Multiple Sclerosis Foundation

# MS Warriors: Battling Autoimmunity

## National MS Education and Awareness Month®


# MS Warriors: Battling Autoimmunity

Dear Readers,

During this year's National Multiple Sclerosis Education and Awareness Month, we want to highlight a topic of importance to anyone with an autoimmune disorder – supporting a healthy immune system. The idea of "supporting" your immune system may seem counterintuitive because multiple sclerosis is a disease where your immune system is literally attacking you. But in this year's booklet, we hope to show you why it's so important, the role your daily activities play, and how to best manage your MS.

In your younger years, you probably never thought that one day your immune system would turn on you, because you were taught in school that it is your body's way of protecting you. But some estimates say up to 50 million Americans have an autoimmune disease. While individual autoimmune diseases affect only small percentages of the population, when autoimmune diseases are looked at as a whole, they are a leading cause of disease, disability, and even death. Moreover, it's often found that treatments that work for one autoimmune disease can work for other autoimmune conditions. These facts highlight the importance of research into autoimmunity itself. Learning more about the immune system – how it functions and the way it malfunctions – can only help.

Autoimmune disease is caused by a malfunctioning immune system, that is over-active or out of balance. Supporting your immune system and doing what you can to reduce inflammation are vital approaches to maintaining the best health possible. In the first part of this booklet, you will learn the key ways to support your immune system. These five pillars of MS management – diet, exercise, sleep, stress management, and medications – all play a crucial role in your immune health. We'll also discuss common questions about MS and the immune system, and how both current and future autoimmune research research can bring about advances in MS treatment.

Your immune system is meant to protect you. But when you have MS, your immune system can seem like your worst enemy. Understanding what goes wrong in the immune system of a person with MS, how medications can help, and how best to support a healthier immune system is vital to living well with the condition. In this year's National Multiple Sclerosis Education and Awareness month activities, we provide a deeper understanding of the immune system, discuss the benefits and advances in treatment, and highlight how you can advocate for autoimmune research in your community.

We hope this theme will empower you to take charge of the factors in your control that contribute to a healthy, balanced immune system and join in with the larger autoimmune disease community in fighting for answers.

Sincerely,
The MS Focus Team

## MS and the Immune System: What goes wrong?

The human immune system is incredibly complex. It is made up of both cells and chemical messengers (called cytokines) that allow for communication between immune cells. When working appropriately, the immune system is highly regulated and has a balance between inflammatory and anti-inflammatory actions. So what goes wrong in MS?

Your immune system is designed to fight off outside invaders. Outside invaders are any germs (i.e., bacteria, viruses, fungi, or toxins) that can cause harm to your body. With MS, your immune system mistakenly identifies the myelin sheath (a layer of insulation around your nerves) as a foreign invader. Once this process starts, your body will start trying to fight off "the invader" and create inflammatory cells that damage the myelin sheath. This repetitive fight leads to scar tissue forming around your nerves.

Normally, the central nervous system is selective about what immune cells can enter. The blood-brain barrier helps protect the human brain from potentially damaging inflammatory cells, chemicals, and other substances. In MS, the blood-brain barrier becomes "leaky," allowing inflammatory cells from the immune system to cross into the brain and spinal cord.

Why do they do this? It's thought that cells inside the central nervous system, called glia, become activated and secrete cytokines that serve as a homing signal for these inflammatory cells. The blood-brain barrier is less effective in a person with MS at keeping these inflammatory cells out. We do not yet know what turns on these glial cells in the first place.

Some of the cells involved in the immune attack on the central nervous system include T-cells, B-cells, and macrophages. T-cells can be further divided into classes called CD4 and CD8 cells. CD4 cells can be further divided into cells called Th1,

Th17, and Th2. The Th1 and Th17 cells are said to be inflammatory in nature and are relatively overrepresented in people with MS. During a relapse, Th1 and Th17 cells may be moving across the blood-brain barrier more easily, resulting in damage to myelin and nerve fibers (axons).

B-cells are immune cells that have two major roles in inflammation. B-cells can become plasma cells, which produce antibodies. Antibodies are crucial in protecting us from foreign invaders like bacteria. They can also be problematic in autoimmune diseases such as MS, where they create autoreactive antibodies (antibodies which falsely identify your own cells as a danger). B-cells also regulate T-cell production and can trigger proinflammatory cytokines.

Finally, macrophages also play a role in the inflammatory damage of an MS relapse. Macrophage comes from the Greek words "makro" meaning big and "phagein" meaning to eat. So, macrophages are big eaters. Think of them as gobbling up bacteria or other undesirable things in your body. Again, this normally helpful cell can be turned against healthy tissue, such as myelin, in the setting of an autoimmune disease.

