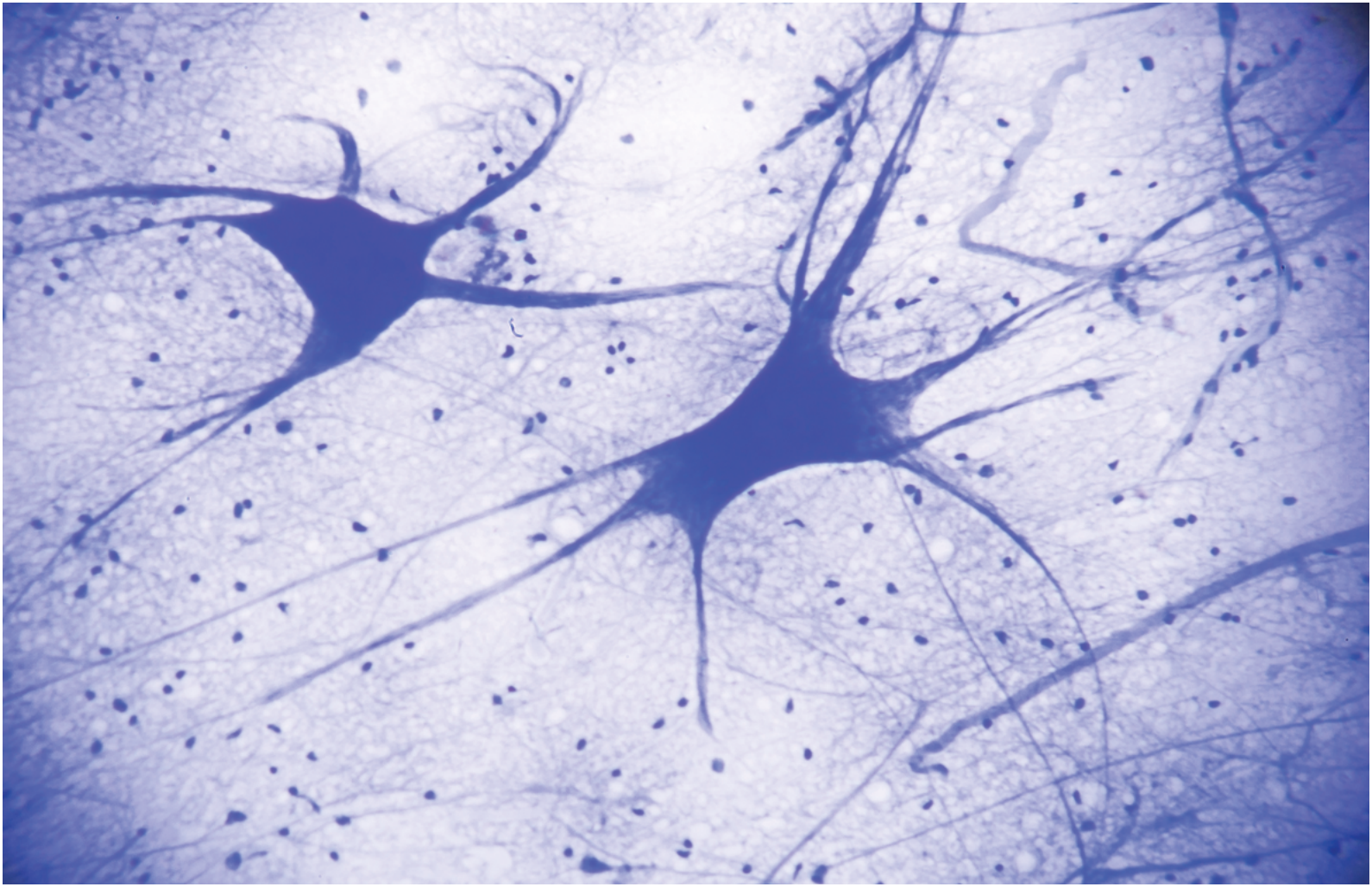

Detect. Differentiate. Diagnose.

