MS ActiveNOW
ACTIVATING YOUR LIFE

A Health Professionals Guide to Understanding Exercise and Multiple Sclerosis

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Written by: Lea Carlyle, Keith Johnston, Scott Rattray and Garry Wheeler

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Photo taken by: Darrel Gregory

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MS Active*NOW*

MS Active*NOW* is a health promotion initiative for persons with multiple sclerosis (MS) designed to:

- Increase awareness of the benefits of daily physical activity and exercise in persons with MS, caregivers, and providers in the health, fitness and lifestyle industry.
- Help fitness providers design exercise programs for persons with MS such that persons with MS may enjoy the benefits of exercise safely and with confidence.
- Increase access to active living and exercise opportunities in the community for persons with MS.
- Increase intention for physical activity and exercise in persons with MS.

MS Active*NOW* uses a combination of information sessions and target specific materials in order to raise awareness and educate persons with MS, fitness and lifestyle professionals and health professionals with regard to the role of exercise in symptom management of MS and to provide a guide for suitable exercises for persons with MS.

Introduction

Multiple sclerosis (MS) is an inflammatory neurological disease that can affect any myelinated structure in the central nervous system (CNS), including the brain, spinal cord and optic nerves. Its etiology is unknown, but genetic, environmental and autoimmune processes are thought to be involved. Much of the permanent disability results from axonal destruction in the very long pathways of the pyramidal tracts carrying motor signals and the dorsal columns carrying sensory information to and from the legs. Symptoms of MS include fatigue, motor weakness, spasticity, ataxia, poor balance, visual disturbances, heat intolerance, depression and bladder and bowel dysfunction[1].

Exercise plays an essential part in the prevention and treatment of many chronic diseases including MS. The benefits of exercise have also been studied and realized in other neurological diseases, but less often explored in MS. Up until recently, exercise as a therapy has been under-utilized in the MS population[2] . This may have been due to neurological functions such as vision, motor function, and ambulation often becoming worse with exercise and therefore exercise was thought to be contributing to the disease process. It was also thought that participating in exercise would cause excessive fatigue preventing the individual from completing basic daily activities. Individuals were therefore often advised by health care professionals to refrain from participating in exercise. However, the worsening of symptoms that occurs with exercise does not cause any further damage to the myelin sheath and will reverse itself upon recovery from exercise.

Exercise is recognized as an important part of symptomatic and supportive treatment in persons with MS[3] and current research indicates that it is safe and beneficial for individuals to participate in exercise, particularly those with mild to moderate forms of the disease[4]. It improves lung function, lower extremity function, muscle power, exercise tolerance, mood and quality of life in MS[5]. The goal of exercise is to improve cardiorespiratory endurance, muscular strength, flexibility, mobility, and prevent secondary diseases. By improving strength and endurance of the cardiorespiratory and musculoskeletal systems, the hope is that persons with MS can maintain physical function and independence as well as experience an enhanced quality of life. In addition, research has found that individuals with MS with low levels of self-reported physical activity described a worsening of MS symptoms.

This review will discuss the physiological and functional limitations of individuals with MS and how these factors may affect participation in exercise. It also reviews the beneficial effects of exercise in regards to MS symptoms as well as in the prevention of other chronic diseases. Guidelines for exercise testing and prescription in MS and special considerations are also included.

Why MS Active*NOW?*

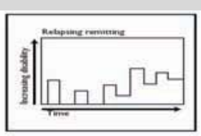
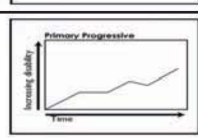
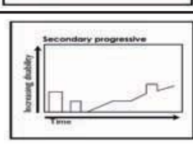
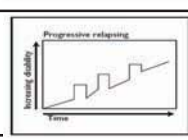
Canadians with disabilities make up approximately 19% of the Canadian population[6]. Despite the importance of physically active lifestyles for maintenance of health, quality of life, and sense of physical well being, people with disabilities and specifically persons living with MS are conspicuously absent from community based physical activity and fitness settings. It has been estimated that only 10% of people with disabilities are physically active, thereby increasing their risk of developing secondary health conditions (e.g., diabetes, cardiovascular disease) that can further impact their quality of life and functional independence[7]. Physical activity is a recognized intervention in the prevention of lifestyle related diseases[8].

Multiple Sclerosis (MS)

What is it?

Multiple sclerosis (MS) is an unpredictable, often disabling disease of the CNS — the optic nerves, brain and spinal cord. The disease attacks the protective myelin covering of the CNS, causing inflammation and often destroying the myelin in patches. In its most common form, MS has well defined attacks followed by complete or partial recovery. The severity of MS, progression and specific symptoms cannot be predicted at the time of diagnosis.

Types of Multiple Sclerosis

Type		Description
Relapsing-remitting		Characterized by clearly defined attacks (relapses) followed by complete or partial recovery (remissions); most common form (75% to 85% at the time of diagnosis).
Primary-progressive		Less common (10 to 15% at time of diagnosis), people with this type of MS have a gradual worsening of MS from the beginning with no clear relapses or remissions.
Secondary-progressive		About half of people with relapsing-remitting MS start to worsen within 10 years of diagnosis, with possibility of increasing levels of disability.
Progressive-relapsing		Relatively rare, combines attacks with steady worsening from the onset of the disease.

Symptoms Associated with Multiple Sclerosis

Symptoms of MS are unpredictable and vary greatly from person to person and from time to time in the same person. MS attacks the protective covering — myelin — of the brain and spinal cord, causing inflammation and often damaging the myelin in patches. When this happens, the usual flow of nerve impulses along nerve fibres (axons) is interrupted or distorted. The result may be the wide variety of MS symptoms, depending upon what part or parts of the CNS are affected. The damaged parts of myelin are often called “lesions” or “plaques”. Evidence exists that permanent damage to nerve fibres may occur in association with the attack on myelin. Not all people with MS will experience all symptoms and often the symptoms will improve during periods of remission. Symptoms may include but are not limited to[9]:

- •Speech problems
- •Unusual and extreme fatigue
- •Loss of balance
- •Problems with coordination
- •Stiffness of muscles
- •Short-term memory problems
- •Visual disturbances (i.e., double or blurred vision)
- •Partial or complete paralysis
- •Spasticity
- •Numbness or pain
- •Bladder and bowel problems

Physiological Limitations of MS

There are physiological aspects of multiple sclerosis (MS) that may interfere with an individual’s ability to exercise. Physiological factors may involve the skeletal, neural, and immune systems. These factors may, in turn, be associated with physical limitations such as ataxia, weakness, fatigue, heat sensitivity, sensory disturbances, spasticity, bladder dysfunction, and visual problems. The following section discusses the physiological limitations of MS which need to be considered when considering exercise and physical activity as an option.

Peripheral Limitations

Research has indicated that skeletal muscle function can be adversely affected by MS. Reduced muscle power and/or endurance, isolated points of weakness in the range of motion (ROM) of the joint and firing oscillation during sustained effort has been found to occur. Ponichtera and colleagues[10] measured the muscle torque at several speeds for both concentric and eccentric contraction on persons with and without MS. It was found that persons with MS had a 22% and 39% lower absolute peak torque of the quadriceps and hamstring muscles, respectively, during concentric muscle action compared to controls. Similar decreases were found in the force of the quadriceps and hamstring muscles with maximal isometric contractions[11]. Force during knee extension and flexion was decreased by 36% and 21%, respectively, compared to healthy individuals. Peak force appears to be affected by the velocity of the contraction as well. When persons with MS performed concentric contractions of the quadriceps and hamstrings, 50% of the individuals were not able to produce any force when the contraction velocity was set at 275 degrees/second[12]. Reduced muscle power and endurance has been found among individuals with MS with mild to moderate disability. There appear to be distinct points of weakness and an increase in the time of contraction during isokinetic knee extension and flexion. Possible reasons for reduced muscle power may partially be attributed to the blocking or slowing of nerve conduction associated with demyelination.