## Supporting Immune Function

If your immune system is on the attack, why would you want to take action that improves immune function? It's important to understand we are not suggesting using "immune boosters" to increase or stimulate your body's immune response. Rather, supporting your immune system means giving your body what it needs to have a healthy and balanced immune response. This will not only help your immune system perform its intended function by protecting you from viruses and bacteria, but can help increase the immune system's anti-inflammatory actions. This can help regulate your immune health.

| | | |
|---|---|---|
| **Immune Booster** | A supplement that's meant to increase the activity of the immune system (such as echinacea or astragalus) | Not recommended for people with MS |
| **Immune Support** | A nutrient needed for the immune system to function optimally, or an action that helps regulate the immune system | Strongly recommended for people with MS |

Immune supports fall in five major areas: nutrition, exercise, sleep, stress management, and medication. Let's examine each of these areas and how it supports your immune health.

## Diet and Nutrition

Every cell in your body needs nutrients to function, including your immune cells. New immune cells cannot be created without proteins and essential fatty acids. Certain vitamins are essential for the growth of immune cells; others play a role in regulating immune response. Minerals such as iron and selenium contribute to






immune cell activity. These few examples demonstrate that good general nutrition is an important way to support your immune health.

So what is the best way to get these vitamins and minerals? While taking a multivitamin can certainly be helpful, the best way to ensure you meet your body's needs is to get your nutrients directly from various fresh foods. This way you also get the needed macronutrients (protein, carbohydrates, healthy fats) and fiber your body needs.

Eating foods with natural anti-inflammatory properties can help to decrease inflammation. Some of these MS-friendly foods are:

- **Fruits and vegetables:** Both fruits and vegetables can help to strengthen your immune system and reduce the oxidative stress on your cells, which in turn can help to improve your fatigue. Oranges, berries, spinach, and kale are all rich in antioxidants and vitamins.
- **Fatty fish:** Fish such as sardines, salmon, and mackerel are rich in omega-3 fatty acids and have anti-inflammatory properties. Consumption of these fish promotes brain health and is shown to remove MS-related inflammation.
- **Whole grains:** Fiber rich whole grains such as quinoa, whole wheat, and brown rice can improve gut health and help with digestion. Studies show whole grains can also provide long-lasting energy.
- **Legumes:** An alternative to meat consumption for protein are legumes. Some of the most common legumes such as beans, chickpeas, and lentils, help with muscle repair and provide energy without the saturated fat found in animal meat products.
- **Nuts and seeds:** Walnuts, flaxseeds, almonds, and chia seeds are rich in fiber, healthy fats, and antioxidants. These qualities can help to support brain health and reduce inflammation.
- **Dairy alternatives:** If you are lactose intolerant or simply do not consume dairy products by choice, there are other options to provide you with essential nutrients such as vitamin D and calcium. Soy milk, almond milk, and coconut yogurt are suitable alternatives.

## Which Diet Should You Choose?

Several diets have been studied for people with MS. While no diet has been proven to have a significant effect on the disease process, all have demonstrated improved general health and well-being, and anecdotal reports indicate some people experience improvement in their symptoms. The chart below compares several of the diets that have been studied in people with MS, showing how much they have in common:

| | Swank | McDougall | Wahls | Mediterranean |
|---|---|---|---|---|
| High in vegetables and fruit | ✓ | ✓ | ✓ | ✓ |
| High in whole grains | ✓ | ✓ | | ✓ |
| Limits animal fats | ✓ | ✓ | ✓ | ✓ |
| Includes Omega fatty acids | ✓ | | ✓ | ✓ |
| Reduces/eliminates dairy | ✓ | ✓ | ✓ | |
| Avoids processed foods | ✓ | ✓ | ✓ | ✓ |
| Reduces sugar intake | | ✓ | ✓ | ✓ |

**TIP:** To learn more about these diets, request or download the booklet *Food to Fight MS*, published by MS Focus. Visit msfocus.org/Get-Educated/Educational-materials/Booklets.

Before choosing which type of diet is beneficial for your specific needs, consult with your healthcare team. Remember, the goal of following specific dietary guidelines is to support your immune system. Eating foods rich in vitamins, antioxidants, proteins, and fiber is crucial to maintaining good immune health.

# Movement and Exercise

Eating proper foods to fuel your body and promote good immune health is only one part of the bigger picture. With consumption of these foods, it is also recommended to keep your body moving.

How does movement benefit your immune system? There are several ways. Exercise reduces stress hormones, which tend to be inflammatory. The increased breathing rate can help flush bacteria out of your airways, and the increased temperature can help your body fight any potential infection. But perhaps more importantly, recent research from Harvard University indicates exercise increases a kind of regulatory T cell (called Tregs) that fights inflammation and helps quiet the immune system.

