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Exhibit A

2 Pages

Subj: **Fwd: AUTOIMMUNE DYSFUNCTION MCTD MIXED CONNECTIVE TISSUE DISEASE**
Date: 12/15/2009 3:25:39 P.M. Eastern Standard Time
From: RetAirForceMan
To: rstanton@stjoelive.com

LeRoy G. Foster, MSgt, USAF, Ret
Life Member of the DAV of New York State
Member of the American Legion Post 777, Celeron, NY
Member of the Vietnam Veterans of America
70% Service Connected 100% Unemployable
Totally and Permanently Disabled from Agent Orange on Guam

From: RetAirForceMan
To: rstanton@stjoelive.com, MPaxton@nas.edu, colonel-dan@sbcglobal.net, mar_vic_cagurangan@yahoo.com, josephmchale@ymail.com, jviolante@davmail.org, srobertson@legion.org
Sent: 12/15/2009 1:54:10 P.M. Eastern Standard Time
Subj: AUTOIMMUNE DYSFUNCTION MCTD MIXED CONNECTIVE TISSUE DISEASE

AUTOIMMUNE DYSFUNCTION IN VIETNAM VETS;
THERE MAY BE A DIAGNOSIS

THE
OKLAHOMA AGENT ORANGE FOUNDATION
P.O. Box 849
Lexington, OK 73051
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In 1980, after years of suffering from an undiagnosed illness I saw a "Barney Miller" episode wherein, Wojohowitz (Max Gail) had a Vietnam Veteran in jail and was looking for answers as to why this veteran thought his exposure to "Agent Orange" was responsible for his actions. Deitrich (Steve Landsburg) mentioned a study that showed immunological dysfunction in Vietnam Vets. The next morning I spent hours on the phone tracing the study mentioned by "Deitrich". Eventually, I actually contacted the researcher who had done the study. This study, although small, showed that 65% of those Vietnam Veterans who were ill had antibodies to their own DNA. With a possible explanation of my own previously undiagnosed illness at hand I became an activist in the "Agent Orange" issue. As I gathered information on the possible health effects of exposure to "Agent Orange"; I found a 1979 General Accounting Office report wherein they instructed the Veterans Administration to pay particular attention for damage to the immune system of those exposed to "Agent Orange". Next, I found a 1981 American Medical Association report that showed damage to the thymus (part of the immune system) in animals exposed to Dioxin (a contaminant in Agent Orange). Shortly thereafter, during the EPA scandal of 1982, Congress turned up a study done in England, of people exposed to 2,4,5-T (half of Agent Orange), that again showed immune system damage. Our own EPA not only had knowledge of the previous study, but did a similar study and found much the same results. The EPA chose to suppress this information. This all occurring while Congress was unraveling, and proving, corporate (DOW) interference with EPA documentation. My wife and I encouraged four Vietnam Veterans to have blood drawn in an effort to duplicate the results of the study mentioned on "Barney Miller". This blood was not sent to the

Exhibit A

university that did the "Barney Miller study" but; coinciden- tally, sent to a university where a researcher had discovered a rare disease in the early 1970's. Not only did the blood work return as expected (having similar results to the "Barney Miller study" -- 3 out of 4 veterans had antibodies to their own DNA), but a diagnosis was sent back with the test results! MIXED CONNECTIVE TISSUE DISEASE (MCTD), an AUTOIMMUNE DISEASE. I feel it is imperative that Vietnam Veterans, who become ill, avail themselves of an ANA profile, looking for antibodies to their own DNA to the FLORESENT SPECKLED PATTERN. These tests should be done periodically: 1) to ensure early detection of a serious disease, 2) if you are ill with an Autoimmune Disease the test will only show positive at specific times of flareup. These tests should be done outside the VA system. Veterans who are ill or become ill with an undiagnosed illness should consult with their family doctor about the possibility of having an ANA profile done particularly if they have the some of the following symptoms: arthritis/arthralgias inflammation and pain in the joints), swollen hands, Raynaud's phenomenon (abnormal redness, heat, and tingling in the fingers after exposure to cold weather), abnormal esophageal motility (difficulty in swallowing), myositis (inflammation of muscle tissue), lymphadenopathy (disease of the lymph nodes), fever, hepatomegaly (enlarged liver), serositis (inflamed condition of the serous membrane), splenomegaly (enlarged spleen), renal disease, anemia, leukopenia (abnormally low white blood cell count), and/or hypergammaglobulinemia (abnormally high immunoglobin levels). I recently spoke to a Vietnam Veteran with symptoms of MCTD who was suicidal because of attempting to function with an undiagnosed illness. As we went over his VA medical records we found lab work that clearly indicated MCTD. The VA had refused to inform him of the problem; thus, creating undue stress, and leaving him with a chronic, debilitating, life-threatening disease and no medical care. Thus, I feel obligated to share the good news that we have uncovered about toxic poisoning. Previously, the U.S. Government's constant denial of the damage from diseases that may be caused by exposure to the various chemical warfare agents (herbicides and insecticides) used in Vietnam has forced many veterans to try to function with undiagnosed illnesses and no medical care. Vietnam Veterans and other victim groups can take heart in the fact that many of the illnesses caused by exposure to chemical warfare agents can be diagnosed

