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# Chronic Fatigue Illnesses Associated with Service in Operation Desert Storm Were Biological Weapons Used Against our Forces in the Gulf War?

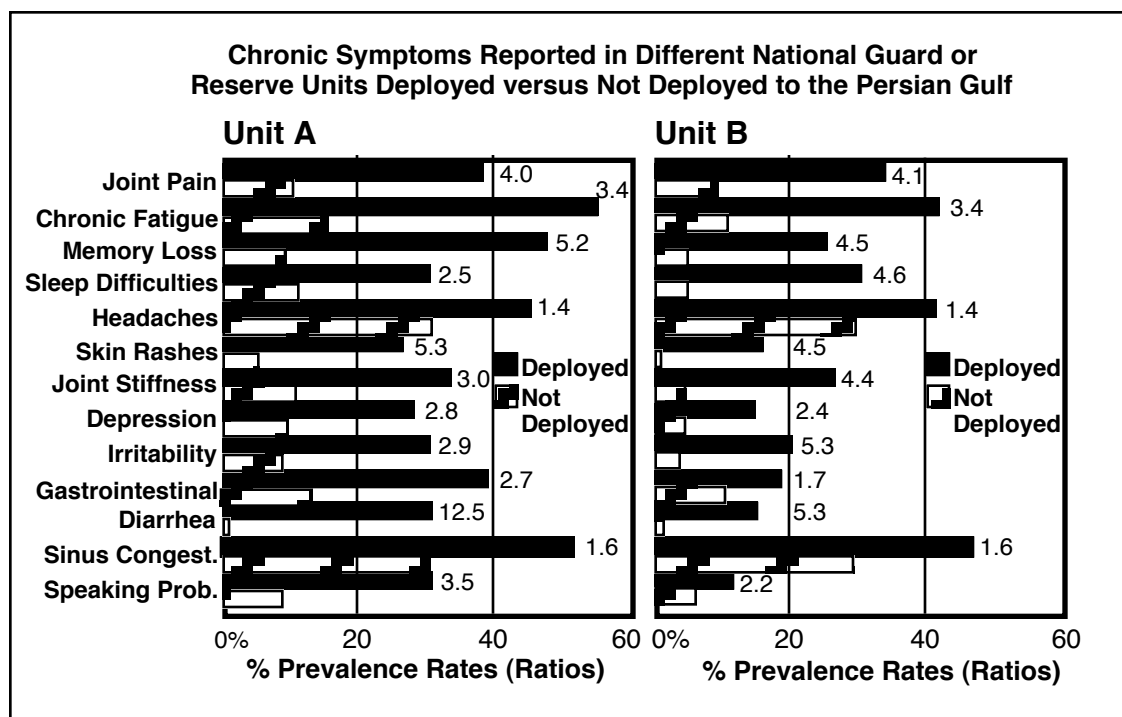
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A large number of soldiers that served in Operation Desert Storm/Shield returned to the U.S. and presented with a variety of unusual signs and symptoms that have been difficult to diagnose. For example, Subject A served in an Army military intelligence unit in Operation Desert Storm and came upon an unusual event in the Iraqi desert. He saw thousands of dead sheep by the road and stopped to investigate. There was no outward manifestation indicative of the cause of the sheeps' death, until he got a closer look. The only thing he noticed that was wrong was that the sheeps' nostrils were red and swollen. But when he looked closer, he noticed that even the insects on the sheep were all dead. Unfortunately, subject A did not have on his NBC (*nuclear/biological/chemical*) protective suit at the time and was probably exposed to agents that have rendered him incapacitated and unable to report to active duty. When subject A returned from the Gulf War to his new post at Fort Meade, MD, he was chronically ill and experienced the signs and symptoms listed in Figures 1 and 2. Along with chronic fatigue syndrome, joint pain, intermittent fevers, headaches, coughing, nausea and gastrointestinal problems, diarrhea, diminished vision and other signs, subject A also had multiple chemical sensitivity (MCS) syndrome, and he has been sick to this day and has been trying unsuccessfully to get help. Then subject A's wife started becoming sick but without MCS, but they have not been able to get effective treatment for their symptoms at military hospitals, including the Army's Walter Reed Medical Center in Washington DC.

