

# Researchers uncover biological rationale for why intensive lupus treatment works

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Researchers at UT Southwestern Medical Center have uncovered the biological rationale for why large doses of corticosteroids given repeatedly over several weeks may help individuals with lupus, a chronic inflammatory disease that affects more than 1 million people in the U.S.

Unlike the [anabolic steroids](#) athletes sometimes use illegally to bulk up muscle, corticosteroids are routinely used to treat inflammation in [lupus](#) patients. The drugs, however, can cause undesirable side effects including [weight gain](#) and acne when taken over long periods of time.

In a study published in a recent issue of *Nature*, researchers at UT Southwestern and other institutions show in blood cells that giving very high doses of intravenous corticosteroids early and frequently in the course of the disease is more effective at killing the cells that drive lupus than giving the standard limited intravenous steroids followed by high doses of [oral corticosteroids](#) over a period of months. The cells used came from lupus patients as well as from animal models of lupus.

"By giving the very high dose early and frequently in the course of the disease, we could actually end up using much less steroids in the long run," said Dr. Marilyn Punaro, professor of pediatrics at UT Southwestern and co-author of the study. "This finding suggests that by doing so, we might be able to get the disease under control more quickly and patients might experience fewer long-term side effects."

Dr. Punaro, who treats patients at Children's Medical Center Dallas and

Texas Scottish Rite Hospital for Children, said her team often uses this treatment plan - referred to as pulse steroids - with lupus patients because they've found it can be more effective than standard treatment at maintaining control of the disease.

The standard treatment involves giving very high doses of steroids intravenously for only a few days. Most physicians then transition to a high oral dose and gradually reduce the amount of steroids to the lowest level at which the drugs are still effective.

Lupus is a debilitating autoimmune disease in which the immune system attacks the body's own tissue and organs, including the joints, kidneys, heart, lungs, brain, blood and skin. The Lupus Foundation of America estimates that 1.5 million Americans have the disease, which affects all age groups. It is 10 to 15 times more likely in adult women than adult men.

The immune system of lupus patients is dysfunctional, causing inflammation throughout the body. In this study, researchers used the [blood cells](#) to investigate why the standard treatment might be less effective in halting the inflammation.

They found that pulse doses of intravenous steroids kill off the cells - called plasmacytoid dendritic cells - producing interferon alpha, a protein that promotes this inflammation. Oral corticosteroids given at much lower doses did not have this effect.

"Now we have the biological rationale for why pulsing is often more effective than standard therapy," said Dr. Tracey Wright, assistant professor of pediatrics at UT Southwestern and another study co-author.

Dr. Punaro, director of the pediatric rheumatology division at UT Southwestern, said the team hopes that this study will lead to

recommendations on ways to treat lupus patients more effectively.

"If the patient receives very high doses of pulse steroids during the induction period, when steroid-sparing long-term drugs - which take a while to work - are being ramped up to an effective level, then our experience has been that we end up using fewer steroids overall," Dr. Punaro said. "Steroids are probably always going to be a short-term fix because they work quickly and powerfully, but we hope that this information will enable physicians to be smarter about how they use [steroids](#)."

The next step, she said, is to use the paper's scientific rationale as the basis for a clinical trial comparing patients who receive the more intensive therapy with those getting standard therapy.

Provided by UT Southwestern Medical Center

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