Skeletal muscle fibers have different mechanical and metabolic characteristics and can be classified based on a variety of criteria. Fibers classified on the basis of their maximal shortening velocity are referred to as slow-twitch and fast-twitch fibers. Slow-twitch fibers develop force and relax slowly and have a long twitch time whereas fast-twitch fibers develop force and relax quickly and have a short twitch time. When slow- and fast-twitch motor units are categorized based on their histochemical characteristics they are known as Type I and Type II, respectively. They differ in their ability to demand and supply energy for contraction, and therefore, their capacity to resist fatigue. Type I motor units are generally fatigue resistant and have a high capacity for supplying energy aerobically. They have limited potential for rapid force development, as characterized by low actomyosin myofibrillar ATPase activity and low anaerobic power[13]. In contrast, Type II motor units are easily fatigued, have low aerobic power, rapid force development, high actomyosin myofibrillar ATPase activity, and high anaerobic power. The properties of a muscle are affected by the regularity with which the muscle is used as well as the duration and intensity of its activity. If muscle fibers are denervated because of severed or destroyed neurons to the skeletal muscles, as is found in persons with spinal cord injury, the muscle fibers become smaller in diameter as well as lose contractile proteins. This condition is known as denervation atrophy. Paralyzed muscles have been found to display a fiber-type transition toward a predominance of Type II fibers and results from both a loss of Type I fibers and a progressive conversion of myosin heavy chain (MHC) I expression toward MHC IIx expression[14]. The greater energy requirement demanded from Type II fibers for contraction would result in greater fatigue.

Research has reported alterations in muscle fibers in patients with MS, with a higher reliance on anaerobic rather than aerobic energy supply compared to healthy controls. Kent-Braun and colleagues[15] investigated whether the changes in skeletal muscle characteristics in MS were consistent with de-conditioning as compared to healthy controls. Analyses of biopsies of the tibialis anterior muscle in MS patients showed that there were fewer type I fibers and fibers of all types were smaller and had lower succinic dehydrogenase (SDH), but not glycerol-phosphate dehydrogenase (GPDH). These results suggest that muscle of MS patients relies more on anaerobic than aerobic-oxidative energy supply than in healthy individuals. There was also a significant association between strength and average fiber cross sectional area (CSA) as well as physical activity and SDH/GPDH. It is suggested that these characteristics are consistent with those observed with deconditioning and may affect function. Garner and Widrick[16] found that biopsies from the vastus lateralis muscle of MS patients showed fewer fibers containing the type IIa MHC isoform exclusively. There was also a significant negative correlation between the Expanded Disability Status Scale (EDSS) and type I MHC expression and a positive correlation between EDSS and the relative expression of pooled fibers containing fast MHC isoforms in the MS group. Type I fibers in the MS group also produced 13% less peak force compared to the control group. This decrease was a result of the significantly smaller CSA and reduced force per fiber CSA of these fibers. The research suggests that the changes observed in fast MHC isoform coexpression and the slight reduction in cross-bridge number, density, or average force that was found may explain part of the muscle weakness and fatigue experienced by individuals with MS.

The resynthesis of phosphocreatine (PCr) has been found to be delayed after muscle stimulation in individuals with MS. Sharma and colleagues[17], found that there was a much greater decline in tetanic force, PCr, and intracellular pH in the MS group compared to controls with 9 minutes of intermittent stimulation of the anterior tibialis muscle. There was also a delay in the recovery of tetanic force following exercise in the MS group which is suggestive of abnormal excitation-contraction coupling. The recovery of metabolites was complete in both groups. Muscle fatigue was also correlated with clinical disability but not with perceived fatigue. These results may indicate that fatigue has both peripheral (impaired metabolism and excitation-contraction coupling) and central (perception of fatigue, upper motor neuron dysfunction) components. Kent-Braun and colleagues[18] also investigated whether skeletal muscle oxidative metabolism was impaired in MS. They found that after intermittent isometric tetanic contractions of the dorsiflexor muscles through stimulation of the peroneal nerve that PCr recovery was significantly delayed in the MS group compared to controls. This indicates impaired oxidative capacity in the skeletal muscle in the MS group. The authors suggest that these findings may indicate that altered muscle function in persons with MS may be the result of intramuscular changes consistent with deconditioning as was also suggested in a similar study. Kent-Braun and collegues[19] found that even in individuals with mild MS, a failure of muscle activation occurred and was indicated by a smaller change in Pi and PCr at the same relative exercise intensity as completed by the control group. However, metabolic factors did not appear to have a significant role in the development of muscle fatigue during voluntary exercise in mild MS.

Central Limitations

Central fatigue, resulting from the inability to sustain the central drive to spinal motoneurons, may also contribute to physiological fatigue. Central fatigue has been investigated in studies of sustained voluntary muscle contraction as well as double magnetic stimulation. Sheean and colleagues[20] studied whether physiological fatigue was peripheral or central in origin in 21 persons with MS. It was found that the MS patients developed greater fatigue during a 45 second maximal contraction of the adductor pollicis muscle compared to controls. Results of central motor conduction time indicated that it was central in origin. Ng and colleagues[21] also found central impairment in 16 MS patients when results of voluntary and electrically stimulated isometric contractions from the ankle dorsiflexor muscles were compared to controls. Maximal voluntary contraction (MVC) was 27% lower in persons with MS. There was also a decrease in central activation ratio (ratio of the maximal voluntary force produced to the total force produced) which indicated an inability to maximally activate the dorsiflexor muscles during a single maximal voluntary isometric contraction. The positive correlations found between CAR and maximal rate of voluntary force development with both MVC and specific strength, suggest that impaired central activation contributes to weakness in MS, but not fatigue.

Peripheral and central mechanisms appear to play a role in the pathogenesis of muscle fatigue in MS. Peripheral changes in muscle performance appear to be related to disuse or de-conditioning whereas muscle fatigue is likely induced by impaired central activation rather than peripheral mechanisms[22].

Cardiac Dysautonomia

The autonomic nervous system (ANS) is responsible for increasing heart rate (HR), maintaining blood pressure (BP), and regulating peripheral circulation and body temperature. Abnormalities in HR and BP are common in approximately 30% of people with MS[23,24] and the disease severity appears to correlate with the decrease in cardiovascular responses[25]. The inability of the HR to increase with exercise is known as chronotropic incompetence and has been shown to increase the risk of mortality in certain individuals. BP and HR abnormalities have been found in response to exercise in MS patients compared to controls[26,27]. It has been found that persons with MS who performed isometric hand grip exercise at 30% of maximal voluntary contraction to fatigue had significantly lower increases in systolic, diastolic, and mean arterial pressure than controls. However, the HR increased normally with exercise which may indicate an abnormal dissociation between HR and pressor response to static work in MS patients. Potential consequences of an inadequate pressor response to exercise may include the body's inability to supply working muscles and the brain with a sufficient blood supply. A reduction in heart rate variability (HRV) may also occur with cardiac dysautonomia in MS patients and may affect the individuals aerobic exercise performance. A high HRV is essential for the body to adapt to changes in the environment.

Visual Sensory Abnormalities

The disease process of MS can affect almost any portion of the visual sensory system including the retina, optic nerve, chiasm, postchiasmal pathways, and the visual sensory cortices and their pathways. Symptoms of visual sensory abnormalities may include difficulties seeing in low light, colour desaturation, sense of disorientation with motion, and loss of depth perception.

Uhthoff's symptom is a visual sensory abnormality that has been associated with an increase in body temperature, for example due to exercise. It is characterized by a transient desaturation of color vision which occurs in response to the increase in body temperature. The symptoms generally last only minutes, but may persist for hours. It is thought that the elevated temperature causes a decrease in axonal conduction in partially or completely demyelinated fibers[28,29]. Elevations in temperature as little as 0.5˚C can produce reversible conduction block in demyelinated fibers[30]. However, reducing body temperature by ingesting cold beverages, taking cool showers, or using cooling devices can improve conduction, thereby, improving symptoms[31]. Identical symptoms may occur in cold conditions as well and is known as "inverse" Uhthoff's symptom. Uhthoff's symptom in addition to other potential disturbances of the visual sensory system should be taken into consideration when persons with MS participate in exercise. Although there is no evidence to suggest that the occurrence of symptoms make MS worse, one must be aware that these symptoms may impair the ability of individuals to move or function sufficiently to protect themselves especially during exercise.

Functional limitations of MS

Many symptoms of MS can affect mobility and, therefore, participation in exercise. Symptoms that may cause problems include spasticity, tremor, ataxia, and foot drop. Most of these symptoms have the potential to affect balance and coordination as well.

Spasticity

Spasticity is a 'motor disorder characterised by a velocity-dependent increase in tonic stretch reflexes that results from abnormal intra-spinal processing of primary afferent input[32]. It generally affects specific muscle groups that are responsible for maintaining upright posture[9] (i.e., gastrocnemius, iliopsoas, hamstrings, and muscles of anterior trunk). Tightness of the gastrocnemius may limit dorsiflexion and affect the ability to perform sitting to standing actions, balance, and gait[33]. A shortened stride length can result from tight iliopsoas muscles which limits hip extension and the ability to have a trailing leg during walking. Tight iliopsoas muscles may also contribute to forward trunk lean affecting posture and balance. Tight hamstrings can also affect stride length by limiting leg extension. The ability to perform tasks that require one to lean forward are also affected. Tightness in the muscles of the anterior truck such as the pecs, intercostals, or rectus abdominus limits trunk extension, rib elevation, shoulder flexion, and external rotation. This affects the ability to maintain an erect posture, decreases pulmonary function, and affects the ability to perform tasks above the head. Spasticity of muscles may be minimal and actually assist with standing or pivoting by providing stiffness in the muscles, but it may also be painful and interfere with activities of daily living (ADLs). Contractures, resulting from spasticity, decreased range of motion (ROM) and potentially lead to a loss of function and an increase in disability. They are difficult to treat once they occur and should be prevented in the early stages of the disease to preserve functional mobility.

