The UCSF Lupus Outcomes Study is conducted by researchers in the Division of Rheumatology at the University of California, San Francisco. We investigate how lupus affects people’s daily lives, the genetic and environmental risk factors for complications of lupus, and what affects quality of care for people with lupus.

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Research Update

Greetings to all Lupus Outcomes Study (LOS) participants! Some of you have been with the study since 2002 and have been interviewed 11 times, others have just recently joined the study. Our sincere thanks to each one of you. We continually strive to ensure that the effort you put into this study is put to good use, in improving the understanding of lupus and care for people with this condition. Since the study began, we have conducted 8,750 interviews among 1,264 individuals with lupus, published 42 papers in medical journals and made over 60 presentations at U.S. and international medical conferences.

In the current issue, we have a report of a study that included many LOS members in the San Francisco Bay Area—the Arthritis Body Composition and Disability (ABCD) study, along with articles about the Lupus Initiative, transitions from pediatric to adult lupus care, and recent findings about an old medication for lupus. We also introduce our newest interviewer, Rosa Castro, and have an update from the UCSF Lupus Genetics Study about possible links between lupus and environmental exposures. We have again included another contribution from a participant in our “Many Faces of Lupus” corner, and describe the work of one LOS participant in raising awareness and funds for lupus research and education. Please keep sending us your stories!

Over the years, we have introduced new topics in the LOS interviews as new areas of research have emerged.

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LOS Researchers and Participants Work to Eliminate Health Disparities in Lupus

Health disparities are gaps in health status or the quality of health care across racial, ethnic, or socioeconomic groups. Lupus is both more common and more severe among members of racial and ethnic minorities. The LOS has played an important role in uncovering some of the reasons for health disparities in lupus. These include genetics, socioeconomic status, health insurance, specialty of the lupus doctor, and health care resources in the community.

LOS researchers are currently involved in a major effort to reduce health disparities in SLE, called the Lupus Initiative, a joint project of the Federal government and the American College of Rheumatology. The Lupus Initiative is designed to improve the diagnosis and treatment of lupus in

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**Lupus Initiative continued**

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populations disproportionately affected by the disease through the education of medical professionals and medical students. The Lupus Initiative has also developed materials for persons with SLE to help them navigate the health care system and to communicate effectively with their health care providers.

Researchers and participants from the LOS have made important contributions to The Lupus Initiative. Dr. Edward Yelin helped develop educational materials that explain how access to experienced providers can make a difference in SLE outcomes, especially for those from disadvantaged backgrounds. Dr. Lindsey Criswell contributed to a video for health care providers about the role of genetics in health disparities, and Dr. Graciela Alarcon provided information about her research on the role of poverty and racial discrimination in health care for lupus.

Dr. Jinoos Yazdany served as an editor and contributed to the materials prepared for US medical schools. Several LOS participants told their stories as part of the educational materials. Our appreciation goes out to these individuals for their contributions to this groundbreaking work.

The research based on the LOS interviews has made major contributions to our understanding of health disparities in SLE. The Lupus Initiative materials are effective ways to make this research accessible to health care providers around the country, even those who do not follow lupus research closely.

For more information about The Lupus Initiative, visit the website at thelupusinitiative.org

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**LOS Participant in the News**

Deidre Gee Baptista, an LOS participant since 2003, and her twin sister, Kirsten Gee Maeda, have been raising awareness of lupus in their own communities and adding their voices to others around the country working to reduce health disparities in SLE. As members of the Lupus Research Institute Coalition, they took part in the March 2013 Lupus Advocacy Day in Washington, DC, lobbying for lupus funding and attending presentations on current issues in lupus education and research. Energized by their experiences in DC, they returned home to California and succeeded in getting resolutions passed to designate May 2013 as “Lupus Awareness Month” in their hometowns of Rocklin and Irvine. Writing in the Lupus Research Institute’s website, Deidre says “We are truly passionate about spreading Lupus awareness and after spending time in DC, we now realize how we can shine some light on the racial disparity, women of color are three times more likely to develop Lupus.” (lupusresearchinstitute.org/lupus-awareness-month). To read more about the Gee twins’ work, see the Placer (CA) Herald article: http://www.placerherald.com/article/rocklin-mom-helps-fight-lupus-research.

Deidre Gee Baptista holding the City of Rocklin Lupus Awareness Month Proclamation.
An update from the SLE Genetics Study

Tying It All Together: The Environment, Interferon, & Lupus

People often ask, what causes lupus? The answer most often refers to both genetic and environmental factors as contributors to the disease. Many large genetics studies -- such as the UCSF SLE Genetics study, which included all LOS participants -- have identified genetic factors important in lupus, and new research continues in this area. However, the environmental factors in lupus have not been well studied. One reason is that the number of environmental factors (diet, medications, sun exposure, and more) that could potentially influence someone’s risk of developing lupus is overwhelming. Essentially, any exposure could be important at a later date, and it is impossible to record everyone’s complete exposure history.

