



MULTIPLE SCLEROSIS: AN IN-DEPTH STUDY ON ITS CAUSES, INCREASING INCIDENCE, CONTROL, PREVENTION AND CURES.

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ABSTRACT The disease is at this point of time is not curable, but research has thrown up various factors which are responsible for the onset of this autoimmune disorder. While the cure is not, at the present, available, there are various ways in which this disease can be managed and most patients live a life which may not be the best but definitely one which is tolerable in the adverse conditions. **Research Question:** The paper will attempt to understand the meaning of multiple sclerosis, increasing incidence, its medical cure as well as the manner in which it can be managed for both the patient and the caregiver. In recent times, there has been an increasing incidence of this disease. An attempt will be made to understand the reasons for its sudden increase in incidence. The most important aspect of making the patient comfortable is an area which will be studied in depth.

KEYWORDS :

INTRODUCTION

This disease is a serious ailment which causes a person to slowly lose control of one's body and movement becomes extremely difficult. It is a disabling disease of the brain and the spinal cord. It could also be a type of autoimmune disorder and it attacks the protective sheath (myelin) which covers the nerve fibers and thus causes communication issues between the brain and the rest of the body.

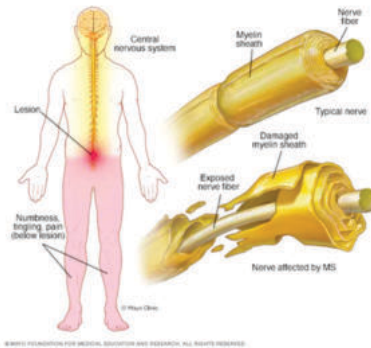


Figure 1: Picturisation Of The Damage Done To The Nervous System Under Multiple Sclerosis
Source: Mayo Foundation For Medical Education And Research

Definition

Multiple Sclerosis is an immune mediated disease. This means that the body's immune system is responding abnormally which leads to the onset of the disease. It is the immune system which is attacking the Central Nervous System (CNS). The CNS is made up of the brain, spinal cord and optic nerves.

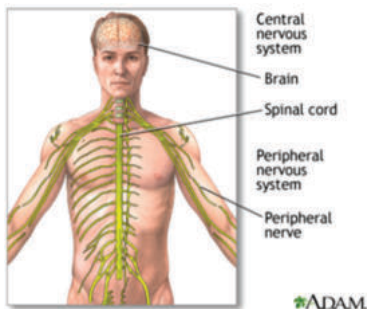


Figure 2: The Central Nervous System
Source: Medlineplus.gov

The immune system is a complex network of organs, cells and proteins that defends the body against infections and it also protects the body's own cells. It keeps a record of every microbe that enters the system, and which it has defeated, and has a memory such that it can destroy it, if it enters the body again. This system is something that humans are born with. This adapts as the body is exposed to microbes and chemicals. It

consists of a large network of organs, white blood cells, proteins (antibodies) and chemicals. The whole system works together to protect the body from foreign invaders (bacteria, viruses, parasites and fungi). The immune system in fact has the ability to recognise those cells which are part of the body and those which are foreign to the body. The moment the foreign germ enters the system, the immune system develops antibodies and protects the host body.

Symptoms Of Multiple Sclerosis (ms)

In MS, the immune system becomes confused and attacks the protective myelin coating around the nerves by mistake. In normal circumstances, the immune system of the body safeguards the protective myelin coating. But suddenly, when the immune system of the body starts giving wrong signals and actually harming what has to be protected, results in MS. The onset of this disease is a result of the system becoming confused and attacking the protective layers. This disease is supposed to be a chronic disease of the Central Nervous System. The fact that it is claimed to be an autoimmune disorder does not hundred percent guarantee that any other system of the body is malfunctioning.

Nerve Disorder

Once the myelin is being attacked, the nerve fibers are left unprotected and this creates lesions. Depending on which portion of the nervous system which is left unprotected, it could lead to symptoms such as numbness, pain or tingling in parts of the body.