Movement with MS can seem daunting. Symptoms such as fatigue, imbalance, and spasticity can make it challenging. However, exercise can also help treat those very symptoms. Use the checklist on the next page and see how many of the exercises are achievable for you. Remember, the checklist is to encourage movement, not to be a competition of how many you can check off.








| | |
|---|---|
| ❑ Stationary bike | ❑ Dancing |
| ❑ Yoga | ❑ Chair yoga |
| ❑ Water aerobics | ❑ Weight training |
| ❑ Walking | ❑ T'ai Chi |
| ❑ Hand dexterity movements | ❑ Gardening |
| ❑ Progressive resistance training | ❑ Rowing |
| ❑ Swimming | ❑ Stretching |

Applaud yourself for checking off any boxes. Not only does movement with MS promote immune health, but it also helps to improve daily moods. If you are having difficulty with movement, consult your healthcare team and ask about physical therapy to help you get started. There are resources available to assist you in creating a movement plan catered to your individual needs.

**TIP:** Through the MS Focus Health and Wellness Program, you can access free adaptive classes such as T'ai Chi, yoga, and dance. Visit msfocus.org/Get-Help/MSF-Programs-Grants/Health-and-Wellness-Program.

## Keeping Your Cool

While exercise is good for your general health and your immune system, the majority of people with MS cope with heat sensitivity. What can you do to keep your cool while you exercise? Try these tips:

1. Exercise indoors – when possible, choose forms of exercise you can do inside, preferably in an air-conditioned room and with a fan.
2. Pick your times – if your preferred form of exercise takes you outdoors, avoid peak sun hours. Mornings and evenings are the safest times to avoid the worst of the heat.
3. Take breaks – incorporate cool-down breaks into your exercise routine. Stop before you get overheated.
4. Stay hydrated – carry a bottle of cool water and sip it regularly.
5. Wear cooling garments – a cooling vest, hat, or neck scarf can help prevent you from overheating.

# Sleep

Exercise and sleep have a harmonious relationship. Exceeding in one and neglecting the other is not beneficial for your body and your mood. When you sleep, you allow your body to rest and recuperate from the day's activities. Even when you feel you have not been that active, your body has repair work to do. But how does sleep play a role in helping boost your immune system?

When we are sleeping, our bodies release cytokines – signaling proteins within the immune system. Cytokines help to regulate inflammation, with both proinflammatory and anti-inflammatory types. When we fall asleep, proinflammatory cytokines trigger the immune system to fight invaders. (This is why sleep often helps us feel better when we are sick.) As the sleep cycle continues, the body sends signals to reduce inflammation. Also, melatonin is released, which counteracts inflammatory stress hormones.

In people who do not get enough sleep, this system of natural inflammation regulation is disrupted. A chronic lack of sleep is known to cause chronic low-grade inflammation that contributes to many health conditions. The tricky part of sleeping when battling an autoimmune disease such as MS is how to manage your sleep and keep a consistent routine.

Symptoms such as restless leg syndrome, bladder issues, or muscle spasms can cause you to wake up repeatedly throughout the night. By not giving your body the daily recommended sleep (seven to nine hours), your body becomes tired the next day. Combine this tiredness with the fatigue you probably feel through your MS and you have an endless cycle of exhaustion. Lack of sleep can also alter your mood and make you more irritable or distraught.

Below are a few questions to ask yourself and to better gauge if you are sleep-deprived. Check off the boxes you feel describe you best.

- ❑ Do you feel sleepy, grumpy, or "down" during much of the day?
- ❑ Do you fall asleep as soon as your head hits the pillow?
- ❑ Do you sleep fewer than seven hours most nights?
- ❑ Do you still feel tired even after having eight hours of sleep or more?

If you checked off any of these boxes, you may be sleep-deprived. Consulting with your healthcare team can help you decide how to approach your sleep routine.

**TIP:** As many as 58 percent of people with MS have a sleep disorder, such as sleep apnea or insomnia. If you have chronic sleep problems, consider asking for a sleep study.

### Get Better Sleep

Healthy sleep habits, often referred to as sleep hygiene, can help you consistently get a good night's sleep. Follow this advice for better rest:

- **Routine promotes rest** – try to go to sleep and wake up at the same time each day, have your meals around the same time, and have the same pre-bed rituals.
- **Avoid stimulants** – stop caffeine at 2 p.m. Quit smoking if you can, but at least avoid nicotine near bed time.
- **Relaxation matters** – reduce bedtime stress by not watching or reading news before bed and instead, engage in calming activities.
- **Reduce sensory input** – keep the room quiet and dark, block out lights on devices.
- **Get cozy** – make sure your clothing, mattress, pillow, and bedding are all comfortable. Keep the room cool – 68 degrees is considered the optimal temperature for sleep.
- **Avoid frustration** – if you find you can't sleep, don't toss and turn and continue checking the clock. After 20 minutes, get up and do something relaxing and try again when you feel ready.

## Stress Management

Sleep, exercise, and nutrition all go together to support your immune system. But one of the largest contributing factors to the state of your immune system is stress. When we feel stressed, we may think our emotions and mental state are the only things being affected, but our bodies also bear the effects as well.

Handling short-term stress is part of the body's natural function and is not harmful. For example, if a large object were about to fall where you are sitting, your stress response would cause your body to surge with adrenaline and cortisol, your heart would beat faster to move blood to your muscles, and you would have the urge to run. Aside from these noticeable effects, this rapid process would also alter the balance of cytokines, T cells, and other immune cells. However, after the danger has passed and this acute stress alleviates, the body resets without a lasting effect on your immune system.

