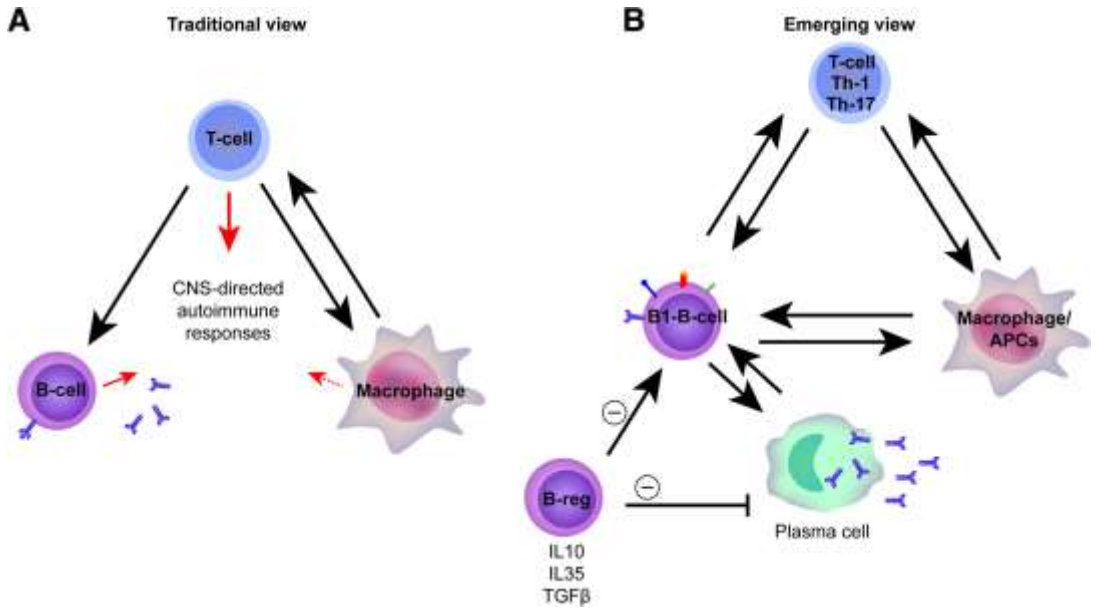
Chronic and acute pain syndromes in patients with multiple sclerosis

