

American Autoimmune

Related Diseases Association, Inc.

New Trends in Autoimmunity for Patients, Researchers and the American Public

Highlights from “The State of Autoimmune Disease: A National Summit”



About American Autoimmune Related Diseases Association

Founded in 1991, American Autoimmune Related Diseases Association (AARDA) is the nation's only non-profit organization dedicated to bringing a national focus to autoimmunity as a category of disease and a major women's health issue, and promoting a collaborative research effort in order to find better treatments and a cure for all autoimmune diseases. AARDA's mission is the eradication of autoimmune diseases and the alleviation of the suffering and socioeconomic impact of autoimmunity through initiating, fostering, and facilitating collaboration in research, advocacy, patient education and public education in an effective, ethical, and efficient manner.

Research Highlights, include:

- providing nearly five million dollars in funds for peer reviewed basic autoimmune research and donor directed specific disease research/fellowships.
- founding of the Center for Autoimmune Disease Research at John Hopkins University Medical Center with a major grant for start-up funding continues to support today. AARDA also sponsors an annual "Autoimmunity Day" program at Johns Hopkins that brings together researchers from many different disciplines who are involved in autoimmune research.
- organizing and/or sponsoring numerous national and international scientific symposia and colloquia as well as cosponsoring several scientific meetings with the National Institutes of Health, American College of Rheumatology, and Clinical Immunology Society.
- working in collaboration with five National Institutes of Health, the U.S. Department of Health and Human Services and other research universities in the U.S. and around the world.

"AARDA has been effective. And I can tell you that they have made an impact on the field. They're deeply appreciated."

- Dr. Robert Carter

Patient Education Highlights, include:

- handling more than 400,000 inquiries per year via phone, email, mail and the internet and developing over 80 patient education information pamphlets.
- hosting 4-5 Autoimmune Public Forums annually in different cities around the country.
- creating the *Autoimmune Walk: Linking Together for a Cure* annual campaign, allowing patients to band together to meet, share experiences and help raise money for research. Walks have been held in Washington, DC, New York City, Chicago, Detroit and Atlanta, among others.

Advocacy Highlights, including:

- initiating, supporting and facilitating the National Coalition of Autoimmune Patient Groups (NCAPG), a coalition of 38 national voluntary health agencies which represent specific autoimmune diseases.
- sponsoring annual Congressional Briefing on Autoimmune Diseases and hosting every several years National Summits on Autoimmune Disease to focus on current and emerging trends.
- successfully advocating for the creation of and/or passage of:
 - NIH Autoimmune Disease Coordinating Committee
 - Legislative language included in the Children's Health Act that required NIH to develop a national strategic plan for autoimmune disease research.

Public Education Highlights, including:

- working with longtime AARDA celebrity spokesperson Kellie Martin who stars in public service and social media campaigns, speaks at patient forums and advocacy events and participates in media interviews.
- creating the "Walk Through Autoimmunity" Curriculum for Grades 3-8 and providing it free to U.S. elementary and middle school teachers to supplement their in-class science lessons.
- conducting ongoing research projects with patients and physicians to better understand autoimmune disease diagnosis, treatment and daily life.

For more information, please visit www.aarda.org or follow AARDA on social media including:

- Facebook (www.facebook.com/Autoimmunity)
- Twitter (@AARDATweets)
- YouTube (www.youtube.com/AARDATube)

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NOTE: By summarizing the ideas from our recent National Summit on Autoimmune Disease, American Autoimmune Related Diseases Association wishes to provide important information and updates to patients, physicians, researchers and those who oversee and set U.S. health and health care policy. We invite anyone with an interested in autoimmune diseases to utilize this report, including the media. It may be reproduced, either in whole or in part, with proper credit given to American Autoimmune Related Diseases Association.

Introduction

Autoimmune disease affects some 50 million Americans and their families. The physical, emotional and economic toll of these diseases is enormous. Autoimmune disease is one of the *top 10 leading causes of death of women* under the age of 65. It encompasses more than *100 diseases*, including psoriasis, Graves' disease, Sjogren's syndrome, multiple sclerosis, rheumatoid arthritis, Crohn's disease and lupus. It is responsible for more than *\$100 billion in direct health care costs* annually.

Since American Autoimmune Related Diseases Association (AARDA) was founded in 1991, autoimmunity has come a long way in terms of being recognized as a major disease category, like cancer and heart disease.

However, there is still much work to be done.

Every March, AARDA and the National Coalition of Autoimmune Patient Groups (NCAPG) celebrate National Autoimmune Diseases Awareness Month to bring much need attention to this major disease category.

"It seems to me that as our knowledge of the actual science behind these conditions increases -- the kind of knowledge on view here today -- the tendency to psychologize and dismiss patients will diminish as well. After all, we don't really think of cancer as being a disease of repression. We don't tell someone who has tuberculosis they're too soulful. We give them antibiotics. I don't want to sound like a Pollyanna, but even with the limited knowledge we have, I think I and many other autoimmune patients are living healthier and more capacious lives than we once did. It's very illuminating to read Henrietta Aladjem's memoir. You realize how hard it was once and how much better it is today. That's thanks to the work of organizations like AARDA and all of you here."
-- Meghan O'Rourke,
journalist, author, poet and autoimmune patient

This past March, we co-hosted the fourth National Summit on Autoimmune Disease which brought together leading experts to advance knowledge and understanding by sharing the most current trends in autoimmune disease research, advocacy and patient issues.