Chronic stress, however, is a different story. In chronic stress, the body does not have the opportunity to return to baseline after a stressful event. This leads to a chronic state of inflammation that is associated with several health conditions. Chronic stress has been shown to be associated with disease onset and disease exacerbations in MS, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, Graves' disease, and other autoimmune conditions.

These effects play a role in your MS management and can cause an exacerbation of other symptoms such as pain, fatigue, and depression. To reduce the stress, let's go through some stress management tips. As you go through this list, you may find some are easy to practice, while others are not in your comfort zone.

Whichever the case, finding ways to manage your stress is essential to lowering stress hormones and inflammation and, therefore, nurturing your immune system to perform efficiently.

## Managing Stress

1. **Identifying your stressors** – When you can identify the things, situations, or relationships causing you stress, you can help to eliminate them in a healthy manner. Take a step back and think about when you are stressed and if any factors influence or worsen the feeling.
2. **Making time for yourself** – Self-care is a way of loving yourself and the body you are in. Whether it is taking a relaxing bath, watching your favorite TV show, or reading a book – do what makes you happy and do it often.
3. **Silencing negative self-talk** – Negative thoughts play a large role in our daily life. Imagine talking to yourself like you would to your child or to your best friend. If the things you currently say are not things you'd say to someone important to you, try and silence them.
4. **Get out in nature** – Sometimes in moments of stress, a walk or roll can be therapeutic. Taking time away from the situation or person can provide clarity. Plus, it allows you to take a breath of fresh air.
5. **Sing** – It may sound childish, but sometimes a little bit of music can improve your mood and reduce your stress. Play your favorite song and sing out your emotions!

- What causes me stress?

_____

_____

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_____.

- How can I reduce that stress?

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# Medication

Science has come a long way since the initial description of MS was made in the 1870s. Since then, treatments to help slow down the disease have been developed, providing people with MS a variety of options.

The goal of disease-modifying treatment for MS is to regulate your immune system. Different treatments approach this complex task in different ways. Among the treatments, some seek to target immune cells (T- and B-cells) directly. Others affect the immune system components that control how and when those cells respond. In both cases, the point of these medications is to calm an overactive immune system and to create a better balance.

This balance is delicate because MS is an autoimmune disease, but your immune system's job is to help fight off infections. If the medication is not effective enough at calming the immune system, you are at risk for disease activity. Being adherent to your medication regimen (taking the right dose consistently) is important in maintaining the balance of your immune system.

The Centers for Disease Control and Prevention (CDC) estimates that non-adherence causes 30 to 50 percent of chronic disease treatment failures. Why do so many people fail to stick to their treatment regimen? What can help?

## 1. Cost

If the cost of your chosen medication is outside your ability to pay, you have a few options. First, contact the drug manufacturer about any financial assistance they may provide. Next, ask about any charities that can assist with the cost. Finally, if no other option remains open to you, talk to your doctor about other options such as generic equivalents which may be more cost effective due to payor formularies.

## 2. Side effects

If you are experiencing a side effect from a medication, make sure to communicate with your doctor. Ask if there are ways to manage the side effect, whether the side effect is likely to go away as treatment continues, or whether you can try a medication with a different side effect profile. Also, keep in mind that potential side effects listed on the medication insert are not guaranteed to happen to you, and that serious side effects – while a warning must be included – are very rare. If fear of side effects prevents you from sticking to your medication regimen, discuss this with your doctor.

## 3. Confusion

When you and your doctor decide on a medication, make sure to take notes or record what the doctor says about when, how often, and how much of the medication to take. Also, some people may stop adhering to their MS disease-modifying treatments because they do not notice improvement. Remember, the purpose of a DMT is to balance your immune system to prevent relapses and slow progression. It will not undo previous damage to your central nervous system, so it's unlikely to bring about much improvement to your existing symptoms.

Adhering to your medication regimen, managing your stress levels, getting plenty of sleep, staying active, and eating with nutrition in mind are the pillars of good health.

With the five pillars in mind and the information presented, take a moment to set an intention for supporting your immune health:

- Knowing that good nutrition can help strengthen my immune system, I will implement the following into my daily diet:

  _____

  _____

  _____

  _____.

- Knowing that increasing my movement is vital and achievable with my MS, I will implement the following movements/exercises into my daily life:

  _____

  _____

  _____

  _____.

- Knowing the importance of sleep and practicing good sleep hygiene habits, I will implement the following into my evening routine:

  _____

  _____

  _____

  _____.

- Knowing the role stress plays in my immune system, I will use the following techniques to better manage my stress:

  _____

  _____

  _____

  _____.

- Knowing the importance of strictly adhering to my medicine regimen, I will address the following issues with my healthcare team:

  _____

  _____

  _____

  _____.

# Healthcare and Your Immune System

While you support your immune system with healthy lifestyle choices, you can also protect your immune system with proper healthcare. This includes regular screenings to head off any problems that may decrease the effectiveness of your immune system or throw off your immune balance, as well as avoiding things that threaten your immune health.