Recognizing Multifocal Motor Neuropathy (MMN)[1,2]

Takeda

About MMN

MMN is an immune-mediated demyelinating neuropathy that causes progressive, asymmetric weakness of the distal limbs with no objective sensory loss.[1]

Whom it affects

Approximately
1-2 in 100,000
people have MMN—about half the prevalence of ALS[1,3]

MEN are affected nearly **3×** more often than women[4]

80%
of patients develop symptoms between 20 and 50 years of age (average age: 40 years)[4]

ALS=amyotrophic lateral sclerosis.

PERSONAL EXPERIENCE

Patient reports showed it may be years before MMN is treated, which may result in symptom progression.[1,5] Without knowledge of their disorder, patients may feel helpless and frustrated about what is happening to them.

Hypothetical patient portrayal; model shown not actual patient.

"I'm 29 years old but started experiencing weakness in my hands when I was 26. Over that first year, I suffered complete wrist drop in both hands. As a fourth-grade teacher, this was tough for me. I dropped pencils and markers in front of my kids, couldn't write on the board without holding one of my wrists up, and I dreaded having to shake parents' hands due to embarrassment about my condition."

—Patient with MMN

Diagnostic criteria and presentation

Key feature	Early signs	Advanced disease	Important to note
CLINICAL			
Asymmetric weakness of distal arm and/or leg muscles[1,4,6*]	• Commonly begins in the fingers or thumb • May include involuntary fasciculations and cramping	• Wrist drop, foot drop, and/or loss of grip strength • Weakness may move proximally as disease progresses	• Symptoms progress slowly or in a stepwise pattern • No progression to generalized immobility
No objective sensory impairment[4*]	• None, or very mild	• None, or very mild	• Absence of sensory impairment is uncommon among other peripheral neuropathies
Muscle mass[1,4]	• Preserved, despite profound weakness	• Decreased due to atrophy	• Muscle mass decreases with disease progression
PHYSIOLOGIC			
Motor conduction block[1,2,7†]	• Present, but may be activity dependent and, therefore, difficult to detect	• Increasing frequency of conduction block may make it easier to detect	• MMN is unique because conduction block is confined to motor axons, a hallmark symptom
Axonal damage and loss[1,2,5]	• Axonal damage and/or loss is correlated with the level of muscle weakness and may be less pronounced in early stages	• Increased axonal damage and/or loss is correlated with muscle weakness and subsequent muscle atrophy	• Advanced axonal damage and/or loss is correlated with muscle weakness and subsequent muscle atrophy
LABORATORY			
Anti-GM1 antibodies[1,7]	• Present in 50%-60% of patients	• Present in 50%-60% of patients	• Presence of anti-GM1 antibodies is a marker for MMN; however, the role of these antibodies has not been well established

*MMN should be considered when patients present with asymmetric, distal muscle weakness with no objective sensory loss.[7]
†Establishing diagnosis based on consensus criteria for confirming conduction block may result in underdiagnosis, as conduction block is not always necessary for a diagnosis if other criteria are met.[6]

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MMN as part of the differential diagnosis

Often presenting with symptoms similar to those of other neuropathies—such as ALS and CIDP—a diagnosis of MMN can be elusive.[1,2]

A thorough patient evaluation can reveal meaningful details that help lead to a definitive diagnosis. Refer to the chart below to quickly see differences among these symptom-sharing neuropathies.

NEUROPATHIES IN THE DIFFERENTIAL DIAGNOSIS: MOST COMMON PRESENTATION OF SELECT SYMPTOMS

Disorder	Motor conduction block	Sensory signs	Anti-GM1 antibodies elevated	Most common clinical presentation of weakness	Distribution of weakness	Tendon reflexes	Elevated protein in CSF	Disease course	Gender distribution, male:female
MMN[2,4,7]	Frequently present*	No	Yes	Distal upper limb	Asymmetric	Normal or decreased in weakened muscles†	No	Slowly progressive	2.6:1
ALS[2,8,9]	Absent	No	Rare	Focal,‡ distal > proximal; upper limb > lower limb	Asymmetric	Increased in weakened muscles	No	Rapidly progressive	1.4:1
CIDP[1,2,4]	Frequently present	Yes	Rare	Proximal and distal	Symmetric > asymmetric	General hyporeflexia or areflexia	Yes	Progressive or relapsing	M < F
Lower motor neuron disease[2,8,10]	Variable	No	Rare	Focal, distal > proximal; upper limb > lower limb	Asymmetric > symmetric	Decreased in weakened muscles	No	Slowly or rapidly progressive	6:1
LSS[2,4,10]	Present*	Yes	Rare	Distal upper limb	Asymmetric	Decreased in weakened muscles	Rare	Progressive or relapsing	M > F

"The tests we do are so operator-dependent and very open to misinterpretation."