Tremor/Ataxia

Demyelination in the cerebellum and its pathways can cause tremors such as an intention tremor or ataxia[34]. Intention tremor is coarse trembling and is most noticeable when performing fine motor, skills such as pushing a button. Ataxia involves gross motor activities such as standing and walking. Tremors can affect any muscle group and ADL such as walking, self-care, sitting balance, and head control. Walking may become difficult because of poor balance and the individual compensates by placing the feet further apart. Tremors may affect participation in exercise because of their effects on balance and coordination. Tremor and ataxia may decrease overall endurance during exercise and increase MS fatigue because of the increase in energy consumption.

Balance/Coordination

Balance and coordination are controlled by the proprioceptive, visual, and vestibular systems along with the generation of motor outputs to coordinate movements of the limbs, trunk, and head in response to external stimuli or to perform voluntary movements. Significant attention and cognitive efforts are required to maintain balance and coordination in MS which occurs automatically in healthy individuals[35]. The combination of increased cognitive efforts, imbalance and incoordination may place a person at increased risk of falls and needs to be considered in relation to exercise participation. Muscle weakness, paralysis, and fatigue can also lead to poor balance and coordination as is seen with foot drop, for example. Weakness or paralysis of the anterior muscles of the lower leg can cause individuals to drag their toe rather than lift it or lift the advancing foot high so that the toes clear the ground known as a ‘steppage gait.’ The toe touching the ground before the heel may cause the individual to trip or lose balance.

Demonstrated Benefits of Exercise

Exercise has no effect on the prognosis or progression of MS, but individuals with MS, particularly mild to moderate disease can obtain similar health benefits from being active as healthy individuals. Persons should be encouraged to maintain or improve cardiorespiratory and muscular fitness early in the disease to offset decreases in functional reserve that generally occur with increasing disability and loss of function as the disease progresses[36]. The effects of exercise on the most common MS symptoms are reviewed.

Physiological

Aerobic Fitness

Aerobic fitness is the ability of the body to transport and use oxygen, relying on the coordination of the cardiac and pulmonary systems. It can be affected by age, gender, regular exercise, bed rest, medications and illness. A high level of aerobic fitness has been associated with lower mortality rates from cardiovascular disease (CVD)[37].

Physical fitness has been shown to improve in MS patients who engage in exercise. Bjarnadottir, and colleagues[38] assessed the effects of an aerobic and strength exercise on physical fitness with an EDSS < 4. The exercise group followed the American College of Sports Medicine's (ACSM) guidelines which included exercise 3 times per week for 20 – 60 minutes at 40 – 50% of VO max for 5 weeks. Intensity was increased after the first 2 weeks. Upon completion of the study, the mean change in VO max was 4.54 mL/kg/min with a mean change in anaerobic threshold of 0.32 L/min. Mostert and Kesselring found similar increasing in 26 patients with MS (12% increase in VO max after three to four weeks).

Muscular Fitness

Muscular fitness is characterized by muscular strength, endurance, and flexibility and plays an important role in the overall physical fitness and health of the individual. A decrease in muscle mass that normally occurs with age is associated with many debilitating conditions such as weakness, poor balance, and increased risk of falls[40].

Muscle fiber type in MS (shift to fast twitch to type II fibres) is consistent with disuse atrophy which may decrease the ability to perform daily activities leading to further disability. Although little research has been conducted on strength training in MS, work that has been completed has shown positive results. De Bolt and McCubbin[41] investigated the efficacy of an 8-week home-based resistance training program in improving balance, power, and mobility in adults with MS. Each person completed 25 – 30 minutes of functional strength training exercises (chair raises, forward lunge, step-ups, heel-toe raises, leg curls) 3 times a week. A periodization method of strength training was used to increase the intensity of the program. Upon completion of the program, there were significant improvements in leg extensor power, but measures of balance and mobility did not change. There were no increases in MS symptoms and there was a good adherence levels to the 8-week program. More recently, Taylor and associates[42] assessed the effects of a 10 week progressive resistance exercise (PRE) program on muscle strength and endurance, walking speed, a 2-minute walk test and a timed stair test in 9 individuals with mild to moderate MS. Individuals performed 10 – 12 repetitions twice a week for the major muscle groups of the upper and lower body. Significant improvements were found in arm strength, leg endurance, walking speed, and a trend in increased distance in the 2-minute walk test. The PRE program also appeared to reduce the impact of MS in physical function in day-to-day life as measured with the physical impact scale (clumsiness, grip, balance, transportation use, and limitations in social and leisure activities) of the MS impact scale (MSIS-29). No incidences of increased lassitude, muscle fatigue, or symptom exacerbation were reported after the PRE program.

Pulmonary Function

There is a decrease in both strength and endurance of ventilatory muscles in persons with advanced MS and even in those with minimal to moderate MS due to motor deficits[43,44,45].As the disease advances, there is progressive weakening of the ventilatory muscles as is seen in the muscles of the extremities and is partially due to deconditioning[46,47]. Values for maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) in persons with advanced MS range from 27-74% and 18-51% of predicted values, respectively[48,49]. Persons with minimal or moderate disability have been found to have MIP and MEP values ranging from 50-77% and 34-60% of predicted values, respectively[44].

Resistive ventilatory muscle training has shown to be beneficial in persons with mild to severe MS. Smeltzer, Lavietes, and Cook[50] demonstrated a significant increase in MEP after 12 weeks of expiratory muscle training which included 3 sets of 10 repetitions twice a day. Gosselink and collegues[43] found that 3 sets of 15 repetitions twice daily for 12 weeks was sufficient to increase MEP and significantly increase MIP. Chiara and associates[47] found that 4 sets of 6 repetitions once a day, 5 days a week increased MEP significantly, but no change in MIP after 8 weeks.

Studies with inspiratory muscle training have also shown positive results. Klefbeck and Nedjad[48] found a significant increase in MIP and MEP after 10 weeks of training doing 3 sets of 10 reps once a day. Weekly progression of inspiratory muscle training was based on rate of perceived exertion (RPE) and MIP beginning at 40-60% MIP. Fry-Welch and colleagues[51] demonstrated that 3 sets of 15 reps once a day over 10 weeks increased MIP, 6-minute walk test time and balance significantly. Inspiratory muscle training started at 30% MIP and progressed weekly based on RPE and symptoms.

It is recommended that pulmonary function be assessed in all persons with MS and that expiratory and inspiratory training be included in rehabilitation programs when respiratory function is decreased.

Immune Function

Multiple Sclerosis is an inflammatory and demyelinating disease of the CNS and is characterized by varying degrees of inflammation. Although the etiology of MS is not fully understood, it is currently thought that a T cell-mediated autoimmune process with a dysregulation of the balance between proinflammatory T helper 1 (Th-1) and anti-inflammatory Th-2 cytokines are associated with MS[52]. Proinflammatory Th-1 cells secrete interleukin (IL)-2 tumour necrosis factor (TNF)-α, interferon (IFN)-γ, and c-reactive protein (CRP) whereas anti-inflammatory Th-2 cells secrete IL-4, IL-5, IL-10, and IL-13[53]. Cytokines are protein messengers that regulate immune responses which are secreted by macrophages, monocytes, lymphocytes, and other cell types. Changes in the concentrations of certain cytokines, in particular IFN-γ and TNF-α, have been associated with changes in disease status[54].

Studies on immune function and exercise in healthy compared to sedentary individuals have demonstrated a "J-shaped" relationship where regular, moderate exercise reduces the risk of infection and prolonged, high intensity exercise increases the risk of infection[55]. Exercise has been shown to modulate immune function through local and systemic cytokine production[56,57]. Interleukin-6 produced by and released from contracting skeletal muscle during exercise has been shown to stimulate anti-inflammatory cytokines such as IL-1 receptor antagonist and IL-10 and inhibit the production pro-inflammatory TNF-α[58].