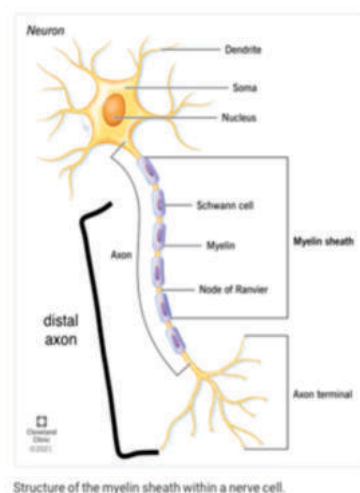


Figure 3: A Nerve Axon
Source: Clevelandclinic.org

The myelin sheath is an extended and modified plasma membrane which is wrapped around the nerve axon in a spiral fashion. It originates and is part of the Schwann cells in the Peripheral Nervous System (PNS) and the oligodendroglial cells in the Central Nervous System (CNS)

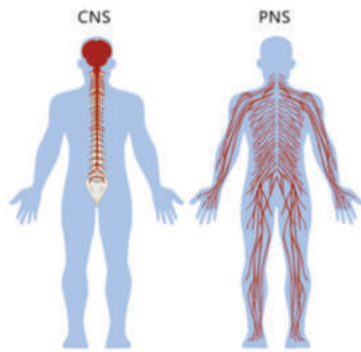


Figure 4: Central Nervous System Vs Peripheral Nervous System
 Source: Partnershipeducation.com

What is important is that each myelin generating cell provides myelin for only one segment for any given axon. In fact, it is an electric insulator, but its property of impulse conduction does not have an exact analogy. It can be seen under an electron microscope as well as a light microscope and it indicates a lipid and protein dependence.

In the PNS myelination, the cells lie up along the axon, with intervals between them, and these intervals would become the Nodes of Ranvier. These nodes are specialized regions in the axonal membrane that are not insulated by myelin. Even though myelin does not exist at the node, the axon is in direct contact with the microvilli of the Schwann cells in the PNS or with the processes of astrocytes in the CNS.

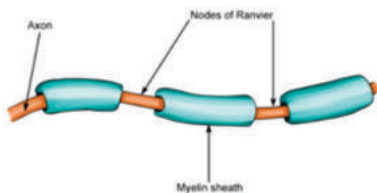


Figure 5: Nodes Of Ranvier
 Source: Mammothmemory.net

Schwann cells serve as the myelinating cell of the PNS and they support cells of peripheral neurons. They are a type of glial cells that help separate and insulate nerve cells. Glial cells, or neuroglia are cells that surround the neurons of the CNS and provide structural and physiological support. These cells support, connect and protect the neurons of the CNS and the PNS. They perform specialized functions and regulate neurotransmission as well as help in the formation of blood brain barrier. The simplistic definition of them is that they hold the nerve cells in place and help them work the way they should. They also maintain homeostasis and clean up debris as well as form myelin. They in fact take care of the neurons and the environment that they are in.

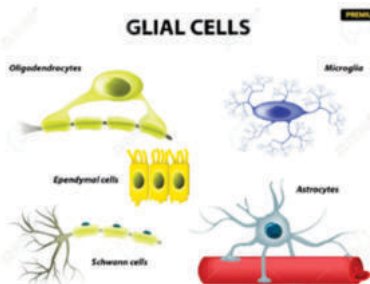


Figure 6: Glial Cells
 Source: 123rf.com

The failure of the immune system in the case of MS leads to neuronal cell death, accompanied by nerve demyelination and neuronal dysfunction. The neurological problems can be categorized as:

1. Multifocal zones of inflammation due to focal T-lymphocytic (these are a type of White Blood Cell which are a part of the

immune system which develop from stem cells in the bone marrow, essentially protecting the body from infections), macrophage infiltrations (when a wound is healing, macrophage infiltration contributes to macrophages which play an important role in suppressing inflammation and initiating wound repair by clearing debris and producing growth factors that support the tissues) and oligodendrocyte (These are myelinating cells of the CNS. They are the end product of a cell lineage which has to undergo a complex and timed program of proliferation, migration, differentiation and myelination again to produce the insulating sheath of the myelin) deaths are the primary causes of myelin sheath destruction.

When the myelin sheath disappears or is substantially damaged in a number of areas, what it leaves is a scar which is called Sclerosis. These scars or lesions affect the:

- Brain stem
- The cerebellum (controls movement and balance)
- The spinal cord
- Optic nerves
- White matter, in some regions of the brain

As more and more breaks develop, these nerve fibers can break or become damaged, which further results in a break in the electric impulses by the brain to the target nerve, resulting in the body not carrying out certain functions.