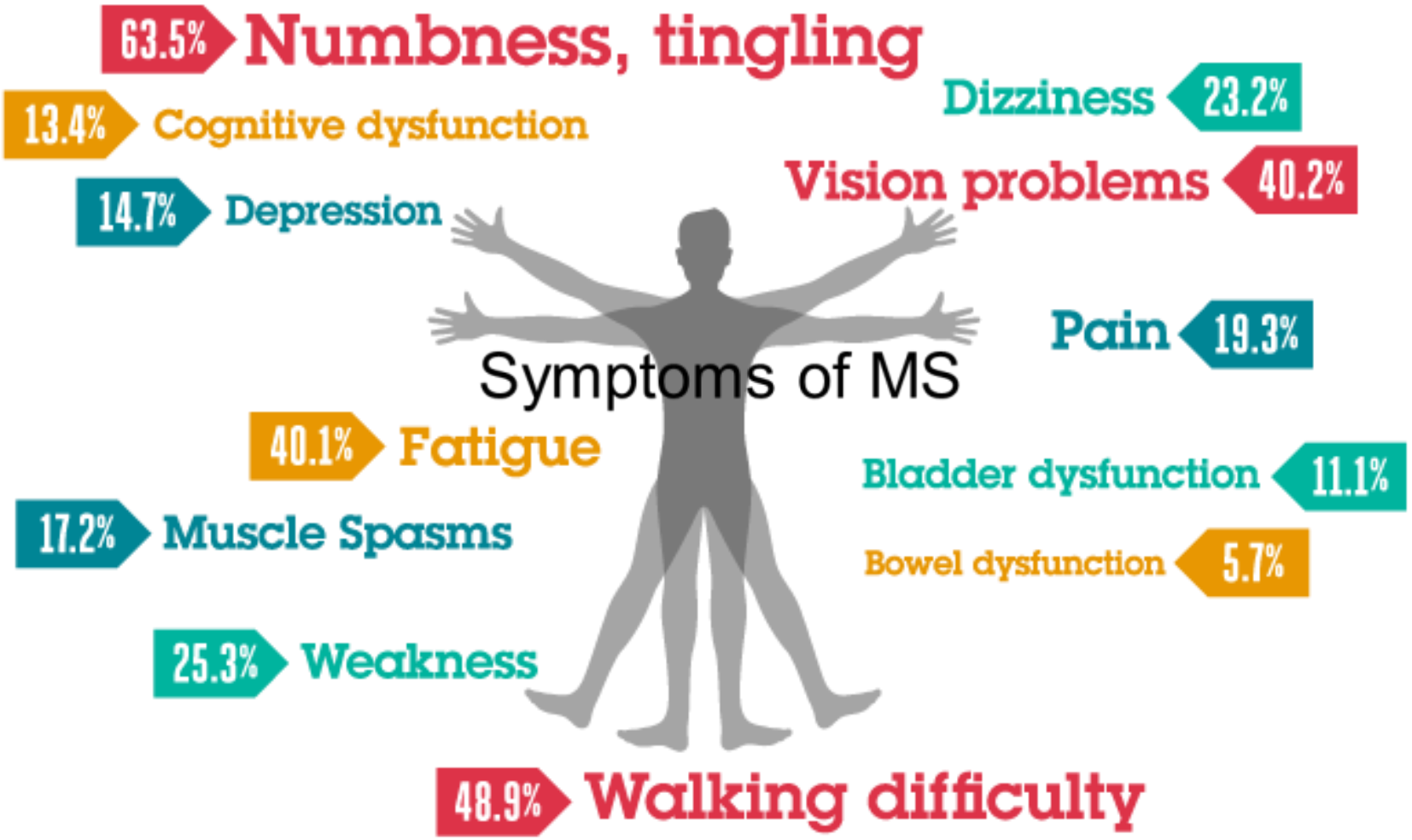
Iman Adibi, M.D.
Assistant Professor in Neurology and Multiple Sclerosis

Pathophysiology of MS

An autoimmune disorder of the central nervous system
Multifocal regions of inflammation/atrophy in gray and white matter
oligodendrocyte death and myelin sheath destruction



Symptoms of MS



Pain in Multiple Sclerosis

- Chronic Pain: pain lasting more than 12 weeks
- Based on underlying mechanisms:
- Nociceptive
- Neuropathic
- Noci-plastic or mixed

Pathophysiology of Pain in MS

Primary :

- demyelination and/or axonal damage
- most commonly in the brainstem and less commonly in the spinal cord

Secondary:

- an indirect consequence of the CNS lesion

Clinical Presentation:

- stimulus-independent

- stimulus-independent: persistent or paroxysmal pain

Underlying Mechanisms

- Ongoing extremity pain (dysesthesia): burning sensation in the lower limbs
- Intermittent central neuropathic pain: trigeminal neuralgia (TN) and Lhermitte's sign
- Painful tonic spasm:
  - specific to MS
  - spontaneous muscle contractions
  - a result of the lesions in the motor pathway (internal capsule and cerebral peduncle)
- Spasticity pain
- MS back pain
  - mechanical-originated pain
  - secondary to : inactivity, muscle weakness, and spasticity

Impacts of Pain in MS

- health-related QoL
- ADL
- mental health
- Social functioning
- Employment
- Sleep
- Pain is highly associated with fatigue, depression, and anxiety
- In case the pain is neuropathic, the degree of interference increases, especially in terms of depression

Risk Factors for Developing Pain in MS

- older age
- longer disease duration
- greater severity of MS
- Gender is a conflicting risk factor, females are more likely to report their pain and to have more severe and neuropathic pain
- mental health problems
- Lower education level
- lower socioeconomic
- marital status

Headache

- headache is more common in MS
- it is unclear whether headache was present before MS
- Headache in MS is thought to have neuropathic and nociceptive mechanisms,(mixed pain)
- migraine three times more common in both men and women with MS than in the general population
- Prevalence of headache in MS is greater than 50%; women being at greater risk
- MS patients with migraine experience greater depression and additional sensory related pain
- onset or worsening severity of headache may predict or be a marker for MS exacerbation
- The frequency and severity of headache may be exacerbated by interferon beta medications, especially at the start of treatment