Some researchers speculate that if exercise can assist in reducing pro-inflammatory cytokines and increase anti-inflammatory cytokines it may be beneficial to the underlying disease course in MS. It has been found that cytokine patterns following 8 weeks of aerobic exercise showed a shift towards TH-1 cytokines as well as an increase in IFN-γ in persons with MS. White, Castellano, and McCoy[59] found significant decreases in proinflammatory cytokine concentrations (IFN-γ, CRP; trend towards a reduction in TNF-α), but no change in IL-2 concentrations. There were also reduced plasma concentrations of IL-4 and IL-10. It was suggested progressive resistance training may have an impact on cytokine concentrations and, in theory, may have an impact on overall immune function and disease course, but state that results need to be confirmed in studies with larger statistical power. Schulz and colleagues[60] assessed if 8 weeks of interval training would lower inflammatory cytokine activity and catecholamine responses in 28 MS patients. Results indicated that interval training performed twice a week for 30 minutes at 75% of maximal watts on ergometry did not show higher levels of the immune parameter, IL-6, in MS patients. There were no changes in endocrine (cortisol, adrendocortico-releasing hormone, epinephrine, norepinephrine) or neurotrophic (brain-derived neurotrophic factor, nerve growth factor) parameters either. With few studies conducted in this area, there is inconclusive evidence on the effects of exercise on immune function in MS. Future research in this area needs to include larger sample sizes with greater statistical power[61].

Much of the research on growth factors, immune function and exercise has not been done specifically in MS. There exists a strong theoretical support for growth factors playing a role in the treatment of MS. The various actions of growth factors may provide valuable treatment possibilities, specifically within the areas of nerve-regenerating effects, nerve-protecting effects and anti-inflammatory effects[62]. Nerve-generating effects may improve nerve function after injury and, if needed, facilitate the development of new pathways. Nerve-protecting effects may prevent nerve injury by making nerves less vulnerable to the disease process of MS. Anti-inflammatory effects may also prevent nerve injury by decreasing immune-system attack on the nervous system. Although the studies of growth factors and exercise in MS are limited, this area of investigation provides clear directions for future research.

Psychological

Depression

Depression is common in individuals with chronic medical conditions and has been found to occur more often in individuals with MS than with other chronic conditions[63]. At least 50% of persons with MS live with depression[64,65] which may result from disease activity such as the onset of exacerbations, neuropathologic changes in areas of the brain, neuroendocrine changes, reaction to loss, and side effects of medication[66]. Individuals living with depression tend to be less physically active and have less physical work capacity compared to the general population[67].

Numerous studies have found positive support for a relationship between exercise and depression in the general population as well as those with chronic diseases[68]. A review by Scully and colleagues[69] found that exercise had a positive influence on depression. Both aerobic and non-aerobic forms of exercise such as walking, jogging, cycling, light circuit training and weight training have been shown to be beneficial. Individuals that maintained their exercise routine over several months tended to have the most positive effects.

For persons with MS, only a few studies have assessed the influence of exercise on depression. Petejan and colleagues[70] showed that after 15 weeks of an aerobic training program (3 sessions per week, 40 minutes each) on a Schwinn Airdyne bike, MS patients experienced less depression and anxiety when the Profile of Mood States (POMS) was used. The POMS is a generic instrument used to measure distinct affective states. Patti and associates[71] used the Beck Depression Inventory (BDI) to assess depression in MS patients involved in 6 weeks of an outpatient rehabilitation program as well as 6 additional weeks of a home program performed 6 days a week. The BDI has been widely used in neurological diseases. There were significant improvements in depression ($p<0.001$) at the end of 12 weeks of exercise in individuals with MS. Wiles and colleagues[72] found a significant improvement in mood and reductions in anxiety and depression measured with the Hospital Anxiety and Depression Scale (HADS) with an 8 week outpatient and home-based physiotherapy program performed twice a week. The outpatient program focused on specific facilitation techniques whereas the home-based program focused on specific functional activities.

Although there appears to be inconsistent findings on the benefits of exercise in MS, psychological well-being still needs to be addressed in individuals with MS as it can influence initiation and maintenance of an exercise program as well as the individuals QoL. Exercise is used as part of the treatment plan for persons with major depression and other chronic diseases and it may be that persons with MS may also have improvements in their psychological functioning with participation.

Quality of Life

Quality of life (QoL) and health-related quality of life (HRQoL) are often used interchangeably in health research. Quality of life is defined by the World Health Organization as a person's "perception of their position in life in the context of that person's culture and value system and in relation to his/her goals, standards, and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs, and their relationship to salient features of their environment." MS has been found to severely affect a person's QoL[73,74,75]. The clinical course of the disease[76],disease duration[77], cognitive function[78], and depression and anxiety[79,80] may contribute to a decrease in QoL. Health-related quality of life is also considered to be multidimensional and generally includes measures of physical, social, and role functioning as well as mental health and general health perception. Other important HRQoL domains to be considered are vitality, pain, and cognitive function[81]. However, HRQoL is concerned more specifically with aspects of life which can be affected by health care and their measures may give a better indication as to the specific areas of life that are most affected by a chronic disease.

A review by Mitchell and colleagues[82] discusses QoL and the generic and specific instruments used in the assessment of MS. Generic instruments measure broadly defined HRQoL issues and can be applied to different diseases. They can also be used to make comparisons between the degree of deficits in different diseases. Generic instruments include the Short Form-36, the Sickness impact profile (SIP), functional status questionnaire (FSQ), and the Nottingham health profile. The SF-36 appears to be the most widely used, but has structural limitations such as floor and ceiling effects which vary according to the severity of the disease being examined.

Physical activity has been found to be associated with an improvement in QoL in persons with chronic diseases[83,84]. Several studies have found physical activity to be associated with an improvement in QoL in individuals with MS. Stuifbergen, Blozis, Harrison and Becker[85] assessed the interrelations between functional limitations, exercise behaviours, and QoL over a 5-year period in 611 persons with MS. They found a positive correlation between exercise behaviours and QoL scores at time 1 suggesting that higher exercise levels were associated with a higher QoL at that time. An increasing rate of change in functional limitations over time was associated with decreases in exercise behaviour and QoL over the 5-year study period. Sutherland, Andersen, and Stoov[86] showed that 10-weeks of water aerobics, 3 times per week resulted in improvements in physical, social, and mental components of QoL in 22 individuals with MS. Health-related QoL was assessed with the MSQOL-54. The MSQOL-54 is a disease-specific instrument to measure QoL in MS patients and is based on the SF-36 QoL instrument. Schulz and colleagues found that an 8 week tailored aerobic fitness intervention enhanced disease specific QoL as measured by the HAQUAMS. The HAQUAMS consists of 38 items reflecting the major dimensions of HRQoL in MS which included fatigue/thinking, mobility lower limb, mobility upper limb, social function, and mood. They did not find any improvements on the generic POMS or SF-36 scales.

Romberg and colleagues did not find improvements in QoL measured with the MSQOL-54 with long-term exercise. The exercise program consisted of 26 weeks of resistance and aerobic exercise with the first 3 weeks completed in an inpatient setting and the remainder completed at home. The authors discuss that the lack of improvement in HRQoL may be the result of a different intervention or the lack of social support from other exercisers when exercising at home. This is consistent with findings from other studies that have found that social support is moderately and independently associated with QoL in individuals with MS[87].

The differences in findings in QoL and exercise in MS research may be attributed to how QoL is defined and measured. Researchers appear to use generic measures of QoL to assess HRQoL when more specific measures may have increased sensitivity to changes in HRQoL.

Functional

Mobility

Difficulty walking is one of the most common challenges for individuals with MS and can be affected by spasticity, tremor, muscle weakness, fatigue, and poor balance and coordination. A decrease in mobility often leads to a decrease in participation in exercise leading to muscle weakness and further impairments in mobility. However, research has shown that exercise is beneficial in maintaining an individual’s independence through increased mobility.

In a randomized crossover trial, Wiles and colleagues[88] assessed the efficacy of physiotherapy in improving mobility in chronic MS. Patients either received physiotherapy for 2 sessions of 45 minutes each week for 8 weeks either at home or at the clinic or received no therapy at all. Main outcome measures were Rivermead mobility index, gait impairments, arm function, mood, and subjective patient and caregiver ratings. Results indicated that there was a significant improvement in the Rivermead mobility index ($p<0.001$) in both group receiving physiotherapy compared to the control group. There were also improvements in mood and subjective well-being. Armutlu, Karabudak, and Nurlu[89] studied the effects of a 4 week neuromuscular rehabilitation program and Johnson Pressure

Splints in patients who had ataxic MS. Ataxia of the lower limbs can affect mobility and activities of daily living. Neuromuscular rehabilitation consisted of proprioceptive neuromuscular facilitation techniques combined with balance training to enhance postural stability and balance reactions. Johnson pressure splints were applied to both lower extremities before the exercise session. Significant differences were found in sensation, anterior balance, gait parameters, and EDSS ($p<0.05$) in pre-and post treatment data. There were also significant differences in pendular movements and dysdiadakokinesia ($p<0.05$). The study group also had improvements in cortical onset-P37 peak amplitude of somatosensory evoked potentials in the right limbs. Non-equilibrium coordination tests did not show a significant improvement which the authors attribute to limb ataxia being potentially more resistant to physical therapy approaches.