Subject B was an Army officer who returned from Operation Desert Storm after service with the 101st Airborne Division (Air Assault) out of Fort Campbell, KY. He was deployed on the deep insertions into Iraq. His unit did not come under enemy fire, and he considered his service relatively uneventful, until approximately six months after he returned to Fort Meade, MD in 1991. What started out as a relative benign series of flu-like illnesses became progressively worse with severe chronic fatigue, coughing, nausea, gastrointestinal problems, intermittent fevers, skin rashes, joint pain, memory loss, vision problems and severe headaches. Then subject B's wife began to have chronic fatigue and gynecological problems, aching joints, headaches, and her stomach began to swell with ascites fluid, causing severe pain, until she looked 9 months pregnant. Even his 7 year-old daughter became ill with similar flu-like symptoms that did not go away and progressively became worse, resulting in chronic fatigue, skin lesions, vomiting, headaches, aching joints, and she failed to gain weight. While this was happening, subject B and his family were under the care of Kimbrough Army Hospital at Fort Meade and Walter Reed



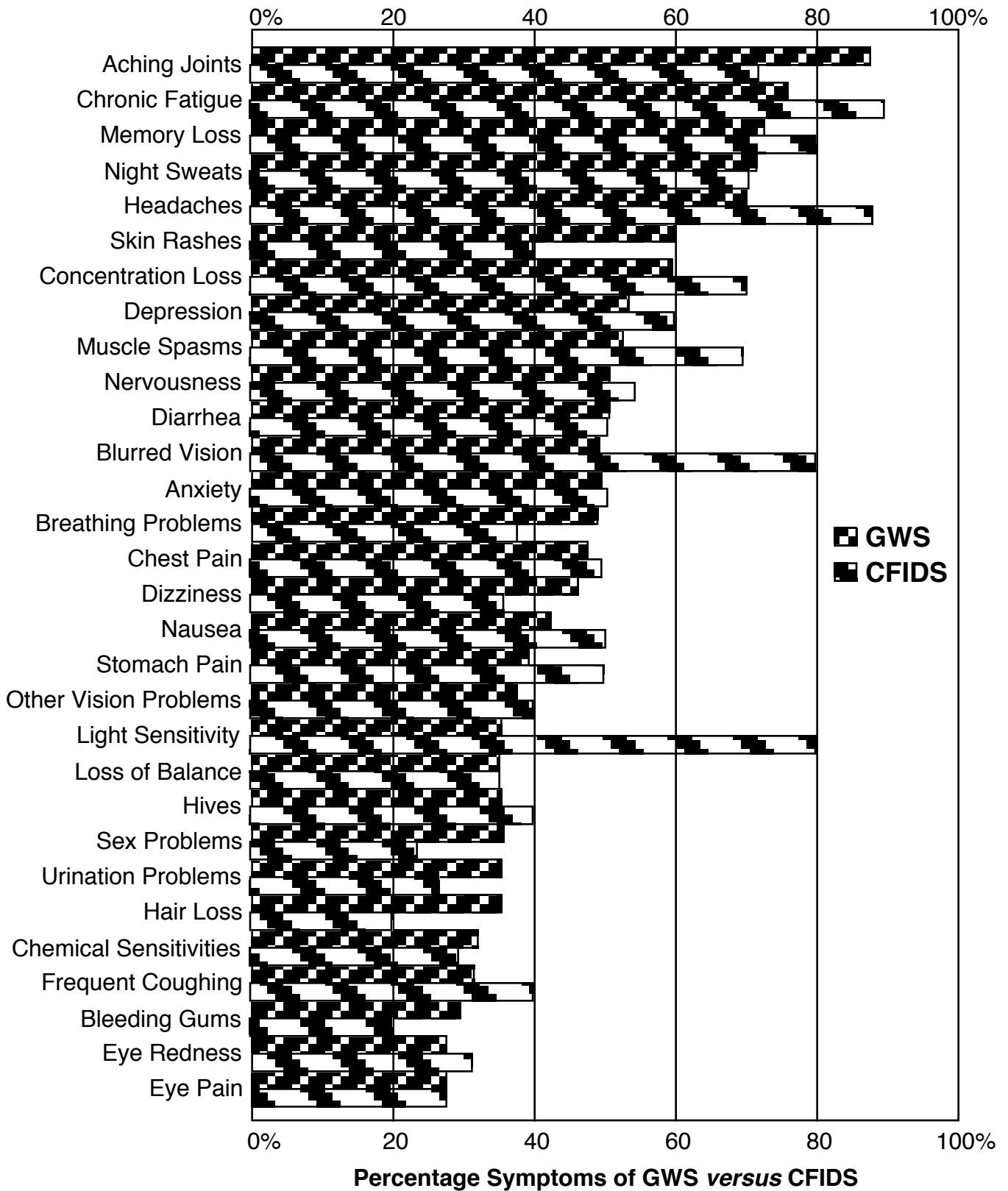
**Figure 1.** Control study on Persian Gulf War illnesses conducted by the CDC. The bars indicate the frequencies of common symptoms in deployed (solid bars) and non-deployed (stippled bars) members of a Air Guard (Unit A) and Air Force Reserve (Unit B) units that approximately equal numbers of airmen deployed or not deployed to the Persian Gulf Theater of Operations.

