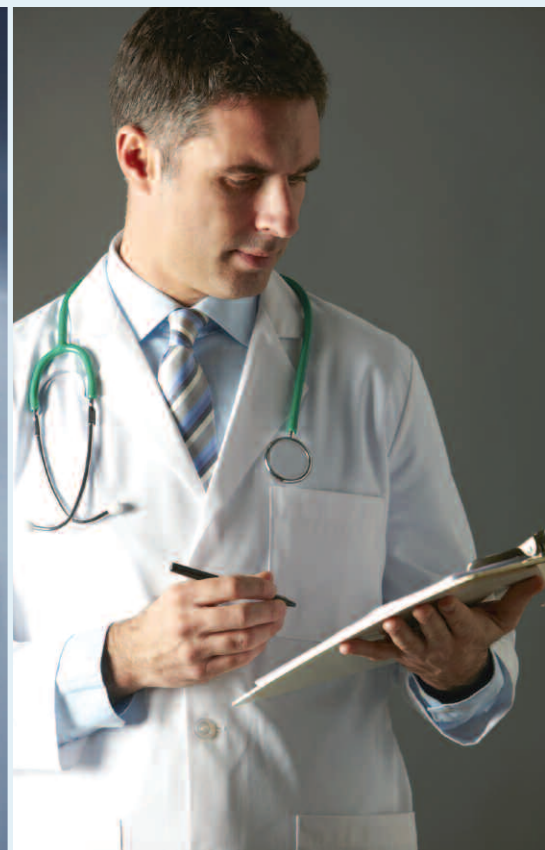


Autoimmune Diseases:



The Growing Impact

By Amy Scanlin, MS

Despite its increasing prevalence, autoimmunity is still not categorized as a “disease,” and research to determine its cause remains hindered due to a lack of focus and funding.

Autoimmunity contributes to more than 100 serious chronic illnesses that involve almost every organ system in the human body. Some of these diseases are cited in the top-10 leading causes of death in women aged 65 and younger, and together, they represent the fourth-largest cause of disability among women in America.¹

The National Institutes of Health's (NIH) Office of Research on Women's Health has named autoimmunity a major health issue that attacks women; 75 percent of autoimmune diseases (ADs) occur in women.¹ It is believed that women's enhanced immune systems make them more susceptible to ADs because, while enhanced immunity makes them more resistant to infection, it also exacerbates the autoimmune response that occurs when the body turns on itself and starts attacking healthy cells.

But, even with the staggering statistics surrounding autoimmunity, it has not yet been categorized as a disease. And despite the fact that the diseases believed to be caused by autoimmunity span many speciality areas, there has yet to be a determination that autoimmunity is the underlying cause.¹

A Brief History

The idea of autoimmunity first came to light in the early 1900s, and the understanding that autoimmunity was in fact a feasible underlying cause for disease was recognized in the 1940s. The term AD was probably first recognized in a 1963 monograph and a subsequent international conference in 1965.² Fast-forward to 1998 when the NIH created the Autoimmune Diseases Coordinating Committee (ADCC) under the direction of the National Institute of Allergy and Infectious Diseases (NIAID).

In 1992, only 67 ADs had been identified.³ Today, there are more than 100, and there are thought to be about 50 million Americans living with autoimmunity, 30 million of which are women. That number, unfortunately, is increasing, particularly within the past decade. According to the American Autoimmune Related Diseases Association (AARDA), while we don't know the reason for the increase, it is largely suspected to be due in part to environmental factors.⁴

ADs affect 5 percent to 10 percent of the developed world's population. The World Health Organization cites being too clean (also known as the hygiene hypothesis) as possibly impacting the prevalence of AD. "The mechanism by which an AD is triggered is still not known, but there is valid research supporting this 'too-clean' theory," says Virginia Ladd, president and executive director for AARDA. "For instance, some treatments for Crohn's and MS [multiple sclerosis] show the inflammatory response is reduced as the body goes after a parasite. Also, on the microbial theory, antibiotics clean out a lot of the good bacteria in the gut. We may have evolved so that our immune systems are decreasingly efficient."