AARDA and NCAPG would like to thank the dozens of experts who participated and the hundreds of autoimmune patients, advocates, policymakers, pharmaceutical industry representatives and others who attended.

The following report synthesizes the key issues that emerged during the daylong summit. We encourage you to read and share the report with your colleagues and partners. A PDF version will be available for downloading on AARDA's web site at www.aarda.org.

Featured Panelists and Speakers

The Doctors/Researchers

- Dr. Robert Carter, Deputy Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases
- Dr. Anne Davidson, Investigator, Feinstein Institute for Medical Research
- Dr. Michael Holers, Head, Division of Rheumatology, University of Colorado
- Dr. William Harvey, Clinical Director of the Arthritis Treatment Center, Tufts University School of Medicine and Chair, Government Affairs Committee, American College of Rheumatology
- Dr. Abid Khan, MidMichigan Health, University of Michigan Health System
- Dr. Frederick Miller, Deputy Chief, Clinical Research Branch, and Head, Environmental Autoimmunity Group, National Institute of Environmental Health Sciences
- Dr. Jennifer Nyland, Assistant Professor, University of South Carolina
- Dr. Noel Rose, Director, Center for Autoimmune Disease Research, Johns Hopkins University

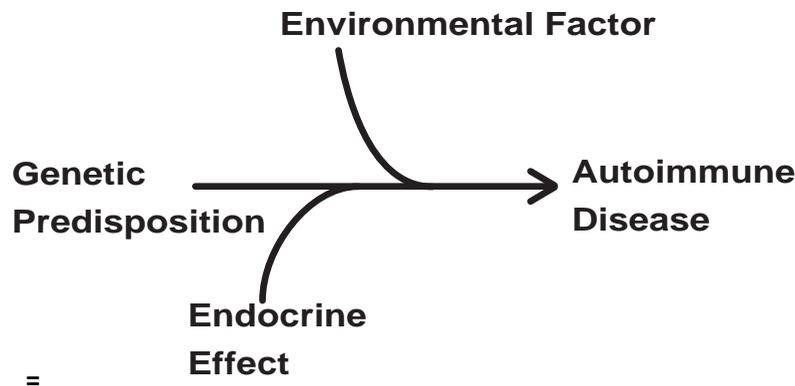
The Patients

- Tracy Evans, Patient
- Beth Harkavy, Patient
- Meghan O'Rourke, Journalist, Author, Poet and Autoimmune Disease Patient
- Tiffany Westrich-Robertson, Patient

The Advocates

- Dr. Dennis Cryer, Chief Medical Officer, CryerHealth
- Stephanie P. Hales, Associate, Sidley Austin LLP
- Virginia T. Ladd, Executive Director, AARDA
- Kellie Martin, Emmy Award-nominated Actress and AARDA Spokesperson
- Georgine Paltzer, ARNet: The Autoimmune Disease Patient Registry
- Michael Reilly, Executive Director, Alliance for Safe Biological Medicines
- Steven Taylor, Chief Executive Officer, Sjogren's Syndrome Foundation

Autoimmune Research: An Overview



Graphic Credit: Dr. Noel R. Rose

It's All in the Genes

- Autoimmune diseases have a genetic precursor, meaning individuals have an inherited predisposition to developing them and it involves a multitude of genes.
- Considerable research has found there are two major types of genes involved in the development of autoimmune disease. The first type is a complicated system called a **histocompatibility complex**, a genetic family that determines what the **lymphocytes** or immune cells detect and how they respond. The other is a multitude of smaller genes that together help regulate the immune system and determine what lymphocytes will do once triggered.

“Trying to understand, even in individuals who don't have an autoimmune disease, how these things are different provides important insights into how genes work together.”

-- Dr. Michael Holers

Autoimmune Diseases Develop in Stages

- With rare exceptions, autoimmune diseases are not pure genetic diseases. Instead, they are diseases that need a necessary trigger in order to manifest.
- Autoimmune diseases develop in stages based on genetic risk and **predictive biomarkers** which include antibodies present in a person's system even though there are no signs or symptoms yet.

The Environment Plays a Key Role Too

- These diseases evolve over time through a combination of genetics and environmental factors. Understanding, on a molecular basis, how and why these genes act the way they do is key. Equally important is understanding the influence external environmental factors have on disease development.
- Today innovative human studies are advancing knowledge by looking at a particular gene in different individuals to determine if differences exist in the expression of that same gene in different individuals and its impact of that difference on the immune response, as well as how outside influences on the genes impact their behavior.

Gender Role in Autoimmune Disease

- Another key to understanding autoimmune disease is how genes express themselves, particularly those related to the body's **endocrine** system. Since these diseases predominantly impact women in the childbearing years, better understanding of the role played by sex-related properties, genes and hormones, in disease development is fundamental.