—Neurologist who treats MMN

"EMG [electromyography] is an acquired skill. Very technical."

—Neurologist who treats MMN

Differentiating MMN from other neuropathies

- ✓ Is there an asymmetrical distribution of distal limb weakness?
- ✓ Is there absence of objective sensory loss?
- ✓ Is motor conduction block present?
- ✓ Are anti-GM1 antibodies elevated?

Please see chart above for more complete information.

CIDP=chronic inflammatory demyelinating polyneuropathy; CSF=cerebrospinal fluid; LSS=Lewis-Sumner syndrome.
*Conduction block may not be detectable and is not always necessary for diagnosis.[2,6]
†Reflexes may be brisk in some patients.[2]
‡Bulbar symptoms at onset may be observed in approximately 25% of patients.[8]

Detect. Differentiate. Diagnose.

The importance of a timely diagnosis

The mean time from symptom onset to diagnosis is **6 years** (range: <1 to 23 years).[6]

Undiagnosed and unmanaged, MMN will progress as patients:

- Experience spreading weakness, making it more difficult to identify asymmetry[4]
- Lose muscle mass due to atrophy[4]

MMN cannot be cured, and disease progression depends on how long patients remain undiagnosed.[1,2]

Hypothetical patient portrayal; model shown not actual patient.

"I had been suffering and searching for a diagnosis for 3 years. [By the time I was diagnosed,] I had lost most of the strength in my hands and had wrist drop. My muscles had begun to atrophy."

—Patient with MMN

Think MMN when patients present with asymmetric, distal muscle weakness without objective sensory loss[7]

Include MMN as part of the differential diagnosis and identify more patients to have the greatest impact.[1,2]

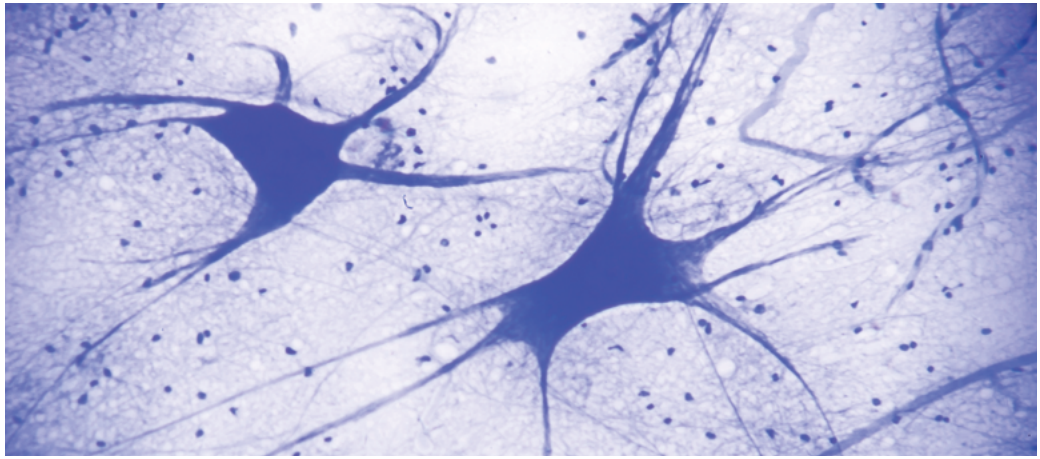
"And this is what excites me to this day—the thrill of making a correct and sometimes obscure diagnosis.... It is incredibly satisfying and empowering."

—Neurologist who treats MMN

Detect. Differentiate. Diagnose.

- Asymmetric, distal muscle weakness that progresses slowly or in a stepwise pattern, commonly resulting in wrist or foot drop, is characteristic of MMN[1]
- Compared with other neuropathies, there is no objective sensory loss in MMN, and it may present with or without motor conduction block[1,2]
- Prognosis is better with early diagnosis[1,2]

Think MMN when patients present with asymmetric, distal muscle weakness without objective sensory loss[7]



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US-NON-0650v1.0 03/20

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