Spasticity

Treatment for spasticity that has shown some benefits have included rehabilitation exercises, such as ROM, stretching, and strengthening exercises, along with neuromuscular blockade, or rehabilitation exercises alone. Solari and colleagues[90] assessed the effectiveness of an inpatient rehabilitation program on impairment, disability, and QoL of 50 MS patients. Results showed that there were significant improvements in disability as indicated by improvements in two or more steps of the motor domains of the Functional Independence Measure at 3 and 9 weeks. There were no changes in impairment in either group as measured be the EDSS. Freeman and associates found that there were significant improvements in MS patients' level of disability compared to a control group after 6 weeks of a multidisciplinary inpatient rehabilitation program[91]. The level of impairment of both groups did not improve.

Rosche and colleagues assessed whether antispastic treatment with a motorized exercise-cycle could be detected by F-wave-amplitude parameters[92]. F-wave amplitudes have been used to demonstrate changes of motor neuron excitability and have been shown to be increased in those with spasticity. This study found a significant decrease in F-wave amplitude, mean F-wave/M-response ratio, and maximum F-wave/M-response ratio EMG recordings of thirty one patients with MS who cycled at 40 revolutions per minute for 30-minutes.This decrease indicates a reduction in motorneuron excitability. A similar study by Motl, Snook, and Hinkle found that 20 minutes of unloaded leg cycling reduced soleus H-reflex and scores on the Modified Ashworth Scale in individuals with MS who were currently taking anti-spastic medications[93].

Fatigue

Fatigue is often the most common and debilitating symptom for individuals with MS[94] and has been reported by approximately 65% of patients[95,96]. Fatigue has been described as an overwhelming sense of tiredness, lack of energy or feeling of exhaustion, or as muscle fatigue without exercise[97]. Fatigue may be separated into primary and secondary fatigue. Primary fatigue relates to the disease itself and may have CNS, neuroendocrinological, immunological, or physiological origins. Secondary fatigue is generally a result of the consequences of MS and may be related to sleep disorders, reduced physical activity, psychological factors, depression, or other factors such as age, gender, disease duration or type of MS. Changes in gait due to disease can also increase the energy required to perform normal daily activities and therefore, fatigue.

Several studies have demonstrated an improvement in fatigue with exercise in MS patients. Recently, Newman and colleagues[98] examined the effects of treadmill walking on walking effort on individuals with mild to moderate MS. After training, oxygen consumption was found to be decreased at rest, comfortable walking speed increased, and 10 meter and walking endurance increased. Oxygen consumption also decreased with an increase in comfortable walking speed. Reported fatigue levels remained unchanged. These findings indicate that aerobic training on a treadmill may alter a motor skill and reduce the effort of walking and potentially reduce the effort and fatigue experienced by some individuals with MS. Petajan and colleagues in a study found significant increases in VO2 max and work capacity in person with MS who exercise. There were also significant increases in mobility, physical functioning, emotionality, and psychological dimensions, as well as improvements in symptomatic fatigue. Oken and colleagues[99] compared 6 months of aerobic exercise with yoga and a wait list control group in individuals with MS. The yoga group participated in a 90-minute class once a week while the exercise group completed stationary cycling combined with stretching exercises once a week. Both groups were encouraged to continue with their exercises at home. The outcomes of interest were fatigue, cognitive function, mood and QoL. Results of this study showed that participants in the yoga and exercise group had significant improvements in general fatigue and in energy and fatigue (vitality). The yoga and exercise interventions did not bring about changes in alertness or attention or any other measure of cognitive function. It was suggested that the improvements in fatigue are more indicative of physical rather than mental fatigue. Rosava and colleagues (2006) found that 3 different training programs (neurophysiologically based physiotherapy; aerobic training; and combined aerobic training and neurophysiologically based physiotherapy) had a positive impact on fatigue. The neurophysiologically based physiotherapy had an impact on the regulation of depression, impairment, disability, handicap, and QoL. Spiroergometric and spirometric parameters were most improved with the aerobic training group.

However, a Cochrane review of randomized controlled exercise trials, completed by Rietberg, Brooks, Uitdehaag, and Kwakkel[100] showed no evidence for improvements in fatigue measured with the Fatigue Severity Scale when exercise therapy was compared to no exercise therapy. Also, best evidence synthesis revealed that there was no evidence that exercise therapy was more effective on fatigue than a control exercise intervention for MS patients[5,39,90]. The authors do discuss the potential limitations of the study including participants and type of exercise program. Studies included diverse participant characteristics which included a large range of disability (EDSS 1 to 6.5), all ages of both females and males, and all types of MS. This makes it difficult to determine the effectiveness of exercise therapy for different types of MS and levels of disability as well as how exercise therapy may affect male and females differently. Also, the review did not control for the frequency, intensity, or duration of exercise therapy which may be important in modifying treatment effects. If types of exercise programs, level of disability, and type of MS were analyzed separately, findings for the effects of exercise therapy on fatigue may be different.

Improvements in fatigue through exercise may be brought about by an increase in muscle strength as well as gait training which may decrease the effort of activities and fatigue.

Reducing Risk of Co-morbidities

A physically inactive lifestyle has been shown to increase the risk of CVD, diabetes, and some types of cancers. Persons with MS are more sedentary than other individuals with other chronic conditions and should, therefore, be encouraged to add daily physical activity to obtain the same physiological benefits from physical activity as healthy individuals.

Physical Activity and Cardiovascular Diseases

Research has shown that physical activity may reduce the incidence of coronary heart disease (CHD) by improving other risk factors known to be associated with CHD such as decreasing BP and hypercholesterolemia and increasing high-density lipoprotein[101,102]. Results of a meta-analysis by Berlin and Colditz demonstrated an association between physical inactivity and an increased risk of CHD in a dose-response fashion[103]. The association was generally stronger when the high activity group in a study was compared to a sedentary rather than a moderate activity group. A more recent review by Kohl also demonstrated that CVD incidence and mortality, specifically ischemic heart disease, are causally related to physical activity in an inverse, dose-response manner. Studies analyzed together demonstrated a lower risk of CVD with subsequent higher levels of physical activity[104]. Sundquist, Qvist, Johnasson, and Sundquist studied the long-term effect of leisure-time physical activity on incidence of CHD among men and women[105]. Results indicated that when leisure-time physical activity increased, incidence rates of CHD decreased. After adjusting for sex, age, socioeconomic status, smoking, and body mass index, men and women who were physically active at least twice a week had a significant reduction in the risk of developing CHD. A review by Fagard assessing the effects of physical activity on the risk factor, hypertension, found that the overall net change in BP averaged -3.4/-2.4 mm Hg in response to dynamic physical training[106]. Baseline BP was an important determinant of the BP response with the hypertensive subjects having a more pronounced BP lowering effect than normotensive subjects. Several epidemiological studies have also identified that a low level of physical activity in both men and women was associated with a higher incidence of developing hypertension[107]. In a sample of 123 women with MS, Slawta and colleagues[108] found that women who participated in low-to moderate leisure time physical activity had significantly lower waist circumferences, lower triglyceride levels, and lower glucose levels than the less active women. This study indicates that the level of activity that the women were able to achieve may be a sufficient amount to decrease their risk of CVD.

Physical Activity and Type II Diabetes

Physical inactivity is one of the many factors contributing to the incidence of type II diabetes. There have been several meta-analysis and reviews evaluating the relationship between physical activity and the incidence of type II diabetes[109]. Most studies have found physical activity to be beneficial for the prevention of diabetes, the management of impaired glucose tolerance[110] and for improving glucose control in diabetics[111]. In a meta-analysis of 10 prospective studies, Jeon and colleagues[112] found that individuals who engaged in regular physical activity of moderate intensity had an approximate 30% lower risk of type II diabetes compared to sedentary individuals. There was a significant inverse relationship between physical activity and risk of type II diabetes in both men and women and this relationship persisted after adjustment for BMI. In individuals at higher risk for diabetes, the addition of moderate physical activity for 150 minutes a week and adhering to a healthy low calorie, low fat diet was found to be more effective at preventing or delaying type II diabetes in persons with elevated fasting and post-load plasma glucose than metformin[113]. However, the evidence that physical activity independent of dietary or weight loss changes in the prevention of type II diabetes in high-risk individuals was found to be equivocal in a recent systematic review[114]. There appears to be a dose response relationship between physical activity and the risk of developing type

II diabetes, but the same pattern has not been found to exist between physical activity and improved metabolic control in type II diabetes.