## How Biological Sex Affects Immune Health

*Please note: In the following pages, we will be discussing immune system differences between male and female biology. Our use of the terms male and female herein are meant to refer in general terms to biological sex, not gender identity.*

Your immune system is unique to you. This complex system varies from individual to individual, since so many different factors affect your immune composition and response. These factors can include those we've already discussed – diet, activity, sleep, stress, the medications you take – but also include things such as what viruses and bacteria you've been exposed to in your life, what vaccines you've had, and surprisingly, even your biological sex.

Biological sex plays a large role in the makeup of our immune system. The X chromosome contains a large concentration of immune-related genes. Females have two X chromosomes, where males only have one. Therefore, females generally have stronger immune responses than males, and may have more resistance to viruses, bacteria, fungal infections, and parasites. However, females are also considerably more likely to have autoimmune disease.

## Sex Differences in MS

- **Prevalence:** When diagnosed before puberty, males and females are diagnosed at the same rate. After puberty, MS is significantly more common in females than males, with a ratio of 3:1. While this makes a strong case for the influence that hormones play in the immune system being a factor, there is still no clear answer as to the cause of this disparity.
- **Clinical Course:** Females experience hormonal changes that can lead to changes in MS-related symptoms during the course of their lives. Sex hormones, such as progesterone and estrogen, fluctuate throughout the reproductive cycle and a decrease in these hormonal levels can exacerbate symptoms of MS. Conversely, during pregnancy, studies show a decreased risk of relapses, particularly in the third trimester, when estrogen and progesterone levels are elevated. This cycle of hormones, and its correlation with MS symptoms, is unique to each individual.

  While fewer males develop MS, males are more likely to have the progressive form of MS, more severe symptoms, and greater disease progression. Studies show males usually have more difficultly recovering after relapses and higher rates of cognitive impairment.
- **Response to Treatment:** Little research has examined whether there are differences in response to treatment between male and female, although it does appear females

have more frequent relapses. However, it's thought that factors such as differences in body composition, hormonal fluctuations, and genetic factors may all contribute to variability in treatment response between genders. Furthermore, females may have more limitations on treatment options if they are considering pregnancy or breastfeeding.

Knowing that biological sex is a factor in MS, it is important to keep up with regular screening for sex-related health issues. Such issues can alter the balance of hormones and thus affect the state of your MS and your immune health in general. And of course, having MS doesn't exempt you from other health issues, such as cancer, heart disease, and stroke, so seeing your primary care doctor regularly is important too.

## Have you Been Keeping up with Your Wellness Check-Ups?

Take a look at the the following charts and see how many of the general wellness exams you have been receiving based on the criteria. If you have some visits to schedule, reach out to your healthcare team.

| *General Health Screening Guidelines for Females with MS* | |
|---|---|
| **Condition** | **Criteria** |
| **Breast cancer** | Mammography beginning at age 35 - 39 to establish a baseline, every one to two years for people age 40 - 49, and yearly for those age 50 and older |
| **Cervical cancer** | For sexually active people, screening every three years after age 18 |
| **Colorectal cancer** | Colonoscopy every 10 years for those age 50 and older |
| **Osteoporosis** | Routine screening in females 65 and older |
| **Well-visit exam** | Every one to three years between ages 18 - 49 and annually for individuals age 50 and older |

| *General Health Screening Guidelines for Males with MS* | |
|---|---|
| **Condition** | **Criteria** |
| **Prostate cancer** | Starting at age 50 and continuing annually. African-Americans or those with family history of prostate cancer, start at age 40. |
| **Testicular cancer** | Monthly testicular self-exam, annual clinical testicular exam. The American Academy of Pediatrics recommends starting at age 18. |
| **Colorectal cancer** | Starting at age 50, continuing every five years for sigmoidoscopy or every 10 years for colonoscopy. Screening recommended earlier for high-risk individuals. |
| **Bone Density Test** | Consult with your healthcare team for a one-time exam, for everyone with risk factors (prolonged steroid use or anticonvulsants, a family history of osteoporosis, and a sedentary lifestyle). |

## New Clues to Sex Differences in Autoimmune Disease

Autoimmune diseases affect about eight percent of the population, but 78 percent of those are female. The reasons for the high prevalence of autoimmune diseases in femles are unknown, but new research could provide a clue.

According to a February 2024 study published in the journal *Cell*, the molecule Xist may play a role in autoimmune diseases. The role of this molecule is to prevent overproduction of certain proteins in people with two X chromosomes (biological females), so Xist is an RNA molecule that is only found in female cells.

Lupus is an autoimmune condition that is particularly uneven in terms of prevalence. It affects a 9:1 ratio of females to males. In an experiment on mice, a Stanford study found that when they activated Xist genes in male mice, the males developed lupus-like autoimmunity at a similar rate to females.

