Section A: Pharmacology, Toxicology, and Biochemistry.

Review Article

Advances in Understanding and Treating Multiple Sclerosis: A Comprehensive Review

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Abstract

Introduction: Multiple sclerosis (MS) is an autoimmune disease resulting in neurodegeneration accompanied by chronic inflammatory response, apoptosis, and neuronal loss. It is characterized by number of signs including paresthesia, spastic paralysis, cognitive impairment, and functional deficits. More than 2 million people worldwide suffering from the disease. The generation and development of MS are heterogeneous and manifold.

Aim and concept of review: The aim of this review is to provide detailed information about the pathophysiology, different treatments, and protective agents as well as animal models used for studying MS in pharmacological experiments. Furthermore, the review sheds light on the molecular mechanisms involved in the pathogenesis of the disease including infiltration of immune cells and expression of inflammatory and oxidative biomarkers that represent a significant indication of the disease.

Conclusion: The review concluded with the potential therapeutic and neuroprotective approaches of management of MS. It provides future perspective concerning with controlling the incidence of MS.

1. Introduction

Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system (CNS). It affects the myelin sheath, a fatty substance that surrounds and protects nerve Fibers, and the nerve Fibers themselves. Damage to the myelin sheath disrupts the transmission of nerve impulses, resulting in a variety of neurological symptoms [1].

2. Prevalence and Epidemiology

MS is estimated to affect approximately 2.8 million people worldwide, with a prevalence of about 1 in 700 people in the Northern Hemisphere and 1 in 2,000 in the Southern Hemisphere [1]. The prevalence varies significantly by geographic region, with the highest rates observed in

Northern Europe, North America, and Australasia. Notably, the prevalence is significantly lower in Africa and Asia.

In Egypt, the prevalence of MS is estimated to be around 17 per 100,000 people. This is lower than the global average, but the exact number of people affected is

unknown due to underdiagnosis and limited data collection [2].

2.1. Global Disparities

Access to diagnosis and treatment, healthcare resources, and awareness of MS vary considerably across different regions. This leads to disparities in disease outcomes and quality of life for individuals living with MS [3].

2.1.1. Challenges in LMICs

Low- and middle-income countries (LMICs) often face significant challenges in managing MS due to:

- **Limited access to diagnosis and treatment:** Specialized healthcare facilities, diagnostic tools like MRI scans, and advanced treatment options are often unavailable or unaffordable in LMICs [4].

- **Financial burden:** The high cost of MS medications and supportive care can be a substantial barrier to accessing treatment in resource-limited settings [5].

- **Lack of awareness and education:** Stigma and misinformation surrounding MS can hinder early diagnosis and access to proper care [6].

- **Inadequate healthcare infrastructure:** LMICs often lack trained healthcare professionals and specialized MS clinics, leading to inadequate care and support [7].

2.2. Opportunities for Global Improvement

Despite the challenges, there are opportunities to improve global MS care:

- **International collaboration and knowledge sharing:** Collaboration between researchers, healthcare professionals, and patient advocacy groups can facilitate knowledge transfer, improve diagnostic and treatment standards, and promote research progress [8].

- **Development of affordable and accessible treatments:** Research efforts are focused on developing less expensive and more readily available treatment options, including generic medications and alternative therapy approaches [9].

- **Telehealth and digital health interventions:** Utilizing digital technologies for remote consultation, patient monitoring, and education can improve access to care, even in resource-limited settings [10].

- **Capacity building and healthcare worker training:** Investing in training programs for healthcare professionals in LMICs can enhance their skills in diagnosing and managing MS [11].

- **Raising awareness and reducing stigma:** Public awareness campaigns and educational programs are crucial for combating stigma, encouraging early diagnosis, and promoting access to care [12].

3. Pathophysiology

The exact cause of MS remains unknown, but it is believed to be a combination of genetic and environmental factors [13].

3.1. Genetic Susceptibility

Genetic factors play a role in MS susceptibility, with several genes identified as having increased risk [14]. However, the exact contribution of each gene is complex and likely interacts with environmental factors.

3.2. Environmental Triggers

Several environmental factors have been linked to MS development, including:

- **Viral infections:** Some viruses, such as Epstein-Barr virus, may trigger an autoimmune response that contributes to MS [15].