Exhibit B
3 Pages

Subj: **OH MY GOSH**
Date: 12/15/2009 7:57:55 P.M. Eastern Standard Time
From: RetAirForceMan
To: rstanton@stjoelive.com

Mixed Connective Tissue Disease

MCTD--A Precursor of Lupus or a Distinct Disease?

Feb 25, 2007 **Elaine Moore**, Lab Supervisor, University of Colorado

Mixed connective tissue disease is a distinct syndrome with features of arthritis, lupus, poymyositis and scleroderma that can progress to lupus or scleroderma.

Mixed connective tissue disease (MCTD) is a **connective tissue disorder** first described in 1972 as a distinct rheumatic disease syndrome associated with a specific antibody to an extractable nuclear antigen (ENA). This early report was based on a group of patients with overlapping clinical features of systemic lupus erythematosus (SLE), scleroderma, and myositis with blood tests showing a distinct autoantibody. This autoantibody was later identified as an antibody to U1-ribonucleoprotein (RNP).

Today, MCTD is recognized as having features of **Raynaud phenomenon**, swollen hands, arthritis/arthralgia, acrosclerosis, esophageal dysmotility, polymyositis, sclerodactyly (scleroderma-like tissue hardening), pulmonary hypertension or interstitial lung disease, and high levels of anti-U1RNP antibodies as well as antibodies against U1-70kd small nuclear ribonucleoprotein (snRNP).

Who is Affected?

Females are 10 times more likely to develop mixed connective tissue disease than males. The typical onset occurs in people aged 15-25 years. In the United States, MCTD is seen in about 3-5 out of 100,000 persons, and it's more prevalent than dermatomyositis and less prevalent than SLE. Internationally, MCTD has a reported prevalence of 2.7 cases per 100,000 population.

Symptoms and Signs

At the time of diagnosis 74 percent of patients show signs of Raynaud phenomenon and 66 percent of patients exhibit symptoms of arthralgia and arthritis. Over time, nearly all patients show signs of Raynaud phenomenon and arthritis, and eventually about 66 percent of patients develop esophageal hypomotility, swollen hands, and pulmonary (respiratory) dysfunction.

Other signs and symptoms seen in MCTD include myositis (muscle inflammation), leukopenia (low white blood cell count), sclerodactyly, pleuritis/pericarditis (inflammation of tissue surrounding the lungs and heart), and rash. Complications include fever, which occurs as a sign of infection, vasculitis, pancreatitis, appendicitis, bowel perforations, trigeminal neuralgia, respiratory distress syndrome, stroke, and secondary Sjogren's syndrome.

Although some researchers recognize MCTD as a subset or early stage of SLE, most researchers consider MCTD a distinct clinical entity with infrequent renal complications. While the prognosis in MCTD is generally good, patients who develop pulmonary hypertension are more likely to have an unfavorable disease course. Overall, about 25 percent of patients with MCTD eventually progress to SLE, and about 33 percent progress to systemic sclerosis. Pulmonary hypertension is the most common cause of death in MCTD, followed by scleroderma renal crisis, heart failure and infections.

Diagnosis

MCTD is diagnosed in patients with symptoms of arthritis, scleroderma, and Raynaud with high titers of antinuclear antibodies with a speckled pattern and high titers of anti-RNP and anti-U1-70kd antibodies. Patients may also have **rheumatoid factor**, Scl-70 antibodies, and antiphospholipid antibodies. Current diagnostic criteria include 3 of the 5 following clinical features: edema of hands, swollen joints (synovitis), myositis, Raynaud phenomenon and acrosclerosis (sausage-like fingers typically seen in systemic sclerosis).

Treatment

The type of treatment used depends on the predominant signs and symptoms and the clinical disease severity. Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to reduce pain and inflammation, which improves mobility and function. Hydroxychlorquine (Plaquenil) is frequently used along with NSAIDs in patients with arthritis.