Physical Activity and Cancer

Evidence shows that physical activity is most protective against colon and breast cancers and overall cancer risk. Data from combined studies has shown that there is a lower risk of colon cancer among men and women who are more physically active[115]. When comparing the most active to the least active among studies, the median relative risk was found to be 0.7 in men and 0.6 for women indicating a 30-40% risk reduction. A dose response relationship has also been found between physical activity and the risk of colon cancer with higher levels of physical activity decreasing the risk of colon cancer. It is thought that physical activity may help decrease the transit time of fecal matter through the colon reducing the exposure of the intestine wall to cacinogens. What is less clear, however, is the amount, intensity and duration of physical activity needed to decrease the risk of colon cancer. Studies examining these variables have found that men who expended ≥ 1000 kcal/week through physical activity had half the rates of colon cancer compared to the less active individuals[116]. Women who engaged in an average of 4 hours/week of moderate intensity physical activity had a 33% reduction in colon cancer rates compared to those expending <2 MET hours/week. A further risk reduction of 46% was seen in women participating in approximately 5 hours/week of moderate intensity physical activity[117].

With regards to breast cancer, the data demonstrates a lower rate of breast cancer among active women. When the most active women are compared to the least active women over all of the studies, studies, the median relative risk is 0.8 and among postmenopausal women it is 0.7 indicating a 20-30% reduction in breast cancer risk. The data also support a dose-response relationship between physical activity and breast cancer. Again, it is unclear as to how much activity is needed to decrease the risk, but some studies have shown that women who spend more than 4 hours/week engaging in moderate or vigorous physical activity had 15-37% lower breast cancer rates compared to less active women[118,119,120]. The potential biological mechanism by which physical activity may decrease breast cancer risk include the alteration of menstrual cycle patterns and exposure to sex hormones, enhancement of immune function, changes in body weight, and changes in insulin like growth factors[121].

There has been extensive research on the role of physical activity in the prevention of CHD, certain cancers, and diabetes with most studies demonstrating that regular physical activity is associated with a reduced risk of these chronic diseases in both men and women. These findings would clearly extend to persons with MS.

Exercise Testing and Prescription

Exercise Testing

Assessment of a baseline fitness level is important in order to design a program of regular exercise. Because symptoms such as lower extremity sensory loss, foot drop, balance, spasticity, and tremor may affect ambulation, modifications to exercise testing equipment may need to be made to provide a safe exercise testing and training environment[122]. Testing on a treadmill is often impractical therefore, upright or recumbent leg cycle ergometry is the preferred modality for exercise testing[123]. When a combination of arm and leg ergometry is used a more accurate test result may be achieved because of the increased recruitment of muscle mass. Research has shown that most individuals are able to reach 85% - 90% of their age-predicted maximum HR and bicycle ergometer testing HRs have been found to be as high as 90 – 96% of expected age predicted maximum. However, there is > 15% error when using regression equations to predict peak VO_2 from submaximal tests in this population. Cardiac dysautonomia or severe muscle paresis in some patients with MS may account for this error[124].

To ensure foot stability and counteract spasticity, tremor, and weakness in the lower extremities, toe clips and heel straps should be used with leg ergometers. It may be common for individuals who undergo maximal aerobic power testing to experience post- exercise fatigue, but an exacerbation of current MS symptoms or provocation of new symptoms has not been found in the 100 tests that have been performed.

Because of the diverse individual abilities and a general lack of research in this area, there are no standard protocols or absolute standards for comparison among individuals with MS. Some recommendations for exercise testing in this population by ACSM[125] include:

- Use of continuous or discontinuous protocol of three to five minute stages.
- Begin with a warm-up of unloaded pedaling or cranking on the leg or arm ergometer.
- Increase the work rate for each stage by approximately 12-25 watts and 8-12 watts for legs and arms
- Monitor HR and BP.
- Terminate the test with volitional fatigue, achievement of maximal HR, or decrease/plateau in VO2 with increasing work rate.

Exercise Prescription

The primary goal of exercise prescription in this population should focus on maintenance of, and when possible, an increase in, physical function, joint flexibility, aerobic endurance, and muscular strength and endurance. It is essential that exercise prescriptions for persons with MS are very individualized due to their varied symptoms. The following paragraphs will discuss the current recommended guidelines by the American College of Sports Medicine (ACSM) for the prescription of endurance, strength, and flexibility training.

Endurance Training

When selecting the mode for endurance training, the individual's symptoms need to be taken into consideration as this will determine which type of exercise will be most appropriate. Petajan and White have suggested using a pyramid (Fig. 1) to classify physical activity based on the individuals' functional level with activities at the base appropriate for individuals with severe paresis and activities at the top for those with little or no motor deficits. Activities at the base of the pyramid include ADL. Assistive devices may allow the individual to complete ADLs with energy remaining to participate in more meaningful activities. The second level of the pyramid includes active leisure activities and built-in "inefficiencies" meaning adding activity to the day by doing things such as parking the car further away from the store, for example. The third level is active recreation which includes activities like house and yard work, gardening, walking, or cycling. These activities have been shown to provide enough of a stimulus to preserve function and independence. Lastly, individuals who have adequate functional capacities and desire can be prescribed a structured cardiorespiratory exercise program. ACSM recommends that structured exercises such as cycling; walking; and low-impact, chair, and water aerobics be performed three times per week for at least 30 minutes. The 30 minutes can be accumulated throughout the day such as doing three 10- minute or two 15-minute sessions. This method is ideal for individuals who have a low level of fitness or who are easily fatigued. This amount of activity allows individuals to complete ADL such as self care, cooking, or ambulating around the house. It is recommended that the exercise HR be maintained at about 60% to 75% of age-predicted maximum HR. More severely impaired or elderly individuals may need to exercise at a lower intensity such as 50% to 65% of maximum HR until their fitness level improves. Individuals who are symptom free should try to achieve an 11-14 rating on the Borg scale indicating a moderate intensity. It is recommended that a perceptual scale be used to monitor intensity since MS symptoms vary from day to day. Adjustments to work rates should be based on daily symptoms and energy levels.

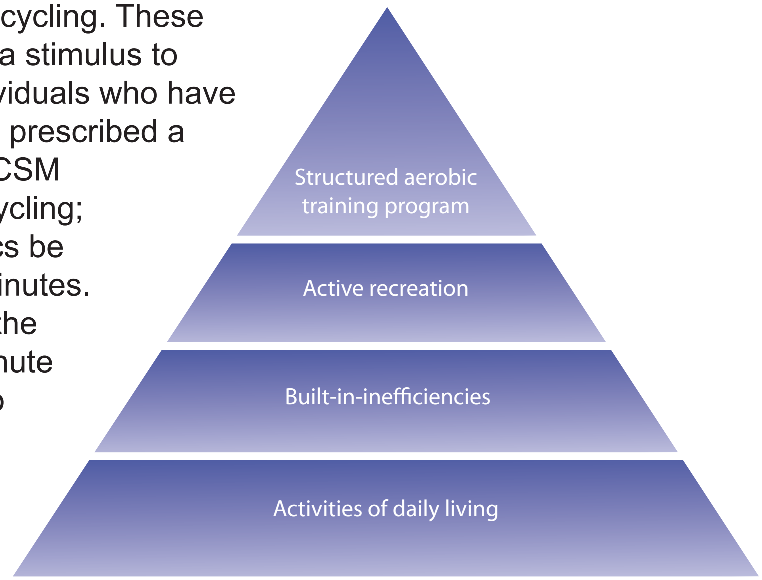


Fig 1. Physical Activity Pyramid

Strength Training

Strength training is important to combat the effects of muscle weakness on activities of daily living (ADL) in persons with MS[126]. Repetition of basic daily activities such as walking, rising from a chair, and climbing stairs results in muscle fatigue and individuals may limit activity leading to muscle atrophy and further muscle weakness.

ACSM recommends that baseline strength levels be assessed before the individual takes part in a strength training program. Traditional methods of strength assessment such as manual muscle testing, one-repetition maximum, isokinetic dynamometry, or functional strength assessment are all appropriate methods. Any modifications done to the strength test to accommodate spasticity or joint contracture need to be documented in order to have similar follow-up tests. Since muscle fatigue generally sets in after repeated movement, it is best to have the individual perform several repetitions in order to assess muscle endurance. These results will better assist in devising programs that will help individuals improve muscle endurance needed to perform daily activities. Functional tests such as sit-to-stand test, get-up-and-go test, or physical performance tests are often useful in determining the individuals' ability to accomplish ADL[127,128].

