The pumpkins are ripening and the political campaigns are heating up…. it must be October. Welcome to our latest issue of the Lupus Outcomes Study (LOS) newsletter. With this issue, we mark the completion of 4,775 interviews among almost 1,200 participants. As always, we thank you for the time and effort you give to this study.

The purpose of the LOS is to follow people with lupus over many years, to identify time trends in treatments, health care access, and physical and mental health outcomes. We truly appreciate your willingness to make time in your lives for the interviews; we couldn’t do it without each and every one of your contributions.

In this issue, we address several topics of interest: employment, primary care in lupus, and the risks of blood clots. In addition, we include an update on the recent advances in understanding the genetics of lupus and other autoimmune conditions. The articles here are mostly brief summaries of longer articles published in medical journals or presented at rheumatology conferences. If you are interested in more information about any of these topics, please contact our office.

Thanks again for being an important part of the Lupus Outcomes Study!

Research Update

The data from the annual telephone interviews have been used in three separate studies of employment. In the first, led by LOS principal investigator Dr. Edward Yelin, we looked at the work history of the members of the Lupus Outcomes Study. We reported that between disease onset and the first LOS interview, hours of work per year declined by about a third among all individuals who had ever worked, but actual hours only declined by 1% among those able to work continuously. Among individuals working at the time of diagnosis, the proportion employed declined by 15% after 5 years and by 63% after 20 years.

Demographics (age, sex, and education) and work characteristics (the physical demands of jobs and the level of control on the job) were the main factors contributing to work loss.

In the second study, Dr. Peter Panopalis and colleagues studied 832 Lupus Outcomes Study participants. These 832 had been screened for memory impairment and grouped into 3 levels of memory function: those...
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whose memories were intact, those with mild-moderate impairment, and those with severe impairment. In the intact memory function group, 54% were employed, versus 41% in the mild-moderate impairment group and 31% in the severe impairment group. The findings suggest that severe memory impairment is an important factor associated with job loss among people with lupus.

The last study, which was recently accepted for publication, was also led by Dr. Yelin. It focused on changes in employment status among LOS participants: stopping work for those with jobs when they were first interviewed, or starting work for those who were not employed at that time. At the beginning of the study, 405 (50%) LOS participants were employed, of whom 96 (24%) stopped working. Older participants were more likely to stop working. Of the 404 LOS participants not employed, 82 (20%) began working. Those with shorter disease duration, better functioning, and shorter time since last employment were more likely to get jobs. Before age 55, low rates of employment among persons with lupus are due to low rates of work entry. Beyond age 55, both high rates of work loss and low rates of work entry contribute to low rates of employment.

The results of these studies using LOS interviews may help in the design of strategies to improve employability of persons with lupus.

LupusLine® -- Peer Support for People with Lupus

Hospital for Special Surgery (HSS) in New York provides a unique service to people with lupus. LupusLine®, established in 1988, is the only national telephone peer support program offering one-to-one emotional support and information to people with lupus across the country and internationally; the program links people who need the service with trained volunteers who have lupus or are a family member of someone with lupus.

In its 20 years, the program has provided support and education through approximately 19,000 client contacts, over 500 of which occurred in the last year. Callers come from the New York area, around the U.S., and even from Canada, South America, and Europe. Twelve active volunteers bring the peer support from their homes into the homes of people with lupus. Several volunteers have worked with the program since its start in 1988 and are still in touch with some of their original clients.

The program’s reputation continues to grow through referrals from rheumatology health professionals, government, and community-based organizations. Since 1990, the program has presented information on various aspects of the unique LupusLine® approach at the national meetings of the American College of Rheumatology. The HSS LupusLine® program is made possible through funding by Rheuminations, Inc., and reaches out to communities we seek to serve in cooperation with the S.L.E. Lupus Foundation.

To access this telephone peer counseling support and education program, please call 866-375-1427 toll-free, or log on to www.hss.edu for additional information.
Blood Clots in Lupus Patients

Lupus can cause arthritis, rashes, and kidney damage. It can also cause blood clots such as strokes or clots in the lungs (known as “pulmonary embolism”). People with lupus experience blood clots more often and at a younger age than those without lupus. Such clots can have long-lasting consequences including paralysis from a stroke, recurrent miscarriages, and can increase the risk of early death. Treatment sometimes requires life-long medication with a blood thinner (such as warfarin), which carries the risk of bleeding. Clearly, we need to improve our ability to identify which lupus patients are at greatest risk for having a blood clot in order to take the appropriate preventive care measures.

