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## Multiple sclerosis: New insights and trends



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## ABSTRACT

Multiple sclerosis (MS) is the most famous autoimmune disease attacking the central nervous system. It attacks people from age 20–50 years old and the females' attacks double than males' attacks. MS is an autoimmune disease affecting principally the central nervous system that cause nerve sheath demyelination followed by axon damage and paralysis. MS symptoms include muscle weakness, weak reflexes, muscle spasm, difficult in move, miss-coordination and unbalance with others. There are many factors may be responsible for MS: microbial, viral, smoking, stress, environmental toxins, contaminated diet, and gout. MS is wide spread in the populations in North Europe and this related to lack of vitamin D due to decrease of sunlight exposure. MS biomarkers include nitric oxide, interleukin-6, nitric oxide synthase, fetuin-A and osteopontin. MS is not a genetic disease where MS occurs when human leukocyte antigen system related genes are changed in chromosome 6. The physiology of MS is monitored by activation of immune-inflammatory, oxidative, and nitrosative stress pathways. MS is including two main steps: (1) myelin sheath destruction and formation of lesions and, (2) inflammation. Four types of MS can be distinguished: relapsing-remitting, primary progressive, secondary progressive and progressive relapsing. Nine treatments have been accepted for relapsing-remitting MS type: interferon  $\beta$ -1a, interferon  $\beta$ -1b, mitoxantrone, natalizumab, glatiramer acetate, fingolimod, dimethyl fumarate, teriflunomide, and alemtuzumab, however, the only treatment used is mitoxantrone for progressive MS but many of MS treatments side effects are recorded. Complementary treatments also used in MS treatments such as: vitamin D, Yoga, medicinal plants, oxygen therapy, acupuncture and reflexology.

## 1. Introduction

Scientist Jean-Martin Charcot is the first one who discovers the disease in 1868 [1]. It is most famous and pronounced autoimmune disease attacks the central nervous system [2]. According to world health organization reports in 2008; actually 2–2.5 million with multiple sclerosis (MS) disease were recorded in the world [3], and approximately 20000 MS patients died all over the world in 2012 comparing to 12000 died in 1990 [4]. MS starts attacks people from age 20–50 years old and the records investigated that females' attacks

double than males' attacks [5,6]. Disseminated sclerosis and encephalomyelitis disseminate are two alternative names of MS. The MS is autoimmune disease combined both genetic and environmental factors such as viral-induced immune disturbances [7]. There are many types of MS, sometimes occurring in isolated neuron (relapsing type) or spreading to few or many neurons (progressive type) [8]. The MS characteristic features are common disability, moving limits, low personal activity-related self-effectiveness, limitation of self-regulatory concepts, socio-demographic factors restrictions, decline employment state, and decrease educational level [9]. The MS symptoms may occur and disappear completely where the permanent neurological problems happen when the disease timely advances [8]. MS symptoms occur when the nerve cells myelin sheath in the central nervous system (brain and spinal cord) start to injure and consequently damaged. MS is associated with many symptoms and these include: physical, mental, and sometimes psychiatric disturbances [10–12], due to the neural damage occurs which block the communication among different parts of the nervous system.

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The mechanism responsible for MS to be appeared can be summarized into two reasons: (1) the immune system destructed the myelin sheath, and (2) failure of the myelin-producing cells to produce new sheathes [13]. The two above mentioned two reasons include numerous genetics and environmental factors *e.g.* heredity, pollution, microbial and viral infections [11,14,15]. The MS is diagnosed depending on the present patient status and the medical check-up investigations.

There are endogenous repair mechanisms to improve from MS disease early phases and these repair mechanisms contains inside local factors control these mechanisms. The natural killer (NK) cells are quickly moved to the organs defined by auto-immunity and NK increasing numbers when inflammatory case occurs. The NK cells are recalled in the brain subventricular zone during the progressive type of MS in both humans and MS animal model. These NK cells are establish very close sub-ventricular zone neural stem cells (NSCs) so consequently the cells begin to secret interleukin-15 and maintain the NK cells function. Furthermore, the NK cells decrease the functional capability of NSCs following MS inflammation so neurorepair is found due to communication of both NK and NSCs cells [16]. There are different types of upper limb rehabilitation can be found in MS incidence and a training program is run directed toward the upper limbs improve limb function and structure but cannot effect on the upper limb capability and performance in MS patients [17].

There is no treatment for MS until now. All the MS treatments try to attempt to improve the neuronal function following MS occurs and stop any progress of the disease [11]. The use of MS treatments in the early stage of MS can induce adverse side effects and can be ineffective at all. The treatments with good results are observed in teenager women where MS appears early with relapsing type with few neurons damaged [18]. MS decreases life with an average 5–10 years than other healthy ones [10,19]. There are many treatments and diagnostic procedures of MS are in the process of development.

