National Institutes of Health

Fact Sheet — *Lupus*

Lupus (systemic lupus erythematosus) is a serious and potentially fatal autoimmune disease that mainly affects young women. The disease often starts between the ages of 15 and 44. The manifestations of lupus are diverse: it can affect many parts of the body, including the joints, skin, kidneys, heart, lungs, blood vessels, and brain. People of all races can have lupus; however, African American women have a three times higher incidence (number of new cases) than white women. They tend to develop the disease at a younger age than white women and to develop more serious complications. Nine times more women than men have lupus, and it is also more common in women of Hispanic, Asian, and Native American descent.

Thirty Years Ago

- A significant number of people diagnosed with lupus faced the prospect that they would die within 5 years of the diagnosis. While patients who were diagnosed with lupus faced an uncertain future, they knew that in addition to the shortened life span, they were quite likely to have a significantly compromised quality of life.
- Treatments for lupus were of limited effectiveness, typically targeting the entire immune system rather than the specific elements of the immune system involved with the disease course in lupus. Therapies were associated with significant and often debilitating side effects.
- Diagnosis of lupus was difficult because the symptoms of lupus are similar to a number of other diseases, and sophisticated tools of molecular medicine were not yet available.

Today

- People who are diagnosed with lupus today have hope for a significantly increased life span and improved quality of life compared with those 30 years ago.
- Seminal studies from the NIH Intramural Research Program determined that treatment with immunosuppressive drugs (cyclophosphamide and prednisone) can prevent or delay kidney failure due to nephritis, one of the most serious and life-threatening complications of lupus.
- A number of genes associated with lupus risk and severity have been discovered. Some are linked in patient populations at high risk for lupus, including African American and Hispanic individuals.
- Basic research on animal models of lupus has identified the novel, targeted, and relatively less toxic therapy of utilizing short peptides (protein fragments) prior to the development of signs of lupus that has resulted in delayed onset of lupus kidney disease as well as prolonged survival and halting of the progression of kidney disease in those who already have lupus.
- A new approach to treatment of lupus is being explored in studies of the medication rituximab (FDA-approved for the treatment of patients with lymphoma). While current lupus treatments work by suppressing the entire immune system, rituximab selectively targets the subset of white blood cells, called B lymphocytes that are at the root of the problem in lupus. Clinical trials to test the effectiveness of rituximab in comparison to standard immunosuppressive treatment are in progress.
- The Epstein-Barr virus or EBV -- the virus that causes infectious mononucleosis -- may be related to the development of lupus in certain people. Studies of changes in the blood of people who later developed lupus identified auto-antibodies that damage target tissues, and for many, the antibodies were first produced in response to EBV infection. This suggests that viruses may be an important environmental trigger in lupus.

- Research has advanced our understanding of the molecular changes that can occur in the brains of people with lupus. The antibodies that attack the DNA of people with lupus can also attack molecules that bind a particular neurotransmitter (glutamate) involved in nerve cell activity. These antibodies can cause death of the nerve cells, and they are present in the fluid of the brain and spinal cord, possibly affecting brain function. These findings may explain why some people with lupus have cognitive symptoms.

Tomorrow

Through advances in medical research, we have a much better understanding of the many factors -- genetic and environmental -- that cause lupus; improved diagnostic abilities to identify lupus far earlier in the disease process before tissue damage has occurred; and targeted, less toxic therapies. Building on these advances, the future for patients diagnosed with lupus is significantly brighter, with genuine hope for longer life and improved quality of life.

- *Prediction*. Genetic studies will allow the identification of those at risk for lupus so that interventions can be made earlier in the disease process. A genetic "signature" was discovered that identifies some lupus patients who will develop such life-threatening complications as blood disorders, central nervous system damage, and kidney failure. Powerful molecular tools will help to predict who is likely to develop lupus, what organ systems are more likely to be targeted, and the severity of disease. Identifying lupus patients at particular risk for severe disease before serious complications arise has implications for early diagnosis and treatment.

- *Personalization*. The variations in disease course and severity that are associated with women and people in minority populations can be eliminated as our understanding of health disparities is improved, and treatments can be targeted to all affected individuals in a personalized way. In addition, some people with lupus have kidney disease, while some have predominantly central nervous system disease. In the future, we will have therapies designed for the specific complications of each lupus patient.

- *Preemption*. Identification of biomarkers of lupus as well as markers of increased susceptibility to the disease will allow preemptive strategies to be developed. Because antibodies in the blood precede diagnosis of lupus by many years, it will be possible to identify patients before disease onset and administer preventive treatments. In addition, results of the ongoing prevention trial in cardiovascular lupus in children will become available, and we will know whether statins (cholesterol-lowering agents) can be used preemptively to prevent cardiovascular and lipid abnormalities in children with lupus. Furthermore, we will have peptide therapies that preemptively block the binding of antibodies to kidneys and brain, and thereby block the injury to organ targets that lupus causes.