One way to study environmental exposures indirectly is to study DNA methylation. DNA methylation has to do with how genes express themselves (or go on to produce proteins). When a gene is not methylated, the gene can be expressed. When a gene is methylat-

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Growing Up with Lupus

Lupus is the second most common chronic rheumatic disease of childhood, with between 10,000 and 15,000 children currently being treated for lupus in the United States. While children with lupus experience many of the same symptoms as adults — in fact, lupus in children is often more severe, with kidney disease being common — they must manage their disease while accomplishing all the other important tasks of growing up. As you can imagine, this is no small job!

All children, with or without lupus, need to learn how to care for themselves independently as they become adults. For example, most young adults need to open a bank account, go to college or get a job, and find their own place to live. However, young people with lupus need to learn many additional skills as they transition into adulthood. They need to learn how to take and refill their medications, make and keep regular doctor appointments, communicate well with their doctors, and maintain health insurance coverage. In addition, most of them will change healthcare providers between the ages of 18 and 21 as they switch from pediatric doctors to adult doctors. This may include switching primary care doctors as well as multiple specialists. Some young adults will need to find new health insurance if their previous coverage was specifically for children. In the medical world, this process of becoming an adult and entering the world of adult health care is called “transition.”

Many of the LOS participants were diagnosed as children, and previous newsletters have highlighted some of our study findings comparing childhood and adult onset lupus. Now, Dr. Erica Lawson, a UCSF pediatric rheumatologist and one of the LOS investigators, is going to recruit subjects for an interview-based study focused on young adults with lupus (ages 18-25) and their rheumatologists. This new study is designed to better understand the challenges faced during the transition process. Together with the Arthritis Foundation, we’ve also developed an online Transition Toolkit designed to help youth and parents prepare for transition, at www.jatransition.org. Our goal is to develop ways to help young people gain the skills they need to transition to adult medical care and become successful, healthy, thriving adults.
Report from the ABCD Study

The body-mind connection: Does fat matter?

Between 2007 and 2012, 172 members of the LOS participated in the Arthritis Body Composition and Disability (ABCD) Study at the UCSF Hospital. This study looked at the relationship between body composition (the amount of fat and muscle in the body), disease activity, and functioning in lupus. Many of you have had a bone density (or DEXA) scan to look at your bones. DEXA scans can also be used to examine how much fat and muscle you have in your body. Using this “whole body DEXA,” we found that half of the study participants could be classified as obese according to the percent of their body that was made up of fat. The whole body DEXA is used mostly for research studies; people do not usually have a DEXA to find out about their body composition. So, in addition to the DEXA, we looked at two other ways of measuring body composition that are easily done at home or in the doctor’s office.

The most common measure of body composition is the body mass index, or BMI, which is a ratio of weight to height. In the general population, a BMI of 25-30 is considered overweight, and a BMI of 30 or greater is considered obese. (To calculate your own BMI, see the box below). Another easy way of estimating body composition is by measuring waist circumference with a tape measure around the body at waist level. For women, a waist circumference of 34.5 inches or greater is considered obese. Some think that waist circumference is more important than BMI because fat that is stored around the waist is more closely associated with cardiovascular disease.

Using these two more common measures, we found that 28-29% of the group would be classified as obese – quite different from the 50% who had excess fat that we found with the DEXA! Why such a difference? We found that women who were classified as obese with DEXA had less muscle and more fat in their arms and legs. While we don’t know why this is, it’s possible that people who are sicker may be less active physically and this may lead to muscle loss.

There are several reasons that these study findings are important for people with lupus. First, having lupus automatically puts people at a higher risk for cardiovascular disease, which can lead to heart attack or stroke. Study participants with higher BMIs or more body fat had an even higher risk of cardiovascular disease. A second reason is that obesity is often linked to problems with physical functioning, such as difficulty with walking and other daily activities. We found that, starting at BMI of 25, functional problems were more common and this became more pronounced as BMI increased further. This was somewhat surprising, because in the general population, functional

More information:

General information on physical activity from the CDC:
www.cdc.gov/physicalactivity/everyone/guidelines/adults.html

Info from the National Center on Physical Activity and Disability:
www.ncpad.org/14weeks/login.php

To calculate your Body Mass Index:
Weight in lbs. / [Height in inches]² × 703
OR see: www.nhlbi.nih.gov/guidelines/obesity/BMI/bmicalc.htm
problems do not show up until BMI reaches the level of obesity, a BMI of 30 or more.