We know about certain risk factors already. For example, lupus patients who have blood clots test positive on blood tests for “anti-phospholipid antibodies” or aPL. However, not all people with lupus who experience blood clots have positive aPL blood tests and not all patients with these positive tests have a blood clot. This is our best clue so far, but it is still very imperfect. Our research group is studying LOS participants and others in the UCSF Lupus Genetics Project to better understand the factors that contribute to blood clots.

In a study just published in The Annals of Rheumatic Disease, we found that the following factors increased the risk that a person with lupus would have a blood clot: smoking, older age at lupus diagnosis, having had lupus kidney involvement, having taken strong lupus medications such as cytoxan, and having had lupus for many years. Many of these findings, such as the strong medication use, having had lupus for a long time, and having had kidney involvement, may just suggest that patients with more severe lupus are at higher risk for having a blood clot. These findings do not mean that these strong medications themselves cause the blood clots and patients should not avoid these potentially life-saving medications. Rather, this suggests to physicians that we need to aggressively manage lupus patients with such severe disease manifestations.

However, at least one of these risk factors – smoking – is modifiable. We already know that smoking makes many aspects of lupus worse, and this is just another reason for patients with lupus not to smoke.

Interestingly, we also found that patients who had taken hydroxychloroquine, or Plaquenil, had a lower risk of experiencing a blood clot. Lupus patients are often on this medication because it also helps to treat arthritis and rashes, so the fact that it may help to prevent blood clots is an encouraging discovery.

Our research group is now trying to determine if certain genes put lupus patients at greater risk for blood clots. As with many aspects of lupus, ethnicity also seems to influence a lupus patient’s risk of clots, and we are currently studying these differences across several ethnic groups, including Caucasians, African-Americans, Asian-Americans, and Hispanics. If we can understand more about the risk factors for blood clots in lupus patients, we hope to be able to prevent such events from occurring.
Earlier diagnosis and aggressive treatment have improved survival for systemic lupus dramatically over the last several decades. When lupus was first studied, many patients died within 5 to 10 years of diagnosis; today, they have near normal life expectancy. Since people are living longer, taking care of the long-term complications of lupus and the other diseases that tend to increase with age have taken on new importance.

Research shows that seeing a rheumatologist on a regular basis improves outcomes for people with lupus, but frequent contact with your primary care doctor or internist is an equally important part of basic lupus care. In fact, those with systemic lupus are at higher risk than the average person for complications such as heart disease and cancer.

In this article, we describe some topics that are important to discuss with your primary care doctor: heart disease and stroke, infections, bone health and osteoporosis, and cancer. Since lupus is a rare disease, not all primary doctors will have experience with following lupus patients long-term. By publishing research in this field, we are trying to increase awareness of all medical professionals to the complications associated with lupus. We ask for your help in this mission as well.

Heart disease and strokes: Know the signs and get screened for traditional risk factors

People with lupus are at higher risk of heart attacks and stroke than the average person. The association between heart disease and lupus was first reported almost 40 years ago, when researchers found an increased number of heart attacks and strokes among women with lupus. Among women aged 35-44, those with lupus were 50 times more likely to have a heart attack compared to those without lupus (for whom heart attacks are extremely rare at these ages). Even among women aged 45-64, those with lupus had more than double the risk of a heart attack than women without lupus.

It is not clear yet why these heart attacks occur in such young women with lupus: some of them can be explained by the high blood pressure than can come with kidney disease or by the high cholesterol that can occur with steroid use. But these “traditional risk factors” do not seem to explain the whole picture.

The best strategy for reducing the rates of heart attacks in lupus patients is still unclear, and research in this area is ongoing. Until such information is available, however, it makes sense to be alert for the symptoms of heart disease and to be screened for the traditional cardiovascular risk factors.

How can you stay heart healthy?

- Ask your primary care doctor to screen you every year for high blood pressure and high cholesterol.
- Keep a healthy weight. If you are overweight, let your doctor know that you are concerned about this affecting your risk for heart attacks and strokes.
- Exercise. No matter what your weight, regular exercise is a good way to keep your heart strong. If you have joint pain, ask your doctor for a referral to a physical therapist to discuss safe ways for you to do aerobic exercise at least 3 times per week.
- If you smoke, talk to your doctor about ways to quit, including setting a quit date, support groups, nicotine gum or patches, or even medication. Check out ‘Resources for Smoking Cessation’ on page 6.
- Know the symptoms of heart attacks and strokes and remind your doctors that these occur more frequently in patients with lupus. See ‘Warning Signs’ on page 6.
Preventing Infections: The Role of Immunizations

Common infections such as the flu and pneumonia can be significant problems for people with lupus, especially those receiving steroids and other drugs that suppress the immune system. One way to reduce infection is to lower the doses of these drugs, but clearly this is not always possible. Another important way to reduce infections is to make sure that you have received the appropriate vaccinations. Recent research has shown that vaccines are safe for people with lupus and that they do not cause flares of lupus activity. Most experts now agree that lupus patients should receive “inactivated vaccinations” recommended for the general population, including the flu shot and the pneumonia vaccine.