Patients with more severe disease are often treated with low-dose corticosteroids, endothelin receptor antagonists, cyclophosphamide, or methotrexate or with cyclooxygenase-2 inhibitors. Patients with secondary pulmonary hypertension are usually treated with prostaglandins such as eposprostenol (Flolan). Patients who show a good response to corticosteroid or NSAID treatment usually have a favorable prognosis.

Resources

Hoffman, Robert, **Mixed Connective-Tissue Disease**, Emedicine, Nov 2006, accessed Feb 10, 2007.

Venables PJ, Mixed connective tissue disease, Lupus, 2006; 15(3): 132-137.

Zdrojewica A, Budzyn-Koziol E, Mixed connective tissue diseases—etiology, pathogenesis, clinical significance, treatment, Posthepy Hig Med Dosw, 1999; 53(5): 751-766.

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multifactorial nature of the process may explain why only relatively few patients develop adverse clinical responses.

The complexity of chemical-induced systemic allergy and autoimmunity is a major hurdle for the development of models predictive for such adverse effects of chemicals. To illustrate the possible mechanisms of chemical-induced autoimmunity, in particular regarding initiation of processes, it is reasonable to consider results of studies with allergenic drugs as well.

Mechanisms through which chemicals cause sensitization of the immune system are very diverse, but they can mostly be categorized according to the general strategy that is followed by the immune system (Janeway & Medzhitov, 2002; Hoebe et al., 2004) (see Fig. 1). According to this strategy, immunization occurs only when cells of the adaptive immune system (T and B lymphocytes) encounter antigen-specific signals (providing so-called signal 1 to the lymphocyte) from antigen-presenting cells in combination with additional, adjuvant-like costimulatory signals (collectively called signal 2). Once sensitized, T cells may activate various effector mechanisms that in turn may cause protective immunity or, depending on the antigen that is recognized and under certain circumstances, adverse (i.e. allergic or autoimmune) disorders. All steps in this process are strongly regulated by a number of factors, including immune, neuroendocrine, and environmental factors (see Fig. 1). Together, this strategy aims to tailor the immune response so as to effectively get rid of the initiating antigen and at the same time to prevent the immune response from persisting or possibly proceeding to adverse effects.

Drugs may interfere with all phases of this immune strategy. For instance, chemicals may interfere with antigen-specific stimulation (signal 1) by forming neoantigens (section 7.2.1), inducing targets for cross-reactivity (section 7.2.2), releasing non-tolerant epitopes (section 7.2.3), or interfering with central tolerance (section 7.2.4). Chemicals may also elicit adjuvant-like processes, reminiscent of danger signals, leading to increased costimulation, and thus provide signal 2 to lymphocytes (section 7.2.5). And obviously, chemicals may directly (e.g. through modification of immune regulatory processes) or indirectly (e.g. through the neuroendocrine system) (section 7.2.6) affect the functionality of the immune system.

Pg 1.
Exhibit C
3 Pages

World Health Organization

7. MECHANISMS OF CHEMICAL-ASSOCIATED AUTOIMMUNE RESPONSES

7.1 General

When discussing mechanisms of chemical-induced autoimmunity, it should be stressed that autoimmunity is an ill-understood phenomenon. It is also important to realize that normal healthy individuals possess natural autoantibodies as well as autoreactive T and B cells to provide a necessary and protective immunological homeostasis (Avrameas, 1991; Schwartz & Cohen, 2000). At the present time, it is not precisely known why on certain occasions autoimmune responses can lead to pathological conditions (i.e. autoimmune diseases). Another important consideration is that mechanisms of systemic allergy may resemble those of autoimmune reactions, at least to some extent.

Compounds can induce the release of neoantigens (cryptic epitopes) or alter autoantigens so that they appear foreign (Griem et al., 1998). Specificity of an immune response induced by a compound may be initially directed exclusively towards this neoantigen, but after a certain time it spreads to include autoantigen-directed responses. For instance, it has been shown that T cells from mice exposed to mercury(II) chloride for only one week responded to mercury(II) chloride or mercury-modified fibrillarin, whereas after eight weeks of exposure, the T cells responded to native fibrillarin as well (Kubicka-Muranyi et al., 1996). This process, referred to as epitope or determinant spreading (Sercarz et al., 1993), may explain why individuals, after a certain period of exposure, have an autoimmune response. Individual properties of patients may determine whether the immune response is eventually more allergy-like or more autoimmune-like in nature.