The pyramid (Fig. 2) by Petajan and White[129] can also be used when devising a strength training program according to the individuals' level of functioning. Individuals with severe paresis can start at the base of the pyramid which consists of passive ROM exercises which are discussed in the section on flexibility training. The second level includes active flexibility and resistive exercises for individuals with extremity weakness but some muscle function. If strength permits, bodyweight resistance exercises are suggested with the number of repetitions completed dependent on the level of fatigue. Exercises can be performed against gravity only, or with gravity eliminated. The third level includes specific muscle strengthening exercises that are adapted to the individuals' disability. This type of program is generally developed by a physiotherapist or exercise physiologist. Individuals should start with a few simple exercises that target specific areas of weakness. Exercises and length of sessions should be selected to accommodate MS-specific problems such as poor balance, coordination, and fatigue. Minimal equipment such as stretch bands or sand bags can be used so exercises can be performed in the home. Finally, for individuals with little or no motor deficits, multi-joint strength training exercises may be performed for the major muscle groups. This program can include 3 sets of 10 to 12 repetitions through a full ROM with individuals reaching moderate fatigue at the end of the third set. This type of program allows the individual to increase strength in opposing muscle groups and perform more complex movement patterns. Strength gains can be maintained through training one or two times per week once a plateau occurs, or if additional increases in strength are desired, the program needs to be adjusted to provide an overload.

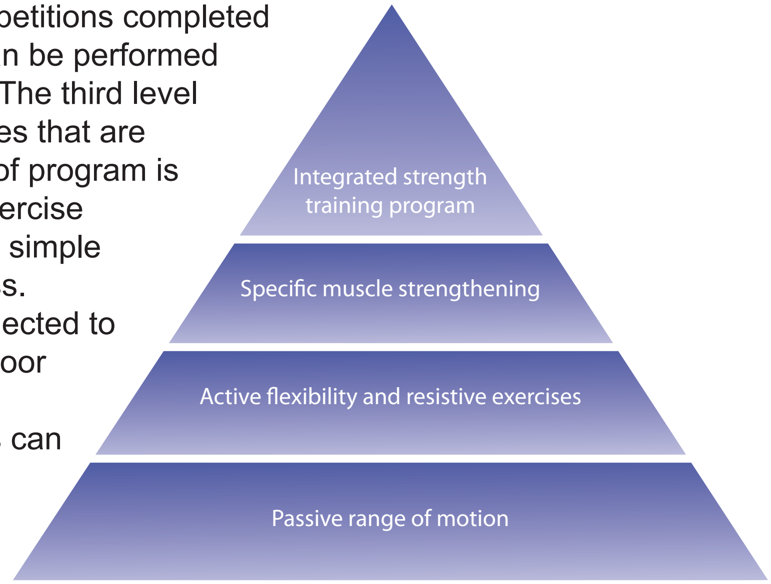


Fig 2. Muscular Fitness Program

Other recommendations by ACSM include:

- Optimizing strength in the unaffected muscle groups to allow for effective compensation and stabilization.
- Make exercises functional
- Allow adequate rest time between exercises
- Emphasize larger proximal muscle groups
- Focus on gentle stretching and ROM rather than strength exercises during exacerbations.
- Weight machines may allow for more controlled movement and postural stability in those with poor balance and coordination.

Flexibility Training

Tightness and contractures of the muscles can occur when the person spends prolonged periods of time in a seated position or lying in bed with his or her head elevated and a pillow under the knees. A thorough program of stretching is necessary to minimize muscle shortening that occurs from spasticity or prolonged bed rest. Passive and active stretching should be performed daily with a focus on the commonly shortened muscles and muscles that cross two joints[130].

ACSM recommends that individuals perform stretching exercises one to two times per day depending on the persons' level of activity and degree of spasticity. Most stretches should be held for 30 to 60 seconds and repeated three to five times. Persons with severe spasticity or contracture may require stretching ranging from 20 minutes to several hours. Dynamic splints or weights with stretches may be needed to induce plastic deformation of connective tissue.

Disability-Adapted Fitness Training

Exercise prescription should be based on a stage adapted approach where the level of exercise is adapted to the level of disability. This is outlined in the Table below.

Disability	Description	Training
None	•No fatigue •No thermosensitivity	Fully exertable, combined endurance and strengthening exercises, but in physiological dimensions, no extreme sports
Mild	•Fatiguability •Perhaps thermosensitivity •Minor balance disturbances	Controlled fitness training, perhaps pre-cooling, supervision to avoid overtraining, long-lasting efforts restricted
Moderate	•Restricted walking •Paresis •Lower limb spasticity •Ataxia •Balance problems	Training program adapted to the deficit, Nordic walking, home exercises, arm-leg ergometry, strengthening of indicated muscle groups, water exercises
Severe	•Loss of daily functions •Walking nearly impossible	Preservation of movements, stretching, focused strengthening, oriented to daily activities, yoga, active/passive training for limbs by motomed
In bed		Preservation of movements, predominately passive, breathing therapy

Adapted from Heesen et al., (2006). Physical exercise in multiple sclerosis: supportive care or putative disease – modifying treatment. Expert Review in Neurotherpaeutics, 6(3).

For further information on exercise testing and prescription, individuals are referred to ACSM's Resource Manual for Guidelines for Exercise Testing and Prescription and ACSM's Exercise Management for Persons with Chronic Diseases and Disabilities. Additional resources can also be obtained from the Multiple Sclerosis Society of Canada (www.mssociety.ca).

Special Considerations for Exercise

Although physical activity is beneficial for individuals with MS, there are several factors that may influence how the individual responds to exercise as well as the amount of improvement one will achieve with exercise. Special considerations are discussed below and are grouped into environmental, physiological, cognitive or functional considerations.

<table>
<tr><th></th><th>Environmental</th></tr>
<tr><td>Temperature</td><td>Increases in body temperature can cause a temporary worsening of symptoms. Several options exist for alleviating temperature increases which can occur with exercise.
1. Exercising in a cool environment such as an air-conditioned gym or in a swimming pool between 26.7 to 29.4 degrees Celsius may help eliminate some of the symptoms that occur[131].
2. Cooling garments such as headbands or vests, wearing light weight clothing, and drinking cold drinks may also help.
3. Surface cooling via water immersion before exercise can significantly reduce core temperature, as well as improve aerobic endurance, reduce sub-maximal exercise heart rate (HR), and reduce the perceived level of exertion[132].
The reduction in core temperature that occurs immediately after cooling persists for several hours, and is associated with significantly less perceived fatigue. Pre-cooling, coupled with exercising early in the day to take advantage of the lower circadian body temperature, might pose less physiological and psychological stress on the individual[133,134].</td></tr>
<tr><td>Hydration</td><td>Persons with MS may severely limit their daily intake of fluids due to bladder function difficulties. This can lead to chronic dehydration and general fatigue, both of which can be exaggerated during exercise. Dehydration also reduces circulating blood volume which may further increase fatigue. Adjustments in medication which help with bladder function, such as oxubutynin, may be needed, along with ensuring adequate fluid intake.</td></tr>
<tr><th></th><th>Physiological</th></tr>
<tr><td>Cardiac Dysautonomia</td><td>Because the ANS is affected in individuals with MS it is important to continually monitor HR, BP, and RPE, during exercise. Orthostatic hypotension may occur and symptoms are often described as dizziness, light headedness, or syncope when moving from a supine to a sitting or standing position. Hypotension may also occur after exercise or with exposure to a hot environment and individuals should be assessed for these symptoms after exercise.</td></tr>
<tr><td>Medications</td><td>Medications that may affect exercise tolerance or response need to be considered when prescribing exercise. Important that a complete history of medications is taken before exercise is prescribed. The following are a few of the medications that may affect the individual during exercise:
• Amantadine HCl (fatigue) may cause dizziness, peripheral vasodilation, and orthostatic hypotension
• Baclofen (spasticity) may cause tachycardia, bladder dysfunction, muscle weakness, and fatigue when taken in high doses.
• Tricyclic (antidepressants) may cause hypotension, tachycardia, tremor, dizziness, and abnormal gait.
• Selective serotonin reuptake inhibitors may cause hypotension and tachycardia.
• Prednisone (acute exacerbation of symptoms) may cause muscle weakness, loss of muscle mass, and hypertension</td></tr>
</table>