Treatment-induced Pains

- Flu- like myalgias
- Headache
- Pain at the injection areas
- Long-term use of corticosteroid

Musculoskeletal Pain

- Weakness
- Deconditioning
- Immobility
- Stress on bones, muscles and joints.
- Steroid use: osteoporosis, avascular necrosis

Musculoskeletal Pain

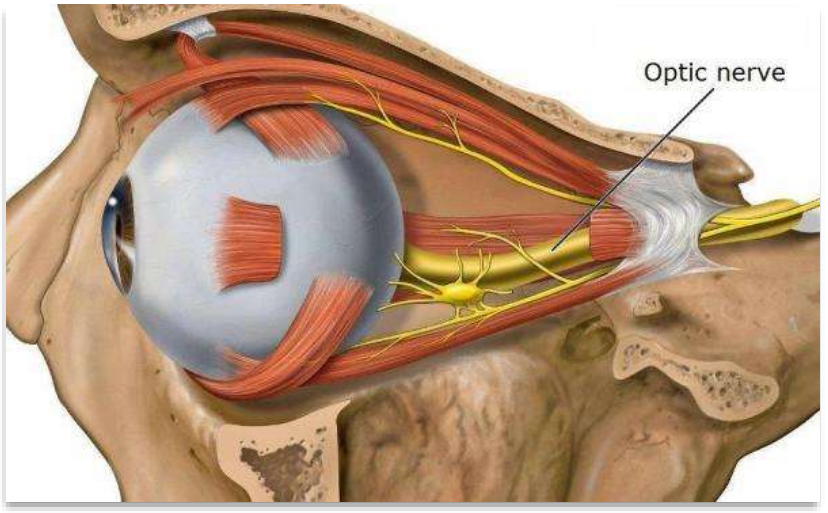
- Prevention is critical to the management of musculoskeletal pain.
- Bone antiresorptive therapies, smoking cessation, calcium and vitamin D supplementation
- Physical therapy
- Frequent position change and proper support relieve stress on muscles, bones and joints.
- Treatment :
  - Acetaminophen
  - nonsteroidal anti-inflammatory agents (NSAIDs)
  - Muscle relaxants

Medications for Paroxysmal Pain:

- Carbamazepine
- Oxcarbazepine
- Gabapentin
- Lamotrigine
- Misoprostol
- Valproic acid
- Topiramate
- Phenytoin
- Baclofen
- Clonazepam
- Capsaicin
- Amitriptyline
- Pregabalin

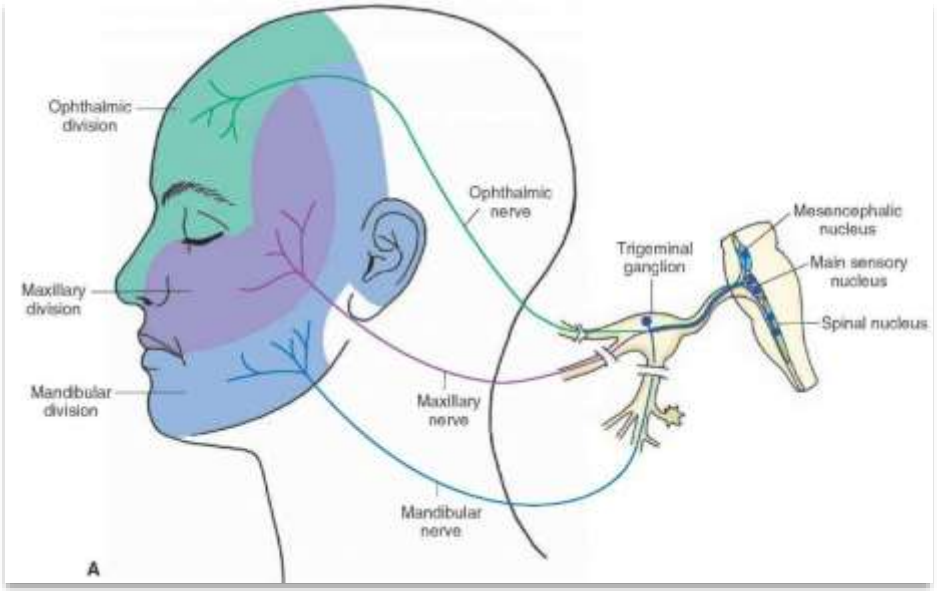
Optic Neuritis

- Inflammation of the optic nerve that activates intraneural nociceptors
- a dull pain sensation
- anti-inflammatory agents such as corticosteroids



