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Gulf War Illnesses: Causes and Treatments

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Gulf War Syndrome or Gulf War Illnesses (GWI) are a collection of chronic illnesses reported by veterans of Operation Desert Storm (ODS, 1991). Between 15 and 18% of the veterans of ODS returned and slowly (6-18 months or more) presented with a variety of complex signs and symptoms characterized by disabling fatigue, intermittent fevers, night sweats, arthralgia, myalgia, impairments in short-term memory, headaches, skin rashes, intermittent diarrhea, abdominal bloating, chronic bronchitis, photophobia, confusion, transient visual scotomata, irritability and depression and other signs and symptoms that until recently have defied appropriate diagnoses (1-3). GWI signs and symptoms are chronic, systemic and in general cannot be placed into ICD-9 diagnosis categories. Also, routine laboratory test results are not consistent with a single, specific disease (1), often resulting in veterans not receiving a clinical diagnosis for their condition. GWI has been reported by various nations (except France) who's forces were deployed against Iraqi units in ODS. Possible reasons for the French Forces escaping GWI casualties will be discussed below as well as some of the possible exposures that occurred, the types of illnesses that resulted from these exposures, and some of the treatments that have been used on GWI patients.

ANALYSIS OF MULTIFACTORIAL ILLNESSES OF THE GULF WAR

Most investigators do not believe that GWI is a separate, new syndrome (2, 3). It has been called Mucocutaneous-Intestinal-Rheumatic Desert Syndrome by Murray-Leisure et al. (4), who placed patients into three broad categories: (**a**) *mucocutaneous lesions* with pustular dermatitis, (**b**) *intestinal disorders* with irritable bowels and (**c**) *rheumatic lllnesses* with large-joint polyarthralgias and night sweats. Minor criteria included: heartburn, rectal fissures, bleeding or hemorrhoids, lactose or meat intolerance, splenomegaly and splenic tenderness, weakness and/or chronic fatigue, headaches, muscle aches, polymyalgias, memory loss, hair loss, fevers of unknown origin, unexplained leukocytosis or neutropenia, nasal ulcers or sores, chronic sinus or nasal congestion, atypical chest pain, new-onset asthma or chronic bronchitis, ear infections or tinnitus and dental infections. Using factor analysis six syndrome categories were described by Haley et al. (3) after studying 249 veterans of the U.S. Navy's 24th Reserve Mobile Construction Battalion. The most important were (**d**) *impared cognition* characterized by problems in attention, memory, reasoning, insomnia, depression and headaches; (**e**) *confusion-ataxia* characterized by problems with thinking, disorientation, balance, vertigo and impotencc; (**f**) *artho-myo-neuropathy* characterized by polyarthralgias and myalgias, muscle fatigue, difficulty lifting and extremity paresthesias (similar to **c**, above); (**g**) *phobia-apraxia*; (**h**) *fever-adenopathy*; and (**i**) *weakness-incontinence*. The last three groups overlapped with groups **d** and **e** and involved weaker clustering in their analysis (4). These groups differed from Post-Traumatic Stress Disorder (PTSD), depression, somatoform disorder

and malingering (4). Baumzweiger and Grove (5) have described GWI as *neuro-immune disorders* that involve the central, peripheral and autonomous nervous and immune systems. They attribute a major source of illness to be brainstem damage due to central, peripheral and cranial nerve neuropathy with demyelination. Their patients tended to have muscle spasms, memory deficits, attention deficits, ataxia, and increased muscle tone, which are often seen in neurotoxin-induced brain stem dysfunction (5). GWI patients can also have chronic bacterial and viral infections that are an important source of morbidity and symptoms (2, 6, 7).

GWI are usually not fatal (8); however, there are now thousands of U. S. veterans dead after service in ODS (6). The possible reasons why these deaths have not been reported in official studies could be due to the limited sizes of study groups and time intervals used for analysis, the lack of information on veterans who have left the Armed Forces, and the primary use of military hospitals for such analyses (9). In the U. S. estimates of between 15,000 and 25,000 or more dead have been advanced, but the exact figures are unknown. The exact figures have not been carefully analyzed so it is difficult to determine if ODS veterans are at higher risk than non-deployed personnel. Although for years the U. S Department of Defense and the U. K. Ministry of Defense officially stated that there were no unique illnesses associated with deployment to ODS (10), just the opposite appears to be the case (3-6), although these studies have been questioned on the basis that similar clusters can be found in non-ODS veterans deployed to Bosnia (11).

In a case control study veterans with GWI have chronic illnesses at higher rates than military personnel from the same units that were not deployed to the Persian Gulf (10). In the four units that were studied, the deployed personnel had a variety of chronic illness signs and symptoms that were not present at the same frequencies in non-deployed personnel (10). For certain signs and symptoms, this difference was dramatic (for example, over 13-times difference in incidence of diarrhea). This study showed that ODS deployment was an underlying risk for contracting chronic illnesses.

