarcoidosis)

What are the Different Patterns (courses) of MS?

- Relapsing-Relmitting MS (RRMS)
- Secondary Progressive MS (SPMS)
- Primary Progressive MS (PPMS)
- Progressive-Relapsing MS (PRMS)

Disease Courses in MS



What are the treatment strategies?

- **Management of MS falls into five general categories:**
 - Treatment of relapses (exacerbations, flare-ups, attacks—that last at least 24 hours)
 - Symptom management
 - Disease modification
 - Rehabilitation (maintain/improve function)
 - Psychosocial support

How are relapses treated?

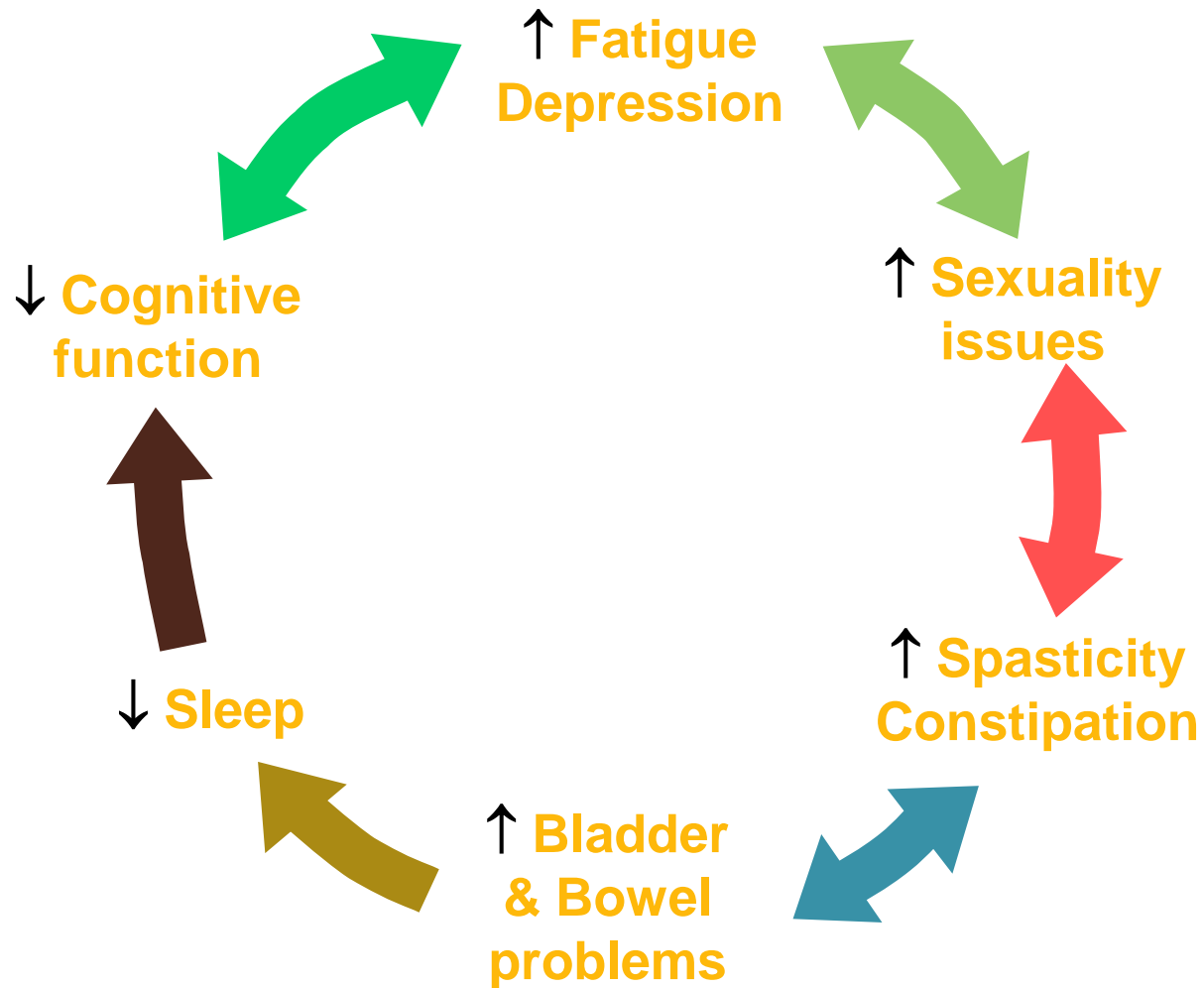
- **Not all relapses require treatment**
 - Mild, sensory symptom are allowed to resolve on their own.
 - Symptom that interfere with function (e.g., visual or walking problems) are usually treated
- 3-5 day course of IV methylprednisolone—with/without an oral taper of prednisone
 - High-dose oral steroids used by some neurologists
- Rehabilitation to restore/maintain function
- Psychosocial support

MS Symptoms vs. Relapses...

