

Inside This Issue

Repairing the Nervous System: Remyelination and Multiple Sclerosis 3

Mayo Clinic Stroke Programs: Providing Acute Care in the Community and Beyond 6

The Science and Art of EMG Testing



Eric J. Sorenson, MD

“Much of neurology hinges on locating the problem. Once you’ve established the location, you have a much greater likelihood of determining the cause and fixing it. One of the great strengths of EMG [electromyography] is its high level of accuracy in localization.” With these words, Eric J. Sorenson, MD, helps explain the importance of EMG in diagnosing and treating neuromuscular disease. Director of the EMG Laboratory in the Department of Neurology at Mayo Clinic Rochester, Dr Sorenson notes that EMG can determine which nerves and muscles are impaired and whether the source is the nerve, the neuromuscular junction, the muscle, the spinal cord, or a combination of structures.

Anyone who has listened to the buzz and crackle of an EMG recording knows that interpreting EMG responses requires fine auditory discrimination and an experienced ear. EMG is not an exact science—neither the test protocols nor the results are black-and-white (Figure). EMG must be conducted and interpreted within the context of the clinical examination and clinical hypotheses. C. Michel Harper, MD, a neurologist and former director of the EMG Laboratory, points out that EMG “is not an end in itself, but rather an extension of the neurologic examination, much as a tuning fork or tendon hammer. It is a tool that allows physicians to probe specific aspects of the nervous system.”

Context and Bias—Sorting the Wheat From the Chaff

EMG is always subject to bias, and in the hands of an experienced electromyographer, bias is helpful and important. Dr Sorenson explains: “Because EMG is so sensitive, it’s not uncommon to have false-positive results, so it is critical to distinguish true- and false-positives, to sort the wheat from

the chaff.” Dr Harper adds: “Narrowing down the pretest probabilities allows us to collect less EMG data to answer the diagnostic question, to recognize incidental findings that have nothing to do with the history or clinical exam findings, and to consider whether an extraneous finding is meaningful or not.”



C. Michel Harper, MD

The more skilled one is at EMG,

- the fewer recordings are needed to answer the diagnostic question.
- the easier it is to attend simultaneously to the electrical response and patient comfort.
- the better one is at distinguishing relevant from irrelevant information and outlier responses.

A large patient volume and varied caseload that includes complex cases such as brachial plexus injuries and rare peripheral neuropathies enhance EMG expertise and specialized skills. Mayo Clinic electromyographers, for example, routinely perform single-fiber EMG, a technique that samples 1 or 2 muscle fibers rather than the standard 10 to 15. It is difficult to perform, not widely available, and 95% to 100% sensitive in diagnosing myasthenia gravis.

Because EMG is not an exact science, training and mentorship are particularly critical. Residents at Mayo Clinic’s 3 sites train for at least 6 months in the EMG lab—this is 3 months longer than most other residencies. Many of their mentors trained under Edward Lambert, MD—one of the forefathers of EMG who established the nation’s first EMG lab at Mayo Clinic in the 1950s—and also with Jasper R. Daube, MD, Andrew G. Engel, MD, Donald W. Mulder, MD, Peter J. Dyck, MD, and others whose contributions to the understanding of neuromuscular disease continue to inform refinements in the technique, science, and practice of EMG.

EMG at Mayo Clinic: One Lab—Integrating Patient Care Across Disciplines and Sites

Mayo Clinic Rochester

- has one of the largest EMG labs in the world.
- conducts more than 15,000 EMG studies a year.
- conducts monitoring in approximately 500 surgical cases a year.

At Mayo Clinic Rochester, 11 neurologists and 4 physiatrists work in the EMG lab and operating room on a rotational basis. Approximately 25 allied health staff and technicians, many with more than 20 years' experience, work in the lab and on surgical cases. While most institutions have separate EMG labs for neurology and physical medicine, Mayo's lab serves both disciplines in patient care and resident training. Dr Sorenson says, "Mayo has a very collegial environment. Everybody shares and does what they do best.