National Institutes of Health Approaches to Autoimmune Disease Research

Patient-Reported Outcomes Measurement Information System
Launched 10 years ago, the Patient-Reported Outcomes Measurement Information System (PROMIS) offers a more meaningful portrait by allowing researchers to bring patient voices and experiences into the outcomes of clinical trials and other types of research.

Accelerating Medicines Partnership

Because many drugs fail in late stage development due to lack of efficacy, NIH created the Accelerating Medicines Partnership (AMP). AMP brings NIH's research community together with the pharmaceutical industry and patient groups. Working collaboratively, they identify targets for drug development that have a high probability for success. Although originally established around drugs for rheumatoid arthritis and lupus, the concept from the outset has been to create a model applicable broadly to all autoimmune diseases and even other disease categories.

Autoimmune Centers of Excellence

The National Institute of Allergy and Infectious Diseases (NIAID) has created the Autoimmunity Centers of Excellence (ACEs) to encourage and enable collaborative research across scientific disciplines and medical specialties, and between basic and clinical scientists.

One of our major problems in research is the decrease in budget that's happened over the last 10 years. In real terms, a more than 25% decrease in funding to the National Institutes of Health has been voted in by two Presidents and I don't know how many Congresses, because of political issues. An understanding of how these [diseases] happen can't progress without research. Keep that at the forefront of an agenda – not only patient advocacy, but advocacy at the level of research funding.

-- Dr. Anne Davidson

Cosponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the NIH Office of Research on Women's Health (ORWH), ACEs support an integrated basic and clinical research program that focuses on treatment or prevention approaches that induce immune tolerance or modulate the immune system. ACEs investigators also explore the immune mechanisms underlying the agents evaluated in these trials – research that commonly is not included in other clinical trial programs.

Cooperative Study Group for Autoimmune Disease Prevention

Established in 2001, the Cooperative Study Group for Autoimmune Disease Prevention's mission is to focus on the prevention of autoimmune disease. The initiative consists of a group of investigators across multiple public and private research institutions focused on advancing understanding of the natural history of autoimmune diseases and the various features they share including genetics, pathways of disease and treatment.

Autoimmune Disease and the Pharmaceutical Pipeline

- Drug development in common autoimmune diseases is fairly robust. Even for the more rare autoimmune diseases, the market is slowly improving.
- There is a growing shift expensive biological to large, complex, molecules.
- Due to genetic analysis biomarkers, biological tailored specifically to more effective and the and the advent of therapies can be patients, fostering efficient treatments.

“Credit Suisse sees some solid upside in big pharma in the coming years... The brokerage firm updated its autoimmune market model and it sees implications for all large cap U.S. pharmaceutical companies in its coverage. Based on multiple conversations with physician experts and companies active in the space, Credit Suisse sees the U.S. autoimmune market growing to \$30 billion by 2025, up from \$20 billion in 2014.”

– Chris Lange, 24/7WallStreet.com
June 8, 2015

Autoimmune Disease and Fatigue: What's the Connection?

Autoimmune Disease and Fatigue: Patients Speak

- At the summit, AARDA released the results of a survey of more than 7,800 autoimmune disease (AD) patients who called fatigue “a major issue” that impacts nearly every aspect of their lives, describing it as “profound,” “debilitating,” and “preventing them from doing the simplest everyday tasks.”
- Much of the panel discussion surrounded patients’ experiences that amplified what the data revealed, including:
 - Almost all patients surveyed reported suffering from fatigue.
 - Nine-in-10 called it a “major issue” and six-in-10 said it is “probably the most debilitating symptom of having an AD.”
 - More than two-thirds said their “fatigue is anything but normal. It is profound and prevents [them] from doing the simplest everyday tasks.”
 - While nearly nine-in-10 said they have discussed their fatigue with their doctor, six-in-10 said their doctors have neither prescribed nor suggested treatment.
 - Three-quarters said it has impacted their ability to work; nearly four-in-10 said they are in financial distress because of it; one-in-five said it has caused them to lose their job and the same number report they have filed for disability because of it.
 - Fatigue impacts nearly every aspect of AD patients’ lives including overall quality of life (89 percent), career/ability to work (78 percent), romantic (78 percent), family (74 percent) and professional relationships (65 percent) and their self esteem (69 percent), among others.

AARDA Spokesperson Kellie Martin on The Pajama Challenge

I've been told that many autoimmune patients have what they call their “pajama days.” Those days when the fatigue is so bad, it's hard for them to accomplish everyday tasks like taking a shower, getting dressed, caring for their children and going to work. A really wonderful woman and multiple sclerosis patient named Kim Radomski had a great idea that she shared with family, friends and AARDA. Kim began challenging everyone she knows to do the Pajama Challenge to raise awareness of autoimmune disease and funds for research. It's simple. First, put on your favorite pair of pajamas. Then, queue up your favorite dance song. Next, tell people you are dancing or pillow fighting in your PJs to support #autoimmune disease patients and raise funds for #AARDA. Finally, challenge 2 or 3 or 4 of your friends and family to don their PJs and donate to AARDA. Oh, and you have to share the videos on social media. That's where the awareness raising comes in.