Another important finding from the study is the connection we saw between higher levels of fat and problems with cognitive functioning – such as memory, concentration, the ability to process information, and the ability to solve problems. Many people with lupus report problems with cognitive function such as memory or concentration. The best tests of cognitive function have to be administered in-person, take quite a bit of time, and need specialists to interpret the results, so most doctors can’t test for cognitive function in their offices. We took the opportunity of our in-person study visits to measure cognitive function. We found that 1 out of 4 people who came in for visits had significant problems with some type of cognitive functioning. When we looked at obesity as defined by DEXA, we found that women who were obese were 3 times more likely to have significant cognitive problems than women who were not obese. Using the more common measures of body composition, we also found that a BMI of 30 or more or a waist circumference greater than 34.5 inches increased the risk of cognitive problems by 50%. Corresponding to this, we also found an association between cognitive problems and physical inactivity. Women who were inactive were twice as likely to have cognitive problems.

So what do these findings mean for you? Try to stay physically active. It’s good for your heart and muscles, it can help you manage your weight and reduce your fat, and it may help your mind. Some research also suggests that exercise is a good way to lessen depression.

You might say that it’s difficult for you to exercise because your lupus gets in the way. But being physically active doesn’t necessarily mean going to the gym or running. Even short walks can be helpful. The Centers for Disease Control and Prevention (CDC) recommends that adults need 150 minutes of moderate or vigorous physical activity per week for health benefits. 150 minutes may sound like a lot, but you don’t have to do it all at once – it’s even better to spread it out. Even 10 minutes at a time is fine. See the shaded box on page 4 for links to information about physical activity in general, and specialized information about physical activity for people with chronic health conditions or disabilities.

In closing, we would like to extend a special thank you to all the participants in the ABCD study. The study visits were long and challenging for many of you, and we truly appreciate all of your time and effort. We are still looking at the information provided during your visits, and expect to be able to report more important findings in the next LOS newsletter.

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**Research Update continued**

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One recently added series of questions asks about experiences with your lupus doctor and your health plan. These questions were developed as part of the US Agency for Healthcare Research and Quality’s Consumer Assessment of Healthcare Providers and Systems (CAHPS) and are used by public and private health plans to assess the quality of care provided to patients throughout the US. However, we do not use these questions to rate any individual doctors, nor will we ever give feedback to any participants’ doctor as to the responses on these (or any other) questions. The information we get from these questions will help us gain better understanding of the patient-provider relationship in lupus care, and how it may affect overall quality of care and the disease progression over time. We appreciate your candid responses to all of the questions in our interviews. Thank you for your continued participation in the study.
In the last 10 years, new evidence has emerged about the benefits of hydroxychloroquine, a drug used to treat malaria for more than 50 years. Most rheumatologists now recommend that all of their patients with lupus take the drug as soon as they are diagnosed.

One of the important early studies that helped us understand the benefits of hydroxychloroquine was published in 1991 in the New England Journal of Medicine. In this study, researchers found that when patients with stable lupus stopped the drug, they were more likely to have a flare. This study and others like it helped us understand that the drug was helping keep lupus in remission. Before this study, hydroxychloroquine was largely used to treat some of the symptoms of lupus, such as rash, oral ulcers or joint pain. Now it had an important role as a preventive medicine in lupus.

Newer studies have found even more benefits of hydroxychloroquine, including that it helps people live longer with lupus. People who take the drug also have fewer long-term complications from lupus, including damage to their organs. It is associated with less frequent blood clotting, cardiovascular events, and better kidney outcomes. Hydroxychloroquine seems to lower cholesterol and blood sugar levels, benefits that might at least partly explain why it is good for the heart and blood vessels. New studies also suggest that hydroxychloroquine use during pregnancy is safe and that it prevents flare-ups of lupus in pregnant women. It seems to control the overactive immune system without increasing the risk of infection, a problem in many lupus drugs.

An important finding is that hydroxychloroquine does not work as well in people who smoke. So it is very important not to smoke if you want to see the full benefits of this drug.

Despite the many benefits of hydroxychloroquine in lupus, safety is an issue, particularly with very long-term use. Very rarely, in about 1 in 2000 people, hydroxychloroquine can lead to damage to the retina, which is the part of the eye that senses light. This is why it is so important to follow your doctor’s recommendation to see an ophthalmologist regularly while taking the medication. Ophthalmologists (but not optometrists) do special testing to look carefully at the retina for side effects of hydroxychloroquine. If any abnormalities are found, they will recommend that you discuss stopping the medication with your lupus doctor. Researchers hope to develop an equally effective form of hydroxychloroquine in the future that does not have these rare eye side effects, and we hope to see clinical trials with these newer medicines soon.