This indicates Xist may play a role in the prevalence of autoimmune diseases such as lupus and MS in females. The research provides a new pathway for study and could lead to future treatments for autoimmune diseases.

## Protecting Your Immune System

Just as healthy habits promote immune health, certain unhealthy habits can damage our immune systems. You can protect your immune system by avoiding certain practices.

1. **Tobacco and nicotine use** – cigarette smoking has been causally linked to several autoimmune disorders, including MS. Smoking reduces the body's antioxidant levels and interferes with the functions of T cells and cytokines. Nicotine itself has been shown to be an immunosuppressant. So quitting smoking, vaping, and other forms of nicotine or tobacco ingestion can help protect your immune function.
2. **High alcohol consumption** – while moderate alcohol use can show a positive effect on inflammation, both chronic alcohol use and binge alcohol use can have negative effects on immune health. High alcohol consumption reduces good bacteria in your stomach and digestive tract and lowers the number of B cells and T cells in your immune system. Fortunately, stopping drinking or reducing alcohol consumption to recommended levels can allow your immune system to return to health.
3. **Excessive chemical exposure** – we are all unavoidably exposed to chemicals in our environment and everyday lives. However, research has shown that people in careers with frequent chemical exposure have a higher risk of autoimmune illnesses. With MS, studies have shown an increase in risk of up to 50 percent for people with high exposure to solvents (which are used in products such as paints, adhesives, cleaning agents, degreasers, and in the production of dyes, plastics, textiles, and inks, etc.). While exposure to any of these is not the direct cause of autoimmune disease, the effects of exposure on the immune system combined with a genetic predisposition to a disease are believed to be a trigger. Reducing our daily exposure to chemicals where possible helps protect our immune systems. If exposure is a part of your work, wear appropriate protective gear.

**TIP:** Speak to your healthcare provider about any challenges you may face with smoking, vaping, or excessive use of alcohol. To learn about alternatives to potentially harmful chemicals, visit the U.S. Environmental Protection Agency's Safer Choice program at: epa.gov/saferchoice.

## Common Questions About MS and Your Immune System

**• I have MS. Does that mean I'm immunocompromised?**

People with MS are generally not considered immunocompromised, unless they are taking an immunosuppressant medication. However, while the damage in MS is caused by an overactive immune system, recent research suggests people with MS may still be more susceptible to infections from viruses and bacteria than a person without MS. It is important to practice good hygiene and take preventative measures to avoid exposure to infection.

**• Are vaccines safe for people with MS?**

Because people with MS may be at higher risk for infections, vaccination is important. People with MS and particularly those on a disease-modifying treatment should avoid "live" vaccines. However, inactivated vaccines and mRNA vaccines are considered safe for people with MS. Depending on the type of medications you take, your doctor may have recommendations on the timing of your vaccinations for optimal immune response.

**• Does my MS medication suppress my immune system?**

No MS medications completely suppress the immune system, but certain medications do target specific immune cells to reduce or suppress immune response. The following chart shows which medications suppress the immune system and to what degree.

| Level of Immunosuppression | Medications |
|---|---|
| Little to no immunosuppression | **Interferons**<br>Avonex, Betaseron, Extavia, Plegridy, Rebif |
| | **Glatiramer acetate** – Copaxone, Glatopa |
| | **Teriflunomide** – Aubagio |
| Mild degree of immunosuppression | **Fumarates** – Bafiertam, Tecfidera, Vumerity |
| | **Natalizumab** – Tysabri, Tyruko |
| Causes targeted immunosuppression | **Anti-CD20 medications**<br>Ofatumumab – Kesimpta, Ocrelizumab – Ocrevus, Rituxumab – Rituxan, Ublituximab – Briumvi |
| | **Cladribine** – Mavenclad |
| | **S1P Modulators**<br>Fingolimod – Gilenya, Tacenso ODT<br>Siponimod – Mayzent, Ozanimod – Zeposia<br>Ponesimod – Ponvory |
| | **Anti-CD52**<br>Alemtuzumab - Lemtrada |

Some of the more immunosuppressive MS therapies are also some of the most effective treatments. Each person must balance the risks of immunosuppression against the risks of MS relapse and progression, and then decide with their healthcare providers which medications are most appropriate for them. But all of us can benefit from taking steps to actively avoid infection, such as handwashing and limiting exposure to people who are unwell. Vaccinations can be an important tool to lessen the risk of certain infections. Be sure to discuss vaccine recommendations for the various MS disease-modifying therapies with your medical team.

## Advocate with the Autoimmune Community

When it comes to advocacy, there is strength in numbers. Although only about one in 300 people have MS, a whopping one in 10 people have an autoimmune disease. When advocating for research, legal protections, social services, or other aspects of life with chronic illness or disability, the autoimmune community is stronger together.