- **Vitamin D deficiency:** Vitamin D is essential for immune function, and low levels are associated with an increased risk of MS [16].

- **Smoking:** Smoking is a significant risk factor for MS, potentially due to its inflammatory effects [17].

- **Gut microbiome:** Recent research suggests that the gut microbiome may play a role in MS development and progression [18].

4. Clinical Features

The clinical presentation of MS is highly variable, with symptoms depending on the location and extent of demyelination. Some common symptoms include

- **Motor weakness:** This can affect any part of the body and may cause difficulty with walking, coordination, and balance.

- **Sensory disturbances:** This can include numbness, tingling, pain, and burning sensations.

- **Visual problems:** This can include blurred vision, double vision, and optic neuritis.

- **Fatigue:** This is a common symptom and can significantly impact daily activities.

- **Cognitive difficulties:** This can include problems with memory, concentration, and information processing.

- **Bladder and bowel problems:** This can include urinary urgency, frequency, incontinence, and constipation [19, 20].

5. Types of MS

There are four main types of MS:

5.1. Relapsing-Remitting MS (RRMS): This is the most common type of MS, affecting about 85% of people with the disease. RRMS is characterized by episodes of worsening symptoms (relapses) followed by periods of improvement or remission.

5.2. Secondary Progressive MS (SPMS): This type of MS develops in some people with RRMS over time. In SPMS, neurological function worsens steadily over time, with or without relapses or plateaus.

5.3. Primary Progressive MS (PPMS): This type of MS is characterized by a gradual worsening of neurological function from the onset of the disease, without relapses or remissions.

5.4. Progressive-Relapsing MS (PRMS): This is a less common type of MS characterized by a gradual worsening of neurological function from the onset, with superimposed relapses and remissions [21].

6. Diagnosis

Diagnosing MS requires a comprehensive evaluation, including a detailed medical history, neurological examination, and diagnostic tests.

6.1. Medical History and Neurological Examination

A thorough medical history helps assessment potential risk factors and identify symptoms suggestive of MS. The neurological examination evaluates various functions like motor skills, coordination, reflexes, and sensation to identify neurological abnormalities.

6.2. Diagnostic Tests

Several diagnostic tests are used, including:

- **Magnetic resonance imaging (MRI):** MRI scans can reveal characteristic lesions in the brain and spinal cord, providing strong evidence for MS.

- **Evoked potentials:** These tests measure the electrical activity of the nervous system in response to specific stimuli, helping to assess nerve conduction pathways.

- **Cerebrospinal fluid (CSF) analysis:** This test examines the CSF for specific markers of inflammation, although its role in diagnosis is becoming less prominent.

7. Treatment

While there is no cure for MS, various treatments can help manage the disease and improve symptoms. These treatments can be broadly categorized into:

7.1. Disease-modifying therapies (DMTs):

DMTs aim to slow down the progression of the disease and prevent relapses. They work by suppressing the immune system and reducing inflammation in the CNS. Examples include [22,28]:

- **Interferons:** Interferon beta-1a and interferon beta-1b are commonly used first-line DMTs. Interferon-β stimulates the generation of anti-inflammatory cytokines while decreasing proinflammatory ones, thus limiting the movement of inflammatory cells in the central nervous system. This anti-inflammatory effect results in a decrease in new MRI lesions and relapse rates. Experimental evidence indicates potential nerve growth factor production, suggesting reparative processes. Despite its benefits, common adverse effects of interferon-β include postinjection flu-like syndrome, skin reactions, mild leukopenia, and reversible thyroid and liver dysfunction.

- **Glatiramer acetate:** a synthetic amino acid polymer mimicking myelin basic protein. This medication acts by mimicking myelin and altering the immune response. This action reduces active MRI lesions and relapse rates. Additionally, MRI studies indicate its impact on measures like brain volume loss and black hole formation, hinting at a potential role in promoting remyelination.

