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Lupus, the Prototypical Autoimmune Disease, and the Military

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Introduction:

Lupus is the prototypical autoimmune disease because it can affect any organ system or tissue in the body. Many experts believe that research on lupus may provide important clues to understanding other autoimmune diseases. In lupus, the body's own immune system becomes unbalanced and incapable of differentiating between foreign substances and its own cells and tissues. In essence, the body attacks itself, causing inflammation, pain and damage to the skin, joints, heart, lungs, blood system, kidneys and brain resulting in significant disability or death.

According to a 2002 National Institutes of Health (NIH) report, lupus and other autoimmune diseases affect an estimated 14 to 22 million people in the United States. The estimated number of individuals with lupus in the U.S. is between 1.5 and 2 million.[i] To put these numbers into perspective, cancers of all types affect an estimated 9 million Americans.

While the causes of lupus are not fully known, it is widely accepted that lupus results from a complex interaction of genes and environmental factors. In recent years, a number of **genes** have been found to play a role in the development of lupus. As well, **environmental factors**, such as hormonal and occupational exposures, ultraviolet light, mental and physical stress, infectious agents, chemicals and toxins and certain drugs are known to trigger the onset of lupus as well as the exacerbation of existing disease.

Overall, lupus annually costs the nation an estimated $31.4 billion in direct and indirect expenditures. The average cost per person with lupus (between the ages of 18 and 65) was estimated to be $20,924, although the cost of lupus kidney disease is much higher at $64,195[ii] and since lupus kidney disease represents about 40% of the total lupus population, overall direct and indirect costs may well exceed $31 billion.

In 2009, as many as 20,000 active duty soldiers and veterans are receiving care for lupus through TRICARE or the Veteran's Administration healthcare system. At this time, we do not have statistics on the number of spouses or family members receiving treatment for lupus in these two federal programs.

Key factors in lupus:

- Ninety percent of people with lupus are women *(The number of women in the military is projected to rise - the number of women veterans is expected to reach 1.8 million in FY 2010)* [iii]
- Lupus is two to three times more common among African Americans, Hispanics, Asian Americans and Native Americans than in Caucasians – a health disparity that remains unexplained [iv] *(38% of all active duty military women are minority women- Minority women account for 55% of Army enlisted women)*
- African-American women with lupus are impacted at an earlier age, experience greater disease severity, have the highest overall death rate among all people with

lupus[v] *(30% of all active duty women are African-American)*

- Eighty percent of new cases are diagnosed in women of child-bearing age – striking people in their prime *(This is also the time when women enter the military)*

- More than 36% of lupus deaths occur in people between the ages of 15-44 [vi] *(the average patient in the U.S. is diagnosed in their 20's and 30's)*

- According to the CDC, African-American women are three times more likely to die from lupus than Caucasian women [vii]

Emerging research data indicates that our U.S. servicemen and women may be at high risk for developing lupus and other autoimmune diseases. Factors such as post-traumatic stress disorder (PTSD)[viii], vaccines[ix], chemical and toxins, ultraviolet light, certain drugs and infectious agents [x] [xi] [xii] have been associated with the development of lupus and other autoimmune diseases.

Few studies have been initiated to examine these issues in depth. As the prototypical autoimmune disease, findings from a robust research effort on lupus may provide clues to the causes of many other autoimmune diseases. **There is an urgent need to expand research to better understand the key factors that place military personnel at risk for developing lupus.**

With respect to environmental exposures in the war theaters today, several recent studies report that immune pathology may be present for a decade before the clinical presentation of lupus. Therefore, it will be important to recognize environmental exposures today, not only to prevent certain diseases, such as lupus, but to understand that clinical expression of a given disease may occur after military service.[xiii]

Vaccinations May Trigger Autoimmunity

In April of 2003, a 22-year old female soldier died due to lung complications caused by an acute attack of previously undiagnosed lupus.[xiv] An expert medical panel concluded that the soldier's death was precipitated by the administration of four pre-deployment vaccines – smallpox- typhoid, anthrax, hepatitis B and measles-mumps-rubella. Because of the complex nature of lupus, it is not untypical for women of this age to have undiagnosed lupus.

According to the Centers for Disease Control and Prevention (CDC), individuals with compromised immune systems, such as lupus patients, should not receive live-virus vaccines, or, importantly, be exposed to anyone who recently received a live-virus vaccine, such as for smallpox.