So many benefits in a single medicine seems almost too good to be true. How exactly can one medication lead to all of the benefits reported in these studies? Research in the laboratory is slowly starting to unravel how hydroxychloroquine works in lupus. It appears that this medication may prevent the activation of the cells responsible for making interferon. Interferons are proteins that are crucial to the body’s ability to fight disease, but they are overactive in lupus and cause unwanted inflammation.
Many Faces of Lupus -- Contribution from a Participant

My name is Kate Mendeloff. I was diagnosed with lupus in 1978, when I was in my second year of graduate school in Directing at Yale School of Drama. I had joint pain, was suffering from depression and had Raynaud’s in my feet, which I first thought was frostbite. I didn’t recognize myself in the mirror. I was terrified and tried to pretend that nothing was wrong. Eventually I was even crawling up and down stairs at school, waiting until my classmates had left the room, so I would not be observed. I did go to the student health service several times, but because I saw different doctors and had different symptoms, my diagnosis was not complete until I was very sick.

I went home to Baltimore for break and when I got off the train, my parents took me directly to the hospital and Dr. Mary Betty Stevens at Johns Hopkins Hospital diagnosed me immediately. It was an incredible relief! I spent the summer and fall recuperating. I had to take time off from school, but eventually finished my degree, only a semester late.

I have had several lupus flares that have been debilitating, a stroke early on, which resolved, but made it clear that I had CNS involvement. I moved with my husband to San Francisco in 1983 and had a high stress job. I was not managing my lupus well, so I was put on prednisone for several months and then had a steroid induced depression/psychosis that was very scary, and involved being hospitalized at UCSF. But, I was very lucky in that my pregnancies seemed to make my lupus better, and since I had my two daughters, in 1986 and 1988, I have been able to maintain a fairly active life. Most of my health problems at this point seem more related to the long exposure to steroids than the lupus itself. But, I am aware that if I push myself, or get too much sun and too little rest, I will still have bad days, so there is no forgetting that this is a chronic disease!

I am a theater director and educator. I teach drama at the University of Michigan and enjoy my work very much. I even direct a summer theater which produces Shakespeare’s plays in the University Arboretum. There is no stage, the audience follows the actors through the woods! I wear lots of sunscreen, a big hat, and sun protective clothing, so I still manage to direct and be outside without too much difficulty.

I do acknowledge that my original goal to be a professional director was not realistic because the long hours and high level of stress, but I feel that teaching theater is a good compromise. I arrange my course schedule to have two days a week when I am able to rest if I need to, and feel very lucky to have the flexibility and support to do what I love and stay as active as I can.

When my older daughter was living in NYC, she did the Lupus Walk. I am very proud of her and am touched that my family and friends are donating time and money for this important cause. I also want to give a shout-out to my mother, Natalie Mendeloff, who was one of the founders of the Maryland Lupus Foundation, now the Mid-Atlantic Lupus Foundation, and who has inspired me in all areas of my life.
ed, the gene can be silenced (or turned off). Diet, exposure to sunlight, medications, or smoking, as well as age and gender, can all affect DNA methylation. Advances in technology now allow researchers to measure the methylation levels of an individual's genes, and to see how methylation is related to particular diseases.

Here at UCSF, we are currently studying how differences in DNA methylation are related to the development of an antibody against double-stranded DNA (dsDNA) seen frequently in lupus. This autoantibody is associated with kidney involvement in lupus as well as more severe disease. For our study, we have examined the methylation status of over 23,000 genes in over 300 women with lupus. We identified 12 genes which are less methylated in lupus patients who have the anti-dsDNA autoantibody compared to lupus patients without this autoantibody. Over half of these 12 genes have a role in the body's response to interferon, a protein released by the immune system that causes inflammation. Of note, these genes have not been previously identified genetic factors important in the development of lupus.

This study is one of the first steps in understanding how DNA methylation and environmental exposures can influence both the risk of getting lupus and how it progresses in individuals with the condition. In the future, we hope this research will provide a better understanding of how lupus develops and lead to the discovery of less toxic medications.

New LOS Interviewer: Rosalba Castro

We are pleased to introduce Rosalba Castro who joined the Lupus Outcomes Study last October to enroll and interview participants in Spanish. Rosa moved to San Francisco from Denver in 2005. Prior to joining the staff here at UCSF, she worked in banking and customer service and completed coursework at the Business and Language Institute. “I love my work!” says Rosa, “Hearing how challenging it is for our participants to cope with their illness has taught me that no matter how bad your situation, there is always hope. I think that it helps people to tell their stories and know that there is someone out there who cares about them.” When she’s not enrolling patients at the SF General Hospital clinic, interviewing participants, or translating study materials into Spanish, Rosa enjoys spending time with her 9 year old son, Eric. Rosa is a wonderful addition to our research team, enabling us to expand the reach of our studies to the Spanish-speaking population.

We want to stay in touch!
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For back issues, go to: pages.medicine.ucsf.edu/lupus/newsletternew.html