1. MS results in the formation of CNS plaques, which are composed of inflammatory cells and their products, demyelinated and transected axons (degeneration of the distal portion of the axon and myelin sheath), and astrogliosis (Astrogliosis is a spectrum of potential, molecular, cellular and functional changes in the astrocytes. It also refers to the reactive astrocytic response to a brain injury. It is an abnormal increase in the number of astrocytes due to the destruction of nearby neurons. Astrocytes normally play a critical role in energy provision, regulation of blood flow, etc. Astrogliosis changes the molecular expression and morphology of astrocytes, and that is why they result in scar formation and may inhibit axon regeneration.) in both white and gray matter. These scars can interfere with the correct transmission of nerve impulses, leading to neuronal dysfunction. Malfunctioning could be in the form of visual disturbances, fatigue, difficulties in thinking and emotional issues.

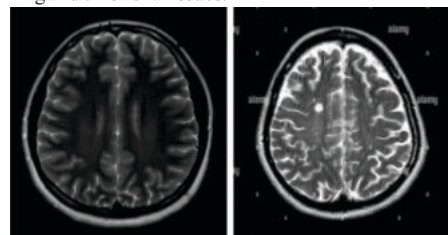


Figure 7: Contrasting Mri Images Of (a) Normal Brain And (b) Ms Brain
 Source: (a) Alamy.com (b) Radiopaedia.org

Brain Deformity

MS is essentially first attacking the nervous system and subsequently the brain. There are four types of MS which have been characterized according to the progression of symptoms over time.

1. Relapsing-remitting MS: This is characterized by attacks and people may completely recover or else be at the situation of disability after the attack. The time period between the attacks is known as remission, and this may vary from weeks, months or even years.
2. Secondary progressive MS: This is normally the second stage when, after the initial attacks, patients start to develop gradual and steady symptoms and deterioration of their body functions over time.
3. Primary progressive MS: Straight away starts with progressively worsening symptoms, with no noticeable relapse. This is not as common as the other two.
4. Progressive relapsing MS: This is very rare and in such cases there are worsening symptoms right from the beginning, with acute relapses.

The symptoms may begin with vision problems, for example blurred

or double vision, moving subsequently to the limbs and muscles, leading to clumsiness and not being able to balance while walking. From hearing to bladder control problems and constant dizziness. Assuming that we are talking about the first and second type of MS, the subsequent symptoms could be mental and physical fatigue, mood changes, cognitive dysfunction which essentially involves the brain and leads to problems in concentration, multi-tasking, thinking, learning and difficulties with memory and judgement.

Besides just affecting the myelin, there could be problems in the blood-brain barrier. Once this occurs, it exposes the brain to the immune system and then the immune system misinterprets the structure in the brain and attacks it, as it considers it foreign. This is the case when it considers myelin as foreign.



Figure 8: Four Types Of Ms
Source: Multiplesclerosisnewstoday.com

Reasons For The Incidence Of The Disease

There have been studies indicating that females are more frequently affected than males. The other factor is that MS is not itself inherited, but susceptibility to MS may be inherited. Studies have indicated that some individuals with MS may have one or more family members who also have MS. Research has shown that dozens of genes and hundreds of variations in the combination of gene variants lead to vulnerability to MS. Studies have discovered some genes which come under this category but there are a number which are still unknown. The ones which have been discovered have been identified in people with other autoimmune diseases such as type -1 diabetes, rheumatoid arthritis or lupus.

Many types of viruses have been found in patients who have been diagnosed with MS. The most rampant one is the Epstein-Barr virus (EBV) (also known as human herpesvirus 4). Most people in their lifetime have been affected by this. There may be only 5% who have not been affected. The ones that have not been affected are at a lower risk of developing MS than those who have. As one grows older, the impact of contracting EBV may develop into an exaggerated immune response, which then results in a higher risk for developing MS than those who contracted the virus at a young age.

Studies have also indicated that those people who spend more time in the sun and subsequently have higher levels of vitamin-D are less likely to contract MS. Researchers have indicated that vitamin -D helps in regulating the immune system, which automatically places a barrier on the body's immune system. Climatic conditions then play an important role in the contraction of this disease.

Smoking is another factor which adversely impacts the brain. Smokers tend to have more brain lesions and brain shrinkage than non-smokers. High consumption of cow milk as a child and adolescent has emerged as an increasing incidence in contraction of MS. This happens because the immune cells of a person with MS could target proteins in dairy (butyrophilin and MOG), as their structure resembles that of myelin. Dairy products also increase saturated fat, which increases the risk of MS. High Body Mass Index and obesity increases the incidence of the disease. Saturated fat, diet and stress are other factors contributing to the rising incidence.

