

Autoimmune Diseases

Autoimmune diseases result from a dysfunction of the immune system. The immune system protects you from disease and infection. Sometimes, though, the immune system can produce autoantibodies that attack healthy cells, tissues, and organs. This can lead to autoimmune disease.

Autoimmune diseases can affect any part of the body. More than 80 autoimmune diseases have been identified. Some are relatively well known, such as type 1 diabetes, multiple sclerosis, lupus, and rheumatoid arthritis, while others are rare and difficult to diagnose.

More than 80 autoimmune diseases have been identified. Some of the more common ones include:

- Diabetes (Type 1)
- Lupus
- Multiple sclerosis
- Rheumatoid arthritis
- Celiac disease



The causes of autoimmune diseases remain largely unknown. There is growing consensus that autoimmune diseases likely result from interactions between genetic and environmental factors. The National Institute of Environmental Health Sciences (NIEHS) is supporting research to understand how these factors work together to compromise the body's ability to defend itself, and develop into autoimmune diseases. NIEHS hopes to find clues that will lead to treatments and cures, or ways to prevent the development of these diseases.

Individually Rare, Collectively Common

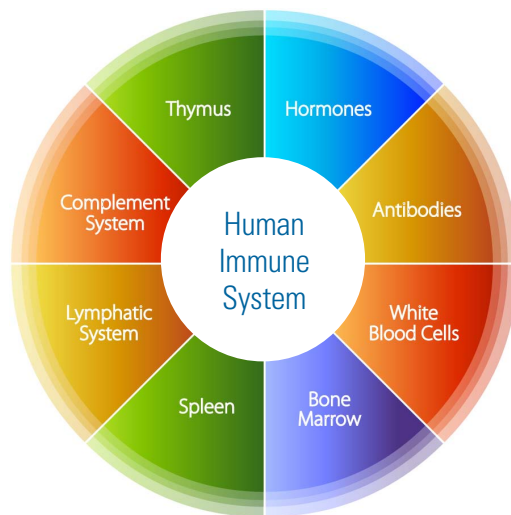
Collectively, autoimmune diseases are among the most prevalent diseases in the U.S., affecting more than 23.5 million Americans. They are more common among women, and while some are more prevalent among white people, others are more common among African-Americans and Hispanics.¹ Autoimmune diseases are becoming increasingly prevalent, for reasons unknown.

Some autoimmune diseases are life-threatening, and most are debilitating and require a lifetime of treatment. There are treatments available to reduce the symptoms and effects from many autoimmune diseases, but cures have yet to be discovered. Since most autoimmune diseases are rare, patients can often spend years seeking a proper diagnosis.

NIEHS and NTP Research Efforts

Unraveling the connections between genetic predisposition and environmental triggers is a major focus for NIEHS and the National Toxicology Program (NTP), an interagency testing program headquartered at NIEHS. Progress is being made through multiple research efforts, some of which are noted below.

- A 2012 study by NIEHS researchers found that over 32 million people in the U.S. have autoantibodies. Earlier studies have shown that autoantibodies can develop many years before the clinical appearance of autoimmune diseases. The study, which looked at the most common autoantibodies, antinuclear



antibodies, found that they are most prevalent among women. This research suggests that the hormones estrogen and progesterone might be affecting the immune system.²

- A study of residents in Libby, Mont., who have experienced significant exposure to asbestos minerals due to mining in the area, suggested a link between asbestos exposure and lesions in the lungs. Sixty-one percent of Libby residents tested had autoantibodies and were more likely to have two types of lung abnormalities.³
- An NIEHS study found associations between ultraviolet radiation from sunlight and the development of an autoimmune muscle disease, myositis, particularly in women.⁴
- Low birth weight and low socioeconomic factors in childhood were associated with the later development of rheumatoid arthritis as an adult.⁵



- Recognizing that individuals are never exposed to one chemical at a time, NIEHS grantees studied what happens when mice are exposed to two suspected triggers for autoimmune diseases. Previous studies had shown that exposure to trichloroethylene, a solvent and degreasing compound, induced autoimmune hepatitis in autoimmune-prone mice. This study found that when the mice were also exposed to mercuric chloride, a compound used as a disinfectant and also in photography, disease development accelerated and a unique, liver-specific autoantibody response occurred.⁶

- NIEHS grantees studying blood samples of Brazilian mothers exposed to methylmercury, an environmental contaminant passed on to humans by eating contaminated fish, found elevated levels of autoantibodies in the blood of both mothers and their fetuses.⁷

- NIEHS and NTP researchers demonstrated that a certain enzyme creates mutations in DNA and is a major player in the development

of autoantibodies. The discovery of the role of this enzyme establishes it as a potential target for therapy in autoimmune disorders, such as lupus.⁸



Unraveling Environmental Triggers

NIEHS brought together an interdisciplinary group of experts to evaluate the state of the science regarding the role of the environment and the development of autoimmune diseases.

