INFOCUS
CELEBRATING 25 Years
American Autoimmune Related Diseases Association, Inc.
A nonprofit association bringing a national focus to autoimmunity, the major cause of chronic diseases
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AARDA launches first worldwide registry for autoimmune disease patients

AARDA is announcing the unveiling of the Autoimmune Disease Patient Registry Research Network, known as ARNet, the world's first fully functioning patient registry for individuals diagnosed with one or more of the 100+ known autoimmune diseases.

The result of two years of beta testing by AARDA, ARNet facilitates research into autoimmunity and autoimmune disease by creating one comprehensive, central database of anonymous patient information. This includes diagnosed diseases and other demographics that investigators around the world can use to enlist patients in clinical research studies.

In addition, ARNet will help researchers answer epidemiological questions, identify trends, and track the number of patients with certain autoimmune diseases and their experience obtaining a correct diagnosis.

Managed by Global Vision Technologies, a pioneering firm specializing in custom-tailored, HIPAA compliant patient registries, the ARNet database currently contains information for nearly 10,000 patients and continues to grow.

Virginia Ladd, Founder and Executive Director of AARDA, says, "With this 'big data' project, AARDA's hope is to drive much-needed clinical research into the numerous and wide-ranging autoimmune diseases, including the rheumatic, neurologic, dermatologic, endocrine, and so on." Mrs. Ladd adds, "This research ultimately will help improve time to diagnosis of these diseases, as well as advance knowledge into causes, treatments, and perhaps cures."

Working in collaboration with the 39-member National Coalition of Autoimmune Patient Groups (NCAPG) and other interested parties, AARDA is encouraging autoimmune disease patients to sign on to the registry, get involved, and be part of the solution as researchers, both academic and commercial, work to understand the puzzle that is autoimmunity.

Mrs. Ladd explains, "ARNet seeks to fill in some of those research gaps and foster projects that uncover knowledge that will benefit all autoimmune diseases."

In AARDA's 2015 Summit Report, Frederick Miller, M.D., Ph.D., Chief, Environmental Autoimmunity Group, NIH National Institute of Environmental Health and Safety, talked about "big data" as an important future pathway for autoimmune disease research. According to Dr. Miller, "This is an historic moment in our time, in autoimmunity. We have a variety of areas that we are able now to 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."

How does it work for patients? Patients who have been diagnosed with one or more autoimmune diseases can register online at AARDA's Web site (www.aarda.org) or the Web sites of participating NCAPG groups. The information is anonymous and made available to researchers interested in looking at the "bigger autoimmune picture."

When investigators identify an individual appropriate for a clinical trial, they contact AARDA or the originating NCAPG group who in turn contacts the patient (who, up until this point, has remained anonymous).

Once the patient agrees, AARDA or the NCAPG group issues an invitation to the patient regarding his/her potential participation in this study, eventually connecting him/her with the researcher.

How does it work for researchers? ARNet is now open to researchers. To utilize the database, researchers may contact the AARDA office (aarda@aarda.org; or 586-776-3900). ■

Do you have your invitation to Downton?

AARDA's 17th Annual Fund Raiser, with its post-Edwardian era Downton Abbey theme, is receiving reservations--even before the invitations have been sent (limited seating is available).

On Saturday, May 20, at 12:30 p.m., guests will step back in time to enjoy an afternoon tea, entertainment, a "Dress Up for Downton" contest, and a silent auction in a stately 1894 Romanesque Revival mansion, The Whitney, located in Detroit.

This benefit event brings funds in support of AARDA's mission--autoimmune research, education, awareness, and patient services. To date, sponsorships have been received from Pfizer and *Hour Detroit* magazine. Silent auction donations are arriving.

The online event and ticket page is available (http://return2downton.eventbrite.com). Or call the AARDA office (586-776-3900, ext. 60). ■

Your thoughts, please...

What do you think about the InFocus newsletter?

To serve you, our subscribers, casual readers, and others, we would like to hear from you. Please take part in our reader survey (quick to complete, we promise). To participate, you may go to **www.research.net/r/InFocusNewsletter**. Or you may call the AARDA office (**586-776-3900**) and we will mail a survey form, plus an envelope, to you.

You are important to us. We thank you, in advance, for your thoughtful evaluation. ■

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President/Executive Director's message

— Virginia T. Ladd

Dear AARDA Friends,

Hello again! Once more we are celebrating March as Autoimmune Disease Awareness Month, during which there will be a number of special PSAs and other media opportunities, including stories in *Prevention Magazine* online; *US News and World Report*; and *Delta Sky*, "Friendly Fire," Special Reports section.

♦ **Perhaps the most exciting start to the month was the launch of ARNet**, the first worldwide registry for autoimmune disease patients. This has been a major undertaking with some starts and stops along the way--but now it's here! All of our contributors over the years had a hand in supporting the expense of ARNet's development. Take a bow!

♦ **Education** remains important. Knowing the importance of reaching young people with autoimmune education, we have established a focus group to gather input from patients up to 35 years old to determine what they want included in the program. This project will take about six months to complete.

A scientific symposium has been scheduled for April on the subject of "Cancer Immunotherapy and Autoimmune Disease." Along with AARDA staff, this program is being planned by Dr. Noel Rose and his assistant at Brigham and Women's Hospital. Also, "Infection and Autoimmune Disease" is the topic of another scientific colloquium scheduled for September 23, 2017, in Washington DC.