Many issues regarding the health effects of vaccines have been raised including those surrounding the potential health effects of multiple vaccines given prior to deployment.

In addition, a Department of Defense (DoD) report indicates that during the administration of the anthrax vaccine to hundreds of thousands of active duty personnel, there were 147 events classified as serious or medically important.[xv] **Lupus and undifferentiated immune affects were cited among the adverse events.**

There has also been much controversy as to whether squalene-containing adjuvants, as part of the anthrax vaccine formulation, were present in the shots administered to military personnel.[xvi]

Adjuvants are substances added to the vaccine to boost the immune response to the vaccine. In animal models, squalene has been used to induce antibodies and precipitate diseases that simulate autoimmune diseases such as lupus and MS. DoD has asserted that squalene was not added to the anthrax vaccine; but, in subsequent tests, traces of squalene were found.

To avert the potentially serious consequences of "live-strain" vaccines in immune compromised individuals, it would be important to identify lupus prior to the administration of vaccines. This is especially relevant since lupus is widely under-diagnosed in the U.S. and underlying disease can be triggered as a result of the use of these vaccines.

Research to detect servicemen and women who may have underlying disease is urgently needed. According to lupus experts, an approach that includes the identification and validation of lupus biomarkers and development of a test to detect those markers should be initiated. A biomarker is a chemical, physical or biological indicator, such as cholesterol, blood pressure or heart rate, which can be used to diagnose disease, measure the progress of disease or monitor/assess the effects of treatment. **Existing lupus research has provided exciting clues about potential lupus biomarkers but research to validate these markers requires further study.**

The Persian Gulf Wars and Lupus (Toxic Exposures)

Environmental and occupational factors have been shown to both exacerbate lupus and trigger the onset of the disease.[xvii]

Toxic exposures have long been hypothesized to cause the majority of long-term health problems experienced by veterans of both Gulf Wars. Neither clinical examination of ill war veterans or specific scientific research has yielded conclusive answers about toxic exposure. In all reports on the matter, there is a clarion call for a more robust medical research effort to expand present knowledge of environmental hazards and the impact on the health of our active duty personnel as well as the lasting effects on our veterans.

The National Academy of Sciences Institute of Medicine (IOM) has completed studies in which they document illnesses related to environmental exposures but additional research is urgently needed since, as they state, "none of the identified toxicological risks have been completely ruled out as possible causes of ill health among veterans."[xviii]

Reports in the literature suggest during the first Gulf War, as well as in Iraq and Afghanistan, exposure to a cocktail of environmental chemical and toxins may have caused a variety of conditions including amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS) and lupus.[xix] Along with the "dirty battlefield," other health threats included exposure to investigational vaccines for anthrax and other nerve agents. The release of sarin gas and related chemicals into the atmosphere during bombing raids on Iraqi chemical-storage bunkers have been chronicled in various reports.

A Department of Veteran's Affairs study states that "*further follow- up of Gulf War veterans and their controls is warranted for evaluating mortality risk of diseases with longer latency periods*." [xx]

It is important to note that recent research strongly suggests that antibodies linked to lupus may have latency periods that extend over decades.

Current research has not clarified the various contributions of toxic exposures to development of diseases such as lupus. **A more robust research effort to better understand the environmental contributions to the development of lupus is urgently needed.**

Other Related Issues

Post-Traumatic Stress Disorder (PTSD)

According to a recent report, troops sent to Iraq and Afghanistan who have post-traumatic stress disorder (PTSD) are three times more likely to develop lupus and other autoimmune diseases.[xxi]

A 2005 Veteran's Administration study states that an estimated 10% of active duty women and retired military women who served in Iraq have PTSD. In addition, a *New York Academy of Medicine* report states that Vietnam veterans who have PTSD more commonly develop autoimmune diseases such as lupus.

Mental and physical stresses are known to affect the neuroendocrine system whose function, in part, is to quiet autoimmunity. In FY 2006, the top three diagnostic categories for millions of women veterans were PTSD, hypertension and depression. As we know, women, especially women of color are at highest risk of developing lupus.[xxii]

Again, having validated lupus biomarkers and a definitive test linked to those biomarkers would help to identify veterans with PTSD who are at highest risk for lupus. In this way, treatment for the disease can be begun early to prevent the disease from progressing and its associated costs from escalating.