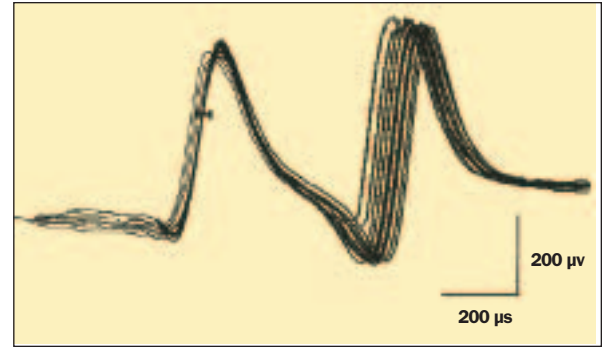


Figure. Two muscle fiber action potentials recorded during single-fiber EMG.

Our EMG lab is an example of that type of integration and collaboration." Dr Harper adds, "In most places, patients get a totally different exam, depending on what 'door' they use to enter the lab. At Mayo, all patients go through 1 door, regardless of the nature of the problem."

EMG techniques, lab organization, and philosophy of practice are consistent across Mayo's 3 sites. The staffs at Mayo Rochester, Arizona, and Jacksonville have a collaborative relationship and gather several times a year to discuss clinical practice, share research, and participate in continuing education.

Pediatric EMG: Combining Expertise and Compassion

The advent of "awake anesthesia" or "conscious sedation" has made EMG in children feasible. It allows compassionate testing under moderate sedation. The patient is awake enough for voluntary movement, but sedated enough to minimize discomfort. Mayo Clinic Rochester conducts these studies in a special suite attached to an operating room with a dedicated nurse anesthetist supervised by a pediatric anesthesiologist. As Dr Harper says, "The art of EMG in children is conducting the test in the shortest time with the least amount of discomfort and working in an integrated way with the anesthesiologists who are experts at titrating sedation in an environment that's really safe. Families of children who have had EMGs elsewhere say the experience at Mayo is just absolutely different."

Brachial Plexus Surgery and EMG

Traumatic and extensive brachial plexus neuropathy can leave an arm useless and be difficult to repair. EMG helps to identify and map out impaired nerves before surgery and to determine if nerve grafts or nerve transfers are needed (ie, if a nerve root is functional). As Dr Sorenson says, "These are delicate surgical procedures, and the more the surgeon knows about what he or she

Table. EMG Referral

Common symptoms that trigger referral

Weakness, numbness, sensory loss, neuropathic pain, or a combination of these findings

Common conditions include

Brachial and lumbar plexopathies

Carpal tunnel and cubital tunnel syndrome

Motor neuron disease

Myopathies (congenital and acquired)

Neuromuscular junction disorders (eg, congenital and acquired myasthenia gravis, Lambert-Eaton myasthenic syndrome)

Nerve terminal disorders

Peripheral neuropathy

Radiculopathies

Common referral sources within Mayo Clinic

Neurology (peripheral nerve, neuromuscular, or general)

Child and Adolescent Neurology

Neurosurgery

Spine Center

Internal Medicine

Orthopedic Medicine (Hand Clinic)

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has to work with before surgery the better.” When the nerves are exposed during surgery, they are directly stimulated with nerve action potentials and EMG. “We also stimulate the motor and sensory cortex, testing the entire motor and sensory pathways,” explains Brian A. Crum, MD, a neurologist who routinely conducts neurophysiologic monitoring during surgery.

Surgical Monitoring

At Mayo, depending on the type of surgical case, other types of neurophysiologic monitoring such as evoked potentials may be used in addition to or instead of EMG to monitor the integrity of the cranial nerves and motor and sensory pathways. In patients with acoustic neuroma, for example, acoustic or auditory nerve and facial nerve function are monitored. Dr Crum states: “The amount of monitoring at Mayo is more extensive than it is in many clinical facilities because our cases are often complex. We participate in several surgical procedures each day. Our goal in all neurophysiologic surgical monitoring is to prevent unnecessary neurologic damage by doing the safest procedure. We are fortunate to have technicians with 20-plus years of experience.”