Trigeminal Neuralgia

- sudden, usually unilateral, severe, brief, stabbing or lancinating, recurrent episodes of pain in the distribution of one or more branches of the fifth cranial (trigeminal) nerve
- 10-15 times more than general population
- Idiopathic trigeminal neuralgia manifests due to neurovascular compression
- in multiple sclerosis due at least in part to enhanced inflammatory activity



Trigeminal Neuralgia

Trigeminal distribution – strictly limited to the distribution of the trigeminal nerve (V2 and/or V3) isolated involvement of the V1 subdivision occurs in <5 percent of patients with TN

Paroxysmal pain - maximal at or near onset, facial muscle spasms can be seen

Continuous dull pain - that is present between paroxysms of pain

does not awaken patients at night

Unilateral – Bilateral involvement in approximately 10 percent

Trigeminal Neuralgia

Trigger zones – Nearly all patients with TN experience triggered pain

Lightly touching these zones

chewing, talking, brushing teeth, cold air, smiling, and/or grimacing

Autonomic symptoms – association with attacks of TN in the V1 distribution

lacrimation, conjunctival injection, and rhinorrhea

The presence of autonomic features, particularly when prominent or severe, is suggestive of the syndromes of short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with autonomic symptoms (SUNA)

Summary of Commonly Used Therapies for Trigeminal Neuralgia

Modality	Assessment
Pharmacologic Therapy	Carbamazepine: moderate level of evidence for long-term benefit, but loss of benefit (failure rate of 50% long term) Other anticonvulsant drugs: oxcarbazepine, lamotrigine, gabapentin—commonly used but low quality or insufficient evidence re: benefit
Peripheral Nerve Intervention	Percutaneous rhizotomy (glycerol): high level of evidence for long-term benefit Radiofrequency thermocoagulation: high level of evidence for long-term benefit Balloon compression: high level of evidence for long-term benefit
Botulinum Toxin	High quality of evidence for benefit
Gamma Knife Radiosurgery	High quality of evidence in favor of long-term benefit. Benefit falls by almost half in 5–10 years, but treatment can be repeated
Microvascular Decompression	High level of evidence for long-term improvement that is maintained over 5 years

The Lhermitte sign

- transient sensory sensation
- lasting seconds
- resembles an electric shock
- radiating down the spine or into the limbs
- It is most often elicited by flexion of the neck
- Resolves spontaneously without treatment
- Treatment:
  - glucocorticoid therapy (a new inflammatory spinal cord lesion)
  - gabapentin, pregabalin, or carbamazepine
  - sodium channel blockers lidocaine and mexiletine (paroxysmal painful tonic spasms and Lhermitte sign)

The “MS hug”- (Anaconda sign)

Dysesthetic phenomenon with gripping, squeezing, constricting, or pressure-like sensations in the thoracic and abdominal regions.

The etiology is variably attributed to neuropathic pain from spinal cord involvement or to thoracic and abdominal spasticity.

The “MS hug”- (Anaconda sign)

Resulting from neuropathy: amitriptyline, gabapentin, pregabalin, or topical compounded creams containing a neuropathic pain medication, a nonsteroidal anti-inflammatory drug (NSAID), and a local anesthetic.

Resulting from spasticity: treatment options include baclofen, tizanidine, and gabapentin.