Recognizing Fatigue as an Early Symptom of Autoimmune Disease

- Many patients complain their doctors don't take their fatigue seriously. From a doctor's perspective, all is good if a patient

1) looks fine, 2) has good disease activity indices and 3) the treatment for their inflammation has kept a potentially major health issue at bay. Yet, patients still complain of fatigue.

“Fatigue is one of the predominant early signs of a large number, and probably most, autoimmune disorders.”

-- Dr. Noel Rose

- For physicians, fatigue is problematic for several reasons. First, while they may have some understanding, there are no easy medical solutions for fatigue. Second, managing autoimmune disease is complex and time-consuming. Finally, unlike pain, no metrics exist that allow doctors to define the impact fatigue has on a patient's daily function.

Status of Research on Fatigue

- The research community's understanding of autoimmune disease fatigue is at a fairly basic level. Research must increase in order to provide patients with effective and efficient treatment.

- What we know:

- a common side effect of certain **cytokines**, which are used to treat disease, is extreme fatigue.
- cytokines also are released during illness as a protective mechanism to make patients rest.

- Several fatigue research areas in the early stages are focusing on:

- the connection between the neurological system - the brain and nerves - and the immune system;

“The overwhelming response AARDA received to this survey shows without a shadow of doubt that fatigue is not a ‘fuzzy’ symptom, it's real. Yet, for too long, it has been ignored and/or misunderstood by the medical community and the public at large. It's time we bring more research funding to this issue to advance understanding and effective treatments for fatigue.”

-- Virginia Ladd

- the role of stress in inflammation and breaking down the “blood-brain barrier”
- the barrier that protects the brain from toxins and other external exposures;
- the connection between the metabolic system and the immune system; and,
- understanding fatigue signals that come from the “periphery” or outside of the brain.

Autoimmunity and the Environment

Autoimmunity and the Environment are Connected

- Studying the connection between autoimmunity and the environment is critical to understanding not only how autoimmunity begins, but how these diseases may eventually be prevented.
- Over the last several decades, studies have shown a significant number of autoimmune diseases increasing in frequency in the U.S. and around the world - sometimes very dramatically, such as with Crohn's disease, multiple sclerosis and type 1 diabetes.
- Mounting evidence for the role of environment comes from a variety of sources, including:
 - studies of identical twins which show relatively few pairs develop either the same or any autoimmune disease at all, despite having the same genetic makeup.
 - animal models or in vitro studies where researchers actually induce autoimmune disease with different environmental compounds, chemicals and other agents.

These increases [in autoimmune disease] can't only be explained by the medical community's ability to better diagnose and treat them. Something else must be going on – and that reason is the great changes in our environment prompted by the last 40 or 50 years of industrialization.

-- Dr. Frederick Miller

Have You Been Exposed?

In food, in the playground and on the walk to work, individuals face numerous external factors. New technologies have been developed that help better assess the what, how and where of these environmental exposures:

- wearable personal monitors that can detect a wide variety of environmental exposures
- mobile health apps and devices that offer new ways of monitoring health and environmental exposures in real time.
- geographic information systems (GIS) or new computer methods that examine large collections of patients over large areas where there are clusters as well as deficiencies of disease and then connect the information with environmental databases in order to shed light on possible disease triggers.

- a “de-challenge” process whereby disease improves after researchers remove a potentially offending agent and then “re-challenge” the redevelopment of disease by reintroducing that agent, thereby demonstrating the agent is the cause of that particular disease.
- the “clustering” of specific autoimmune diseases by season, geographical location and birth date – all suggesting something occurred around those times and in certain areas leading to the development of disease.
- studies demonstrating that environmental agents can alter the structure of cells, making them appear to be foreign invaders, resulting in either an activation or suppression of the immune system.

The Interplay of Genetics and Environment

- Everyone has genes that are responsible for regulating the gene response to different environmental exposures. An individual’s genetic risk for developing autoimmunity is based on how their genes respond to different such exposures.
- Rheumatoid arthritis offers a good lesson in how genes and the environment work together to produce disease. It has been long recognized there are genes that increase the risk of rheumatoid arthritis. Smoking is an environmental factor that drives the development of rheumatoid arthritis and other autoimmune diseases. When smoking and genes are working together, the risks for developing rheumatoid arthritis become **additive**. By studying how smoking can affect these genes, researchers are learning how this drives rheumatoid arthritis at the earliest stages.

Infectious and Non-Infectious Agents

- Infection is the perfect environmental trigger because it does the two things necessary to prompt autoimmune disease. It stimulates specific lymphocytes that cause disease and does so in just the right way to trigger an autoimmune response.
- While the understanding of infection as a trigger for autoimmune disease is still in its infancy, current data suggest both infectious agents and non-infectious agents play a role.
- Infectious agents include bacteria, viruses and parasites. The microbiome represents the

The new study [reported March 16, 2015 online in the journal *Arthritis & Rheumatology*] is the first to find an increased risk of certain autoimmune disorders, the researchers say.