All autoimmune diseases have a common underlying mechanism – an immune system that becomes reactive to the body's own cells. But aside from the fact of simply being autoimmune in nature, the approximately one hundred autoimmune diseases have other similarities. People living with autoimmune diseases, though their conditions may be very different, still have much in common.

**Nearly all autoimmune conditions cause:**

- Fatigue
- Pain
- Inflammation
- Difficulty with activities of daily living

**Like multiple sclerosis, autoimmune conditions typically:**

- Affect more women than men
- Are diagnosed from late adolescence to age 50
- May take years to get a diagnosis
- Progress over time
- Are linked with increased rates of depression and anxiety

Autoimmune diseases also frequently gang up on a person. About 25 percent of people with autoimmune diseases have more than one autoimmune condition. This is referred to as polyautoimmunity.

Interestingly, treatments for autoimmune diseases can have more than one use. Steroids are used to treat flare-ups in many autoimmune diseases. Biologic treatments that target immune cells also frequently help more than one condition. For example, rituximab (off-label) is not only used in MS but in rheumatoid arthritis and autoimmune skin diseases. Some biologic treatments may be used in five or more autoimmune conditions.

The underlying mechanisms, many symptoms, and many of the treatments are common to several autoimmune conditions. For these reasons, research into one autoimmune disease can have benefits for other autoimmune diseases – perhaps even all autoimmune diseases.

## Orphan Drug Research

Because a single autoimmune condition usually affects only a small percentage of the population, at times it may not seem like a wise financial investment for drug developers to pursue an experimental treatment. Even a more common autoimmune disease such as MS, which affects one million Americans, is small in comparison to conditions such as high cholesterol, for which 47 million Americans are treated every year, or the 40 million being treated for migraine. Nearly 95 million Americans are treated for high blood pressure. Yet some of the 100 autoimmune diseases, affecting 200,000 Americans or less, are classified as "rare diseases". For these conditions, there would seem to be little incentive for companies to invest millions or billions of dollars in research. However, the government addressed this issue with the Orphan Drug Act in 1983.

An orphan drug is a drug for a rare disease or condition. Some rare disease treatments have been “orphaned” or discontinued because there was not enough financial incentive to continue development or production. The Orphan Drug Act incentivizes drug development for rare diseases.

## Understanding the Orphan Drug Act

Here are the five key provisions of the Orphan Drug Act that all lead to encouragement and incentives for pharmaceutical companies to invest in further research.

1. **Orphan Drug Designation:** The ODA allows drugs intended for the treatment, diagnosis, or prevention of rare diseases to be designated as orphan drugs by the FDA. This gives many incentives to sponsors, such as tax credits for qualified clinical testing expenses, eligibility for orphan drug grants, and exclusivity in the market upon approval.
2. **Market Exclusivity:** Orphan drug designation grants the sponsor of the designated drug a period of market exclusivity. This means during the time an orphan drug is approved and being sold in the market, no other drug with the same active ingredients and indication for the same disease state can be approved by the FDA. This period of exclusiveness is generally seven years and will begin on the first day of FDA approval of the drug.
3. **Tax Incentives:** Sponsors of orphan drugs are eligible for tax credits. The tax credits can be put towards qualified clinical testing expenses that occur during the development of the designated drug.
4. **Grants:** The ODA authorizes the FDA to award grants that support clinical testing of orphan drugs. These grants can help with covering the costs linked to conducting clinical trials and further contribute to the betterment of treatment for diseases such as MS.
5. **FDA Assistance**: The FDA helps sponsors pursuing orphan drug generation and approval, including guidance on regulatory requirements, an expedited review processes, and access to scientific expertise on related information.

Since orphan drugs are a niche product in the pharmaceutical market, the prices of these medications can be high. To help with this issue, the federal government created the Inflation Reduction Act in 2022 termed The Inflation Reduction Act. The aim of this law is to curb inflation through different sectors, such as government budgeting, and lower prescription drug prices. For those of you who have or will be receiving Medicare in the near future, the Inflation Reduction Act can help with covering higher costs for prescription drugs.

## Here are some benefits that come from the IRA:

### Part D Advances

People with Medicare will benefit from lower prescription drug costs and a redesigned prescription drug program. Benefits include:

- Access to recommended adult vaccines without cost-sharing.
- A yearly cap ($2,000 in 2025) on out-of-pocket prescription drug costs in Medicare.
- Expansion of the low-income subsidy program (LIS or "Extra Help") under Medicare Part D to 150 percent of the federal poverty level starting in 2024.

### Changes to Part B

- Changes in the Medicare Part B program will improve access to high quality, affordable biosimilars for people with Medicare.
- The Inflation Reduction Act makes Medicare stronger for current and future enrollees. It makes healthcare more accessible, equitable, and affordable by lowering what Medicare spends for prescription drugs and limiting increases in prices.

### Inflation Rebates in Medicare

The new law requires drug companies that raise their drug prices faster than the rate of inflation to pay a rebate to Medicare.. This will lead to a stronger Medicare for current and future enrollees and discourage unreasonable price increases by drug companies.