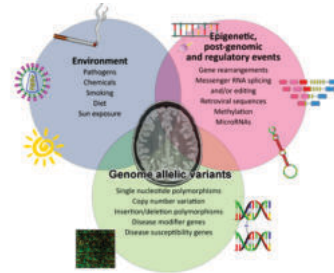


Figure 9: Various Causes Of Multiple Sclerosis
Source: Ucsf.edu

Preventions And Cures

MS is a growing global health challenge affecting a larger and larger number of people every year. There has been an immense amount of research and progress made on the understanding and treatment of MS in the last several decades. The problem is in the cures, which has remained elusive. There seems to be a lot of knowledge gaps in arriving at the right set of cures.

The primary aim of the pathway to cures should be:

- Stopping the MS disease process
- Restoring lost function by reversing damage and symptoms
- Ending MS through natural alternative medicines

There is a National Multiple Sclerosis Society, which is focused on achieving breakthroughs in the cures for MS. As breakthroughs in knowledge about the disease increases, effective development of measures that could target different cells and mediators are being researched on, eventually resulting in the improvement in the quality of life of people suffering from MS. These measures are essentially of the type that modulate the adaptive immune system and or impact immune cell trafficking.

Immune cell trafficking (ICT) includes all aspects that control the localisation of cells, including adhesion and homing, retention and recirculation. Adhesion is a central and clinically relevant step of gut homing and it depends on the endothelial cell adhesion molecules and integrins on the surface of immune cells.

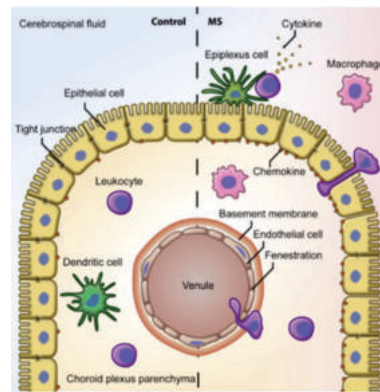


Figure 10: Immune Cell Trafficking
Source: Sciencedirect.com

An altered cell trafficking is a crucial step for diseases like rheumatoid arthritis and MS. Research on the central role of the gut has progressively emerged. The microbiota-driven imprinting of certain cell trafficking phenotypes in the intestine seem to be actively involved. The essential importance of this discovery is that the gut is the main area involved in immune mediated pathology. E.g: gut-liver, gut-joint and gut-brain access. The main idea in this pathway of research is to find therapeutic approaches that would specifically interfere with the homing, retention, egression and recirculation of immune cells.

Cell trafficking mechanisms, along with these axes include the induction of pathogenic immune cells at the interface with the intestinal microbiome (The types of human microbiota include bacteria, archaea, fungi, protists and viruses, are found inside the intestine and on the skin, and their homing to extra intestinal sites is a

possibility. This is an important but yet nascent field for future therapeutic intervention.)

Vitamin D is another observation which could reduce the risk of MS and affect the course of the disease. The two questions that are to be answered is whether Vitamin D can prevent MS and if Vitamin D is an effective treatment for MS. There are random clinical controlled trials which are being undertaken but conclusive results are still not within reach. It also depends upon the design on which the trial is conducted (this depends upon strength, men, women, and the extent of supplemental Vitamin D). Evidence does suggest that Vitamin D is an important MS prevention but the questions that have been mentioned in the beginning are difficult to conclude.

There are strong genetic determinants of MS as well as environment, which have a great impact on the contracting of the disease. Vitamin D nutrition and cigarette smoking have been identified as a causal factor for MS. Genes play an extremely important role in the risk associated with contracting the disease.

It has also been known that MS is rare between the tropics, and increases in frequency with the increasing latitude in both hemispheres (latitude gradient). A large part of the spread of the disease was also due to the initial migration that took place in fledgling countries in regions of high MS risk (British Islands) to areas of low risk (South Africa or Australia). This also indicates the years in which there is a sudden increase in MS. For example, in white US women, there is a threefold latitude gradient among those born in 1921 to 1946, but no gradient to those born after 1946.