Army Medical Center. They never received a diagnosis, explanation or treatment for their illnesses, even after extensive testing. Later they found out that several families of Gulf War veterans at Fort Meade had similar health problems and nowhere to go for help. These families were being told that they had psychological problems, but they claim and can prove with documentation that they are sick and deserve proper treatment.

Subject C was an Air Force Special Operations intelligence officer attached to the 5th Special Forces Group based at King Fahd Airport west of Dhahran and the 160th Special Operations Aviation Regiment at King Khalid Military City. He was involved in the Special Forces operations, but remained in Saudi during the war. However, the area where he was stationed was under constant SCUD missile attack during the war. After his return to the U.S., he noticed that he had a constant sore throat, night sweats, shortness of breath, dizziness, joint pain, short term memory loss, vision problems, diarrhea and other bowel problems, skin rashes and severe to moderate chronic fatigue. He eventually left the military and has not been able to obtain appropriate treatment from VA hospitals for his illness.

Another Special Forces officer now in DELTA ONE (Delta Force) at Fort Bragg was subject D, a Navy officer in charge of the SEAL units that were involved in some of the most sensitive covert missions during Operation Desert Storm. He presented after the Gulf War with chronic fatigue, fever, stomach cramps, joint pain, skin rashes, memory loss, dehydration, headaches and heart pain and other symptoms shown in Figure 2. His vision became so diminished that physicians at Womack Army Hospital were considering surgery. He stated to us that he had "every conceivable test conducted, treatments, etc., known to the military with zero results, zero answers and zero relief."

Although most military, VA, and civilian doctors agree that these Gulf War veterans have medical problems, they have been unable to diagnose the exact syndrome. This has resulted in the misinformation that the Desert Storm veterans do not have health problems. That they do have undiagnosed medical conditions was carefully shown in a control study by the Center for Disease Control (CDC) in Atlanta.<sup>1</sup> The CDC epidemiologists studied hundreds of airmen from an Air National Guard unit from Pennsylvania that were deployed to the Persian Gulf and compared their health problems to similar numbers of members



**Figure 2.** Comparison of symptoms in approximately 650 Desert Storm veterans suffering from Desert Storm Illness with symptoms of CFIDS (From Nicolson and Nicolson<sup>2</sup>).

of the same unit that were not deployed (Figure 1). They also studied Air Force reserve and active duty units in Pennsylvania and Florida. In these four units the deployed members had a variety of chronic illness symptoms that were not present in the same frequencies in the undeployed members of the same units.<sup>1</sup> Even with this controlled study, some military and VA physicians still don't even believe that Gulf War Syndrome (GWS) exists, and they do almost nothing to treat the illnesses associated with Operation Desert Storm.

Approximately 50,000-100,000 Desert Shield/Storm veterans, and in many cases their family members, share similar but individually unique sets of signs and symptoms (see Figure 2)<sup>2</sup> that cannot be easily explained. Since collectively these signs and symptoms are not well established as criteria for particular diseases and they do not readily fit into common diagnosis categories used by military and VA hospitals, many physicians simply list the diagnosis as unknown, or worse, they conclude that their patients have psychological problems, such as Post Traumatic Stress Disorder [PTSD].

Most military personnel that we interviewed were particularly disdainful of a "psychological explanation" for GWS. We have been told repeatedly by veteran combat soldiers that the Desert Storm conflict was not particularly stressful as far as wars go. Indeed, the involvement of multiple organ systems and multiple, seemingly disparate signs and symptoms of GWS have baffled most physicians and have not allowed them place patients into a single working case definition that would enable them to get appropriate treatment. Using PTSD and other psychological profiles for GWS seems like a convenient cover to most Gulf War veterans. In fact, the signs and symptoms of GWS almost exactly fit the profile for Chronic Fatigue-Immune Dysfunction Syndrome (CFIDS).<sup>2</sup> Thus the DoD is probably correct in their stance that GWS is not a new syndrome, and from the signs and symptoms we believe that it is a CFIDS-like disorder.<sup>2</sup> Even Major General Ronald Blanck, commanding officer of Walter Reed Army Medical Center in Washington D.C., agrees that GWS "symptoms list fit a CFIDS-like illness."<sup>3</sup>