ADs such as diabetes and MS are quite rare in less-developed

areas of the world like Africa and Asia, and yet they are on the increase in societies that have a modern infrastructure.³ Part of the reason is the health structure within less-developed nations and the diseases on which they are primarily focusing. In Africa, for instance, healthcare officials are so overwhelmed with diseases such as AIDS and malaria, they are not closely looking at ADs. However, says Dr. Noel Rose, director of the Johns Hopkins University's Center for Autoimmune Disease Research, "We have pretty good data from industrialized countries that are showing a true increase in AD, and we have been able to separate that true increase from a greater awareness of AD. After all, you diagnose what you are looking for. Data from Scandinavian countries such as Finland and Sweden — countries with a good national health scheme — are showing solid diagnostic measures. The consensus shows that AD rates are going up and at fairly significant rates. There is huge speculation, however, as to why."

Possible Theories of AD Development

Why so many people have multiple ADs and why they tend to run in families seems to point to genetics. Those who have a genetic predisposition to ADs will have a two- to five-times greater chance of developing one (or more) than those who have none.⁵ It is estimated that about one-third of a person's risk of developing AD is due to hereditary factors, and the rest belongs to the environment. "We know in broad terms that there is a genetic component in every AD," says Dr. Rose.

Even with the staggering statistics surrounding autoimmunity, it has not yet been categorized as a disease.

In January 2012, the National Institute of Environmental Health Sciences reported that 32 million people in the U.S. have autoantibodies, most commonly antinuclear antibodies (ANA). Some who have ANA go on to develop ADs, and some do not.⁴

Finding genetic markers is an area of research that scientists are really excited about. "That is the real problem that is holding back progress," says Dr. Rose. "In most cases, we don't see a patient until the damage has been done, and you can't reverse that damage. What we want to do, and are slowly working our way toward, is finding early genetic markers that will allow us to begin to see patients earlier when AD may be reversible or even earlier before it develops to tell them of their risk.

Genetics, whether someone is high risk or low risk or somewhere in between on the scale, is the kind of information we'd like to be able to impart on patients. Susceptibility is not an all-or-nothing prospect. We can give patients advice when we know there is enough risk, and in certain groups where there is a pregenetic disposition, antibodies rise years before the disease presents. The type and number of antibodies are becoming predictive clues but are not at the clinical level yet."

One promising area that has provided a better understanding of why women tend to develop AD more than men is the link between the hormone estrogen and the immune response. The sex hormone estradiol has shown to induce a lupus-like disease in highly susceptible mice. Estradiol makes B cells that produce autoantibodies resistant to apoptosis — autoantibodies that normally destroy them. According to the study, when mice that were susceptible to lupus were treated with the hormone prolactin, "autoantibody-producing cells that are usually eliminated by the immune system survived, and the mice developed lupus symptoms."⁶

Currently, scientists are actively studying only 24 of the more than 100 ADs. This makes it harder to find a generalized way of connecting the diseases to one or some causal factors that would connect them into a disease category to better enable diagnoses and find treatments. A better understanding of ADs in the medical community can lead to earlier diagnosis and better management of symptoms, particularly through efforts such as community-based triage centers rather than emergency room visits and hospital stays.⁷ This also affects funding; if ADs are not looked at in their totality, the impact of those diseases as a whole will be lessened and so, too, may the dollars put toward research.

Currently, scientists are actively studying only 24 of the more than 100 ADs.