Bladder Dysfunction	Persons with MS may need to urinate frequently during exercise especially if certain exercises place pressure on the bladder. Additionally, accidental bladder voiding may occur during exercise due to the negative affects of MS on neurological function[135]. Individuals should make sure that the bladder is voided before exercise and intermittently during the exercise session, particularly if they are drinking fluids to prevent dehydration and overheating[136].
	Psychological
Cognitive	Many with MS will have some level of cognitive deficit which may, in turn, affect their ability to follow an exercise program. Deficits may occur with memory[137], abstract reasoning and problem solving[138], attention and concentration[139], and speed of information processing[140]. Individuals may require additional time for information processing as well as multiple forms of information presentation to ensure understanding of their exercise program. Written instructions of exercises may be required in addition to verbal cues[122].
Emotions	Emotional factors, such as depression and anxiety may affect motivation to engage in and adherence to an exercise program so constant reinforcement and counselling may be necessary for some persons.
	Functional
MS Exacerbation	Exercise programs need to be flexible in order to accommodate MS exacerbations. Modifications may be required when the individual resumes their activity because of residual neurological deficits from exacerbations. Depending on the severity of the exacerbation, light activity such as gentle stretching and ROM exercises are encouraged to avoid deconditioning. Individuals may present with new MS signs and symptoms during an exacerbation which may require corticosteroid therapy[36], in turn, potentially causing muscle weakness and decreased sweating further affecting ability to exercise.
Fatigue	Fatigue affects the time of day that is best to exercise. In general, fatigue from MS worsens later in the day, so it may be best to schedule exercise earlier in the day. Fatigue may also affect the results of motor testing and therefore evaluation of muscle strength[127]. Within an exercise regimen, a balance between rest and exercise is needed to avoid becoming overly fatigued. Also, resting for 10-15 minutes several times a day can be just as restorative as prolonged periods of rest which may include sleeping.
Balance and Coordination	Some symptoms of MS can lead to a loss of coordination and balance. Exercising while fatigued may lead to poor coordination and balance, and may compromise personal safety (i.e., individuals with ataxia, spasticity, sensory deficits, and foot drop may find it difficult to walk on a treadmill without handrails). Several simple considerations may help alleviate these problems during exercise: 1. Ankle and foot orthotics can to correct foot drop and prevent tripping. 2. Mechanically synchronizing combined arm/leg ergometers help with coordination. 3. Exercises such as stationary cycling, rowing, aquatics or therapeutic standing[141] can be selected and supervised in individuals with these symptoms. 4. Exercise areas should be kept free of obstacles and well lit.

Benefits of Specific Exercises

	Benefits
Aquatics	Provides optimal exercise conditions by reducing the effects of gravity, and helps with weakened extremities attain a greater ROM. Movements are more efficient and can be performed with less energy limiting fatigue[9]. Chest-high water provides support, enabling a person to stand and maintain balance for exercises with less effort than on land. The resistance water provides can be utilized for strengthening muscles, while reducing body heat that generated by exercise. Water temperature between 80 and 84 degrees F is generally recommended[142]. Studies have shown an improvement in peak VO2 and lactate threshold[143] as well as reduced levels of anxiety and depression, and increased freedom of movement, relaxation, energy and social interactions[144].
Yoga & Tai Chi	Assists in decreasing stress, and improving relaxation and balance. These activities involve slow, controlled movements of specific muscle groups and breathing exercises that require attention from the individual. Yoga studies have shown significant improvements in general fatigue and vigour for persons with MS[99]. Tai Chi has been shown to significantly improve balance, posture, flexibility, muscle strength, and well being[145,146] as well it has also been shown through research to relieve stress and make connections between the mind and body[147]. More studies are needed, but preliminary results suggest that these activities may help improve fatigue, depression, and balance in individuals with MS[148].
Chair Exercises	Chair exercises are a good alternative to standing exercises. Strengthening and stretching exercises can be adapted to be performed while seated and will allow for the conservation energy while preventing excess fatigue.
Group Programs	Studies on exercise in persons with chronic diseases, have found that persons who exercise in a group not only receive the physiological benefits of exercise, but also important aspects of socialization, support, and motivation. Since isolation and depression can occur in individuals with MS, group exercise programs may be beneficial.

Getting a Person with MS Started

One of the hardest things to do for persons with MS when deciding to become active is knowing what they should do or how to go about it. Here are some helpful tips for you to remember in helping them get started towards exercising and being active. In addition, it also covers aspects they should remember when exercising or being active.

Before a person with MS starts any exercise program they need to:

- A person with MS should consult with a physician prior to beginning any exercise program. You or their primary physician can direct them to a physiotherapist or exercise specialist who can devise an exercise program specific to their needs; if you or their physician feels this is needed.

- A person with MS should inquire with local facilities for programs or activities that interest them. They can also check with their local MS Society of Canada Chapter or Division for programs and activities within their community.
- Ensure that the person with MS picks an activity that they will enjoy doing. This will help with continuation in the program and being active.
- Have the persons with MS get family and friends involved – exercising and being active is more enjoyable when it's done with a partner or group. As well family and friends will then also receive the benefits of being active and healthy.

To avoid fatigue and reappearance of MS symptoms a person with MS needs to:

- Know their own limits and not exceed them. The person with MS should do as much as they feel they can do. They do not need to add to their fatigue by working to the point of exhaustion. Also it is okay for them to take breaks between activities or exercises.
- Wear light clothing and exercise in a cool environment (symptoms of MS can get worse with overheating).
- Avoid heat exhaustion and not overdo it! The person with MS should and needs to stay cool. When a person with MS feels fatigue, they should stop and rest or change exercises.
- Take a ‘time-out’ and stop exercising when a MS relapse occurs.
- Ask questions or ask for advice on exercise, physical activity, symptom management and how their body may respond to activity and exercise.

Things to remember as a health professional:

Don’t hesitate to ask for advice. Understanding multiple sclerosis and impact and affects of exercise can be difficult at times, there are experts in the field that can help in this regard (i.e., MS Society of Canada, MS Neurologist).

Listen to the person with MS. They know their body the best, as they are the ones experiencing MS (i.e., MS symptoms, what they can and cannot do, and the impact that fatigue has upon their life and activities of daily living).

It’s important for people with MS to be active NOW!! So, they too can enjoy the physical and emotional rewards of being in the best shape they can be.

Summary

In this guide we have addressed the physiological and functional limitations of MS that may affect an individual's ability to exercise, the potential benefits that could be gained from participating in exercise as well as some of the guidelines for exercise testing and prescription have been presented. For many individuals with chronic conditions, including MS, refraining from participating in exercise due to their symptoms leads to a decrease in functional capacity and muscle weakness leading to further immobility. As this pattern progresses, it eventually affects the individual's ability to carry out even the basic functions of daily living and may lead to a decrease in the individuals QoL. Exercise plays a key role in preventing de-conditioning in MS and maintaining physical function and individuals should be encouraged to maintain or improve aerobic and muscular fitness early in their disease to offset the decrease in functional reserve that generally occurs with increasing disability and loss of function as the disease progresses. Exercise programs also provide a valuable opportunity for social interaction and support which may assist in maintaining or improving a person's QoL.

Need More Information?

For more information on exercise and MS, contact your local chapter of the MS Society of Canada. This can be done by calling 1-800-268-7528, by email (active@mssociety.ca) or by accessing the MS Active*NOW* website (www.mssociety.ca\alberta).

Resources

DVDs

Title	Year	Publisher
Body, Mind and Soul: Adapted Yoga Exercises	2008	MS Society of Canada, Hamilton Chapter
Exercise and MS	2007	MS Society of Canada, Alberta Division
About MS	2007	MS Society of Canada, Alberta Division
It's Your Choice- Exercises for Fitness & Well-Being for Individuals with Multiple Sclerosis	2007	Toronto Rehab, Toronto, Ontario

Books

Title	Author(s)/Organization	Year	Publisher
Understanding MS and exercise: A fitness and lifestlye providers guide	MS Society of Canada, Alberta Division	2008	Priority Printing
Activating your life: A guide to excercise for persons with multiple sclerosis	MS Society of Canada, Alberta Division	2007	Priority Printing
Excersises for Multiple Sclerosis	B. Hamler	2006	Hatherleigh Press
Multiple Sclerosis: A Self-Care Guide to Wellness	N. Holland & J. Halper	2005	Demos Medical Publishing, NY
Managing the Symptoms of Multiple Sclerosis	R. Schapiro	2003	Demos Medical Publishing, NY
Everybody stretch: A physical activity workbook for people with various levels of multiple sclerosis	J. Fowler	2003	Multiple Sclerosis Society of Canada
Stretching for people with MS: An illustrated manual.	B. E. Gibson	2003	National Multiple Sclerosis Society.

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Notes

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Contact the
MS Society of Canada, Alberta Division

Phone: 1-800-268-7582
Email: active@mssociety.ca
Website: www.mssociety.ca/alberta
Address: #150, 9405 - 50 Street
Edmonton, AB T6B 2T4

OUR MISSION

To be a leader in finding a cure for multiple sclerosis and enabling people affected by MS to enhance their quality of life.