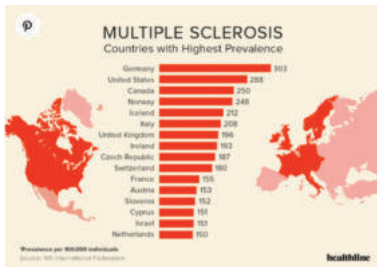


Figure 11: Incidence Of Ms Worldwide
Source: Healthline.com



Figure 12: Pathways To Cures For Ms
Source: nationalmssociety.org

Psychological And Psychiatric Support For The Disease

For primary progressive MS, Ocrelizumab(Ocrevus) is the only FDA (Food and Drug Administration) approved disease modifying therapy (DMT). It has been seen that in patients who receive this treatment, the disease is likely to progress less. It kills certain blood cells and has shown to be effective in the spread of the disease.

Ayurvedic cure, here it is important is to discover the dominant dosha and the Laghana therapy(which means “to fast and to reduce”, involving dieting,fasting etc),as a cure for MS which concentrates in the removal of Ama(these are toxin-undigested metabolic waste) along with excess Pitta/Kapha dosha(the body functions are governed by three basic entities called Vata, Pitta and Kapha) from the body.

This form of treatment essentially bases its analysis on undigested toxin waste, which remains in the body system. Some of the ways in which it can be removed/reduced is by fasting and yoga. Yoga limits itself to further deterioration of the disease by reducing the subsequent inability with respect to movement.

Homeopathic Treatment requires a lot of patience as it tries to treat the body's immune system, and this takes a long time to adapt.

Homeopathy cannot be considered a miracle cure for patients suffering an advanced stage of Multiple Sclerosis.

Chinese Herbal Medicine has also been used to reduce the side effects of hormones and immunosuppressins. They cannot cure the disease, but can control the side effects that arise due to the continuous usage of alopathic drugs.

CONCLUSION

MS has become quite common either due to the greater knowledge of the disease or maybe due to a larger number of people contracting the disease. The awareness of the disease has increased tremendously leading to MS Day being celebrated on 30th May every year. This just indicates the increasing need to spread awareness of the ailment, knowledge about prevention and help in managing the disease.

There is no 100% cure for the disease. The only way is to manage it with various types of medicines, both in the traditional and alternative fields. The psychological mindset of the patient is an extremely important factor in controlling the spread of the disease. The positive attitude goes a long way in controlling the spread of the disease as well as managing it. The reasons like smoking, intake of vitamin D, genetics, environment are some of the known factors that have been discovered. These should be taken cognizance of, if one has to prevent the onset of such a disease. Researchers are working on trying to find a cure, but when this will happen is an unknown factor.

REFERENCES

- Ghasemi, N., Razavi, S., & Nikzad, E. (2017). Multiple Sclerosis: Pathogenesis, Symptoms, Diagnoses and Cell-Based Therapy. DOAJ (DOAJ: Directory of Open Access Journals), 19(1), 1–10.
- Haussleiter, I. S., Brüne, M., & Juckel, G. (2009). Review: Psychopathology in multiple sclerosis: diagnosis, prevalence and treatment. Therapeutic Advances in Neurological Disorders, 2(1), 13–29.
- Immune cell trafficking across the barriers of the central nervous system, in Multiple Sclerosis and Stroke; Melissa A, Lopes Pinheiro, Gigs Kooij et al; Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease, March 2016
- Kalb, R., Brown, T. L., Coote, S., Costello, K., Dalgas, U., Garmon, E., Giesser, B., Halper, J., Karparkin, H. I., Keller, J., Ng, A. V., Pilutti, L. A., Rohrig, A., Van Asch, P., Zackowski, K. M., & Motl, R. W. (2020). Exercise and lifestyle physical activity recommendations for people with multiple sclerosis throughout the disease course. Multiple Sclerosis Journal, 26(12), 1459–1469.
- Walton, C., King, R., Rechtman, L., Kaye, W., Leray, E., Marrie, R. A., Robertson, N., La Rocca, N., Uitdehaag, B. M. J., Van Der Mei, I., Wallin, M. T., Helme, A., Napier, C. A., Rijke, N., & Baneke, P. (2020). Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. Multiple Sclerosis Journal, 26(14), 1816–1821.
- Yang, J., Rempe, T., Whitmire, N., Dunn-Pirio, A., & Graves, J. (2022). Therapeutic Advances in Multiple Sclerosis. Front. Neurol., 03 June 2022 Sec. Multiple Sclerosis and Neuroimmunology, 13.
- Zundler, S. (2022). Gut immune: Interorgan communication and immune mediated inflammation. Nature Reviews Gastroenterology and Hepatology.