♦ **Research** happenings include the 18th Annual Autoimmunity Day, a program for researchers, at the Johns Hopkins University Deborah and Noel R. Rose Center for Autoimmune Disease Research, being planned by AARDA's newest Scientific Advisory Board member Dr. Patrizio (Mario) Caturegli, Director of the Center. Dr. Rose will be one of the speakers.

Also in the area of research is our support of "young investigators" plus a grant for relapsing polychondritis research (see article in this newsletter).

An autoimmune summit meeting has been scheduled for March 28, at the National Press Club, in Washington DC. The discussions will consider advocacy and research.

♦ **Advocacy** issues have been addressed through ads in several Washington DC publications. These ads have addressed issues such as the renewal of the Prescription Drug User Fee Act (PDUFA), the Fastercures legislation (which passed and was signed by the President), and the need for autoimmune disease patients to have access to specialists.

Also, AARDA's Advocacy Committee has been very active on both federal and state levels on the subjects of biosimilar naming, access to and cost of medicines, and non-medical switching.

So...readers can see that AARDA has been on the move over the past months. Much done and much to do! With the generous support of our AARDA friends, individual and corporate, the autoimmune mission forges ahead. Any contribution is gratefully accepted; and since Annual Appeal contributions were down this year ($45,251 compared with $55,774 in the previous year), we are looking to find ways to recoup that loss. As readers know, we at AARDA are optimists (and good managers)! Stay on board for the March 2018 report.

Best wishes to all,

Virginia

Creative supporters keep "grassroots" alive

With imagination and energy, AARDA friends keep coming up with new ideas to raise funds, spread awareness, and educate. We are grateful for the planners/volunteers for these grassroots events.

• "Mooooovin' On 5K," Trico High School, Campbell, IL - Saturday, April 1 - sponsored by Jackson County Farm Bureau Women's Committee

• Autoimmune Awareness Luncheon (awareness, not fund raiser) - Houston, TX - Saturday, March 18 - privately sponsored

• Tammy Cassidy & Friends CD Project - 50 percent of sales to AARDA - To order: www.cdbaby.com/cd/Tammycassidy4

• Mrs. Colorado International Monthly Fund Raisers for AARDA - Greater Denver area - Birgit Daniels, Mrs. Colorado International. Her first event raised $900.00.

#Autoimmune Heroes - May we introduce. . . ?

Readers of past issues have been introduced to AARDA's Autoimmune Heroes as we celebrate our 25th Anniversary. Now proudly we present more Heroes who have served AARDA with special distinction during most of those years.

Betty Diamond, M.D., is a 14-year member of AARDA's Scientific Advisory Board which she has served as Chair since 2004. During her time with AARDA, she has given her time and expertise to journalists working on stories about autoimmune disease, from research breakthroughs to new treatments options. She also has contributed articles to various AARDA publications and has made time available for advice as needed.

Dr. Diamond is Head of the Autoimmune Disease Center at the Feinstein Institute at Northwell Health where her groundbreaking research has focused on the induction and pathogenicity of anti-DNA antibodies in systemic lupus erythematosus. She showed that somatic mutation of immunoglobulin genes can generate autoantibodies in mice and humans, making the germinal center a focus in disease pathogenesis.

Her laboratory also has demonstrated that a subset of anti-DNA antibodies cross-reacts with the NMDA receptor. These antibodies can mediate neuronal apoptosis in the hippocampus, leading to a memory deficit or, in the amygdala, leading to a behavioral alteration and showing that autoantibodies can cause aspects of neuropsychiatric lupus and create a paradigm for antibody-mediated changes in brain function in many conditions.

Dr. Diamond received the Outstanding Investigator Award of the American College of Rheumatology, in 2001; the Lee Howley Award from the Arthritis Foundation, in 2002; and the Recognition Award from the National Association of MD-PhD Programs, in 2004. She was elected to the Institute of Medicine, in 2006. Dr. Diamond is an elected Fellow of the American Association for the Advancement of Science, has served on the Scientific Council of the NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases and the Board of Directors of the American College of Rheumatology. She is a past President of the American Association of Immunologists.

About AARDA, Dr. Diamond says, "Since its inception, AARDA has been committed to advancing our knowledge of the science of autoimmunity and improving the lives of those with autoimmune disease. The experience of the patient has been the driver for all organizational activities. This commitment by AARDA to patients is at the core of my own commitment to AARDA."

Robert H. Phillips, Ph.D., was a founding member of AARDA's Scientific Advisory Board which he still serves. He also has been a member of AARDA's Board of Directors over the past years and again has been elected to that position. Dr. Phillips has authored a number of brochures for AARDA on coping skills for autoimmune disease patients and their families and friends. In addition he has volunteered his time to speak at numerous public forums across the country to share best practice coping techniques.

Over the past 25 years, Dr. Phillips has helped raise awareness for autoimmune disease and other illnesses and has shared his expertise on improving ability to cope with medical illnesses through his nationally audio-streamed radio show "Coping Conversations" (www.CopingConversations.com). Guests have included Virginia Ladd and Dr. Noel Rose, among many other celebrities and experts.

