NEEDS ASSESSMENT OVERVIEW

Multiple sclerosis (MS) affects an estimated 4.5 million people worldwide of whom more than 400,000 reside in the United States. Approximately 200 newly diagnosed American patients a week are faced with the prospect of losing physical, cognitive, and psychological abilities due to multiple sclerosis (1).

In the past, the decisions for diagnosis and treatment multiple sclerosis, were primarily based on a neurologist's experience rather than on evidence, but now consensus recommendations are being developed owing to the accumulation of evidence-based clinical data. Continuing medical education is required for neurologists to establish a better baseline that considers all of the latest available treatment options with respect benefit to safety risks and individualized comorbidity concerns.

Multiple sclerosis medicine has been an expanding clinical field of exceptionally limited guidelines. The last American Academy of Neurology (AAN) guidelines for the treatment of MS were issued 15 years ago and they only included β-interferon and glatiramer acetate (2). The treatment landscape has flourished considerably over the past fifteen years, with more than 16 medications now currently approved and these are widely prescribed for the treatment of MS in the United States, and other agents nearing approval. MS treatment options have become increasingly complicated as the available disease modifying therapies (DMTs) have increased. Fortunately a draft of guidelines for treating MS has been released by independently by both the American Academy of Neurology and the largest european collaboration ever, including the European Academy of Neurology (3, 4).

A study by the American Academy of Neurology reveals that by 2025 there will be a 19% increase in demand for neurologists with wait times for an appointment at 45 business days (5). Neurologists are increasingly burdened with greater numbers of multiple sclerosis patients. It is more important than ever that they are comprehensively educated and efficient to the highest of standards (6).

Given the recent new clinical therapeutics entering the market, and recent changes in disease treatment perception, neurologists need to be educated as to how to more accurately treat MS patients. By learning the latest AAN and European Academy of Neurology (EAN) guidelines for diagnosis and DMT treatment, neurologists will be able to more effectively reduce relapses and the adverse events associated with disease modifying therapy.

EDUCATIONAL AND CLINICAL GAP ANALYSIS

GAP #1: Neurologists may not be aware of the latest guidelines from the American Academy of Neurology and the European Academy of Neurology for treating multiple sclerosis.

The goal of the neurologist treating multiple sclerosis is to delay relapses, reduce fatigue, improve the quality of life, and ideally halt disease progression. It is essential that

neurologists are made aware of the latest discoveries identifying MS co-morbidities since co-morbid disease conditions can dramatically affect MS outcome. New AAN and EAN guidelines both independently stress the importance of considering co-morbidities before selecting disease modifying therapies. Medical education is needed to ensure proper disease modification therapy selection and administration. The American Academy of Neurology has issued 31 statements describing their consensus recommendations for starting, switching, and/or stopping DMTs.

Neurologists must be made aware of the new consensus treatment-specific treatment recommendations for both American and European 2017 guidelines. ***Mitoxantrone is no longer recommended at all for MS because of safety issues.*** Alemtuzumab, fingolimod, or natalizumab is recommended for patients with very active MS, while azathioprine, cladribine, minocycline, or leflunomide should be used for relapsing MS patientsa who do not have access to approved DMTs. ***Natalizumab should not be used in patients positive for JC virus antibodies.*** Clinicians must be trained to follow up either annually or according to medication−specific risk evaluation and mitigation strategies.

Neurologists should be aware of the reasons for not initiating DMT therapy in particular as related reproduction and vaccinations. Women should stop their DMT prior to conception and not start DMTs during pregnancy, while men must be counselled men with MS on their reproductive plans regarding treatment implications before initiating teriflunomide or cyclophosphamide. The National Multiple Sclerosis Society does not recommend use of live vaccinations in people with MS for teriflunomide, fingolimod, daclizumab beta, or alemtuzumab (7). Moreover, the MS Society advises against using live attenuated vaccines for prespecifed time periods after stopping therapy.

Clinicians should be made aware that it is important to discuss a change to a non−injectable in patients who report pain or “injection fatigue” on injectable DMTs. Better compliance has been observed for oral DMTs fingolimod, teriflunomide, and dimethyl fumarate.

Neurologists should know that discontinuation of DMT is recommended for patients who do not have ongoing relapses and have not been ambulatory (EDSS ≥7) for at least 2 years. Clinicians should know how to assess the likelihood of future relapse based on patient age, relapse history, and gadolinium enhancing lesion.