- **Natalizumab:** This monoclonal antibody targets inflammatory cells and prevents them from entering the CNS, as it interacts with α4 integrin receptors on lymphocytes, impeding their adherence to the blood–brain barrier and entry into the CNS. This action results in a decrease in contrast-enhancing and new MRI lesions, relapse rates, and cumulative progression probability. Furthermore, it diminishes the proportion of new MRI lesions evolving into persistent black holes, indicating a potential inhibition of axonal damage mechanisms.

- **Fingolimod:** This medication works by trapping lymphocytes in lymph nodes, preventing them from reaching the CNS. It operates by internalizing sphingosine-1 receptors on lymphocytes, impeding T-cell migration from secondary lymphoid organs to circulating blood. In a placebo-controlled trial, patients receiving fingolimod exhibited diminished MRI activity and relapse rates. Furthermore, a pivotal trial reported reduced brain volume loss in patients on the drug compared to those on placebo, suggesting potential dual effects of fingolimod—anti-inflammatory and neuroprotective [29].

- **Dimethyl fumarate and teriflunomide:** These medications modulate the immune system by activating a specific pathway.

- **Traditional immunosuppressants:** Cyclophosphamide and azathioprine, explored for their immunosuppressive potential in MS, act by different mechanisms—cyclophosphamide as a DNA alkylating agent and azathioprine as a purine antagonist affecting DNA replication. MRI studies support their efficacy in reducing inflammatory activity within the CNS. However, their safety profiles include notable adverse effects.

Cyclophosphamide therapy is associated with leukopenia, heightened infection risk, nausea, and alopecia. Azathioprine therapy carries a potential long-term risk of malignancy linked to treatment duration and cumulative dose.

7.2. Symptomatic therapies:

These medications aim to manage specific symptoms of the disease and improve quality of life. They include [23]:

- **Corticosteroids:** These medications reduce inflammation and can be used to treat relapses using this mechanism:

inhibiting lymphocyte activation and decreasing the production of proinflammatory cytokines. This, in turn, diminishes the migration of immune cells into the CNS, reducing brain MRI activity, specifically the number of contrast-enhancing lesions.

However, their application is restricted due to established contraindications and adverse effects, such as diabetes, hypertension, and osteoporosis.

- **Muscle relaxants:** These medications help manage spasticity and muscle stiffness.

- **Pain medications:** These medications are used to manage pain, including neuropathic pain.

- **Fatigue management:** Lifestyle modifications and medications can help manage fatigue.

- **Cognitive rehabilitation:** This therapy helps improve cognitive function and memory.

- **Bladder and bowel management:** Medications, dietary changes, and pelvic floor exercises can help manage bladder and bowel problems.

8.Studies [27]

8.1 Animal models:

Animal models have played a crucial role in understanding the pathogenesis of MS and developing new therapies. Some common animal models used in MS research include:

- **Experimental autoimmune encephalomyelitis (EAE):** This is an autoimmune disease induced in animals that shares many similarities to MS, EAE is the most widely used animal model for studying MS. Researchers induce an autoimmune response in animals (such as mice or rats) by injecting them with myelin proteins or peptides, which leads to the development of MS-like symptoms. EAE has helped elucidate the underlying mechanisms of MS, test potential therapies, and evaluate the efficacy of immunomodulatory drugs.

- **Transgenic and Knockout Mouse Models:** These models involve genetically modifying mice to express specific genes associated with MS or to lack certain genes related to immune function. By studying these mice, researchers can investigate the role of specific genes, proteins, or immune cells in MS development and progression.

- **EAE Subtypes:** EAE can be induced in animals using different methods and with various myelin antigens. These variations result in different subtypes of EAE that mimic different aspects of MS pathology. For example, some EAE models primarily exhibit inflammatory demyelination, while others emphasize axonal damage or progressive disease. These subtypes help researchers investigate specific aspects of MS and test targeted therapies.

- **Genetically Engineered Animal Models**: Besides transgenic and knockout mouse models, other genetically engineered animal models have been developed to study MS. For instance, mice expressing a humanized form of the immune system, known as humanized mice, allow researchers to investigate human-specific immune responses in an MS-like context.

- **Non-human Primate Models:** Non-human primates, such as monkeys, can also be used as models for MS. These models offer advantages due to their genetic similarity to humans and the similarities in their immune systems and nervous systems. Non-human primate models provide a closer approximation to human MS pathology and can be valuable for testing therapeutic interventions.