The classical working case definition of CFIDS was proposed by the CDC. CFIDS is characterized by persistent or relapsing, debilitating fatigue or easy fatigability in a person who has no previous history of similar symptoms, that does not resolve with rest and is severe enough to reduce or impair average daily activity below 50% of the patient's premonitory activity level.<sup>4</sup> In addition to the absence of clinical conditions that could easily explain the symptoms, such as cancers or autoimmune diseases, patients present with mild fever, sore throat, muscle pain, generalized muscle weakness, headaches, painful lymph nodes, sleep difficulties, and neuropsychologic complaints, such as memory loss, light sensitivity, confusion, irritability and depression.<sup>4</sup> These signs and symptoms closely parallel those found in GWS (Figure 2).<sup>2</sup> Thus GWS is not a separate syndrome; it appears to be a CFIDS-like disorder as we proposed previously.<sup>2</sup>

Some of the Desert Shield/Storm veterans that have multiple chronic symptoms may eventually have their diagnoses linked to chemical exposures in the Persian Gulf, such as oil spills and fires, smoke from military operations, chemicals on clothing, pesticides, chemoprophylactic agents, chemical weapons and others. In some cases, this exposure may have resulted in multiple chemical sensitivity or MCS, such as seen in subject A. MCS shares some but not all of the symptoms listed in Figures 1 and 2, including immune system dysfunction,<sup>5</sup> but in many of the soldiers the infectious nature of the illnesses and the spread of the illness to immediate family members precluded simple explanations, such as exposure to toxic chemicals that were present at some Gulf locations or exposure to Iraqi chemical weapons. In these patients, the chronic symptoms and moderately contagious nature of the illness are consistent with chronic infections that can cause CFIDS-like symptoms.<sup>2</sup>

The medical problems experienced by many Desert Storm veterans, and in some cases their immediate family members, is one of the ongoing mysteries of the Gulf War. In an attempt to answer criticisms that the DoD and VA were not taking these problems seriously Gulf War Registration Units and Desert Storm Referral Centers were established by the Dept. of Veterans' Affairs to document health complaints. Next, a Technology Assessment Workshop was organized by the National Institutes of Health (NIH) with the task of examining information and reports on Gulf War Illnesses, recommending working case definitions for these illnesses, developing plausible etiologies and biological explanations for the illnesses, and finally recommending future research efforts to understand, diagnose and treat the illnesses.<sup>6</sup> In fact, some of the aforementioned tasks, such as the establishment of initial workshops and Referral Centers at VA hospitals were accomplished.

Unfortunately, the lack of any concrete results and, for the most part, the lack of significant progress in assigning diagnoses and initiating effective treatments for veterans and their families for their Gulf War illnesses have not received appropriate priority, even with the political pressure of various veterans organizations. Also, the politicians in Washington do not seem to be very interested in this issue. Even worse have been the catagoric statements of some officials, such as John Deutch, then Deputy Secretary of Defense, that chemical or biological weapons *were not used* during Desert Storm, effectively eliminating these important sources of the illnesses from careful consideration by military and VA hospitals.

In 1994 a national panel was convened to discuss the medical problems of Gulf War veterans. The NIH Technology Assessment Panel issued a Workshop Report on Desert Storm Illnesses<sup>6</sup> that was meant to address fears that these illnesses were not being taken seriously and to establish practical working case definitions for the chronic illnesses associated with Operation Desert Storm. Unfortunately, the Workshop Report issued by the Technology Assessment Panel<sup>6</sup> did little to address the Gulf War veterans' and their families charges that next to nothing was being done to help them. Earlier this year the Institute of Medicine (IOM) of the National Academy of Sciences criticized the government's efforts as "intrinsically unsuitable for systematic study of the health effects of the Gulf War." While several departments (DoD, Veterans Affairs, Health and Human Services) are arguing over appropriate clinical studies and better coordination, tens of thousands of Persian Gulf War veterans remain chronically ill without much help for their plight.