There is a great focus in researching the etiology of autoimmune-related diseases, instead of a primary focus on treating a singular disease.¹ In 2003, etiology of AD received about 45.5 percent of research funding, followed by the study of genetic links (14.6 percent) and the environment (5.4 percent).⁷

While more crossover research among the different diseases is needed to confirm a causal link, one area that is being heavily investigated is the environment. Scientists are trying to determine if vaccines, female hormones, UVB radiation exposure, fetal blood cells, stress, vitamin D deficiency and toxins impact autoimmune prevalence.⁴ Doctors know, for instance, that

certain drugs such as procainamide and hydroxyzine can induce a lupus-like syndrome in genetically-susceptible individuals. When an individual is taken off the drug, the symptoms go away. As well, certain substances in the diet such as iodine can exacerbate thyroid disease. "If someone gets too much iodine in their diet, they are likely to develop AD of the thyroid," says Dr. Rose. "In our society, we have a diet heavy in fast food with lots of salt." Also, metals such as mercury, gold and silver can induce lymphocyte proliferation and subsequent autoimmunity. And, a selenium deficiency has been linked with autoimmune thyroiditis and cardiomyopathy, but improvements can be seen by some when taking selenium supplements.⁷

"We have a small list of exposures of things we know anything about," says Dr. Rose. "In some diseases like lupus, the effects of sun exposure is well-defined. We know of a few drugs where in a small percentage of people, they will trigger AD. That's probably in those who are genetically predisposed and the disease needed a little kick that the drug provides. We also have to put smoking on that list. We have lots of anecdotal information but don't have solid evidence yet as to these environmental risks. With the human genome project, it is possible that someday we will be able to have a more complete picture."

Scientists are also working to determine if infections and/or viruses may induce type 1 diabetes and MS, as well as lupus and rheumatoid arthritis.

Fiscal Impacts

In March 2011, the AARDA released a study on the fiscal burden of ADs. Because those diseases are not lumped together as one group, it is difficult to get a true cost for patients, insurance companies, federal government and research institutions. However, it is estimated that the 100-plus diseases together cost upward of \$86 billion¹ to perhaps hundreds of billions of dollars in both direct and indirect costs.⁷ And, some feel that number is too low, given the fact that the direct and indirect cost of the seven most common ADs (Crohn's, ulcerative colitis, lupus, MS, rheumatoid arthritis, psoriasis and scleroderma) reaches \$50 billion alone.³

One reason the diseases are a funding challenge is because each disease is tracked independently, not collectively, under a nonexistent umbrella category of AD. So the true cost of ADs together is not actually known. The Agency for Healthcare Research and Quality also does not have codes for all the 100-plus individual ADs, making a thorough tracking of disease and costs nearly impossible.⁴

Additionally, because the totality of ADs is not documented, and thus its impact is not obviously significant, its funding for research falls short compared with diseases with a clearer impact. For example, the NIH estimates the direct cost for all ADs to be about \$100 billion, while the costs of cancer are estimated to be about \$57 billion, and heart disease and strokes about

\$200 billion. Yet, research funding in the year 2003 equaled about \$591 million for ADs, \$6.1 billion for cancer and \$2.1 billion for heart disease and strokes.⁸ This number does not take into account funding from other sources such as the Centers for Disease Control and Prevention and the Department of Veterans Affairs. “Unfortunately, as a whole, AD [research] is very underfunded. Even within AD, we see most funding going to three or four diseases and not the rest,” says Ladd of the AARDA.

Working with AD Patients

Patients often are misdiagnosed or not taken seriously when first presenting with symptoms that could be related to autoimmunity. This is because their symptoms are often vague and come and go, compounding the difficulty of diagnosis. A 2001 survey by the AARDA found that more than 45 percent of patients with ADs are first labeled as chronic complainers.¹ “Many times, it is such a long process to be diagnosed, they are just happy to have an answer,” says Ladd. “I just spoke to one person with lupus who took eight years to be diagnosed because her doctor wouldn’t send her to a specialist — she was too young, too stressed. ... It took a car accident and an MRI where they saw that she’d had a stroke before she was sent to a specialist. And, it usually takes a specialist to diagnose AD. Generally, a family doctor just doesn’t treat patients with those conditions.”