Many multiple sclerosis cases do not have strong scientific evidence for treatment. Combined with the dearth of guidelines up until now for treating neurologic conditions this has even led to development of new anonymous interactive surveys that neurologists can use using to read how their colleagues around the world handle individualised patients (8). This has been a valuable resource for rare neurological conditions anti-NMDA syndrome, where the best treatments have come from observational studies, not clinical studies. Neurologists should be made aware of this new approach to connecting with their community. This is expected to be

useful for multiple sclerosis going forwards given how poorly understood and widely divergent cases of multiple sclerosis.

GAP #2: Neurologists may not be aware of the mechanisms of action and respective safety efficacy for all currently available FDA-approved DMTs.

There are currently 15 FDA-approved DMTs to consider (7, 9). All of these are for use in relapsing forms of MS. Only one approved specifically for primary progressive and another is approved for secondary progressive MS. Neurologists should be aware of all administration-route categorical DMTs. There are 8 injectables, 3 oral, and 4 infusion administered FDA-approved options currently to consider (7). Oral DMTs such as teriflunomide, dimethyl fumarate, and fingolimod are exceptionally convenient, while injectables peginterferon beta, daclizumab beta, ocrelizumab, and alemtuzumab are dosed once every 2 weeks, monthly, every 6 months, and annually, respectively.

Neurologists must consider the mechanism of action and pharmacodynamics of immune system effects because these can impact the efficacy and safety of the next agent. Accordingly neurologists should be aware that current FDA-approved DMTs MS can be grouped those exerting immunological effects on a day-to-week (interferon beta-1a and 1b, peginterferon beta-1a, glatiramer acetate, dimethyl fumarate, teriflunomide), week-to-month (fingolimod, natalizumab, and daclizumab beta), or month-to-year timescale (teriflunomide if the rapid elimination procedure is not implemented, alemtuzumab, and ocrelizumab) (9). Moreover neurologists should understand which therapies work via reversible mechanisms of action as these facilitate switching to others within short time frame of discontinuation if safety considerations allow, while other DMTs with longer-term effects can limit the scope of subsequent pharmacotherapy.

Side effects occur in at least 2-5 percent of participants based on clinical trials (7). Less is known about long-term outcomes with newer FDA-approved DMTs like daclizumab. Accordingly, the recently approved DMT daclizumab is only available through a Risk Evaluation and Mitigation Strategy program. ***Prescribing neurologists and nurse practitioners must be enrolled and trained.*** Neurologists must be aware that liver function testing is recommended prior to starting treatment and daclizumab should be discontinued in cases of significant transaminase elevation since daclizumab can cause severe liver injury.

Neurologists should also be made aware of the Multiple Sclerosis Emerging Therapies Collaborative, which was launched in 2011 (10) with the goal of disseminating evidence-based information MS-specific US FDA-approved treatments towards achieving optimal individualized disease treatment and medical decision-making. Pamphlets for each respective DMT are regularly updated, include a wide variety FAQs, and are available on the website.

GAP #3: Neurologists may not be aware of patient priorities to foster shared decision making with transparent disease monitoring.

Multiple Sclerosis is a chronic and disabling disease which profoundly affects the quality of life of the person from the moment of diagnosis until the end of their life. The goal of the neurologist treating a MS patient is to improve adherence to long-term therapy and the perceived benefits of treatment. Towards this end a particular focus should be devoted to cultivating the physician–patient relationship (11).

Survey analysis suggests that neurologists may be able to use psychological and interpersonal dimensions to target and improve health care outcomes. By becoming more responsive to patients' needs and preferences and physicians may deliver better quality care because ultimately a patients' involvement in the improvement of health care can lead to the best long-term treatment outcomes.

New survey-based research indicate that patient-neurologist communication and particularly patient input into the treatment decision-making process is likely influence patient satisfaction with treatment (12). Shared treatment decision encourages treatment adherence and improves patient satisfaction. Neurologists should be made aware of effective shared decision-making communication techniques to designed to achieve optimal clinical outcomes.

Closing gaps in the physician's understanding of life of the multiple sclerosis patient may improve communication and outcomes. ***Online surveys by The Race to Erase MS reveal differences in understanding of patients as compared to neurologists with respect to disease etiology and ways to better manage the effects of living with disease*** **(13)**. Neurologists should improve their recognition of patients' priorities and patient education.