Dr. Phillips says, "I have been involved with AARDA since its inception because of the long professional relationship I have had with Virginia Ladd. I believed then and believe now in the formative and ongoing principles of the organization and its importance in increasing public awareness and advocacy for individuals affected by autoimmune disease. My professional specialty in helping people cope with medical problems creates a beneficial synergy with AARDA for the people they serve."

Noel R. Rose, M.D., Ph.D., Chairman Emeritus of AARDA's Scientific Advisory Board, was a founding member of that Board and its first Chair. From AARDA's earliest years, he has volunteered his time and expertise to AARDA as advisor, mentor, speaker at numerous public forums and scientific symposia, and author of several AARDA patient education brochures. He also plans AARDA's medical professional meetings.

Dr. Rose is an immunologist, pathologist, and molecular microbiologist. He founded and provided nearly two decades of leadership to the Center for Autoimmune Disease Research at Johns Hopkins University Bloomberg School of Public Health, in Baltimore, Maryland. During that time, he served as Professor and Chair of the Department of Immunology and Infectious Diseases. Now, recently retired, he has moved to Brigham and Women's Hospital, Harvard Medical School, where he holds the position of junior faculty member.

Commonly referred to as "the Father of Autoimmunity," Dr. Rose's pioneering research some 50 years ago at Wayne State University, in Detroit, Michigan, was instrumental in establishing the concept of autoimmune disease and helped immunologists understand, for the first time, that the immune system is capable of directing a response to healthy tissues and organs of the body, not just to invading foreign viruses and bacteria.

Dr. Rose is co-editor of the classic textbook *The Autoimmune Diseases*, now in its 5th edition. He has published more than 760 articles in peer-reviewed journals, has edited or co-edited some 22 books, and has served as an editorial board member of more than 27 journals. Dr. Rose has served as an autoimmunity expert for the World Health Organization (WHO) and the Institute of Medicine of the National Academy of Sciences. He also served as Chair of the National Institutes of Health (NIH) Autoimmune Diseases Coordinating Committee.

Through his work, Dr. Rose has provided mentoring and nurturing of the next generation of autoimmune and other disease researchers in the United States and abroad.

About his association with AARDA, Dr. Rose says, "I have been presented with many awards during my career, but this award means the most to me. I often refer to AARDA as the little mouse that roared. It is a small organization that has changed the biomedical world. I am extremely pleased to be involved and will continue to work towards a cure for autoimmune disease patients."

Virginia T. Ladd, RT, Founder, President, and Executive Director of AARDA, had a vision to found an organization to bring a national focus to autoimmunity and increase collaboration in autoimmune research, education, awareness, and advocacy. Now, 25 years later, she has seen the birth and growth of such an organization.

With more than 30 years of involvement in the nonprofit community as a patient advocate and educator, Virginia has served leadership roles in a number of organizations. Prior to founding AARDA, she served as President and Executive Director of the Lupus Foundation of America. She was instrumental in the formation of the International Alliance of Patients' Organizations (IAPO), an alliance dedicated to advocacy for patient-centered health care, and is an Immediate Past Member of its Board of Governors.

Virginia Ladd was the founder of the National Coalition of Patient Groups (NCAPG) and serves as its facilitator. NCAPG is an organization of 39 national autoimmune disease-specific groups that advocates tirelessly on key issues, including patient safety, step therapy, access to medicine, and the Affordable Care Act.

She has shown a commitment to the National Institutes of Health (NIH), serving on several committees that include the Autoimmune Diseases Coordinating Committee; the Public Interest Committee for the National Institute of Heart, Lung and Blood; the Public Interest Group for the National Institute of Environmental Health Sciences; and the Panel of Experts for the NIH Autoimmune Diseases Research Plan. Virginia also has contributed Board service to the United Nations NGO Health Committee and the National Health Council.

Since the very beginning of AARDA, Virginia Ladd, as the Founder, realized its incredible potential and the obvious need that existed for the type of services it was to provide. As the years passed, AARDA's tremendous growth, with its national and international recognition and results, dwarfed even her original optimism. Although autoimmune diseases have not been conquered and the efforts still have a way to go, Virginia's passion for the autoimmune cause has inspired the dedication of so many to the AARDA team that she has no doubt that all the hard work will eventually bring the cure so desperately needed.

Virginia says, "I knew when I started AARDA that it would be a long and difficult task. If successful, it would impact significantly the lives of those who suffered with an autoimmune disease. Working with the AARDA team to accomplish the mission has been a joy and a passion of my life. AARDA has an important future as it moves onward toward meeting its long-term goals."

Gerald (Jerry) Ladd has given service to AARDA from its very beginning 25 years ago as its Director of Operations, handling the accounting, office management, and Combined Federal Campaign (CFC) program. He worked behind the scenes to get AARDA off the ground, securing its footing and helping it grow to become the successful and respected organization that it is today. He was the founder and first editor of AARDA's quarterly newsletter *InFocus*.

Paying close attention to the day-to-day running of AARDA, Jerry has allowed others to focus on the organization's mission to eradicate autoimmune diseases, the alleviation of suffering, and the socioeconomic impact of autoimmunity through fostering and facilitating collaboration in the areas of education, public awareness, research, and patient services in an effective and efficient manner.

Jerry also has served as AARDA's go-to travel and events booking agent, with a talent for arranging deals for staff, guest speakers, and meeting space that, over the years, has saved AARDA untold amounts of money which can be redirected to programming and research.