Whether performing a complicated brachial or lumbar plexus repair, removing a brain, spine, or peripheral nerve tumor, determining the nature

and source of muscle weakness of unknown etiology, checking the accuracy of a diagnosis of myasthenia gravis, or managing a routine carpal tunnel procedure, the success of EMG depends on more than state-of-the-art equipment. Prestudy narrowing of the differential diagnosis based on clinical findings, sensitivity to patient comfort, a steady hand, experienced visual and auditory discrimination skills, and efficient data collection in the lab and during surgery can make EMG a valuable extension of the neuromuscular examination and an important tool in surgical repair.

Patient Referrals

Referrals from within the Mayo Health System can be made directly to the EMG lab in Rochester. Referrals from outside the Mayo system generally go through the individual departments (Table).

Because a direct correlation between the neurologic examination findings and EMG study is so critical, patients may be required to have a repeat EMG, regardless of the how recent their previous EMG may have been. Dr Harper notes, “Referring physicians don’t have to worry about ordering an EMG ahead of time, because once the patient is at Mayo, the EMG, if it is indicated, will be done within 24 to 48 hours.”

Repairing the Nervous System: Remyelination and Multiple Sclerosis

Acute inflammatory demyelination, limited remyelination, progressive axonal loss, and development of multifocal sclerotic plaques—this is the typical sequence of injury to the brain in patients with multiple sclerosis (MS). For patients, this

translates into a difficult-to-predict course of sometimes benign but often debilitating inflammatory attacks that are commonly followed by degenerative decline. For physicians, it represents one of the most common reasons for neurologic referral, a major cause of disability in their young adult patients, and a heterogeneous and

enigmatic neurologic disease.

MS occurs when a confluence of poorly characterized genetic and environmental factors initiates an immune-mediated response directed at brain components. T cells break through the blood-brain barrier, mistakenly identify healthy myelin-producing cells or their myelin products as foreign, and attack and destroy them.

Symptomatic treatments are often successful, but no treatment can stop the progression of the disease. As Claudia F. Lucchinetti, MD, a neurologist and MS researcher at Mayo Clinic Rochester, puts it, “We’re still at a point where many patients worsen, despite therapies that impact the inflammatory aspect of the disease. So the focus of MS research is understanding why this occurs and what can be done about it.”



Claudia F. Lucchinetti, MD, Moses Rodriguez, MD, and Brian G. Weinshenker, MD

Downregulating the Immune System—Positive or Negative?

Paradoxically, the inflammatory immune response that produces demyelination also induces remyelination, a natural repair process of demyelinated tissue. Natural remyelination is spotty, patchy, and limited in the central nervous system (CNS). Yet suppressing inflammation may prevent it altogether.

Twenty years ago, when the idea that the CNS could repair itself was unheard of, Moses Rodriguez, MD, a Mayo Clinic neurologist and researcher, was trying to prove that stimulating the immune system would aggravate an MS-like illness in animals. In fact, the animals' condition improved and they showed evidence of remyelination, indicating CNS repair not only was possible, but also was enhanced by increased inflammation directed against the CNS. Converging lines of evidence, including brain biopsy and autopsy tissue analysis, confirmed that remyelination, as well as demyelination, occurs in humans with MS.

Today, uncovering the mechanisms of successful and unsuccessful remyelination in MS is considered a critical step in preventing disease progression. Myelin sheath destruction results in acute, usually transient and reversible inflammatory attacks that interfere with axonal conduction of neuronal impulses. But failure to remyelinate eventually leads to axonal death and the chronic, irreversible motor, sensory, and cognitive deficits of late-stage MS. It is this chain of events—from acute attack to downstream destruction—that Mayo researchers want to prevent.