Headaches

- The prevalence of headaches in MS patients is higher than from the general population by greater than 50%
- Migraine headaches, more common in RRMS
- Tension-type headaches, more common in PMS and elderly men
- There is no difference in the treatment approach for headaches in patients with multiple

sclerosis compared with the general population :

- Balance
- Dizziness
- Fatigue
- Weight gain

Neuropathic Pain

- The prevalence is as high as 86%
- Most commonly presents as extremity pain
- it is relatively rare in the earlier stages
- occurrence of pain early in the disease course was linked to increased disability, depression and fatigue
- TREATMENT:
  - Antidepressant medications (TCA,SNRI)
  - Anticonvulsant medications
  - Cannabinoids
  - Spinal stimulation therapies
  - off-label use of low-dose naltrexone

Neuropathic Pain

Physical Therapy and Exercise Programs

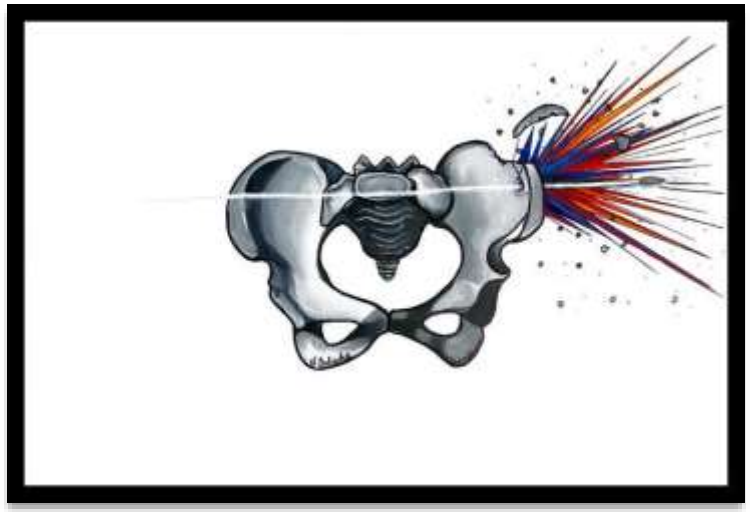
- reduce sensation of painful stimuli
- supply a generalized anti-inflammatory effect
- may slow disease progression in multiple sclerosis
- may even promote regeneration of neural tissues

Neuromodulation

- targeted electrical or chemical neuronal stimulation or inhibition
- Intrathecal baclofen pumps with functional electrical stimulation
- Deep brain stimulation
- Spinal cord stimulation
- Transcranial magnetic stimulation

Pelvic Pain Syndromes

- noncyclic pelvic pain
- persisted for three to six months or longer
- unrelated to pregnancy
- nerve impingement or entrapment: peripheral nerve block or surgical release
- Initial pharmacologic treatment
  - NSAID, Acetaminophen, Muscle relaxants
  - Physical therapy
  - Trigger point injection
  - Nerve block



Pelvic Pain Syndromes

- Anticonvulsants (gabapentin and pregabalin)
- TCA
- SNRI
- Other antiepileptics — Antiepileptic sodium channel blocking agents, such as phenytoin, carbamazepine, oxcarbazepine, lamotrigine, tiagabine, and topiramate,
- CBT
- Exercise
- Acupuncture
- Neuromodulation
- Canabinoids

Painful Tonic Spasms

- Abrupt onset of abnormal posturing of an extremity
- Sudden tightening of a limb, clawing of a hand or arm, or kicking out of a leg
- Spasms last less than two minutes and are often evoked by touch, movement, hyperventilation or emotion
- Typically unilateral but occasionally bilateral
- Arise from a lesion in pyramidal and extrapyramidal tracts or hyperactivity of the central motor fibers caused by a lesion in the internal capsule, cerebral peduncle, medulla or spinal cord
- Management includes treatment with antiepileptic agents, lidocaine, and botulinum toxin

Spasticity

Increased muscle tone and involuntary contractions of skeletal muscle cause pain.

evoked by noxious stimulation such as a pressure ulcer, a full bowel or bladder, urinary tract or other infection

Spasticity

Spasticity management:

- ruling out the cause of noxious stimuli
- Non-pharmacologic; stretching, range of motion exercises and splinting
- Pharmacologic management :
  - centrally acting therapies; baclofen, clonidine, tizanidine; anticonvulsants, benzodiazepines and gabapentin
  - peripherally acting drugs dantrolene sodium
  - invasive treatments, intrathecal baclofen, botulinum toxin injections and phenol/alcohol injections
  - Oral cannabis extract (add-on)