Even worse, there has been little attempt until recently to enlist medical and scientific specialists to help in this problem. In addition, up to 1995 there had not been any appropriation of funds to conduct proper research into the possible causes or potential treatments of GWS. Previous attempts at appropriating funds for research on Gulf War illnesses were blocked by DoD, because they claimed that they duplicated ongoing DoD efforts. This policy has changed recently, however, and the DoD and the Department of the Army have set aside \$4 million for Gulf War Illness studies to be awarded late in 1995 or early in 1996.

In their frustration, Gulf War veterans representing all 50 states met March 10-12, 1995 at a Unity Conference of Gulf War veterans organizations in Dallas under the direction of Air Force reserve Maj. Denise Nichols, R.N. to exchange, discuss and disseminate information on patient registration, medical and employment assistance, legislation, and medical/scientific issues of importance to Gulf War veterans. One of us (G.L.N.) was asked to chair the Medical Panel where environmental, chemical and biological sources of GWS were considered. Indeed, an important conclusion of this panel which was similar to other panels was that there appeared to be no single cause or source for the collection of illnesses called GWS or Desert Storm Illness.<sup>7</sup> Patients seem to fall into several categories, some with only MCS, some with chronic fatigue syndrome (CFIDS) without MCS, some with only a few of the symptoms listed in Figure 2, and some with most if not all of the symptoms in the figure.<sup>7</sup>

One of the first things that the panel did was dismiss a psychological origin of Gulf War Illnesses. Not that psychological problems did not exist among the soldiers in Desert Storm, but after careful assessment of the symptoms of the overwhelming majority of Gulf War veterans, the symptoms did not fit with a psychological origin of the diseases.<sup>7</sup> Parasites such as *Leishmaniasis* and bacteria such as *Cholera* are endemic to the Middle East and could be the cause for symptoms in at least some of the soldiers with GWS; however, diagnostic tests are available for many of these agents, and there have been no reports that they are the causes for symptoms in a large number of patients with GWS. In some cases the explanation has been attributed to known parasitic diseases, such as infections by *Leishmania tropica*, probably spread by a sandfly. This can result in viscerotropic leishmaniasis.<sup>8</sup> However, many of the common symptoms of GWS do not fit with this explanation, and diagnosis of leishmaniasis is uncommon in Gulf War veterans. Nonetheless, it is unclear how prevalent leishmaniasis infections are in GWS patients.

A member of the panel at the meeting in Dallas,<sup>7</sup> William Rea, M.D., Director of the Environmental Health Institute in Dallas, has been treating Desert Storm veterans with GWS and MCS. Similar to many nonveteran MCS patients, Desert Storm veterans with MCS responded to pollutant avoidance, vitamin and nutrient supplementation, allergin tolerization and physical therapy.<sup>9</sup> This subset of GWS patients showed marked improvement in their MCS symptoms after such combination therapy.

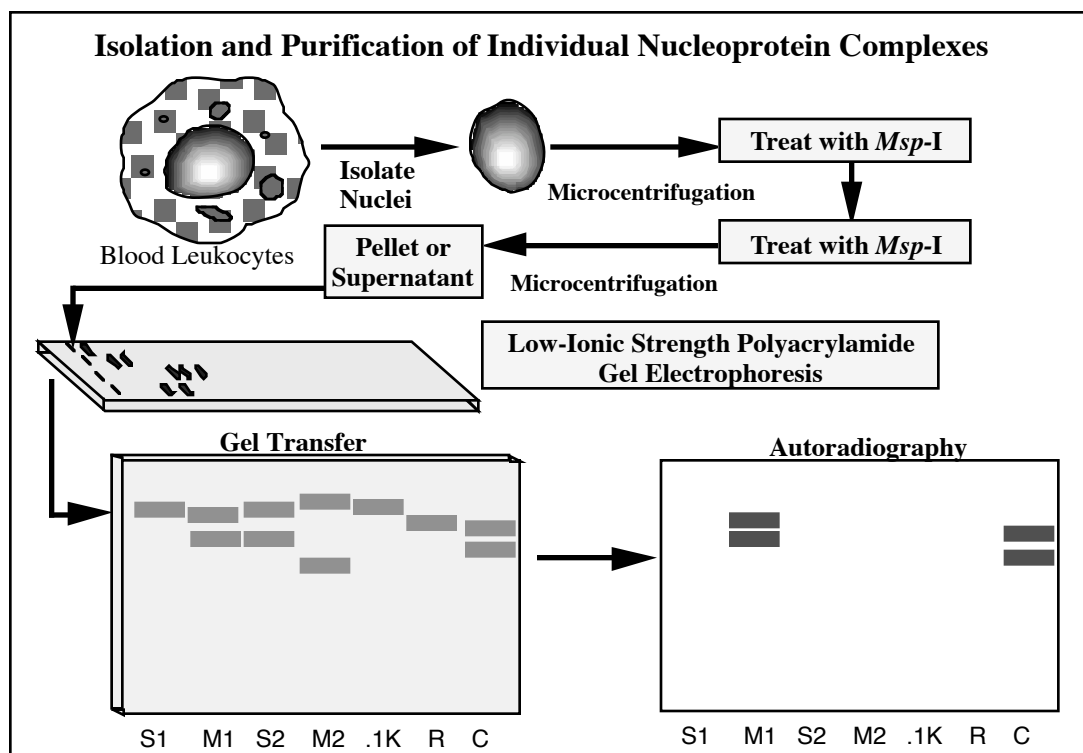
MCS in Desert Storm veterans could have been the result of environmental exposure to chemicals in the air or by direct contact or the use of chemical weapons. Many units reported the use of chemical weapons in Desert Storm. Most of these reports have been abruptly dismissed by the DoD, but the authors of this article find it difficult to dismiss the rather large number of these reports, and most importantly, the number of individual testimonies that indicate that many soldiers had immediate, classic symptoms of chemical attacks while the NBC alarms were sounding. These are also documented in the logs of units that served in Persian Gulf. We feel strongly that the use of chemical weapons by Iraqi forces cannot be dismissed. In testimony to the U.S. Senate Banking Committee chaired by Senator Reagle, representatives from the Army's chemical warfare command indicated that over 14,000 chemical weapon alarms sounded during Operation Desert Storm, and some soldiers in NBC units received medals for identifying the types of chemical weapons that were used. In addition, the widespread use of experimental drugs and vaccines against chemical and biological weapons have to be questioned, because if contaminated with infectious agents, these can cause some of the signs shown in Figure 2.