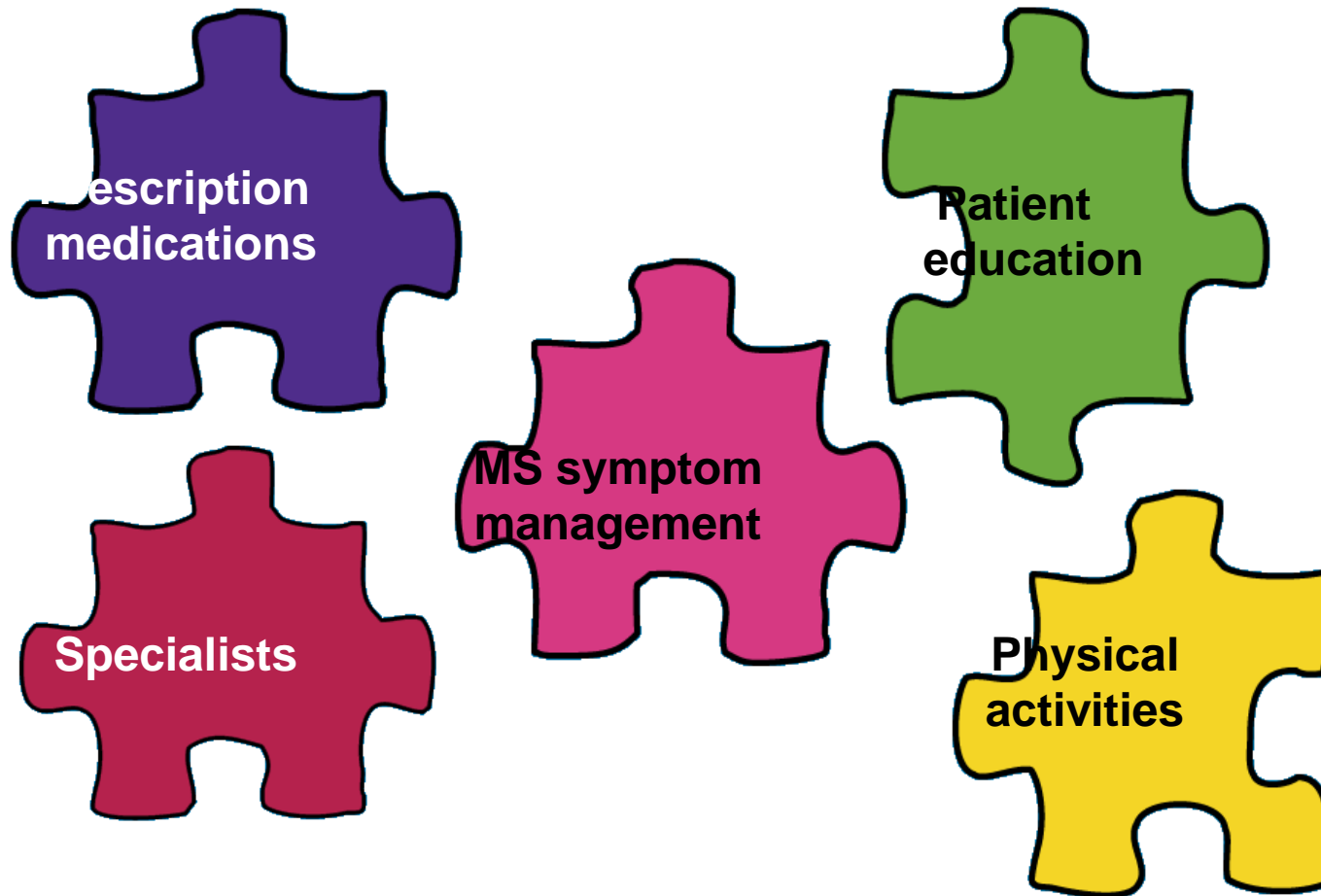
How Are They Different?