Autoimmune diseases arise when the immune system launches an abnormal attack on the body’s own tissue. The conditions seen in this study -- which also included lupus and systemic sclerosis -- affect joints, muscles and connective tissue throughout the body.

The diseases were not common. In the 12 years following 9/11, the researchers found 59 new cases of autoimmune conditions among more than 13,600 firefighters and other recovery workers who were potentially at risk. But their odds of getting such a diagnosis rose 13 percent for each month they spent at the Twin Towers site, the findings showed. And workers who spent 10 months there had a threefold higher risk than those who were on-site for one month.

- Amy Norton, Healthday

Infection to Prevention: From Rheumatic Fever to Autoimmune Myocarditis

Looking to the Past for Clues to Future Prevention

Under the leadership of Dr. Noel Rose, researchers at Johns Hopkins University are using Rheumatic fever -- an autoimmune disease caused by infection that has been cured or nearly eliminated in the developed world -- as window into how autoimmune diseases may potentially be prevented.

Rheumatic fever is a disease whereby the genetics are triggered by a specific pathogenic organism, a bacterium known as the beta hemolytic streptococcus, the strep that causes common sore throats. In 1944, the bacterium was first treated successfully with antibiotics.

This scenario offers a path for the prevention of other autoimmune diseases at relatively low cost. Rather than tampering with genes to eradicate disease, which is risky and expensive, Rose believes it is preferable to identify the organism causing the disease and separate the patient from that organism, thereby preventing and hopefully eradicating the disease.

The challenge, however, is that unlike rheumatic fever, for most autoimmune diseases there is not a good one-to-one ratio of infection to disease.

With that in mind, Rose's team is looking at inflammatory heart disease or autoimmune myocarditis, the major cause of heart disease in people under 40. He and his team are tracing the progression of disease from infection to autoimmunity in order to get clues for earlier diagnosis, treatment and prevention. Using animal models, they can study the disease from the outset, rather than just at the end when patients are very sick. Here's how....

They infect mice with a virus they believe is involved -- Coxsackie virus. This produces viral myocarditis, an infectious disease they then eradicate from the heart. But, some mice go on to develop a second disease called autoimmune myocarditis.

The research team is now trying to dissect this process and see what the virus is doing to initiate the autoimmune process. They've isolated a peptide called cardiac myosin that is responsible for the autoimmune disease. They then induce autoimmune myocarditis by injecting mice with this peptide.

If the mice go on to develop disease, researchers have been able to identify in those mice biomarkers or cytokines, which are basically genetic traits. Cytokines are the mediators of inflammation and higher levels are an early sign that the mouse will go on to develop a potentially inflammatory autoimmune disease. However, researchers believe they can actually block those particular cytokines and prevent the disease. If, indeed, they accomplish this, it will be a major milestone in autoimmunity prevention.

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large collection of organisms that live inside and on us. Certain parts of our personal microbiomes are important in protecting against disease so a change in the microbiome may increase susceptibility autoimmune disease.

- Non-infectious agents include drugs, biologic agents, foods, medical devices, occupational exposures (to silica, beryllium, vinyl chloride), tobacco smoke, UV light, pollution, stress and xenobiotics like heavy metals (mercury), pesticides and petrochemicals.

Xenobiotics and the Development of Autoimmune Disease

- The xenobiotic mercury is the subject of studies to understand if and how it affects the development of autoimmunity and autoimmune disease.
- Environmental exposures to mercury can come from occupational exposures, such as dentists who use amalgams or Brazilian miners amalgamating gold in the Amazon, as well as from consumption of water, arsenic and contaminated foods like rice and fish.
- Studies using small animal models are looking at what happens to the immune system of mice when they are exposed to mercury, both inorganically (occupational exposure) and organically (from consumption).
- In one such study, researchers found they can induce a lupus-like disease which is made considerably worse if the mice were first exposed to a low dose of mercury.
- Another study involving autoimmune myocarditis – an autoimmune heart disease – has shown when researchers expose mice to mercury alone, it does not cause the disease. However, if mice are previously exposed to mercury and then infected with a disease-triggering virus, the heart stops pumping and the mice go into heart failure.
- The good news then is some environmental factors like mercury may not on their own cause disease, but can exacerbate disease if exposed to the xenobiotic previously.

Advocating for Autoimmunity

Biosimilars: Managing Patient Safety

- As biologic therapies reach the end of their patent protection, there must be standards in place for the approval of biosimilar drugs on the basis of analytical and clinical comparison to the already marketed biologic product.

- Biosimilars are similar but can never be identical to the original approved branded product. They are not a 'generic' version, like those for chemically-based drugs.

- For people whose immune systems are already compromised and prone to attacking their own healthy tissues and cells if it perceives them to be foreign invaders, the introduction of any new substance is potentially life-threatening. The differences in manufacturing, however small, have the potential to cause a similar negative immune response. Known as **immunogenicity**, this response can cause further disease and damage to the cells, tissues and organs of AD patients.

- There is still much work to be done to educate physicians and patients about these and other safety concerns surrounding the use of biosimilars, including the need to:

- Establish distinguishable names for all biosimilars.
- Prevent substitution of one biologic or biosimilar for another biosimilar without physician/patient knowledge.
- Create guidelines for **extrapolation**, ensuring clinical evaluation is conducted for each indication.