- **Cuprizone model:** This model uses the copper chelator cuprizone to induce demyelination in the brains of rodents.

8.2 In-Vitro Studies:

8.2.1 Cell Culture Models:

- Primary human oligodendrocyte cultures: These cultures are used to study the biology of oligodendrocytes, the cells responsible for producing myelin. Researchers can investigate how different factors, such as disease-associated mutations or potential therapies, affect the growth, survival, and function of these vital cells.

- Microglia cultures: Microglia are immune cells that play a complex role in both inflammation and repair in the CNS. Studying them in vitro allows researchers to dissect their specific functions and understand their contributions to MS pathogenesis. These studies can inform the development of therapies targeting microglia activity to modulate their inflammatory response and promote neuroprotection.

- T-cell cultures: T-cells are the main immune cells involved in MS. In-vitro studies using T-cell cultures can help identify the specific T-cell subsets involved in the disease and understand

their activation mechanisms. This knowledge helps researchers develop targeted immunotherapies that suppress the pathogenic T-cell response while preserving beneficial immune functions.

8.2.3 Co-culture Models:

Co-culture models involve growing different types of cells together to study their interactions in a more physiologically relevant context. This allows researchers to investigate how different cell types, such as oligodendrocytes, microglia, and neurons, communicate and influence each other's behavior in the context of MS. For example, co-culturing oligodendrocytes and microglia can help understand how microglia can both promote myelin damage and support myelin repair under different conditions.

8.2.4 High-throughput Screening (HTS):

HTS is a powerful technique used to rapidly test a large number of compounds simultaneously to identify potential new drugs for MS. These compounds can be tested on in-vitro models to assess their ability to:

- Suppress inflammation and T-cell activation.

- Promote myelin repair and remyelination.

- Protect neurons from damage.

- Improve cognitive function.

HTS can accelerate the drug discovery process by quickly identifying promising leads for further development.

8.2.5 Organoids:

Organoids are three-dimensional structures cultured in the lab that resemble specific organs, including the brain. Brain organoids have been developed to study MS and offer several advantages over traditional cell culture models. They provide a more complex and realistic environment that better mimics the human CNS, allowing researchers to study how different cell types and signaling pathways interact in disease development. Additionally, organoids can be used to test potential therapies in a more controlled and efficient manner compared to animal models.

8.2.6 Myelin-oligodendrocyte Culture Models

Oligodendrocytes are responsible for producing myelin, the protective covering of nerve fibers that is damaged in MS. In vitro models using oligodendrocyte cultures derived from animal or human cells allow researchers to study the processes involved in myelin production, maintenance, and repair. These models aid in understanding the mechanisms of demyelination and remyelination in MS and provide a platform for testing potential remyelination therapies.

8.2.7 Blood-Brain Barrier (BBB) Models

The BBB plays a critical role in regulating the passage of substances between the bloodstream and CNS. In vitro BBB models, which consist of brain endothelial cells cultured on permeable membranes, are used to investigate how the BBB is disrupted in MS and how immune cells infiltrate the central nervous system. These models also help evaluate the effectiveness of drugs in crossing the BBB and reaching their targets.

Benefits of In-vitro Studies:

- Reduced complexity: In-vitro studies allow researchers to focus on specific cells and pathways involved in MS, making it easier to understand the disease mechanisms.

- Cost-effective: In-vitro models are relatively inexpensive and can be used to screen a large number of potential therapies quickly.

- High-throughput: Techniques like HTS allow researchers to test multiple compounds simultaneously, accelerating the discovery of new treatments.

- Ethical considerations: In-vitro studies avoid the use of animals, raising fewer ethical concerns.

Limitations of In-vitro Studies:

- Artificial environment: In-vitro models cannot fully replicate the complex environment of the human body, potentially leading to misleading results.

- Limited cell types: Most in-vitro studies use a limited number of cell types, which may not fully represent the diversity of cells involved in MS.

- Lack of interactions: In-vitro studies often lack the complex interactions between different cells and tissues that occur in the body.

Future Directions:

In-vitro studies will continue to play a crucial role in advancing MS research. Future research will focus on developing:

- More sophisticated models: These models will better mimic the human CNS by incorporating additional cell types and interactions, including vascular and glial cells.