Two Phases of MS, Two Patterns of Tissue Injury

The Inflammatory Acute Phase

The early phase of MS is characterized by intense inflammation, focal demyelination, and limited remyelination during acute attacks of neurologic dysfunction. It occurs in the context of T-cell invasion across the blood-brain barrier. Axons may or may not recover during this phase. Symptoms are treated with varying degrees of success by immunosuppressive, anti-inflammatory, or immunomodulatory drugs, alone or in combination. Plasma exchange, first studied in a controlled trial at Mayo Clinic as a possible “rescue therapy” for catastrophic refractory episodes, is effective in some forms of MS.

The Chronic Progressive Phase

There is no treatment for the chronic progressive phase. Not only myelin, but also neurons are injured in the cerebral and cerebellar cortices. Global tissue destruction in chronic MS occurs in

the context of a relatively intact blood-brain barrier. Because the process is compartmentalized in this way, it is likely less accessible to the effects of anti-inflammatory or immunomodulatory treatments.

The smoldering inflammation, demyelination, and axonal injury of this phase probably begin during earlier inflammatory attacks. The process affects demyelinated plaques as well as normal-appearing white matter. Wallerian degeneration and loss of trophic support from growth factors associated with healthy oligodendrocyte cells are likely involved. Researchers believe that perturbed interactions between axons and myelin sheaths interferes not only with conduction and remyelination, but also with axonal outgrowth and connectivity. Eventually demyelination disturbs the delicate balance and complex physiology of the entire CNS.

Brian G. Weinschenker, MD, a neurologist and MS researcher at Mayo Clinic Rochester, reports that patients often see the change from the acute to the chronic phase as an abrupt switch. However, even in early MS, MR spectroscopy shows reduction of axonal density. The brain has considerable reserves, but at some point, axonal death reaches a tipping point, and patients begin to experience progressive loss of neurologic function.

The question is, can it be prevented and, if so, how? The answer may lie in therapeutic remyelination.

Remyelination: Keeping Axons Alive

Remyelination keeps axons alive, but natural remyelination is limited. Could the process be stimulated therapeutically? Even without reestablishing conduction, keeping axons alive might limit or prevent the diffuse damage and lasting disability of chronic MS.

Therapeutic remyelination has become a beacon of hope, and the team of MS neuroscientists and neurologists at Mayo Clinic are in the forefront of research to make it a reality.

Patterns of Natural Remyelination

Are some people better at remyelination than others? It turns out they are. The MS Lesion Project, funded by the National Multiple Sclerosis Society and led by Dr Lucchinetti and a diverse international group of collaborating scientists, identified more than 700 people with MS who underwent brain biopsies. From these data, they discovered not only evidence of remyelination, but 4 distinct MS subtypes. Two show evidence of good natural remyelination. Two do not. In a separate study funded by the National Institutes of Health, Dr Lucchinetti and colleagues are investigating whether genetic predisposition contributes to suc-

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successful natural remyelination.

Antibody 22, a Key to Remyelination

Early thinking about therapeutic remyelination focused on transplanting cells such as oligodendrocyte progenitor cells and on administering neurotrophic growth factors. However, there are numerous unresolved issues in cell transplantation, and growth factor strategies have had serious adverse effects and disappointing results.

Dr Rodriguez, Larry R. Pease, PhD, and colleagues were on another track—the search for natural human monoclonal antibodies that would promote repair. Some of these antibodies are involved in the demyelination; some in remyelination. As Dr Rodriguez says, “Each MS lesion is its own little world composed of destructive and protective factors. We tried to enhance the reparative factors.”

In 2001, as Dr Lucchinetti’s team was uncovering MS subtypes, Dr Rodriguez and his colleagues discovered the natural monoclonal autoantibody they were after. Unlike the antibodies made by industry to fight cancer, it is an immunoglobulin of the M type (an IgM). They labeled it “number 22.” Then, using DNA from the patient in whom they discovered it, they sequenced and reproduced it in recombinant form.