Ultraviolet Light, Certain Drugs and Smoking

Sunlight, specifically ultraviolet light, can trigger lupus rashes. In fact many people don't get lupus until they have had bad sunburn. In recent decades, most of operations theaters have been in hot, sunny climates.

A variety of commonly used prescription drugs can trigger lupus in genetically predisposed individuals. For example, sulfa antibiotics can trigger lupus flares. Other drugs known to trigger lupus are: hydralazine, procainamide, quinidine, carbamazepine, penicillamine, phenytoin, among others.

Smoking has also been linked to the worst form of lupus skin disease called discoid lupus.[xxiii]

Conclusions

Growing evidence suggests that there are factors involved in military service that have the potential to increase the risk of development of lupus among servicemen and women. Individuals at highest risk for lupus are young, minority women whose ranks are growing in the military.

An expanded research program through the Department of Defense is urgently needed to answer key questions related to the immune response of military personnel when vaccines are administered, when toxins and chemicals are present in the theaters of operation and when post-traumatic stress disorder occurs.

With respect to the administration of vaccines, knowing whether or not the soldier has undiagnosed lupus or another autoimmune disease is central to preventing morbidity and mortality associated with the disease. Presently, there is no way of identifying underlying lupus or autoimmune diseases in active duty personnel if

clinical presentation of the disease has not occurred.

There are many gaps in our understanding of the adverse effects of vaccines on vulnerable populations. The case of the death of a 22-year old female soldier given live-strain vaccines prior to her deployment to Iraq is particularly troubling since the soldier had underlying lupus which could not be detected prior to the administration of the vaccines.

Undiagnosed lupus is prevalent in the U.S.; therefore, the events which unfolded in this case could very well be repeated not only in the uniformed services but in the general population. In addition, questions have been raised concerning the interactions of multiple vaccines prior to deployment and in the field of operations which should be addressed by an expanded research effort. As well, the adjuvants which may have been present in vaccine formulations have come under scrutiny.

Lupus is a complex disease which is difficult to diagnose. While there are multiple tests that can be administered to detect lupus, these tests are not definitive and must be interpreted by a knowledgeable physician. The identification and validation of lupus biomarkers, those physiologic markers which can help to detect disease, assess progress of disease and monitor treatment effectiveness and the development of a definitive test to detect those markers, could be invaluable in identifying military personnel with compromised immune systems who, according to the CDC, should not receive vaccinations containing live strains.

The short and long term health effects of chemicals and toxins on our active duty soldiers and veterans have been chronicled in reports and studies being conducted by federal agencies and institutions. In all of these reports there has been a call for a greatly expanded research effort to better understand the contributions of environmental exposures related to diseases developed by active duty personnel and veterans. There is no better group to study than individuals with compromised immune systems because they may in fact be the proverbial “canaries in the coal mine” providing early warning of the health effects of various chemical and toxins present in theaters of operation.

This is especially the case since recent studies report that immune pathology may be present for a decade before the clinical presentation of lupus. It will be important to recognize environmental exposures in the war theaters today to not only prevent certain diseases, such as lupus, but to understand that clinical expression of a given disease may occur after military service.

In addition to the issues related to vaccines and toxic exposure, there are other factors which may contribute to the increased risk of developing lupus as a consequence of military service. For example, there is a three-fold increase in autoimmune diseases among military personnel with PTSD. Early identification of lupus in this growing population will be important to detect the disease early in its course. This is especially important in lupus since the disease can progress to irreparable damage to single and/or multiple organ systems of the body.

We believe that the identification and validation of lupus biomarkers and the subsequent development of a test to detect those markers will identify servicemen and women who can then be protected from the morbidity and mortality associated with live strain vaccines. Biomarker and test development will also be invaluable in

identifying immune compromised individuals diagnosed with PTSD. In addition, a robust research effort focused on immune compromised individuals and various toxic exposures is an approach which has the potential to reliably provide information that will serve to protect the health of our veterans and as well as our non-veteran populations.

The Lupus Foundation of America (LFA)

The Lupus Foundation of America is the foremost national voluntary nonprofit organization dedicated to the fight against lupus. Our mission is to find the causes of and cure for lupus and provide support, services and hope to all people affected by lupus. The Foundation vigorously pursues its mission through programs of medical research, education and advocacy. Through its nationwide network of more than 300 affiliates, chapters and support groups, the Foundation provides assistance to the more than 1.5 million people affected by lupus, their families and caregivers. For more information about the LFA, visit our website at www.lupus.org or call 202-349-1155.

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