- Advanced technologies: Techniques like organoids and gene editing will provide further insights into MS pathogenesis and identify novel therapeutic targets.

- Personalized medicine: In-vitro models derived from individual patients can be used to develop personalized treatments tailored to their specific genetic and disease profile.

9. Prognosis

The prognosis for individuals with MS varies depending on the type and severity of the disease. However, with early diagnosis and effective treatment, many individuals with MS can lead fulfilling and productive lives.

10. Research and Future Directions

Significant research is ongoing to understand the complex mechanisms underlying MS and develop more effective treatments. Some promising areas of research include [24]:

- **Neuroprotective therapies:** These therapies aim to protect and repair damaged nerve cells.

- **Immunomodulatory therapies:** These therapies aim to target specific components of the immune system responsible for the autoimmune response in MS.

- **Stem cell therapy:** This therapy has the potential to repair damaged tissues and promote regeneration.

- **Gene therapy:** This approach aims to correct or replace defective genes responsible for MS susceptibility.

- **Personalized medicine:** This approach aims to tailor treatment strategies to individual patients based on their unique genetic and disease characteristics.

11. Psychological Impact of MS

Living with MS can have a profound psychological impact, leading to anxiety, depression, and emotional distress. Factors contributing to this impact include [25]:

- **Fear of the unknown:** The unpredictable nature of the disease and the uncertainty about its progression can cause significant anxiety.

- **Loss of control:** Feeling a loss of control over bodily functions and daily activities can lead to feelings of helplessness and frustration.

- **Social isolation:** Social withdrawal can occur due to physical limitations, fatigue, and fear of stigma.

- **Depression:** The emotional burden of living with a chronic disease can lead to depressive symptoms.

- **Body image concerns:** Visible physical changes, such as changes in gait or muscle spasticity, can negatively impact self-esteem and body image.

11.1. Body Image Concerns

Visible physical changes associated with MS, such as changes in gait or muscle spasticity, can significantly impact self-esteem and body image. These changes can lead to feelings of shame, embarrassment, and social anxiety. Additionally, the fear of further physical deterioration can exacerbate these concerns.

To address body image concerns, it is important to:

- **Focus on abilities:** Emphasize what the body can still do rather than focusing on limitations.

- **Engage in adaptive activities:** Explore physical activities that are safe and enjoyable.

- **Connect with others:** Join support groups or connect with individuals who understand the challenges of living with MS.

- **Seek professional help:** If body image concerns are causing significant distress, consider seeking therapy from a mental health professional specializing in body image issues.

By promoting body acceptance and positive self-esteem, individuals with MS can better cope with the challenges of the disease and improve their overall well-being.

12. Managing MS and Maintaining Quality of Life

Effective management of MS requires a multifaceted approach that addresses both physical and psychological needs. This includes [26]:

- **Adherence to treatment:** Taking medications as prescribed and attending all scheduled appointments is crucial for managing the disease and preventing relapses.

- **Healthy lifestyle:** Maintaining a healthy lifestyle, including regular exercise, a balanced diet, and adequate sleep, can improve overall health and well-being.

- **Stress management:** Learning relaxation techniques and managing stress effectively can help reduce anxiety and depression symptoms.

- **Social support:** Building a strong network of family and friends can provide emotional support and reduce social isolation.

- **Psychological therapy:** Cognitive-behavioural therapy and other forms of psychotherapy can help individuals cope with the emotional challenges of living with MS.

- **Financial planning:** Planning for the financial implications of MS, including accessing disability benefits and managing healthcare costs, is crucial.

- **Patient advocacy and support groups:** Connecting with patient advocacy groups and support groups can provide valuable information, resources, and emotional support.