Number 22 differs from other antibodies. First, it is an IgM, the largest type of antibody with 5, rather than 2 binding sites (Figure 1). Second, it occurs naturally in many individuals and species and is very primitive in evolutionary terms. It is the body’s first and most rapid line of defense, often referred to as the “innate immune response.” Because it is natural, it carries few if any adverse effects, unlike industry-synthesized IgGs. Dr Rodriguez and his team found that it promoted remyelination in approximately 50% of lesions in mice with a virus that mimics MS and was effective in more than 85% of animals tested (Figure 2). They immediately set about producing enough to take to human trials. Now, in conjunction with a Good Manufacturing Practices facility at the University of Minnesota, they have made enough to be steps away from a US Food and Drug Administration–approved phase 1 clinical trial to test the safety of this antibody in humans.

The Next Steps: Taking Remyelination to Clinical Trial

The Right Patients at the Right Time

The next steps are equally critical. As Dr Weinshenker says, “To be successful, we need a great tool, and we need the right patients at the right time. The challenge is to find them.” The right time is early in the disease when it is amenable to

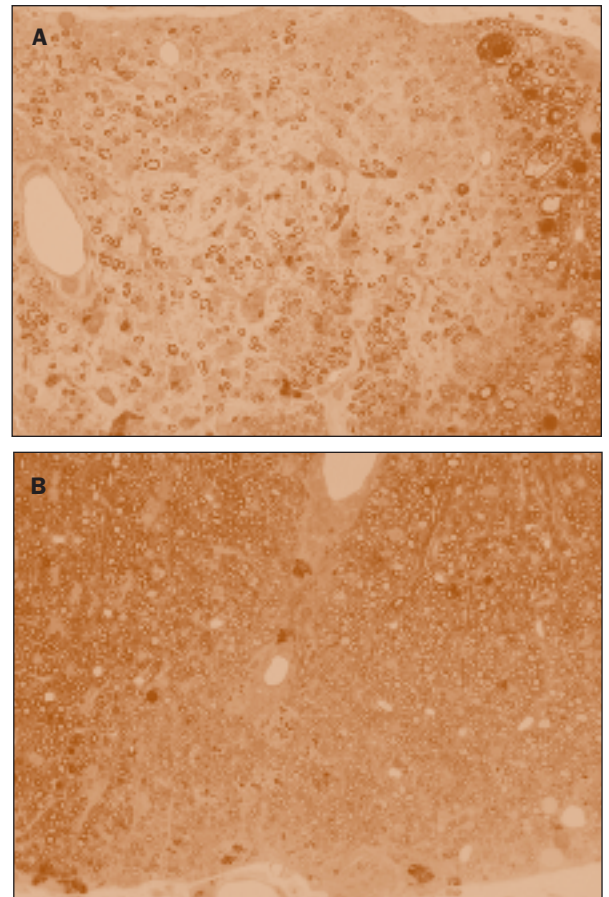


Figure 2. Photomicrograph of mouse spinal cord demonstrating limited repair in an untreated animal with demyelinating disease (A) and marked remyelination in an animal treated with a single 100-µg dose of the remyelination-promoting human IgM rHIgM22 (B).

treatment. The right patients would seem to be patients who are “good natural remyelimators” who fall into the 2 MS subgroups in which oligodendrocytes and/or progenitor cells are available to respond to IgM number 22. It is important to identify patients with the potential to repair using noninvasive tools. In the past year, the MS Lesion Project has found a strong correlation between evidence of remyelination on biopsy and a pattern of “ring enhancement” in MS lesions that shows up on MRI scans. This finding could greatly enlarge the pool of candidates for clinical trials.

Measuring Outcomes

- Is there a critical period for remyelination?
- Are factors affecting endogenous remyelination the same in the acute and chronic phases of the disease?
- How much myelin is needed for success?
- How many axons need to be repaired to prevent diffuse tissue damage?
- Can axon outgrowth be promoted through remyelination?



Figure 1. A schematic of an IgM. An IgG would consist of just one of the subunits.