Neurologists should be made aware of which topics should be thoroughly discussed with multiple sclerosis patients towards achieving shared-decision making. Particularly, clinicians must be made aware to counsel patients on the importance of commitment to adherence to DMTs (3, 4). The safety, route of administration, lifestyle, cost, efficacy, common side effects, and tolerability in the choice of DMT must all be transparently communicated to the patient. Ongoing dialogue and monitoring with patients with MS is required for optimal treatment outcomes.

GAP #4: Neurologists may not be aware of recent updates in the guidelines for diagnosing multiple sclerosis and the particularly utility of central vein sign.

Three consensus guidelines for MRI-based imaging for multiple sclerosis have been released within the past year (14-16). The success and effective therapeutic treatment of any medical condition is dependent upon proper differential diagnosis. Training and experience is needed in order for qualified professionals to perform accurate multiple sclerosis diagnosis. Neurologists most routinely see referred patients with T2 lesions on recent head or spinal

magnetic resonance imaging scans. This is frequently diagnosed at multiple sclerosis since MS is the most common CNS demyelination disorder. However, patient questioning and proper MRI analysis can reveal a diagnosis for many other similar neurodegenerative diseases.

Neurologists should be aware of the consensus statement developed by the NAIMS cooperative to evaluate the central vein sign as a signature for diagnosis of MS **(15).** Standardization of MRI protocols and lesion selection criteria are used to assess central veins. Neurologists should realize that a brain gadolinium-based MRI is recommended for the diagnosis of MS, while a spinal cord MRI is recommended if the brain MRI is nondiagnostic or if the patient is presenting with symptoms are characteristic of the spinal cord lesions (16).

PROPOSED AGENDA

I. Review of consensus guidelines for starting, switching, and stopping DMTs.

II. Cover the mechanisms of actions for DMTs and how this impacts on individualized treatment decisions.

III. Advise neurologists of the differences in provider versus patient perceptions and needs with the goal of cultivating optimal shared decision making with regular monitoring and compliance.

IV. Review of guidelines for differential diagnosis and consensus advancements in MRI-based multiple sclerosis diagnosis.

EDUCATIONAL LEARNING OBJECTIVES AND PROGRAMMATIC LINKAGE TO GAPS

Learning Objective 1

Current Practice	**Neurologists may not be aware of the latest guidelines from the American Academy of Neurology and the European Academy of Neurology for treating multiple sclerosis.**
What Should Happen	**Neurologists should be educated about current and emerging therapy options for multiple sclerosis so they can explain treatment options and potential side effects to patients.**
Learning Objective	**Evaluate the recent guidelines for the use of the wide variety of DMTs with particular attention to concerns for adverse events.**

Learning Objective 2

Current Practice	**Neurologists may not be aware of the mechanisms of action for the latest FDA approved DMTs.**
What Should Happen	**Neurologists should be educated how DMTs work so they can have a better understanding of which DMTs are likely to be better suited for individual patients.**
Learning Objective	**List the mechanisms of action for respective FDA-approved DMTs.**

Learning Objective 3

Current Practice	**Neurologists may not be aware of patient priorities to foster shared decision making with transparent disease monitoring.**
What Should Happen	**Neurologists should be educated about gaps in physician-patient perceptions and concerns of disease progression versus DMT risk.**
Learning Objective	**Counsel patients about the risk versus benefits of DMTs and listen to patients with respect to their disease progression concerns and lifestyle.**

Learning Objective 4

Current Practice	**Neurologists may not be aware of recent updates in the guidelines for diagnosing multiple sclerosi.**
What Should Happen	**Neurologists should be educated about the latest advances in the diagnosis of multiple sclerosis, particularly utility of central vein sign.**
Learning Objective	**Evaluate the guidelines used for the differential diagnosis of multiple sclerosis.**

CONCLUDING STATEMENT

MS is an extremely variable illness. The course of disease progression is nearly impossible to predict on an individual patient. Understanding and communicating the factors influencing MS patient care by a trained neurologists and developing policies for convenient and appropriate access to care is critical to optimizing outcomes among this population. The expertise of a neurologists properly trained in shared decision-making is essential to the successful of administration of DMTs.

This educational program will increase physician awareness of multiple sclerosis patient shared decision-making, diagnosis, and treatment. Physicians will learn new AAN, EAN, and NAIMS recommended guidelines describing the diagnosis and treatment of MS. Physicians will become more aware of recommendations as well as DDX that have the potential to improve the likelihood of properly treating the cause of disease. Physicians will become aware of emerging therapies for the treatment of MS and most important adverse drug response concerns.

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