Some soldiers were probably exposed to chronic toxic environmental conditions during Desert Shield and Desert Storm that can produce some of the signs listed in Figure 2, such as chronic coughing and pneumonitis. Continuous exposure to fine sand particles (< 1 mm diameter) can result in hyperergic lung conditions, and in more severe cases pneumonitis. This disease was first reported by Andr as Kor enyi-Both and his collaborators.<sup>10</sup> Dr. Kor enyi-Both was the Commanding Officer of the Army's 316th Station Hospital in Desert Storm and has been examining the inhalation of very small sand particles that produce what he has called Al Eskan Disease, a pneumonitis that causes flu-like symptoms and eventually immunodepression that can result in opportunistic infections.<sup>7</sup> Environmental stress and infections can result in the activation of endogenous human viruses. Dr. Howard Urnovitz of the Calypte Biomedical Corporation in Berkeley discussed his findings that up to 85% of veterans (and their families) with GWS have antibodies to certain human viruses in their urine.<sup>7</sup> These viruses are human endogenous retroviruses (HERVs), and they are associated with a variety of autoimmune disorders.<sup>11</sup> The high frequency of HERV activation in GWS may be symptomatic of exposure to chemical and biological agents during Operation Desert Storm.

Many of the symptoms of GWS can be reproduced by chronic infections.<sup>2</sup> Dr. Edward Hyman of New Orleans has been examining Desert Storm veterans for the presence of bacteria in their urine and has found that many Gulf War veterans have evidence of bacterial infections.<sup>12</sup> He has successfully treated many of these veterans and their families with broad spectrum antibiotics.<sup>7</sup> The U.S. Senate Banking Committee has documented the transfer of dangerous bacteria (such as *Anthrax*, *Brucellosis*, *Botulinum* and other disease-causing bacterial strains) from U.S. companies to the Iraqi Atomic Energy Commission well before Desert Storm. And these were only the *unclassified* biological agents that were sent from the U.S. with Commerce Department blessing to Iraq.

After listening to the health complaints of many veterans of Desert Shield/Storm, including our step-daughter who served with the Army's 101st Airborne Division (Air Assault) in the deep insertions into Iraq, and their inability to convince military hospitals and VA Medical Centers that they are suffering from the same major symptoms listed in Figure 2, we suggested that most of these symptoms can be explained by aggressive pathogenic mycoplasma infections.<sup>13</sup> The variable incubation time of GWS, ranging from months to years after presumed exposure, the cyclic nature of the relapsing fevers and the other symptoms are consistent with a disease caused by biological agent(s).