With deep respect for the life-saving roles that volunteers can make, it is no surprise that Jerry has given so much support to AARDA and other worthwhile organizations.

As to his history with AARDA, Jerry comments that he is "proud to have been a small part of this success story that is AARDA and will always remember with pride the millions of autoimmune disease sufferers whose lives have been (and will be) made better by its existence."

Patricia Barber has more than 20 years of service to AARDA, first as a member of its Corporate Advisory Board and then as an AARDA staff member, starting as a Meeting Planner and gradually moving to Advocacy Coordinator, then to Patient Educator, and eventually to Assistant Director, a title that she wears today.

In her various roles with AARDA, she has lent an ear and provided compassion to untold numbers of autoimmune patients over the years who were seeking diagnosis. She has helped them navigate the health system and present their symptoms in the best possible ways to doctors and other health care professions when, many times, these symptoms were dismissed.

Pat works in collaboration with AARDA's Board of Directors, its volunteer corps, and the members of the National Coalition of Autoimmune Patient Groups to raise funds for research and advocate for increased awareness of autoimmunity and autoimmune disease.

How did Pat come to AARDA? She explains, "The financial institution that I worked for donated a small room right above my office to Virginia to get AARDA off the ground. After leaving my banking career after 26 years, I volunteered for several months and then said 'yes' to becoming an employee. After all, who can say 'no' to Virginia?"

Pat says, "My many years of involvement in the autoimmune community have exposed me to the multiple obstacles facing patients and the medical community in diagnosing and treating many autoimmune diseases. Through advice, education, collaboration, and administration, utilizing my business background and educational growth opportunities, I have been able to couple my compassion for all patients and their families with my own deep personal interest in the family connection in autoimmune disease."

Eula Hoover - When intrepid autoimmune visionary Virginia Ladd remarked 25 years ago that she would start an autoimmune organization if she had an office, Eula Hoover said, "I know where one is available rent free." A short time later, upstart AARDA was ensconced in a little second floor office of a Detroit bank building. AARDA had its first home.

Working and volunteering for a fledgling nonprofit organization means doing whatever needs to be done. That describes much of Eula's 25 years with AARDA--typing, writing, stuffing envelopes, speaking, setting up meetings, working with the AARDA Board of Directors, answering telephones, proofreading, cleaning, recruiting volunteers,

Article continued on page 7

Young investigators receive AARDA grants

Looking to the future for autoimmune research, the AARDA Board of Directors supports a "Young Investigators" grants program which allocates $20,000 to each winner of the grants applications. Applicants submit their applications which are read by the appropriate members of AARDA's Scientific Advisory Board who then make their recommendations.

For the most recent program, eight applications were received from which five winners were chosen. Checks were sent to the following in December:

♦ **William Bracamonte-Baran, M.D., Ph.D.** - As one of the reviewers wrote: "Well trained and productive, with an important study of innate lymphocytes in autoimmune myocarditis. This is an unexplored area that could suggest new therapeutic targets."

The title of Dr. Bracamonte-Baran's project is "Unique Functionality of Heart Resident Innate Lymphoid Cells on Autoimmunity." He writes: "The present project is aimed to characterize heart ILCs [innate lymphoid cells] and its role in autoimmune cardiac diseases." Dr. Bracamonte-Baran is a Postdoctoral Fellow at Johns Hopkins University.

♦ **Paulina Chalan, Ph.D.** - Dr. Chalan is a Research Fellow at the Johns Hopkins University School of Medicine, Department of Pathology. Her project title is "On the association between serum soluble CTLA-4 and hypophysitis secondary to ipilimumab administration." Her research focus is to elucidate the mechanisms driving the pathology of autoimmune endocrine diseases, in particular hypophysitis development, a chronic inflammation of the pituitary gland. She writes: "The ultimate goal is to develop tools that enable clinicians to predict the onset of a common and severe side effect of cancer immunotherapy."

♦ **Jolien Suurmond, Ph.D.** - Dr. Suurmond is a Postdoctoral Trainee at The Feinstein Institute for Medical Research, in Manhasset, NY. Her project title is "Studies of Systemic and CNS Lupus." The study will address how diminished function of the inhibitory receptor FcgammaR11RB, a genetic risk factor for SLE, can lead to autoantibody production in SLE and may provide novel therapeutic targets to restore tolerance in germinal center (GC)-matured B cells. Dr. Suurmond writes: "Mechanisms are in place to maintain tolerance in healthy individuals. However, the regulation of autoreactive B cells arising through GC responses is only poorly understood."

♦ **Toshihiro Tanaka, Ph.D.** - Dr. Tanaka is a Postdoctoral Scholar at the University of California, Davis, whose project is entitled "Mechanism of Gender Bias in Primary Biliary Cholangitis." As Dr. Tanaka writes, "Female bias is one of the hallmarks of autoimmunity, and although many explanations have been offered, the specific mechanisms that lead to gender differences remain enigmatic." He says, "This is particularly true of primary biliary cholangitis, a model autoimmune disease which is overwhelmingly female predominant (90 percent)." Dr. Tanaka and his team propose that the data that they will present are important not only for primary biliary cholangitis but also for other female dominant human autoimmune diseases. He says that the study will provide important insights and will lay the ground work for potential therapeutic approaches.

