### **Autoimmune Diseases and Your Environment**

Autoimmune diseases are conditions in which the immune system attacks healthy cells in the body. A healthy immune system can defend the body against disease and infection; however, if the immune system makes a mistake, it can create autoantibodies, which target and react with a person's own healthy cells, tissues, and organs, leading to autoimmune diseases. This attack can affect any part of the body, weakening bodily functions and can even be life-threatening.

Research at the **National Institute of Environmental Health Sciences** (NIEHS) suggests that factors in our environment and lifestyles may contribute to autoimmune diseases.<sup>1</sup>

There are more than 100 autoimmune diseases. Some are well known, such as Type 1 diabetes, multiple sclerosis, lupus, and rheumatoid arthritis, while others are rare and difficult to diagnose. Many patients suffer for years before getting a proper diagnosis. Most of these diseases have no cure, and there are few effective treatments to ease symptoms.

## Autoimmune diseases are rising, especially in women

Data shows that autoimmunity and autoimmune diseases are increasing in many parts of the world. They affect at least 1 in 20 individuals in the adult U.S. population, with substantial personal and societal costs.<sup>2</sup> In the United Kingdom, research suggests 1 in 10 people are affected by autoimmune diseases.<sup>3</sup>



Differences in sex are especially linked to the chance of developing an autoimmune disease. These diseases are twice as likely to afflict women than men.<sup>4</sup> The reasons underlying the higher prevalence of autoimmune diseases in women are not yet understood, but there is new information about differences in immune responses in females.<sup>5,6</sup> Autoimmune diseases can also affect males and females differently.

Research increasingly suggests that autoimmune diseases likely result from the interactions of environmental and genetic risk factors. Autoimmune diseases seem more common when people are in contact with certain environmental exposures, including smoking, crystalline silica exposure from working with quartz or granite, and solvent exposures, such as paint thinners and cleaners.<sup>7</sup> The National Institutes of Health (NIH) established an Office of Autoimmune Disease Research<sup>8</sup> within the Office of Research on Women's Health to better coordinate and accelerate research on autoimmune diseases across NIH. One of their initiatives, called the Exposome in Autoimmune Diseases Collaborating Teams Planning Awards (EXACT-PLAN), has awarded grants to develop several autoimmune disease research networks to advance the study of the exposome (the totality of all environmental exposures and our body's response to them across the lifespan) in autoimmune diseases.

#### What is NIEHS doing?

For decades, NIEHS has researched how the environment may affect the development of autoimmune diseases. Research progress had led to discoveries, such as:

- **Determining impact** NIEHS in-house researchers found that one type of autoantibody, called antinuclear antibodies (ANAs), has increased nearly 50% in the U.S. in less than 30 years. Teenagers in the study experienced a nearly 300% increase in ANAs between 1988 and 2012.<sup>2</sup>
- Finding therapeutic targets Researchers analyzed gene regulation in children and adults with an autoimmune disorder called dermatomyositis and found key signaling pathways that could be potential therapeutic targets. The unique analysis of transcript and protein expression together enabled the identification of key pathways involved.<sup>9</sup>





 Identifying risk factors for rheumatoid arthritis – Rheumatoid arthritis is a chronic (long-lasting) autoimmune disease that primarily affects joints.

- Stressful life events Varied, stressful life events may increase the risk of developing rheumatoid arthritis or lupus, another systemic autoimmune disease.<sup>10</sup> Children who experience adverse life events, such as abuse, poverty, or discrimination, may be at greater risk of developing rheumatoid arthritis in adulthood.<sup>11</sup>
- Agricultural chemicals Exposure to some pesticides may play a role in the development of rheumatoid arthritis in male farmers.<sup>12</sup> The same study shows that in women who live on farms, an increased chance of developing rheumatoid arthritis was associated with other types of farm-related exposures, such as painting and using solvents.<sup>13</sup>
- Proximity to hog farms Researchers found that people who lived within 8 miles of a large swine feeding facility in North Carolina were more likely to have an increased risk of autoimmune disorders, such as rheumatoid arthritis, than those who lived farther away.<sup>14</sup>
- Genetics NIEHS-funded researchers are close to discovering why a genetic risk that increases the chance of developing rheumatoid arthritis is amplified by environmental pollutants, like cigarette smoke.<sup>15</sup>

- Identifying risk factors for myositis Myositis is a chronic (long-lasting) autoimmune disease that affects muscles and results in weakness. Dermatomyositis is a form of myositis that includes photosensitive skin rashes.
  - Risk from ultraviolet (UV) radiation –
    Short-term UV radiation exposure, as from outdoor sunlight, may affect the onset of adult and juvenile dermatomyositis, an illness with muscle weakness and skin rashes.<sup>16</sup>
    The chance of illness increased as the UV index increased to high levels in the month before symptoms began.<sup>17</sup>
  - Genetic factors in autoimmune muscle disease – Using DNA samples from myositis patients of European ancestry, NIEHS researchers identified primary genetic risk factors associated with this autoimmune muscle disease.<sup>18</sup>
  - Effective treatments for some patients with myositis include targeted biologic drug therapies.<sup>19</sup>
- Using mice to identify new genetic causes of autoimmune disease – In-house scientists at NIEHS have discovered that IRGM1, a protein in mice that helps cells clear their damaged parts, is important in preventing autoimmune disease.<sup>20</sup> Mice that had the IRGM1 gene removed develop findings very similar to patients with Sjogren's syndrome, an autoimmune disease that damages the salivary and tear glands, among other organs. Some variants of IRGM, a similar gene in humans, have been associated with increased risk for autoimmune disease in people.<sup>21</sup>
- **Role of nutrition** Vitamin D may help prevent immune dysfunction in older populations.<sup>22</sup> For lupus patients, NIEHS-funded researchers found that dietary micronutrients — choline, folate, and vitamin B12 — may improve symptoms.<sup>23</sup>



# NIEHS is recruiting for clinical studies on autoimmune disease:

- Adult and Juvenile Myositis investigates the causes, immune system changes, and medical problems associated with myositis, an inflammatory muscle disease that can cause chronic muscle weakness. Adults and children diagnosed with myositis may enroll by completing questionnaires, undergoing a detailed medical evaluation and other testing, and donating blood and urine samples.
- The MYORISK Study seeks to understand the environmental factors that may result in dermatomyositis or polymyositis, a form of myositis that causes muscle weakness on both sides of the body.
- To volunteer for a study on the causes of, and possible treatments for, autoimmune diseases, visit https://joinastudy.niehs. nih.gov.



### **Five Common Autoimmune Diseases**



For more information on the National Institute of Environmental Health Sciences, go to **https://www.niehs.nih.gov**.

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- <sup>14</sup> Ayala-Ramirez M, et al. 2023. Association of distance to swine concentrated animal feeding operations with immune-mediated diseases: An exploratory geneenvironment study. Environ Int 171:107687.
- <sup>15</sup> Fu J, et al. 2018. Shared epitope-aryl hydrocarbon receptor crosstalk underlies the mechanism of gene-environment interaction in autoimmune arthritis. Proc Natl Acad Sci USA 115(18):4755-4760.
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