We strongly suspected that mycoplasmas, a group of small microorganisms related to bacteria but without cell walls, some of which can invade cells, might be involved in some of the GWS. In general, this type of microorganism can cause chronic infections that yield unusual signs and symptoms. Usually mycoplasma infections produce diseases limited to particular tissue sites or organs, such as urinary tract or respiratory infections. However, the types of mycoplasmas that we have detected in Desert Storm veterans and that may be causing the chronic fatigue and other symptoms in GWS are very pathogenic, colonize a variety of organs and tissues, and are difficult to treat.<sup>7,13</sup> Even pathogenic mycoplasmas that can invade cells and tissues, such as *Mycoplasma fermentans* (incognitus strain) or *Mycoplasma penetrans*, should be treatable with multiple courses of oral antibiotics, such as doxycycline or ciprofloxacin.<sup>14</sup>

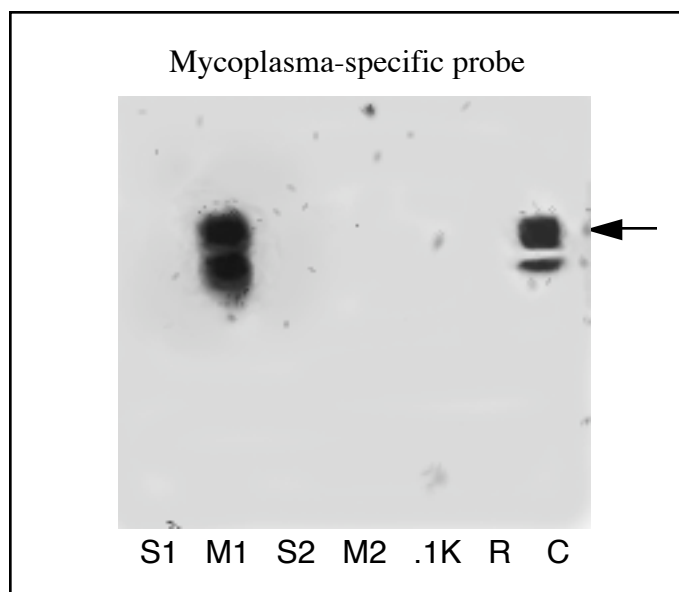


**Figure 3.** Methods used to purify Nucleoprotein Complexes from the white blood cells of veterans of Operation Desert Storm with GWS.

In the absence of sensitive and reliable clinical tests for invasive mycoplasmas, we suggested that physicians consider empirical treatment of GWS with antibiotics like doxycycline.<sup>13</sup> In fact, of the 73 Desert Storm veterans that we followed who had most of the signs and symptoms listed in Figure 2 and were able to find treatment, 55 indicated that they had good responses with doxycycline, and they eventually returned to normal duty.<sup>13</sup>

The invasive, pathogenic mycoplasmas that are associated with service in Operation Desert Storm are not easily detected but can be identified by a technique that we developed called Gene Tracking.<sup>15</sup> In patients with GWS Gene Tracking starts with the preparation of the nucleoprotein complex fractions from leukocyte nuclei of GWS patients' blood. Once the blood leukocytes are obtained, their nuclei are prepared and exposed to a restriction enzyme, *MspI*, that cuts DNA at specific sites to release specific nucleoprotein complexes. The nucleoprotein complexes are then separated by native (nondenaturing) low-ionic strength gel electrophoresis in the absence of chelating agents and transferred onto a Nytran paper support (Figure 3).<sup>15</sup> Once they are immobilized on the Nytran paper, they can be probed using a radioisotope-labeled (usually <sup>32</sup>P-labeled) oligonucleotide that will only bind to a specific DNA sequence. In the example shown in Figure 4, we have probed the nucleoprotein fractions obtained from the blood leukocytes of a GWS patient with a probe specific for *Mycoplasma fermentans* (incognitus strain). In Figure 4 a mycoplasma-specific gene was found in nucleoprotein fraction M1 purified from the leukocyte nuclei of a GWS patient. This suggests that the mycoplasma has penetrated deep into the nucleus of the patient's blood cells.

In our preliminary study on veterans with GWS-CFIDS and their families, we have found evidence of mycoplasmal infections in about 55% of the GWS patients' blood leukocytes. All of these GWS patients were very ill, so it is unlikely that approximately one-half of all veterans with GWS have mycoplasmal infections. In addition, not every Desert Storm veteran had the same type of mycoplasma gene sequences inside their leukocytes. So far, the majority of the mycoplasma gene sequences that have been identified in GWS patient's blood are from *Mycoplasma fermentans* (incognitus strain). As discussed above, pathogenic invasive mycoplasmas, such as *M. fermentans* (incognitus strain) or *M. penetrans*, should be treatable with multiple courses of antibiotics, such as doxycycline (200 mg/day for 6 weeks per course).