The immune system is highly host-specific (for instance, based on MHC haplotypes). Whether exposure to a chemical results in immune-related diseases may depend more on a patient's individual predisposing characteristics and circumstances of exposure than on the characteristics of the chemical itself (Lehmann et al., 1993). The

found (De Heer et al., 1995). TCDD also resulted in the appearance of autoimmune nephritis in young male mice exposed monthly to the chemical and reduced the time to postnatal onset of autoimmune nephritis in male offspring of autoimmune-prone mice receiving a single fetal exposure (Silverstone et al., 1998). Thus, it is proposed that TCDD at prenatal exposure may have the potential to cause defective thymocyte–epithelial cell interactions and antigen presentation on thymocytes, thereby altering normal development of self-tolerance and leading to expression of autoimmunity (Holladay, 1999). The proposal was also supported in autoimmune-prone mice (MRL/lpr mice) exposed prenatally to TCDD, which showed a significant dose-related increase of urinary protein and autoantibodies to single-stranded DNA (ssDNA) (Smith & Germolec, 2000). These findings suggest that developmental exposure to dioxins may accelerate the onset of genetic expression of autoimmune predisposition. Repeated TCDD treatment of mice increased serum IL-6 levels accompanied by higher titres of tissue-specific autoantibodies (H.J. Kim et al., 2003). However, before any firm conclusion on an association of TCDD exposure with autoimmunity or autoimmune disease can be drawn, additional evidence is required.

8.3 Pesticides

8.3.1 General

Pesticides are widely used worldwide in agriculture, public health, and several indoor conditions. Current evidence related to pesticide autoimmunogenic potential is summarized in Table 8. Hexachlorobenzene is the most intensively studied pesticide in the context of autoimmunity, and it will therefore be addressed separately at the end of this section.

There is some evidence, either in animal models or following human exposure, that several pesticides used currently or in the recent past can cause slight changes that could be interpreted as "autoimmune-like effects". However, data supporting this hypothesis are scarce. In some cases, the mere inclusion of observed changes as indicative of autoimmunity is even questionable, whereas in other cases, results of one study have not been confirmed by a subsequent study. Only few compounds that are no longer in use today (i.e. mercury derivatives, hexachlorobenzene) have been

DEPAP, but not aniline or other 3-(*N*-phenylamino)-1,2-propanediol derivatives, induced both apoptosis and necrosis in human peripheral blood lymphocytes in vitro in a time- and concentration-dependent fashion. In short-term cell cultures, possibly representative of the toxic oil syndrome acute phase, DNA degradation occurred rapidly. Apoptosis preceded membrane damage. In longer-term cultures, cytotoxicity was characterized by necrosis. As the cells die, abnormal forms of autoantigens are released, activating autoreactive lymphocytes, which could ultimately initiate autoimmune disease (Gallardo et al., 1997; Lahoz et al., 1997).

8.2 TCDD (dioxins)

Dioxins are unintended by-products of natural events and human-made processes such as manufacturing, incineration, paper and pulp bleaching, and exhaust emissions. Immunotoxic effects of dioxins have been studied primarily with respect to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), the most toxic congener of dioxins and an important immunotoxicant (Vos & Moore, 1974).

There are two cross-sectional studies that suggest autoimmune responses in dioxin-exposed persons. In inhabitants in Viet Nam exposed to Agent Orange containing TCDD, the concentration of circulating immune complexes and antinuclear antibodies was elevated, with an increased number of circulating lymphocytes (Kozhevnikova et al., 1991). Their elevation was also detected more frequently in 18 TCDD-exposed workers than in 15 matched controls (Jennings et al., 1988). In a larger controlled study on workers in a German pesticide-producing factory, however, there was no significant correlation between autoantibody levels and polychlorinated dibenzo-*p*-dioxin (PCDD) / polychlorinated dibenzofuran (PCDF) concentrations in blood lipids (Jung et al., 1998). There are recent reports also indicating no induction of antinuclear antibodies in patients intoxicated with PCBs and dioxin contaminants in rice oil (Nagayama et al., 2001) and in Korean veterans exposed to Agent Orange (H.A. Kim et al., 2003).

Prenatal exposure of mice to TCDD modulated fetal antigen expression on thymocytes and inhibited thymocyte maturation (Blaylock et al., 1992). In TCDD-treated mice, moreover, thymic epithelium distribution of MHC class II molecules was found (De Waal et al., 1992), but potent autoreactive V beta 6+ cells were not