♦ **Marcela A. Ferrada, M.D.** - AARDA and the Relapsing Polychondritis Awareness & Support are sharing equally the cost of this grant. Dr. Ferrada is a Staff Clinician in the Critical Care Medicine Department, Clinical Center, the National Institutes of Health. Her study is entitled "Immunological Basis of Relapsing Polychronditis in a Mouse Model." Dr. Ferrada says, "Our goal is to generate new insights and potentially provide answers as well as generate new questions regarding the immunology of the disease." Dr. Ferrada also is conducting a survey to have a better understanding of the disease in children.

We look forward to having reports from these young investigators who give us hope for the future. ■

Nutrition, skills, and knowledge

Sorry, Pres. George H.W. Bush--it's that broccoli again. Researchers at the University of Illinois, Champaign, in a study of older adults, found that lutein, a pigment found in leafy greens, is linked to the preservation of "crystallized intelligence." This is the ability to use the skills and knowledge one has acquired over a lifetime.

Lutein, one of several plant pigments acquired through diet, is found not only in leafy green vegetables but also in cruciferous vegetables, such as broccoli, and in egg yolks, reported Marta Zamroziewicz, leader of the study along with Illinois psychology professor Dr. Aron Barbey.

"Previous studies have found that a person's lutein status is linked to cognitive performance across the lifespan," said Zamroziewicz. "Research also shows that lutein accumulates in the gray matter of brain regions known to underlie the preservation of cognitive function in healthy brain aging." She said that lutein accumulates in the brain, where it embeds in cell membranes, likely playing "a neuroprotective role."

The Illinois researchers collected blood samples from 122 participants, aged 65 to 75, to determine blood serum levels of lutein. They also imaged participants' brains using MRI to measure the volume of different brain structures. Results showed that subjects with higher blood serum levels of lutein tended to do better on tests of crystallized intelligence. Zamroziewicz said that while serum lutein levels reflect only recent dietary intakes, they are associated with brain concentrations of lutein in older adults, reflecting long-term dietary intakes.

Dr. Barbey said, "We can only hypothesize at this point how lutein in the diet affects brain structure. It may be that it plays an anti-inflammatory role or aids in cell-to-cell signaling." He reflects, "But our finding adds to the evidence suggesting that particular nutrients slow age-related declines in cognition by influencing specific features of brain aging." ■

-Excerpted from "Study Links Nutrition to Brain Health and Intelligence in Older Adults," Diana Yates, Illinois News Bureau, December 13, 2016, Brain in the News, January 2017

Don't wash your hands? Hygiene hypothesis good? bad?

Since the 1950s, there has been an alarming increase in autoimmune diseases and allergic disorders while the rate of some other diseases, e.g., mumps, measles, tuberculosis, has decreased. In the 1990s, scientists began to think that, in some way, the decline in infections was causing human immune systems to malfunction. Between the two eras, in 1989, came the "hygiene hypothesis," or "we're too clean for our own good." Needless to say, many scientists have objected to that.

Dr.Graham Rook, emeritus professor of medical microbiology at University College London, says, "We know an awful lot now about why our immune system's regulation is not in terribly good shape, and it's got absolutely nothing to do with hygiene." Instead, new evidence points to a different hypothesis, one that suggests that early exposure to a diverse range of friendly microbes, not infectious pathogens, is necessary to train the human immune system to react appropriately to stimuli. If this new hypothesis is true, then reducing personal hygiene will not have an impact on rates of chronic inflammatory and allergic disorders but actually will increase infections. Still, the hygiene hypothesis continues to be embraced by the public; and because various changes in Western lifestyle are disrupting our exposure to microbes, it's not easy to devise an equally simple and appealing replacement theory.

What about incidences of both disease and food allergies? Prevalence of food allergy in preschool children is now as high as 10 percent in Western countries, but remains just 2 percent in areas such as mainland China. The number of cases of type 1 diabetes (T1D) in Finland per year is 62.3 per every 100,000 children, compared with just 6.2 in Mexico and 0.5 in Pakistan--and so it goes with other diseases. Then, looking beyond allergies, scientists studied parasites. Eventually epidemiological studies began to break down the link between disease-causing germs and reduced risk of allergy. It was found that measles and many respiratory diseases proved not to be protective against allergic diseases; and, in many cases, they even increased the risk.

In 2003, Dr. Rook and colleagues proposed a new explanation for the rise of immune disorders--the"old friends" hypothesis. The hypothesis suggests that early and regular exposure to harmless microorganisms, "old friends," present throughout human evolution and recognized by the human immune system, train the immune system to react appropriately to threats. Dr. Rook likens the immune system to a computer. It has software, but it needs data, in the form of exposure to a diverse set of microbes, to train it to identify threats appropriately. He says, "It's not about just learning what to attack, but learning what to tolerate."

However, hygiene did not stop playing a role in Rook's hypothesis. Dr. Marsha Wills-Karp, chair of environmental health and engineering at Johns Hopkins Bloomberg School of Public Health, says. "We're talking about a number of factors, not just one. It's the diet, sanitation, antibiotic use, parasites, and more. She says, "We've altered all of those simultaneously and overwhelmed the host's ability to modulate the immune system."