How can you protect yourself from infections?
- You should receive the flu shot (but not the nasal spray) every year.
- You should receive the pneumonia vaccine as recommended.
- Ask your doctor if you are up to date on your other routine vaccinations.

Cancer screening

Some research suggests that people with lupus have an increased risk of cancers. Research into this complication is still ongoing, but preliminary data shows that lung cancers and blood cancers may occur at slightly higher rates in people with lupus compared to others. The reasons for the increased risk of these cancers in lupus are unknown, but theories include problems with the immune system failing to attack early cancer cells, or rare side-effects of medications.

How can you protect yourself from cancer?
- Have an annual physical examination by your primary care doctor.
- If you smoke, talk to your doctor about ways to quit, including setting a quit date, support groups, nicotine gum or patches, or even medication.
- Stay up to date on your routine cancer screening, including Pap smear, mammogram, and colonoscopy.

Bone Health: Get Screened for Osteoporosis and Prevent Bone Thinning

People with lupus are more likely to have a bone fracture, especially of the hip and spine, after minor trauma: almost 10% will break a bone at some point after their diagnosis. This is because of osteoporosis, or thinning of the bones. Osteoporosis can occur as people grow older, especially in post-menopausal women. People with lupus are at higher risk for osteoporosis because of chronic inflammation and frequent steroid use, possible early menopause, and because of low vitamin D levels that can occur from avoiding the sun.

How can you stay bone healthy?
- Talk to your doctor about calcium and vitamin D supplements and getting enough of these in your diet.
- Ask your primary care doctor to screen you for osteoporosis with a bone mineral density test if you are over 60 years old or have been taking steroids for over 3 months.

Conclusion

Advances in the treatment of lupus have helped lupus patients to lead longer and healthier lives. As a result, screening lupus patients for risk factors for heart disease and stroke, osteoporosis, and cancer has become more and more important. By educating patients and their primary care doctors, we can continue to improve care and outcomes for people with lupus.
Heart Attack Warning Signs

The American Heart Association website provides the following information:

Some heart attacks are sudden and intense — the “movie heart attack” where no one doubts what’s happening. But most heart attacks start slowly, with mild pain or discomfort. Often people aren’t sure what’s wrong and wait too long before getting help.

Here are the signs that can mean a heart attack is happening:

- **Chest discomfort.** Most heart attacks involve discomfort in the center of the chest that lasts more than a few minutes, or that goes away and comes back. It can feel like uncomfortable pressure, squeezing, fullness or pain.

- **Discomfort in other areas of the upper body.** Symptoms can include pain or discomfort in one or both arms, the back, neck, jaw or stomach.

- **Shortness of breath** with or without chest discomfort.

- **Other signs** may include breaking out in a cold sweat, nausea or lightheadedness.

As with men, women’s most common heart attack symptom is chest pain or discomfort. But women are somewhat more likely to experience some of the other common symptoms, particularly shortness of breath, nausea/vomiting, and back or jaw pain.

Stroke Warning Signs

The American Stroke Association says these are the warning signs of a stroke:

- **Sudden numbness or weakness of the face, arm or leg, especially on one side of the body**

- **Sudden confusion, trouble speaking or understanding**

- **Sudden trouble seeing in one or both eyes**

- **Sudden trouble walking, dizziness, loss of balance or coordination**

- **Sudden, severe headache with no known cause**

If you experience these symptoms, be sure to get medical help right away. **Calling 9-1-1** is almost always the best way to get the help you need.

Source: American Heart Association

http://www.americanheart.org/presenter.jhtml?identifier=3053

Resources for Smoking Cessation

http://www.smokefree.gov/ A comprehensive list of telephone and web-based information and support, from the US Centers for Disease Control and Prevention and the National Cancer Institute.