- **Complementary and alternative therapies:** Some complementary and alternative therapies, such as yoga, acupuncture, and massage therapy, may offer relief from specific symptoms. However, the effectiveness of these therapies varies, and it is essential to consult with a healthcare provider before starting any new treatment.
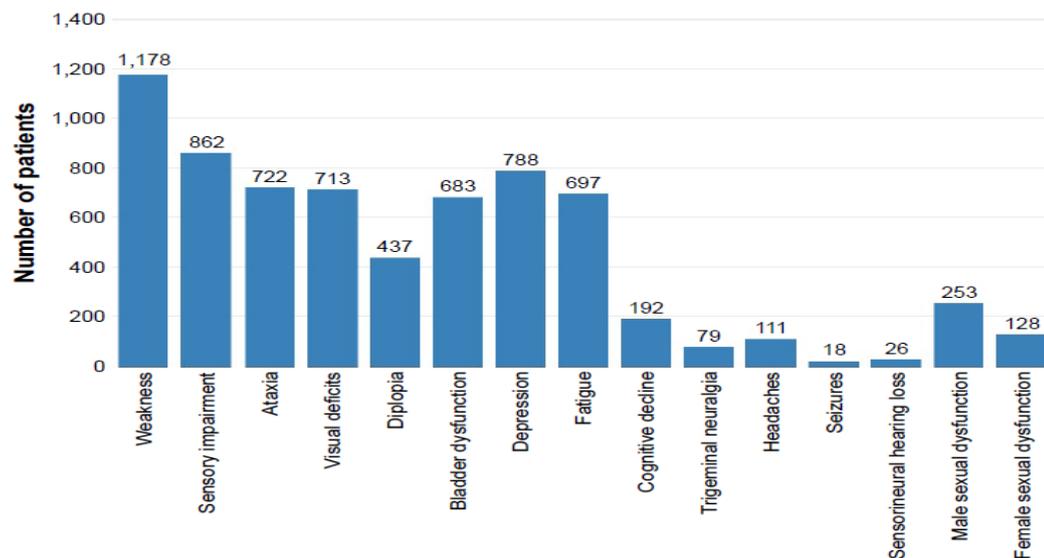
Figure 1: Symptom frequency during disease course in multiple sclerosis patients.

Despite the conventional belief that the Middle East and North Africa (MENA) countries have a low to moderate risk of developing multiple sclerosis (MS) [30], recent studies show that the prevalence of MS is rising in this region [31,32]. Even though Egypt is the most populous nation in the ME and the Arab world, little information is currently known regarding the clinical traits and demography of MS patients there [33,34]. The purpose of this study was to describe the clinical and paraclinical characteristics, as well as the patient demographics, of four tertiary MS referral hospitals in Egypt.

The first and follow-up MRI results for 2,536 brain and 1,007 cervical spinal cord cases were reassessed. Given that this was a retrospective investigation, several scanners and imaging procedures were used. Coordinators on-site evaluated the imaging results, standardizing the retrieved data for specific radiographic features such as typical vs atypical lesions, supratentorial versus in fratentorial position, active lesions, and black holes.

The diagnostic plan and demographic information for each patient comprised After 1,717 patients' medical records were first examined, 136 (7.9%) of them were later removed because missing information was not available. 1,078 (68.2%) of the 1,581 patients that were included were female. The ages of the enrolled individuals ranged widely from 6 to 60 years old, with a mean age of 29.94±8.65 years. Seventy-two percent of the patients lived in Greater Cairo (1,139 out of 1,581). Our cohort (n = 514, 32.5%) had about a third quit their occupations due to illness, and 44 (2.8%) had changed jobs as a result. 157 patients (9.9%) had a divorce brought on by illness, with women making up around two thirds of the cases (n = 105). Forty-one patients (2.6%) had unresolved diagnoses for MS at the time of data collection, out of 1,404 patients (88.8%) with a diagnosis. Regarding the age at which the disease manifested itself, 97 of 1,404 (6.9%) patients had childhood onset MS (age at onset of 18 years), whereas 49 (3.5%) had late-onset MS (age at start of 50 years).

- **Clinical characteristics of MS in the study:** Of the 1,054 individuals identified, RRMS accounted for 75.1% of all cases; 285 patients (20.3%) had SPMS, and 65 patients (4.6%) had PPMS. The majority of patients (616 of 1,404 [43.9%]) presented with motor symptoms, followed by sensory symptoms (465 of 1,404 [33.1%]). A small percentage of patients (3.9%) presented with atypical symptoms (Table 2). The disease onset in almost one-third of our cases (n=471 [33.6%]) was polysymptomatic. The follow-up period for all centers was between 1 and 156 months, with a mean of 53.2±78.3 months (median 39 months).Thirteen people (0.9%) passed away from complications connected to MS throughout this time. 32 individuals (2.28%) in all mentioned having a family history of MS [35].