- MS symptoms are chronic or ongoing indicators of MS lesion damage in the brain, spinal cord, and/or optic nerve
- MS relapses are sudden flare-ups of disease activity (including new or worsening symptoms) that typically last several days to several weeks or months

Cycle of MS Symptoms: Related and Interdependent



The Recommended Approach to Managing MS Symptoms



Managing MS Symptoms

SYMPTOM	PHARMACOLOGICAL Treatment
Fatigue	<ul style="list-style-type: none">• CNS stimulants: eg, modafinal• SSRIs: eg, fluoxetine
Pain	<ul style="list-style-type: none">• Anticonvulsants: carbamazepine, gabapentin, phenytoin• Duloxetine hydrochloride

Managing MS Symptoms

SYMPTOM	PHARMACOLOGICAL TREATMENT
Cognitive dysfunction	<ul style="list-style-type: none">•No symptomatic medications have been shown to be beneficial

Managing MS Symptoms

SYMPTOM	PHARMACOLOGICAL TREATMENT
Bladder dysfunction	<ul style="list-style-type: none">• Anticholinergic/antispasmodic: eg, oxybutynin, tolterodine
Bowel dysfunction	<ul style="list-style-type: none">• Constipation: stool softeners, bulk-forming agents, rectal stimulants, mild laxatives• Fecal incontinence: anticholinergics (for hyperreflexive bowel)

Managing MS Symptoms

SYMPTOM	PHARMACOLOGICAL TREATMENT
Mobility impairment	<ul style="list-style-type: none">• Dalfampridine (Ampyra) to improve walking (speed; weakness)
Spasticity	<ul style="list-style-type: none">• GABA agonists (oral or intrathecal baclofen)• α- Agonists (tizanidine)• Anticonvulsants (gabapentin, clonazepam, diazepam)• Botulinum toxin

Who is on the MS “Treatment Team”?

- Neurologist
- Urologist
- Nurse
- Psychiatrist
- Physiatrist
- Physical therapist
- Occupational therapist
- Speech/language pathologist
- Psychotherapist
- Neuropsychologist
- Social worker/Care manager
- Pharmacist

How is the disease course treated?

- **Thirteen disease-modifying therapies are US FDA-approved for relapsing forms of MS:**
 - Glatiramer acetate
 - Interferon beta-1a
 - Interferon beta-1b
 - Dimethyl fumarate [oral]
 - Fingolimod [oral]
 - Teriflunomide [oral]
 - Alemtuzumab [inj]
 - Natalizumab [inj]
 - Mitoxantrone [inj]

What do the disease-modifying drugs do?

- All reduce attack frequency and severity, reduce lesions on MRI, and probably slow disease progression.
- These medications are not designed to:
 - **Cure the disease**
 - **Make people feel better**
 - **Alleviate symptoms**

What are New Therapies under Investigation?

- **Anti-LINGO (opicinumab):** LINGO-I is a protein in the central nervous system whose role is to halt myelination and prevent the survival of neurons.
- **Amiloride, Phenytoin, and Sodium Channel Blockade:** The accumulation of salt and potassium within the cells of MS lesions may possibly contribute to cellular injury and neurodegeneration.
- **MIS416:** This “therapeutic vaccine” is a potent activator of the innate immune system, which provides immediate defense against infection but does not result in long-lasting or protective immunity.
- **Transdermal Administration of Peptides**
- **IL-17 Modulators**
- **Intravenous immunoglobulin:**
- **Plasma exchange:**

What's New Directions in MS Research

- Vitamins and Minerals
 - Vitamin D3
 - Omega-3 fatty acid
 - Lipoic Acid
 - Biotin (MD1003)
- Stem Cells
- Biomarkers
- Genetic Studies

So What is summary About MS?

- MS is a chronic, unpredictable disease.
- The cause of MS is still unknown
- MS affects each person differently; symptoms vary widely.
- MS is not fatal, contagious, directly inherited, or always disabling.
- Early diagnosis and treatment are important:
 - **Significant, irreversible damage can occur early on**
 - **Available treatments reduce the number of relapses and may slow progression**
- Treatment includes: relapse management, symptom management, disease modification, rehabilitation, emotional support.

THANK YOU
FOR YOUR ATTENTION