- There is a serious need for patient data collection on effectiveness of biosimilars so doctors have a comfort level recommending these treatments to patients.

- Since biosimilars have been on the market in Europe for more than a decade, there are calls for the European Medicines Agency to take a leadership role in the regulatory world in terms of not just naming, but basically harmonizing standards worldwide. The U.S. Food and Drug Administration(FDA) also needs to provide guidance since the Affordable Care Act established

A key tenet of medicine is first do no harm, so that basically the implication there is whatever you do, whatever your decision, you have to use your best judgment, your best knowledge, to be sure that you're not going to do harm. That what you are choosing with your patient is most likely to have a beneficial outcome and less likely to have a negative one.

--Dr. Dennis Cryer

The FDA approval [of the first biosimilar in the US in March 2015] really was not the end of solving all of the challenges with regards to biosimilars, it was really the beginning. It essentially left as many unanswered questions as it answered in terms of the main policy challenges.

-- Michael Reilly

a pathway for it to approve biosimilar drugs in the U.S. for interchangeable use with brand name biologic medicines.

Access to Specialty Medicines

Despite recent positive advances in the treatment of autoimmune diseases, a number of barriers prevent patients from accessing them. Among those highlighted at the forum:

Costs and Insurance Reform

- Myriad problematic practices by insurance companies, including:
 - reducing and/or denying coverage of these specialty medications
 - the growing practice of co-insurance
 - decreased reimbursements for providers for administration of infusion drug therapy
 - limiting the number of providers available within network who care for autoimmune disease patients
 - changing the provider network in between open enrollment periods
 - allowing more access to co-pay assistance programs, both at the federal and private pay levels

- Another way to control costs of medications is to streamline the research and development process so that industry can bring treatments to market and offer them at decreased cost.

“Instead of having a fixed dollar amount of co-payment, which you're all probably familiar with, insurers may impose a percentage based payment -- 30, 40 or 50 percent of \$20,000+ is just not affordable to the average American. None of the people who have to take these medications chose their disease or chose their treatment. It's not an elective procedure. We believe that this practice [of co-insurance] needs to end.”

Dr. William Harvey

Insurance Companies Playing Medical Expert

- The role of prescribers for biologic medicines is very important and should be the sole purview of physicians. Yet, often times, insurers are making these decisions.

- The insurance company practice known as “fail first and step edit therapies” is dangerous and should be abandoned. This practice -- which is tantamount to practicing medicine without a license -- involves insurers insisting patients try a particular medication first until it has proven ineffective and fails before they will cover the one the patient's doctor originally prescribed. In the meantime, patients get sicker before they are properly treated.

Patient Perspective: Getting an Autoimmune Disease Diagnosis

A number of patient surveys underscore the lengthy process involved in getting a correct autoimmune disease diagnosis – an average of five years and visits to five different doctors. During that time, patients spend money on expensive tests, doctor visits, treatments that don't work and, often times, psychiatrists. It's frustrating, time-consuming and expensive not only for them but also for the U.S. healthcare system. At the summit, discussion focused on new strategies for patients and doctors that could help expedite a proper diagnosis.

For Patients.....

How to Tell Your Symptom Story: Not Fatigued, “Function-Impaired”

- Don't start the conversation with your doctor complaining of chronic fatigue. Instead, emphasize the difficulty you're having “functioning” --whether it's at work or home -- and challenge him/her to find out why.

Prepare Your Story, Succinctly

- Don't be afraid to script your story. Have a timeline of specific symptoms, event by event. Write it down on a piece of paper to hand your doctor so you don't forget anything. Most important, keep it short and sweet.

- Scripting can help a doctor get you answers quicker.

Focus on Mid-Michigan Health Autoimmune Disease Center

The first Autoimmune Disease Center in the United States is located at the University of Michigan's Health System's MidMichigan Health. Helmed by Dr. Abid Khan, the center focuses on diagnosing patients with suspected or confirmed autoimmune disease, and providing them with compassionate care by the proper specialist.

Here's how it works. Patients are referred because they have either been diagnosed with an autoimmune disease or they're suspected to have one. The center functions as a triage center – with two tiers. The first tier determines if they have autoimmunity, a non-autoimmune condition, or are in the “gray” area.

In the second level of triage, the course taken depends upon how they are categorized during tier one.

“As William Osler said, listen to your patient, he's telling you the diagnosis. Physicians do not have the time or the skills to listen about fatigue. They're not taught this. The patient needs to be empowered with that knowledge. There's another message for patients, too, and that's how they describe their chronic fatigue – they should not describe their fatigue as fatigue.”