The experts identified future research directions, identified promising mechanistic theories and animal models, and identified some specific environmental agents that may be involved in the development of autoimmune diseases.^{9, 10, 11}

The findings include:

- Exposure to solvents, which are used in thousands of products, including paint thinners, cleaning supplies, and nail polish, contributes to the development of systemic sclerosis.
- Smoking contributes to the development of two types of rheumatoid arthritis.
- Exposure to fine particles of crystalline silica, a basic component of quartz, granite, and many other minerals, contributes to the development of several autoimmune diseases. Workers exposed to these minerals are particularly at risk.
- Eating gluten, present in wheat and some other grains, contributes to the development of celiac disease, a disorder that affects the small intestine and commonly causes chronic diarrhea and fatigue.
- Taking certain supplements containing L-tryptophan, an essential amino acid used as a dietary supplement, contributes to development of eosinophilia myalgia syndrome, an incurable and sometimes fatal condition involving severe muscle pain.

¹ HHS (U.S. Department of Health and Human Services Office on Women’s Health) Autoimmune Diseases Fact Sheet. [accessed October 23, 2012].

² Satoh M, Chan EK, Ho LA, Rose KM, Parks CG, Cohn RD, Jusko TA, Walker NJ, Germolec DR, Whitt IZ, Crockett PW, Pauley BA, Chan JY, Ross SJ, Birnbaum LS, Zeldin DC, Miller FW. 2012. Prevalence and sociodemographic correlates of antinuclear antibodies in the United States. *Arthritis Rheum* 64(7):2319-2327.

³ Marchand LS, St-Hilaire S, Putnam EA, Serve KM, Pfau JC. 2012. Mesothelial cell and anti-nuclear autoantibodies associated with pleural abnormalities in an asbestos exposed population of Libby MT. *Toxicol Lett* 208(2):168-173.

⁴ Love LA, Weinberg CR, McConnaughey DR, Oddis CV, Medsger TA Jr, Reveille JD, Arnett FC, Targoff IN, Miller FW. 2009. Ultraviolet radiation intensity predicts the relative distribution of dermatomyositis and anti-Mi-2 autoantibodies in women. *Arthritis Rheum* 60(8):2499-2504.

⁵ Parks CG, D’Aloisio AA, Deroo LA, Huiber K, Rider LG, Miller FW, Sandler DP. 2012. Childhood socioeconomic factors and perinatal characteristics influence development of rheumatoid arthritis in adulthood. *Ann Rheum Dis*; doi:10.1136/annrheumdis-2011-201083.

⁶ Gilbert KM, Rowley B, Gomez-Acevedo H, Blossom SJ. 2011. Coexposure to mercury increases immunotoxicity of trichloroethylene. *Toxicol Sci* 119(2):281-292.

⁷ Nyland JF, Wang SB, Shirley DL, Santos EO, Ventura AM, de Souza JM, Silbergeld EK. 2011. Fetal and maternal immune responses to methylmercury exposure: a cross-sectional study. *Environ Res* 111(4):584-589.

⁸ Jiang C, Zhao ML, Waters KM, Diaz M. 2012. Activation-induced deaminase contributes to the antibody-independent role of B cells in the development of autoimmunity. *Autoimmunity* 45(6):440-448.

⁹ Miller FW, Alfredsson L, Costenbader KH, Kamen DL, Nelson LM, Norris JM, De Roos AJ. 2012. Epidemiology of environmental exposures and human autoimmune diseases: Findings from a National Institute of Environmental Health Sciences Expert Panel Workshop. *J Autoimmun*; doi:10.1016/j.jaut.2012.05.002 [Online 25 June 2012].

¹⁰ Selmi C, Leung PS, Sherr DH, Diaz M, Nyland JF, Monestier M, Rose NR, Gershwin ME. 2012. Mechanisms of environmental influence on human autoimmunity: A national institute of environmental health sciences expert panel workshop. *J Autoimmun*; doi: 10.1016/j.jaut.2012.05.007.

¹¹ Germolec D, Kono DH, Pfau JC, Pollard KM. 2012. Animal models used to examine the role of the environment in the development of autoimmune disease: Findings from an NIEHS Expert Panel Workshop. *J Autoimmun*; doi:10.1016/j.jaut.2012.05.020.