1-800-QUIT-NOW (1-800-784-8669) Provides support for people trying to quit smoking, including free quit coaching, a free quit plan, free educational materials, and referrals to local resources, from the Centers for Disease Control and Prevention.

http://www.lungusa.org/site/c.dvLUK9O0E/b.22931/k.8550/Smoking_Cessation_Support.htm The American Lung Association’s website for smoking cessation. Includes a link for their free on-line smoking cessation program, Freedom From Smoking®.
Recent Advances in the Discovery of Lupus Susceptibility Genes

Systemic lupus is known to be caused by a complex combination of genetic and environmental factors. Before 1980, researchers knew of only one lupus susceptibility gene (a gene that increases risk for development of lupus). For several decades, progress in identifying these genes was quite slow. With the publication of the human genome sequence in 2001, researchers had access to a wealth of new tools and technologies for identifying disease genes. In the past 5 years, research and understanding of the genetics of lupus has flourished.

This was a very exciting year for lupus genetics. Several high-profile genetics studies were published that identified many additional lupus susceptibility genes. These studies took advantage of the newly developed technology for genome-wide studies. Researchers are now able to identify disease risk genes by using a large number of genetic markers scattered across the entire genome. These studies examine nearly half a million genetic markers at one time! This technology has been used to identify disease susceptibility genes for disorders such as cancer, schizophrenia, and autoimmune conditions.

Two genome-wide association studies published in 2008 in the New England Journal of Medicine and Nature Genetics identified six new genes associated with systemic lupus. Many of these genes influence the immune system’s function and regulation. As a result of enrollment in the UCSF Lupus Genetics Project, participants in the UCSF LOS study contributed to both genome-wide association studies. These studies not only identified new susceptibility genes but, by combining and reanalyzing the results, researchers will likely be able to uncover even more genes in the future. Despite these recent advances, however, there is still not enough known to develop a genetic screening test for lupus. Further research on the genes identified in these recent studies will shed light on lupus disease progression as well as uncover potential new targets for treatment.

One Interviewer Departs…..

Rosemary Prem

When not conducting interviews for LOS, Rosemary Prem could often be found roaming the beaches of San Francisco with her dog, Sophie. But these days, you are more likely to find her on the shore of Lake Michigan than the Pacific. Rosemary has returned to the University of Wisconsin at Green Bay, to complete her college degree in Human Development, after a break of many years. Says Rosemary, "I am truly inspired to complete my Bachelor’s degree after talking with so many people who have this life challenging disease and continue to live life to its fullest. It makes me feel sure that any of my obstacles can be overcome. I am very grateful to all the amazing people who have shared their stories with me during my time with this study." And we, in turn, are grateful to Rosemary for her years of work on LOS, and wish her all the best in her scholarly pursuits!

Interviewer updates continued on page 8
**Put on Your Walking Shoes for Lupus**

Join The Alliance for Lupus Research (ALR) in the quest to prevent, treat and cure lupus, a deadly autoimmune disease. Show your support on Saturday, November 1st, at the **Walk with Us to Cure Lupus Walkathon** being held at Justin Herman Plaza in San Francisco. Check in starts at 9:00 AM with the ALR Walk starting at 10:00 AM. 100% of your contributions to the ALR goes directly to support lupus research programs. Visit [walk.lupusresearch.org](http://walk.lupusresearch.org), or call 206.919.6270 for more information.

The Alliance for Lupus Research (ALR) is a national voluntary health organization based in New York City that was founded in 1999 and is chaired by Robert Wood Johnson IV, a member of the founding family of Johnson & Johnson. Our mission is to find better treatments and ultimately prevent and cure systemic lupus erythematosus (SLE, or lupus), a debilitating autoimmune disease. Since its founding, ALR has given more money to lupus research than any non-governmental agency in the world; to date $50 million has been committed. Because our Board of Directors pays for all administrative and fundraising costs, one hundred percent of all donations from the public, and the proceeds of our signature grassroots fundraising program, Walk with Us to Cure Lupus, go directly to support research programs.

Join us for these west coast ALR walks:

- San Luis Obispo ALR Walk - October 25, 2008
- San Francisco ALR Walk - November 1, 2008
- Los Angeles ALR Walk - November 15, 2008
- Seattle ALR Walk - May 17, 2009

To see walks for other areas of the United States visit: walk.lupusresearch.org.

Together, we will find a cure!

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**….. and Another Interviewer Returns**

Jessica Spry, who long-time study participants may remember from past interviews, rejoined the LOS staff as of September, 2008. Jessica took a couple of years off to care for her two young sons, one of whom was having significant health problems of his own. Now that both boys are back in school, Jessica is back on the phones for the LOS, and we’re thrilled to have her back on the team!

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**We want to stay in touch!**

Please let us know if you have moved or changed phone numbers.

Contact Stephanie Rush
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