-- Dr. Abid Khan

- For those with confirmed autoimmunity, proper tests are run, the university lab analyzes the results and specialty pathologists read the slides and provide the diagnosis. That diagnosis is then confirmed by an autoimmune disease specialist who then takes over patient care.
- For those with non-autoimmune disease conditions, the same process ensues with a patient given a non-autoimmune disease diagnosis.
- Those in the gray area are the most challenging and fascinating. Many do not have conclusive evidence of autoimmune disease. The center takes on these patients, stays in contact with them, tracks new symptoms and asks them to come back every few months for re-assessment. Some of these patients eventually are diagnosed with an autoimmune condition. Others who are not diagnosed with autoimmune disease may be dealing with psychosocial issues. Emotional stress may, in fact, be what is causing their unexplained symptoms. The center has successfully treated these patients with a combination treatment of counseling and antidepressants.

The reality of taking this long for a diagnosis leaves the patient suffering needlessly and often sustaining more severe and irreversible organ damage. And that is the truth in many of our diseases. We need to catch it early so we can get them on disease-modifying drugs or immunosuppressants to slow down the disease state so that we don't have the irreversible organ damage.

-- Dr. Stanley Finger, Vice Chair
AARDA Board of Directors

For Doctors...

Ramp Up Need: Autoimmune Education in Medical School

- A recent AARDA survey found nearly two-thirds of family physicians are uncomfortable or stressed when diagnosing an autoimmune disease. Nearly three-quarters do not believe they received adequate training for treating these diseases, with roughly six-in-10 reporting they had a total of only one or two lectures on autoimmune disease throughout their entire medical education and training. The take-home message here is two-fold:

What is the Autoimmune Disease Patient Registry – ARNet?

In order to advance autoimmune disease research, it is critical that National Coalition of Autoimmune Patient Groups come together with researchers and perhaps pharma as well, to build a registry of autoimmune patients.

AARDA has spearheaded ARNet – the Autoimmune Disease Patient Registry Research Network – to do just that. ARNet's goal is to create one comprehensive, central database that is anonymous and includes patient information, diagnosed diseases and other demographics. In doing so, it will enable researchers who might be interested in looking at the bigger picture to do a query on multiple data sources at once.

With ARNet, AARDA is creating the “big data” source on autoimmunity. Ultimately, having access to this information could lead to decreasing the time to proper diagnosis and treatments, increasing collaboration among researchers and raising awareness of autoimmune disease.

Equally important, ARNet gives researchers access to patients for their clinical research. Today, ARNet's database represents some eight participating patient groups, providing information on 67,000 patients with 2.34 million data points.

For more information about participating, contact AARDA at 586-776-3900.

- 1) American medical schools should include vigorous immunology courses as part of its basic education.
- 2) Residency programs should include an "Introduction to Autoimmunity" education course where residents are introduced to autoimmunity the way they are introduced to oncology – as a mechanism of disease that needs to be thought of collectively across disciplines.

AUTOIMMUNE PATIENTS ON AUTOIMMUNE DISEASE, CHRONIC ILLNESS AND THE GENDER ISSUE

Beth Harkavy

My future once seemed bright, but now I wasn't sure that I had one beyond being ill. I had to go on medical leave from my Ph.D. program and stop working completely. I saw more than 40 physicians over a period of three years. By the time I found myself at Hopkins in 2011, where I was eventually diagnosed, I had been dismissed countless times. Some doctors insinuated that my illness could all be in my head, something which I later learned is experienced by many, especially female patients, who are the ones who mostly have autoimmune disease.

Tracy Evans

There is a lot of frustration when something overtakes your body. Doing big dinners and having family over, which I love to do, decreased. Doing things with my boys like playing basketball --that became less. And the hospital visits increased. I sought disability starting in 2006. I got a letter from Social Security saying I am disabled and I would be eligible, but the lawyer did not do some things on time. As a result, my credits had expired from working for 10 years.

Tiffany Westrich-Robertson

I would say to my dad, "You're in your 70s and there are things you can't do anymore, right?" And he'd say, "Yeah, yeah, I'm not as fast as I used to be. I can't juggle as much." And I said, "Okay, well, you were prepared for that because everyone knows that by the time you reach a certain age you have to give up certain things. What happens when you're 35 years old and you suddenly can't do anything anymore? All at once? And you weren't expecting it?"

Meghan O'Rourke

It can be very hard to understand the trajectory of one's own illness, or communicate it to others. Illness narratives in the popular culture usually have startling beginnings -- the fall at the supermarket, the lump discovered in the abdomen, the doctor's call. Not mine and probably not many of yours.

All this murkiness that we've been talking about here is compounded by the fact that autoimmune patients tend to be women and we know that gender, along with race, has real implications on care in medicine.

What this suggests to me is that many doctors, indeed many of us, have difficulty accepting women's self reports of illness symptoms. Women's complaints are turned into subjective, emotional issues rather than seen as a reflection of a hard or objective physiological reality.

It seems to me that for complicated reasons, when women are sick, the first question we ask is not often what's wrong with them, but why something is wrong with them. For all of these reasons, research into the concrete manifestations of autoimmune disorders is critical.

PATHS FOR THE FUTURE

Over the course of the summit, the following areas emerged as having great potential in preventing, diagnosing and treating autoimmune diseases.

Big Data

- Big Data will be the 21st century way of doing human research, allowing investigators to access human-related data as opposed to only data from reductionist research in animals.
- If researchers can look at enough people, conclusions can be drawn.
- Expanding this approach to autoimmune diseases could have enormous promise.