## An Unintended Consequence

While these changes provide for tangible benefits to consumers, the IRA may have unintended consequences on drug development. The problem is specifically with orphan drugs that might have more than one use.

Under the IRA, Medicare will be able to negotiate directly with drug manufacturers to lower the price of some of the costliest single-source brand-name Medicare Part B and Part D drugs. This means people with Medicare will have increased access to innovative, life-saving treatments, and the costs will be lower for both them and Medicare. Thankfully, the lawmakers had the foresight to exempt orphan drugs from this negotiation, so the incentives of the Orphan Drug Act will not be reduced. However, there was a change that specifically affects the incentive to research orphan drugs for use in other conditions. Because drugs for autoimmune conditions may be found to be effective in more than one condition, this is significant.

Under the new law, if a company with an orphan drug chooses to do research to see if that drug can treat another condition, they lose orphan drug protections. While it would make sense to lose those protections if the drug is approved for use in a broader population, in this case the benefits are removed before the company even knows if the drug will work for a second condition. This removes the incentive to find out.

To address this issue, a bipartisan bill was introduced into the House and Senate late in 2023, called the ORPHAN Cures Act. This bill would protect the incentives that boost rare disease drug development, undoing the unintended consequences of the IRA that are already having a chilling effect on research funding. Supporting the ORPHAN Cures Act is one way you can advocate for research that may benefit the autoimmune community.

**How can you help?** Contact your representatives and ask them to support the act. Let them know why this issue matters to you, as part of the broader autoimmune disease community. Remind them that the first drugs for multiple sclerosis were developed under the Orphan Drug designation, and without that jumpstart to MS treatment research, it's unlikely we would have the treatment options we have today.

**Contact your congressperson:** house.gov/representatives/find-your-representative

**Contact your senator:** senate.gov/senators/senators-contact.htm

## Tips for Writing to Your Representative

- Address the letter: Use "Dear" followed by the member's title and last name. For example, "Dear Congressman Smith" or "Dear Senator Smith". For a member of the House of Representatives, you can use "Dear Mr. or Ms." For the Speaker of the House, use "Dear Mr. or Madam Speaker".
- Include your contact information: Include your name, title, physical address, and email address.
- Keep it brief: Keep your letter brief and concise. Limit your letter to one page or 500 words if you're writing an email.
- Be courteous and reasonable: Write legibly (if you are writing a hand-written letter) and be brief and to the point. Mention the bill in question and give your reasons for supporting or opposing it.
- Make it personal: Tie the issue to your personal expertise or experience. If you don't have a personal story, explain why the issue is relevant to your district or state.
- State your subject clearly: State your subject clearly in the subject line or the first sentence of the letter.
- For an email, be sure to include a specific and clear subject heading, such as: Please support "bill name", "bill number".

### Office of Autoimmune Research Established at NIH

In 2023, by order of Congress, the National Institutes of Health established the NIH Office of Autoimmune Disease Research. As autoimmune disease primarily affects females, the OADR has been placed under the existing Office of Women's Health Research. The OADR's role is to enhance and coordinate the NIH's research efforts into autoimmune disease.

Learn more at: orwh.od.nih.gov/OADR-ORWH

# Get Involved

Just like the ORPHAN Cures Act and the establishment of the Office of Autoimmune Disease Research, there is much going on in the greater autoimmune disease community that is relevant to those of us with MS. While it's important to maintain in touch with the MS community, consider expanding your advocacy and support resources to include the larger autoimmune population.

## Below are some resources to help you get started:

- **The Autoimmune Association, autoimmune.org**

  For over 30 years, the Autoimmune Association has been a pioneer in serving autoimmune patients, sponsoring research, advocating for access to healthcare, and fostering collaboration to identify and explore the common threads that link autoimmune diseases.

- **National Organization for Rare Diseases, rarediseases.org**

  NORD's mission is improving the health and well-being of people with rare diseases by driving advances in care, research, and policy. Their motto is "Alone we are rare. Together we are strong."

- **Global Autoimmune Institute, autoimmuneinstitute.org**

  The Global Autoimmune Institute's mission is to empower solutions in the diagnosis and treatment of autoimmune disease through research, education, and validation while supporting multidisciplinary approaches to wellness.

- **Advocacy and Awareness for Autoimmune Disorders Association, godoaaida.org**

  AAIDA exists to provide support and advocate for the greater than 25 million Americans living with immune disorders. AAIDA works to promote research and create better awareness of immune disorders.

Giving yourself time and the support required to help you battle through your autoimmune disease that is labeled as MS can be difficult. With the ups and downs of MS itself, it can seem daunting to reach out to anonymous people. But the benefit of reaching out to others is knowing there are people out there who can share their experiences and allow you to have a safe space to share yours. While autoimmune diseases may not be as prominent as other diseases in the medical field, a small number of individual groups can help to create one large group. Share your voice with others and remember, you are not alone in this battle with your immune system.

Multiple Sclerosis Foundation

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