- The most frequent symptom reported was motor weakness, which was followed by sensory abnormalities. Conversely, the least common symptoms were sensorineural hearing loss and seizures. Figure 1 shows the frequency of symptoms that MS patients developed over the course of their illness.

13. Conclusion

Multiple sclerosis (MS) remains a complex and challenging chronic disease, but significant progress has been made in understanding its mechanisms, developing effective treatments, and improving the quality of life for individuals living with MS. This review has highlighted the current state of knowledge regarding MS, encompassing its prevalence, pathophysiology, clinical presentation, diagnosis, and treatment options. While the journey towards a cure continues, ongoing research and innovation offer promising avenues for further development.

Currently, the focus lies on several key areas:

1. Disease-modifying therapies (DMTs): Continuous research aims to develop more effective and personalized DMTs with improved safety profiles and targeted mechanisms of action. This includes exploring novel therapies like neuroprotective and immunomodulatory approaches, alongside advancements in stem cell therapy and gene therapy.

2. Improved diagnostics and monitoring: Refining diagnostic tools and developing reliable biomarkers will lead to earlier and more accurate diagnosis, allowing for prompt intervention and personalized treatment plans.

3. Addressing global disparities: Bridging the gap in access to specialized care, diagnostic tools, and medication across different regions is crucial. Telehealth and digital health initiatives can play a vital role in overcoming geographical and resource limitations.

4. Enhancing symptom management: Developing innovative strategies to manage specific symptoms like fatigue, pain, cognitive dysfunction, and bladder and bowel problems is essential for improving overall well-being and quality of life.

5. Mental health support: Recognizing and addressing the significant psychological impact of MS is crucial. Integrating mental health interventions into routine MS care and providing access to specialized support services are vital for promoting resilience and emotional well-being.

6. Patient empowerment and advocacy: Empowering individuals with MS through access to accurate information, education, and support networks is crucial. This fosters a sense of ownership and control over their health, promoting self-management and active participation in treatment decisions.

7. Research funding and collaboration: Continued investment in research, both public and private, is essential to accelerate progress. Fostering international collaboration and knowledge exchange between researchers, healthcare professionals, and patient advocacy groups will expedite breakthroughs and ensure equitable access to advancements.

In conclusion, while challenges remain, the future of MS management holds immense promise. By harnessing the power of scientific advancement, global collaboration, and unwavering commitment to patient well-being, we can move closer to a world where individuals with MS can thrive and live fulfilling lives free from the limitations imposed by the disease.

Disclosure

The authors report no conflict of interest.

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14. Glossary

- *demyelination:* *the process by which the myelin sheath is damaged or destroyed.*

- *autoimmune response:* *an abnormal immune response directed against the body's own tissues.*

- *relapse:* *a worsening of symptoms in MS*

- *remission:* *a period of time when symptoms improve or disappear.*

- **disease-modifying therapy (DMT):** *a medication that aims to alter the course of MS and slow down the progression of the disease.*

- **neuroprotective therapy:** *a treatment that aims to protect nerve cells from damage.*

- **immunomodulatory therapy:** *a treatment that aims to modulate the immune system to prevent it from attacking the myelin sheath.*

- **stem cell therapy:** *a therapy that uses stem cells to repair or replace damaged tissues.*

- **gene therapy:** *a therapy that aims to correct or replace defective genes.*

- **personalized medicine:** *a medical approach that tailor's treatment to the individual patient based on their unique genetic and disease characteristics.*

15. Additional Resources

- *National Multiple Sclerosis Society: https://www.nationalmssociety.org/*

- *Multiple Sclerosis International Federation: https://www.msif.org/*

- *American Academy of Neurology: https://www.aan.com/*

- *Mayo Clinic: https://www.mayoclinic.org/diseases-conditions/multiple-sclerosis/symptoms-causes/syc-20350269*

- *National Institutes of Health: https://www.ninds.nih.gov/*