Oftentimes, insurance becomes a barrier to referrals to specialists, and that may continue. According to Ladd, “Access to specialists is not part of the essential benefits plan in the Affordable Care Act. There is no definition of quality care, and it may be left to the states as to whether they want to include it.”

ADs are not a single disease group, explains Ladd. They are different from patient to patient, and it is important to take patients through what an AD is, give them background on the disease, and how to cope with a chronic illness and overcome challenges. “Developing coping mechanisms is very important,” says Dr. Rose. “AARDA does a great job of putting on forums across the country where we try to explain what an AD is and how it happens. We are trying to demystify medicine and let people know that this is not just some unnamed thing; it is a known entity, and medicine is looking at it.”

“These treatments have become very sophisticated, and it takes a lot to follow the patients through them,” says Ladd. “It can be a real challenge tackling AD, especially when more than one disease presents. It’s a major problem! We don’t have one center in the U.S. that specializes in AD. If you have cancer, you have a selection of oncology centers to go to, but with AD, there is not.”

That means patients must take a more active role in managing their disease as they seek assistance from multiple specialists for each condition. “Patients tend to coordinate their own care, and sometimes one doctor treats with things another doctor may not. For instance, with diabetes, a doctor may not

want a patient to take a corticosteroid because it gets their sugar out of balance, but a rheumatologist may want them to,” says Ladd. It can get tricky. “It is difficult because we have a medical system based on specialties, and AD doesn’t often fit into a speciality. If you have a disease, you want to go to the guy who knows the most about it.”

Patients often are misdiagnosed or not taken seriously when first presenting with symptoms that could be related to autoimmunity.

There are many fine people working on the issue of AD, and that field of people is growing. “Johns Hopkins has Autoimmunity Day each year, and others are coming on board,” says Ladd. “This year, the University of Michigan will sponsor a public forum in June for patients and physicians.”

While there is still a long way to go toward understanding AD, a brighter future is surely ahead as we learn more about the triggers, treatment and how they all link together. ❖

AMY SCANLIN, MS, is a freelance writer and editor specializing in medical and fitness topics.

References

1. American Autoimmune Related Disease Association. Autoimmunity: A Major Women’s Health Issue. Accessed at www.aarda.org/women_and_autoimmunity.php.
2. Mackay IR. Travels and Travails of Autoimmunity: A Historical Journey from Discovery to Rediscovery. *Autoimmun Rev*, 2010 Mar;9(5):A251-8. Accessed at www.ncbi.nlm.nih.gov/pubmed/19883799.
3. American Autoimmune Related Diseases Association. Comprehensive Report on the Global State of Autoimmune Diseases, March 3, 2010. Accessed at www.aarda.org/press_release_display.php?ID=53.
4. American Autoimmune Related Disease Association. 32 Million Americans Have Autoantibodies Targeting Their Own Tissues According to NIH Study, Results Highlight Larger Health and Policy Issues Says Patient Group, Jan. 18, 2012. Accessed at www.aarda.org/press_release_display.php?ID=67.
5. Rose NR. The Common Thread. American Autoimmune Related Diseases Association. Accessed at www.aarda.org/common_thread_page3.php.
6. *Progress in Autoimmune Disease Research*. NIH Autoimmune Disease Coordinating Committee Report to Congress, March 2005. Accessed at www.niaid.nih.gov/topics/autoimmune/documents/adccfinal.pdf.
7. American Autoimmune Related Disease Association. New Report on Economic Burden of Autoimmune Disease Released for National Autoimmune Diseases Awareness Month, March 22, 2011. Accessed at www.aarda.org/press_release_display.php?ID=63.
8. American Autoimmune Related Disease Association. Autoimmune Statistics. Accessed at www.aarda.org/autoimmune_statistics.php.