

Accelerated Cure Project for MS

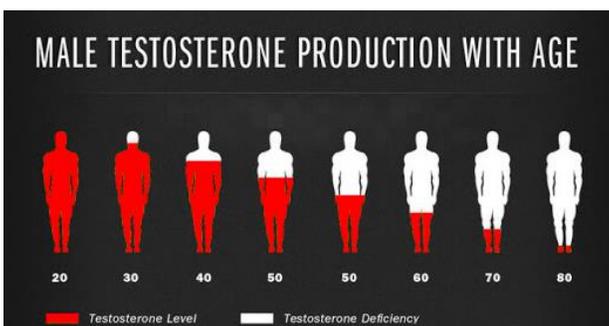
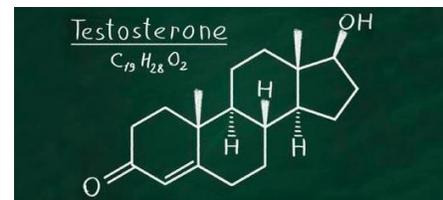
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Accelerating research towards a cure for multiple sclerosis

Does Testosterone Protect Against MS?

Although men are three times less likely to develop MS than women, their disease course tends to be more severe. There are also gender differences in the age of onset and subtype of MS. Women generally develop the disease at a younger age and usually have a relapsing-remitting course. In most cases, men develop MS later in life and it typically follows a more progressive course. Researchers are working to better understand the role that testosterone plays in the development of MS and disease progression.



Researchers at the [Partners Multiple Sclerosis Center](#) at Brigham and Women's Hospital in Boston are conducting the [CLIMB study](#) (Comprehensive Longitudinal Investigation of Multiple Sclerosis) to, among other things, observe testosterone levels in men with MS. This is a large-scale, long-term study of patients with MS. Subjects in the study have neurological exams

and MRI scanning performed on a yearly basis. They also donate blood samples and complete quality of life and mood questionnaires at the same interval. Interim results from the study, published in 2006, revealed that a large proportion of men with MS have low testosterone levels. [Recent research](#) has shown reduced testosterone is, in fact, a risk factor for MS in males and lower levels may impact MS risk as early as the [prenatal period](#). After the age of 30, most men begin to experience a gradual decline in testosterone. The delayed development of MS in men is thought to correlate with age-related reduction of testosterone levels. Data from the CLIMB study also reveals a potential association between low testosterone levels and increased disability.

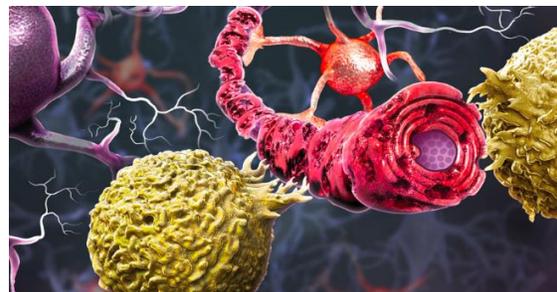
The question is: Would testosterone be an effective treatment for MS? Researchers have shown that testosterone has a [neuroprotective effect](#) in animal models. A small [pilot study](#) in male MS patients at UCLA demonstrated that testosterone therapy led to significant improvements in cognitive function and slowed brain tissue loss. However, larger [placebo-controlled trials](#) are needed to confirm these preliminary results.

Testosterone therapy is known to have other benefits, however it is associated with significant risks and undesirable side effects. Men have reported such benefits as an increase in muscle mass and strength, improved bone density, less fatigue and improved sexual function. Older men treated with testosterone have also shown improvement in memory and cognitive function. However, these beneficial effects must be weighed against possible serious risks. These include an increased risk of hypertension and heart disease, increased hemoglobin (the oxygen-carrying cells in the blood), increased risk of cancer or worsening of preexisting cancer, and emotional instability. Testosterone therapy also has a long list of other noteworthy [side effects](#) ranging from addiction to a reduction in sperm count (which can lead to infertility).

Researchers have recently uncovered a testosterone-regulated pathway associated with demyelination that could hold the key for new treatments for MS.

Investigators at Northwestern University identified a “[guardian molecule](#)” in a mouse model of MS called [cytokine IL-33](#) (IL-33) that appears to protect males from disease. The immune system of an individual

with MS overproduces a type of immune cell called [T helper 17 cells](#) (Th17), which can directly attack the myelin sheath. Researchers found that, in male mice, testosterone resulted in the production of IL-33, which was seen to trigger a pathway that prevented the production of Th17.



Furthermore, when female mice with disease were treated with IL-33, their symptoms were eliminated. Recognizing that these results have yet to be replicated in human studies, scientists speculate that lower testosterone levels in women (which hypothetically are insufficient to activate this protective pathway) could be the reason MS is more prevalent in women.

There is a variety of [disease modifying therapies](#) approved for the treatment of MS. Most work by suppressing the immune system and leave patients more at risk for infection and feeling unwell. Treatment with testosterone is not a viable option for MS patients as its neuroprotective effect has yet to be confirmed and its risks outweigh its benefits. However, the newly discovered pathway testosterone regulates holds great promise in the development of more targeted therapies. Finding a way to activate IL-33 production or emulate this pathway through an approach other than testosterone could revolutionize MS treatment.