GWI IS NOT PTSD

Since the signs and symptoms of GWI are not well established as criteria for particular illnesses found in ICD-9 diagnosis categories (1-3), patients have often been diagnosed with an "unknown" disorder, or a somatoform disorder, such as Post-Traumatic Stress Disorder (PTSD) (1, 11, 12). GWI has a number of significant signs that are different from PTSD, such as neuro-muscular problems, skin disorders, gastrointestinal problems, muscle and joint pain and temperature abnormalities (intermittent fevers) (2-6). A recent psychiatric analysis indicates that PTSD cannot explain symptoms of GWI with fatiguing illness (13).

The variable incubation time of GWI, ranging from months to years after presumed exposure, the cyclic nature of the relapsing fevers and the other chronic signs and symptoms and their appearance in immediate family members are consistent with organic not psychological disease (2, 3, 5, 6). The syndromes most similar to GWI are Chronic Fatigue Syndrome (CFS) (or myalgic encephalomyelitis, ME) and Fibromyalgia Syndrome (FMS) (2, 7). We have proposed that the signs and symptoms found in many GWI patients may be caused by chronic exposures to chemical mixtures and host responses to infectious agents, resulting in cytokine abnormalities and a variety of other responses that result in a CFS/ME- or FMS-like disorder (2). When the signs and symptoms of GWI were compared to the signs and symptoms of CFS/ME, the similarity was striking (7). CFS/ME 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 premorbid activity level. In addition to the absence of clinical conditions that could easily explain the symptoms, such as malignancies or autoimmune diseases, patients present with mild fever, sore throat, arthralgia, myalgia, generalized muscle weakness, headaches, painful lymph nodes, sleep difficulties, and neuropsychologic complaints, such as memory loss, photophobia, confusion,

transient visual scotomata, irritability and depression. These signs and symptoms closely parallel those found in GWI (7). This suggests that GWI is not a "new" syndrome; it is a CFS/ME/FMS-like disorder (2). Interestingly, patients with chronic illnesses that do not have evidence of chronic infections do not display as many signs and symptoms as GWI or CFS/ME/FMS (7).

There are some differences between GWI and CFS/ME/FMS that may be important in determining the various possible causes of GWI. Haley et al. (3) and Baumzweiger and Grove (5) have stressed that unlike CFS/ME and FMS, GWI is associated with ataxia and increased motor tone, symptomatic of brainstem dysfunction, such as cranial nerve and peripheral nerve demyelination, brainstem inflammation, limbic system involvement and personality behavioral changes. Using proton magnetic resonance to measure the ratio of plasma homovanillic acid and 3-methoxy-4-hydroxyphenylgycol Haley et al. (14) examined GWI patients for evidence of basal ganglia injury and found reductions in the left basal ganglia dopamine production, supporting the theory of brain stem injury to dopaminergic neurons in the basal ganglia. The documentation of brain stem damage in GWI patients strongly suggests that stress-related causes, such as PTSD, are very unlikely. Although stress can exacerbate chronic illnesses, stress alone is unlikely to be the cause of more than a small fraction of GWI (11, 15).

POSSIBLE CAUSES OF GWI: CHEMICAL EXPOSURES

Part of the confusion in diagnosing GWI is that the overlapping chronic signs and symptoms displayed by GWI patients can be caused by quite different types of exposures. Gulf War participants could have been exposed to chemical, radiological and/or biological agents, or more likely combinations of these (Figure 1) (3-7, 11, 12, 15). Accurate diagnosis and successful treatment of GWI cohorts will depend on identifying the underlying exposures, because these illnesses are treated differently if their origins are chemical, radiological or biological (15).

Gulf War veterans were exposed to a variety of chemicals, including insecticides, such as the insect repellent N,N-dimethyl-m-toluamide and the insecticide permethrin, battlefield smoke and fumes and smoke from burning oil wells, the anti-nerve agent pyridostigmine bromide, solvents used to clean equipment and a variety of other chemicals, including in some cases, possible exposures to low levels of Chemical Warfare (CW) agents (15). CW exposure may have occurred because of destruction of CW stores in factories and storage bunkers during and after the war as well as possible offensive deployment of CW agents (12, 15).

Low level exposures to mixtures of chemicals, such as organophosphates, can result in chronic illnesses (3, 5, 11, 15), including chronic neurotoxicity and immune supression. Abou-Donia and Wilmarth (16) found that combinations of pyridostigmine bromide, N,N-dimethyl-m-toluamide and permethrin produce neurotoxicity, diarrhea, salivation, shortness of breath, locomotor dysfunctions, tremors, and other impairments in healthy adult hens. Multiple Chemical Sensitivity Syndrome (MCS) and Organophosphate-Induced Delayed Neurotoxicity (OPIDN) are examples of chronic illnesses caused by multiple chemical exposures (Figure 1) (16). Patients with these syndromes can present with many (but not all) of the signs and symptoms found in GWI patients, and in fact, many GWI cases may eventually be explained by complex chemical exposures (3, 14, 16, 17). In these patients, memory loss, headaches, cognitive problems, severe depression, loss of concentration, vision and balance problems, chemical sensitivities, among others, typify the types of signs and symptoms found in chronic chemically exposed patients (16, 17). Arguments have been advanced that such exposures do not explain GWI or that they may only be useful for a small subset of GWI patients (11), but these arguments are for the most part are based on reviewing studies on the effects of single agent exposures, not the multiple, complex exposures that were most likely encountered by veterans of ODS. Since it is unlikely that any one type of exposure will explain the multiple signs and symptoms found in GWI patients, studying subsets or clusters of patients is not as limiting as has been suggested (11).