Cesarean births have been linked to increased risk of allergy and asthma; owning a pet or growing up on a farm is protective against them; and antibiotic use, which kills off both good and bad microbes, in youth has been linked to asthma, cow's milk allergy, intestinal bowel disease (IBD), and eczema.

Dr. Wills-Karp says, "The gut microbiome has changed considerably between folks who live in underdeveloped countries and developed countries, and we're beginning to hone in on some specific bacteria. She adds, "It still fits with the concept that there is some microbial exposure that used to protect us, and that we've lost." For example, Western diets, lacking in plant fiber and other diverse foods that nourish commensal [eating at the same table] species, appear to disrupt the healthy microbiota in our gut.

Instead of targeting environmental factors, researchers hope that, eventually, they will be able to identify which regulatory pathways train the immune system. Dr. Wills-Karp says, "If we could find common pathways, we could adopt drugs or probiotics to activate [those pathways] to condition the immune system properly in early life." Early life is the key. Any intervention likely needs to be done by 3 or 4 years of age, by which time a child's microbiome is established and the immune system has completed much of its training.

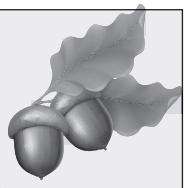
Dr. Maria Yazdanbakhsh, of Leiden University Medical Center, says that, from an immunological standpoint, any therapeutic intervention also needs to be specific. Individuals could be treated with a personalized microbial mixture that induced immune regulatory cells. She says, "It's a big challenge, but we need to start thinking about it."

In the meantime, the "hygiene hypothesis" name keeps popping up--some suggest calling it the "hygiene hypothesis misnomer." Some experts now speak of "targeted hygiene," eliminating the spread of pathogens while promoting steps to restore a diverse microbiome. For example, teach your children to wash their hands after handling raw chicken but also encourage them to play outside in the dirt. Dr. Rook says, "If your children have been out in the garden and come in with slightly grubby hands, I, personally, would let them come in and munch a sandwich without washing."

Unfortunately, seemingly conflicting messages, such as "wash your hands sometimes, but not others," or "use antibiotics, but only when needed," can be difficult to communicate to the general public. However, conveying those messages will be key to reversing the rise in autoimmune and allergic disorders. ■

--Source: "Cleaning up the hygiene hypothesis," Megan Scudellari, Science Writer, Proceedings of the National Academy of Sciences, February 14, 2017

The acorn's promise: a mighty oak!



Our fund for a National Autoimmune Diagnostic and Treatment Center, inspired by the Acorn's Promise, is growing. Yes, we know that we need a major philanthropist to make our acorn fund burst into a mighty oak--but AARDA friends are keeping the hope alive. The fund now has grown to $31,432.92.

As one contributor wrote, "This donation is to help the 'acorn' grow. I hope this National Autoimmune Diagnostic and Treatment Center is in full growth soon."

Yes, while most of us can afford only a twig on the mighty oak, it is very satisfying to know that all of us can be a part, even a tiny part, of this Center that is so desperately needed. Won't we be proud to see our little acorn release its promise?

The AARDA Board of Directors, under the leadership of Board member Michael Linn and President/Executive Director Virginia Ladd, is devising a campaign to procure major funding for the National Autoimmune Diagnostic and Treatment Center. How exciting to see this enormous project develop from a dream to what surely will be reality.

If an internationally known organization (AARDA, of course) can start with canister donations at Kmart, why doubt the power of a little acorn? Let's encourage it. ■

Heros *(continued from page 4)*

providing information and referrals to inquirers, representing AARDA with community groups, and eventually receiving the title of Executive Assistant and editing AARDA's quarterly newsletter, among other things. What better way to utilize a background in teaching and volunteering, from local to international?

Eula says, "Never a dull moment! It's been tremendously exciting to go from "autoimmune? what's that?" to a growing understanding that "autoimmune" is a category of disease encompassing more than 100 diseases. We've also seen autoimmune patients gain the respect and understanding of the medical community--much less of the "it's all in your head" dismissal.

"I have been privileged to work with compatible, capable, and dedicated AARDA staff. I've seen an amazing variety of support for the autoimmune effort--office and fundraising volunteers; local contacts; speakers; Board members; in-kind donors; grassroots volunteers; corporate, foundation, and individual donors; internationally known researchers who see the real-life autoimmune patients behind their research; and, yes, Kmart shoppers who, 25 years ago, dropped coins into our canisters! It's been an enriching experience." ■

AARDA Memorial / Tribute Program

Write or call us for full details of this program. It can be handled by mail or by phone using Visa, MasterCard, or American Express. Memorial and Tribute contributions bring great satisfaction to donors AND to the recipients (or their families). They also help greatly in our ongoing fight against all autoimmune diseases.

American Autoimmune Related Diseases Association

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To our readers: Autoimmune diseases are conditions in which the body's own immune system can (among other things) cause damage to the skin, joints, and internal organs. Although most autoimmune diseases are not yet preventable or curable, most can be controlled to varying degrees. It is because of the wide variance and severity that **the individualization of medical management** is so important. It is vital that persons diagnosed with (or suspected of having) an autoimmune disease consult with their physician or with the appropriate division at a major teaching hospital to assure proper evaluation, treatment, and interpretation of information contained in this newsletter. Opinions expressed in this newsletter do not necesarily reflect the views of the American Autoimmune Related Diseases Association or its Scientific Advisory Board.

Grab your shoes--Autoimmune Walk season is coming!