Epigenetics

- The next area of research is epigenetics – the understanding of the process that determines not only the presence of genes, but what activates them.

The T-Cell

- Antibodies are still the basis of diagnosis. However, researchers do know T-cells orchestrate the autoimmune response. Yet, they are only beginning to examine the specificity of T-cells and the fine genetic structure of the T-cell receptor.

Diet and Autoimmune Disease

- Substantial research is needed to understand how diet influences the development of autoimmune diseases.

Focus on the Spleen

- The spleen is home to many of the immune cells that cause the damage of autoimmune disease. Yet, very little research has focused on the spleen. Consequently, there is no clear way to study autoimmune diseases broadly across the heart, the lungs, the brain, the kidneys, the skin, and the other organs they target.

We used to think weather was completely chaotic, we could never predict it. Yet, by simply looking at all of the warning signs, we now can predict weather pretty well. I'm wondering if anybody knows who had that idea first? It happens to have been Benjamin Franklin, our greatest scientist, who you may remember was Postmaster General of the United States. He developed the simple system of getting all of his postmasters to tell the weather in their community at a certain time. He found that the weather that occurred in Pittsburgh on Monday occurred in Philadelphia on Tuesday. He didn't know why, he didn't know what all of the air currents were doing, and he couldn't measure all the details. But from the chaos of weather, he was able to make a prediction. What I want to do at the moment is see how we can predict the development of autoimmune disease by seeing all the warning signs that a disease process is occurring following initiation of an autoimmune response.

-- Dr. Noel R. Rose

Super Enhancers

- All proteins in the body are made by cells. And proteins are what drive an individual's physiology, including the pathology that causes autoimmune diseases. Researchers have been studying the factors that regulate how those proteins are made and the role of each cell's promoters and enhancers. With current technologies, researchers can pull down all the promoters in the cell, all the active enhancers in the cell, and look across all the regions that are driving expression of protein within a cell.

- In doing this, researchers have found a group of enhancers that control what a cell is. In immunity, for example, T-cells play an important role in autoimmunity. And within the larger group of T-cells, there are different types of T cells that are controlled by a specific set of these super enhancers that regulate which proteins are expressed.

- Using this type of cutting-edge technology that looks across the cell globally could revolutionize understanding of what regulates a cell, how that changes in autoimmunity, and how that responds to therapy.

It has not been hard to find physicians who have had the same experience that patients have had trying to get a diagnosis for themselves or their loved one. They can have every bit as much of a problem, even though you would think they have much more access to getting to the right place. But again, it's the barrier of being believed initially when the symptoms aren't so bad and can mimic many others.

--Virginia Ladd

Fatigue Mapping

- In order to better understand the profound fatigue from which autoimmune patients suffer, physicians need a tool to help them "map" the source of the fatigue. In the mapping process, physicians -- along with their patients -- try to pinpoint when the fatigue started and examine other factors like stress, diet and sleep patterns that may be at play to determine if there is a correlation.

- Making these correlations could give doctors more precise information that enables diagnosis, determines treatments and relieves patients' fatigue.

Involve Physicians with Autoimmune Diseases

- Create a directory of physicians who have autoimmune disease or who have family members with autoimmune disease to help educate other physicians and advocate for better diagnostic tools and treatments for patients.

I think this is an historic moment in our time, in autoimmunity. We have a variety of areas that we are able to now collect information about in so many new and exciting ways. And we are organized, I think, to the point now where we can utilize our organizations and our groups together to make important advances here.

-- Dr. Fred Miller

Glossary*

Cytokine: A small protein released by cells that has a specific effect on the interactions between cells, on communications between cells or on the behavior of cells. Cytokines include the interleukins, lymphokines and cell signal molecules, such as tumor necrosis factor and interferons, which trigger inflammation and respond to infections.

Endocrine System: The glands and parts of glands that produce endocrine secretions. It helps to integrate and control bodily metabolic activity, and include especially the pituitary, thyroid, parathyroids, adrenals, islets of Langerhans, ovaries, and testes.

Extrapolation: The inference of one or more unknown values on the basis of that which is known or has been observed.

Major Histocompatibility Complex: A group of genes that code for proteins found on the surfaces of cells that help the immune system recognize foreign substances.

Immunogenicity: The property enabling a substance to provoke an immune response, or the degree to which a substance possesses this property.

Lymphocyte: Any of the nearly colorless cells formed in lymphoid tissue (i.e., the lymph nodes, spleen, thymus, and tonsils) that constitute between 22 to 28 percent of all white blood cells in the blood of a normal adult human. They function in the development of immunity and include two specific types, B cells and T cells.

Predictive biomarker: A specific physical trait used to measure or indicate the effects or progress of a disease, illness, or condition.

Xenobiotic: A chemical compound foreign to a given biological system. With respect to animals and humans, xenobiotics include drugs, drug metabolites, and environmental compounds such as pollutants that are not produced by the body. In the environment, xenobiotics include synthetic pesticides, herbicides, and industrial pollutants that would not be found in nature.

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