**Figure 4.** Identification of mycoplasma gene sequences by Gene Tracking in a leukocyte cell sample taken from a soldier who served in Operation Desert Storm, and who now has GWS. The figure is an autoradiogram that shows the binding of a radioactive probe against a specific mycoplasma gene DNA sequence in *Mycoplasma fermentans* (incognitus strain) to isolated nucleoproteins. The arrow shows the expected specific binding position of radioactive probe against the mycoplasma genetic sequences in nucleoprotein fraction M1. The positive control is shown in lane C. The results indicate that this soldier is infected with *Mycoplasma fermentans* (incognitus strain).

Of the Desert Storm veterans who had most of the GWS-CFIDS symptoms listed in Figure 2, most had good responses with doxycycline, and after multiple courses of antibiotics eventually recovered.<sup>13</sup> We feel from Dr. Rea's results<sup>9</sup> that it is also important for these patients to practice pollutant avoidance and begin vitamin and nutrient supplementation and physical therapy.

We consider it quite likely that many of the Gulf War veterans suffering from the GWS-CFIDS symptoms may have been infected with microorganisms, quite possibly pathogenic invasive mycoplasmas and other pathogens (bacteria), and such infections can produce the symptoms shown in Figure 2 long after exposure. This would also explain the apparent mildly contagious nature of GWS in some veterans and the appearance of similar GWS-CFIDS symptoms in their immediate family members.

In our preliminary study on a small number of Gulf War veterans and their families we have found evidence of mycoplasmic infections in about one-half of the patients' blood that we have examined. Not every Gulf War veteran had the same type of mycoplasma DNA sequences inside their white blood cells. Of particular importance, however, was our detection of highly unusual DNA sequences in the same nucleoprotein complex fractions by the same Gene Tracking technique. These highly unusual DNA sequences included a portion of a retrovirus genome (the HIV-1 *env* gene), but not all of the genes that make up the virus. Thus these soldiers were not infected with the HIV virus, because the virus cannot replicate with only the gene that we detected. Interestingly, the specific DNA sequence that we detected encodes a protein that if expressed on the surface of the mycoplasma and would enable the mycoplasma to bind to many cell types in the body, and even enter those cells by an endocytotic mechanism similar to that used by the HIV virus. The presence of the viral envelope gene in the mycoplasma could be due to genetic manipulation, or much less likely natural causes, but the importance of this event would be that a relatively benign mycoplasma could be converted to a much more invasive and pathogenic organism that is capable of attacking many organ and tissue systems. Such findings suggest that the mycoplasmas that we have found in Gulf War veterans are not naturally occurring organisms, or to be more specific, they could have been genetically manipulated to be more invasive and pathogenic (potent biological weapons). Of course, the CFIDS-like symptoms can be the result of chemical exposures as well as chronic infections, and this would



be consistent with our findings of pathogenic microorganisms in the blood of a fraction of soldiers who have GWS.

In our sample of Gulf War veterans, the soldiers that were involved in the deep insertions into Iraq and those that were near Saudi and Kuwaiti SCUD B impact sites, particularly those missiles that caused air bursts but not high explosive ground bursts, may be at highest risk for contracting the mycoplasma infections that we feel are a major culprit in GWS-CFIDS. Our results and those of other investigators on other possible causes of GWS strongly suggest that there are multiple causes for these illnesses, including chemical and biological agents that cause persistent chronic symptoms.

Although they were quite ill with GWS-CFIDS, subject B and his entire family have almost completely recovered after several cycles of doxycycline treatment, vitamin and nutrient supplementation and physical therapy over the last year. Our step-daughter left the Army, completely recovered after antibiotic therapy and will be entering medical school. Subject C left the Air Force, fully recovered his health after several cycles of doxycycline, and is now studying to enter the priesthood. The commanding officer of the SEAL units, subject D, has completely recovered after several courses of doxycycline treatment, has recently been promoted and is now serving in DELTA ONE at Ft. Bragg, NC. Other members of his command have similarly completely recovered from GWS after several cycles of antibiotic treatment. Unfortunately, subject A still suffers from MCS as well as CFIDS, and because of his MCS he could not take antibiotics and has not fully recovered from GWS.

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