Actually, any season is good for an AARDA Autoimmune Walk. To date, walks are scheduled from July through November, from DC to Los Angeles. Check AARDA's Walk Web site (www.AutoimmuneWalk.org) for Walk news. Find your shoes, choose a team name, and recruit your team members. Then let Walk Coordinator Deb Patrick know that you and your team members are ready to go.

Autoimmune Walk

LINKING TOGETHER FOR A CURE

- Bowling Green, KY - Saturday, July 8 - Ephram White Park
- New York (Manhattan), NY (formerly Tri-State) - Sunday, September 10 - Hudson River Park
- Arlington, VA (DC Metro) - Saturday, September 16 - Bluemont Park
- Atlanta, GA - Saturday, September 23 - Piedmont Park
- Detroit, MI (Metro Detroit) - Saturday, September 30 - Lake St. Clair Metro Park
- Los Angeles, CA - Saturday, November 18 - Culver City Park

And who says that you can't enjoy an AARDA Autoimmune Walk without walking? Bring your friends (and maybe some chairs--just in case), put your chair in a good spot, declare your goal (or support a walker on the spot), and join kindred spirits for a good cause. ■

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Study may show protection in inflammatory bowel disease (IBD)

Researchers at the University of Texas Medical Center, Dallas, have identified a gene that protects the gut from inflammatory bowel disease (IBD). This disease involves a chronic or recurring immune response and inflammation of the gastrointestinal tract. The two most common inflammatory bowel diseases are ulcerative colitis, which is limited to the large intestine, and Crohn's disease, which can affect any part of the digestive tract.

Under normal conditions, the body maintains a balance between the intestinal tract's ability to respond to disease-causing bacteria and tolerance of normal "companionable" good bacteria that aid digestion. Normally mucus lines the intestines and forms a protective barrier, the mucosal barrier. This barrier protects the intestinal walls from both the disease-causing and beneficial bacteria. However, if the bacteria somehow breach the mucus layer and reach the intestinal walls, inflammation is the result.

In a mouse study, the scientists found a mutation in the Gatm gene and used gene-editing technology to confirm this link. The scientists determined that the Gatm gene is required for the rapid replenishment of the intestinal mucosal barrier.

Nobel Laureate Dr. Bruce Beutler, senior author of the study, said that the Gatm gene is needed for the synthesis of creatine, a substance made in the liver that travels to the barrier cells and allows them to utilize energy in an efficient manner.

In the experiments, mice with two copies of the recessive Gatm mutation showed symptoms similar to people with IBD: diarrhea, weight loss, and the death of cells lining the intestine. The symptoms improved when the mice received creatine in their drinking water. The researchers explained that creatine is necessary for providing the energy needed for the rapid replenishment of the mucosal barrier.

Dr. Beutler said, "Mutations in this gene and others needed for mobilization of energy in cells may account for some cases of IBD in humans." He said that current therapy tends to focus on reducing the inflammatory response. "However," he added, "proper healing of the mucosal layer and cells that line the digestive tract is essential to long-term remission. This study indicates that healing requires effective energy metabolism."

Dr. Beutler commented, "Knowing these genes may help us to understand how IBD occurs in humans, and how to treat it." ■

--Source: "UT Southwestern scientists discover gene that protects gut from IBD," UT Southwestern newsroom, February 2, 2017

Why more women than men in autoimmune disease?

While more women than men experience autoimmune diseases in one form or another, researchers still are searching for the "why." Much of the existing work on gender differences in autoimmune diseases focuses on sex hormones by investigating the effects of hormones on women's immune systems. However, researchers at the University of Michigan decided to explore the "why" from a new angle, gene expression.

Because the laboratory of Johann Gudjonsson, M.D., Ph.D., senior author of the study, has focused on autoimmune diseases of the skin, the researchers decided to take a broad approach with this study by investigating gene expression in the skin of healthy subjects. This study included biopsy samples from 31 females and 51 males. Dr. Gudjonsson said that it is important to examine changes to the skin in diagnosis and treatment of autoimmune diseases because, for example, 4 out of 11 criteria for a lupus diagnosis relates to the skin, signifying features such as rashes.

The researchers found striking differences in gene expression between the women and the men. Dr. Gudjonsson reported, "Our team identified a gene expression difference between the sexes that is associated with susceptibility to autoimmune disease."

According to first author Yun Liang, Ph.D., "Many of those genes had immune function and overlapped with genetic pathways and risk genes that related to autoimmune diseases." This led the team to identify what they are calling VGLL3, a "master regulator" of the female-based immune network.

Dr. Gudjonsson said, "This previously unknown inflammatory pathway promotes autoimmunity in women." He observed that this study provides direction for future investigations into the identified pathway and how it is regulated. It also might put increased focus on women's unique biology.

The researchers say that this is one of the first studies to demonstrate conclusively that it is critical for immunological research to study and analyze female and male samples differently.

"Learning more about these disease processes in each gender will provide opportunities for therapeutic interventions we did not imagine before, including both prevention and treatment," said Dr. Gudjonsson. ■

--Source: Excerpted from "U-M researchers identify gene expression linked to gender differences in autoimmune diseases," University of Michigan Health System, Ann Arbor, December 20, 2016

~EDITOR'S NOTE~

The information on these pages is provided without implied recommendation, solely as a service to those who may be interested. As with all research projects, interested parties should thoroughly question and have a complete understanding before considering participation.