## 2. MS symptoms

MS is an autoimmune disease affecting principally the central nervous system (brain and spinal cord) that cause nerve sheath demyelination followed by axon damage and consequently paralysis [20]. There are many and distinguished lesions found in the lower urinary tract as pronounced symptoms in MS patients [21]. On the other hand, MS is a major important reason of disability of a neurological origin in the young adults where depression is the most observed psychiatric disorder in MS [22]. Central and peripheral auditory disturbances are always appeared in MS [23]. On the other hand, the typical optic neuritis is usually the presenting symptom of MS [24]. The sleep disorder, exhaustion, and pain interfering are among other symptoms associated with MS [25].

MS symptoms depend on the specific nerve attack in the central nervous system and may lead finally to loss of sensitivity in sensation such as muscle weakness, weak reflexes, muscle spasm, difficult in move; miss-coordination and unbalance with others; problem in speech, optic problem, feeling tired, acute or chronic pain, and bladder and bowel difficulties. Depression is always associated with MS due to variable mood of MS patients. In addition to, thinking and emotional problems are also observed in MS. There are many factors increasing MS disease symptoms *e.g.* viral infections such as cold, influenza, and gastrointestinal

problems. Females are more sensitive to MS than males especially during 3 months after baby birth. Other factors do not effect on MS to be found such as vaccination, breast feeding, and physical status [10,25,26]. The expanded disability status scale (EDSS) is a well-known test of MS-associated disability, in addition to, other clinical investigations [27,28]. Stress also is a main cause of MS [29]. Figure 1 reveals MS main symptoms [30].

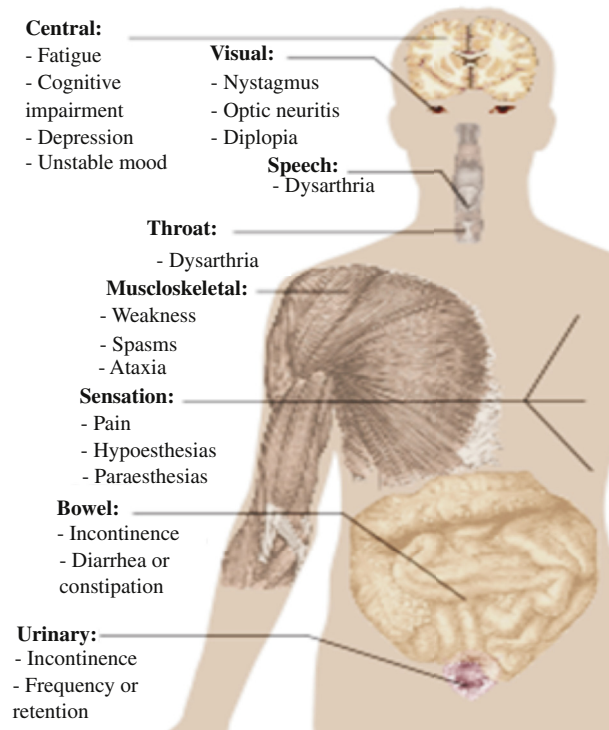


Figure 1. MS main symptoms [30].  
[https://en.m.wikipedia.org/wiki/Multiple\\_sclerosis](https://en.m.wikipedia.org/wiki/Multiple_sclerosis)

## 3. MS causes

Up to date, there are no reasons for MS incidence, however, there is a combination of environmental and hereditary factors including pollution, viral and bacterial infections, and stress may be included. There are many factors may be responsible for MS and these factors can be summarized into: microbial, viral and other infections.

### 3.1. Microbial infection

The infection with microbes has been associated in the main processes of introducing and increasing the incidence of MS [34]. MS can be induced by many microbes [11], where moving from one place to another increase microbial infection to induce MS [14,15].

The infectious disease (paratuberculosis) mainly affects wild and domestic ruminants. This disease induced by *Mycobacterium avium paratuberculosis* (MAP), where MAP correlated to MS incidence. The MAP DNA was found in 4/7 (57.14%) goat, and in 14/25 (56%) sheep cheese using qPCR. In goat, MAP produced type S strain of MAP, and this MAP occurs in quantities ranged from  $1.8 \times 10^4$  to  $6 \times 10^4$  MAP cells/g of cheese. In this study, 56.57% and 66.60% of cheese tested showed positive results for MAP and these can lead to increased incidence of MS in human [35].

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