Is it schizophrenia or Dalmau's disorder?

A new research project is under way with the possibility of releasing thousands of patients from their schizophrenia diagnosis. Many of the patients may suffer from a treatable autoimmune disease discovered only a decade ago by Dr. Josep Dalmau, a former University of Pennsylvania researcher now at the University of Barcelona.

Researchers at Houston Methodist Research Institute, led by Houston Methodist physician Dr. Joseph Masdeu, a professor of neurology at Houston Methodist, are beginning a study to determine how common the autoimmune disease is in patients who have been labeled schizophrenic. The "lowball" estimate is that about 5 percent of the 3.2 million Americans diagnosed with schizophrenia actually suffer from Dalmau's immune disorder. Dr. Masdeu suspects that the percentage may be even larger--a striking prediction, given that the disorder can be reversed totally with immunotherapy treatments.

"These patients develop symptoms that can fool any psychiatrist," says Dr. Dalmau.

The disease, known as anti-NMDA receptor encephalitis, received national attention in 2012 when *New York Post* writer Susannah Cahalan published a book, *Brain on Fire*, about her experience with the disease. The disease, most common in children and young adults, is caused by an immune system gone haywire. The body creates rogue antibodies that attack proteins in the brain called NMDA receptors, resulting in psychotic symptoms.

Dr. Dalmau says, "What's amazing is, once you remove the antibody, we cure it. These patients are completely back to normal." One study found evidence of the NMDA-attacking antibodies in one out of every 10 schizophrenia patients.

Dr. Masdeu has begun enrolling patients in a study, in partnership with Texas Children's Hospital and Michael E. DeBakey VA Medical, that will analyze the spinal fluid of schizophrenic patients. He says that the blood serum, used in past studies, is not so sensitive as spinal fluid which is more likely to have the antibodies.

Dr. Masdeu hopes to develop a diagnostic test that could be given to all schizophrenic patients. This could offer hope to families who have watched loved ones suffer for years. ■

--Source: Excerpted from "Houston researcher: Do thousands with schizophrenia have a treatable immune disorder?" Mike Hixenbaugh, Houston Chronicle, February 17, 2017

Lyme disease treatment options need evaluation

Researchers of a recent study of Lyme disease and current treatments point out that the incidence of Lyme disease is increasing dramatically in the United States, with an estimated 300,000 new cases annually. Likewise, rare manifestations of the disease, including post-infection complications, may be increasing.

The researchers caution, "It is important to be aware that a spectrum of infectious and autoimmune joint disorders may occur within the context of Lyme disease." Such patients may have active B burgdorferi infection in joints, antibiotic-refractory Lyme synovitis, or another form of autoimmune arthritis following Lyme disease.

Lyme arthritis is a condition known to be a late manifestation of Lyme disease, with approximately 60 percent of patients with Lyme disease not treated with antibiotics developing Lyme arthritis. Although many patients with Lyme arthritis respond well to antibiotic therapy, other patients can experience post-infectious antibiotic-refractory arthritis. An alternative plan for treatment is needed for these patients.

The researchers write, "Prior to our evaluation, these patients had often received additional antibiotics for presumed Lyme arthritis, without benefit. We prescribed anti-inflammatory agents, most commonly disease-modifying anti-rheumatic drugs (DMARDS), resulting in improvement."

The researchers say, "Delaying appropriate DMARD treatment of autoimmune joint disorders, by pursuing further therapy with antibiotic agents, may lead to poorer clinical outcomes." ■

--Source: "Reconsider Post Lyme Disease Treatment Options, Study Says," Aisha T. Langford, Ph.D., M.PH, Rheumatology Network, February 1, 2017

Sleep, a mystifying process

Yes, sleep has proved to be one of the most mystifying processes of the human body; for centuries it has confounded physicians and scientists. It also has vexed sleep apnea sufferers who struggle with machines, nose patches, oral appliances, and even an implant--but that may be another story.

One of the latest studies, at Harvard Medical School and the VA Boston Healthcare System, reveals that sleep may be regulated in part by several brain-based immune proteins called inflammasome NLRP3. The researchers say that the inflammasome, which works by unleashing a cascade of immune molecules in response to inflammation and infection, emerges as a central promoter of sleep following such events.

Results of the study show that the inflammasome recruits a sleep-inducing molecule to trigger drowsiness following sleep deprivation and exposure to a bacterial toxin. Senior study investigator, Mark R. Zielinski, instructor in psychiatry at Harvard Medical School, says, "Our research points, for the first time, to the inflammasome acting as a universal sensing mechanism that regulates sleep through the release of immune molecules."

While needing further study, observations suggest that the inflammasome, the "constellation of sleep-regulating proteins," may play an evolutionary role as a guardian of brain health and vitality that wards off the effects of sleep deprivation and infection. Dr. Zielinski comments that inflammasome activation following infection suggests that this immune mechanism may have a brain-protective role.

The researchers say that the results, if replicated in other studies, may become the basis of therapies for people with chronic sleep disorders and sleep disturbances secondary to other diseases. ■

--Source: Excerpted from "Study Points to a Universal Immune Mechanism as a Regulator of Sleep," Newsroom: Harvard Medical School, February 2, 2017

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