For most patients, the signs and symptoms of GWI began to present between six months to two years or more after the end of the war. This slow onset of clinical signs and symptoms in chemically exposed individuals is not unusual for Organophospate-Induced Delayed Neurotoxicity (OPIDN). As mentioned above, exposure to organophosphates was probably quite common in ODS veterans . That delayed, chronic signs and symptoms similar to OPIDN were caused by multiple low-level exposure to nerve agents, anti-nerve agents and other organophosphates remains a distinct possibility (18), especially in certain subsets of GWI patients (16). This is considered unlikely by Sartin (11), who argued that low-level single agent exposures do not usually cause OPIDN.

Low levels of CW agents were present in the Persian Gulf region from the bombing of CW factories and storage facilities (and their demolition after the war), and the probable offensive use of CW delivered by SCUD B (SS1) missiles, aircraft or vehicles outfitted with CW sprayers or by artillery shells and rockets, CW mines and other sources (12, 15, 19). Iraqi Armed Forces were known to have extensive stores of such weapons, and intelligence reports indicated that orders to use offensive CW agents were given. In testimony to the U. S. Congress, Army CBW officers indicated that over 14,000 CW alarms sounded during but not before or after the ODS air/ground offensive, and some soldiers were given medals for identifying the types of CW that were released (19). Extensive stockpiles of mustard (blister agent HN or HT), lewisite (blister agent L), sarin (nerve agent GB or GF), tabun (nerve agent GA) and other CW agents were present in the region, and an unknown quantity of these weapons were released into the atmosphere during the air campaign and by the destruction of Iraqi storage bunkers after the conflict (12, 19). That low level exposure to nerve agents combined with anti-nerve agents and other organophosphate exposures may have resulted in delayed casualties in at least some subsets of GWI is a possibility that cannot be so easily dismissed (11).

POSSIBLE CAUSES OF GWI: RADIOLOGICAL EXPOSURES

Depleted uranium (DU) was used extensively in ODS, and it remains an important contaminant of the battlefield (6). DU, a by-product of uranium processing, was used in armor-penetrating ammunition and in protective armor on tanks and other vehicles. Depleted uranium contains about 30% U-235, a dangerous radioisotope with a half-life of over 4 billion years (6). When a DU penetrator hits an armored target, it disintegrates due to the resulting kinetic energy transfer that results in extreme heat and formation of uranium oxide particles. The uranium oxide particles that form are usually small, and due to their high density they settled quickly onto vehicles, bunkers and onto the surrounding sand where they could be easily inhaled. One particle of $<5\ \mu$m in diameter trapped in the pulmonary system for one year can result in 272-times the annual whole body radiation dose permitted U.S. radiation workers (6). Fortunately, exposure can be monitored, and studies on DU exposures should be initiated as soon as possible to determine the prevalence and extent of uranium oxide exposure.

In addition to battlefield DU contamination, civilian nuclear reactors in Iraq were destroyed during the air campaign. This may have resulted in the release of long half-life isotopes like Sr-90, U-235, or Co-90. This could have resulted in some blow-back exposures, since the prevailing winds in the region were generally unfavorable. Unfortunately, there appears to be no available assessment of regional contamination from the release of nuclear reactor materials (15).

POSSIBLE CAUSES OF GWI: ENVIRONMENTAL EXPOSURES

In addition to the chemicals released by burning oil well fires and ruptured petroleum pipelines, soldiers were exposed to fine, blowing sand. The small size of sand particles (~ 0.1 mm) and the relatively constant winds in the region resulted in some inhalation. The presence of small sand particles deep in the lungs can produce a pulmonary inflammation disorder that can progress to pneumonitis or Al-Eskan Disease (20). This usually presents as a pneumonia or flu-like condition

that can eventually progress to more widespread signs and symptoms, including fibrosis, immunosuppression and opportunistic infections. Although it is extremely doubtful that many GWI patients have Al-Eskan Disease, the presence of silica-induced immune suppression in some soldiers could have resulted in the appearance of opportunistic chronic infections in these patients (12, 15).

POSSIBLE CAUSES OF GWI: BIOLOGICAL EXPOSURES

Parasites such as Leishmaniasis and Schistosomiasis and bacteria that cause Malaria and Cholera are endemic to the Middle East and could be the cause of illnesses in at least some of the veterans with GWI (4). Characteristic signs and symptoms occur in these illnesses, and diagnostic tests are available for most of these agents. Moreover, there have been no reports that they are the cause of illness in large numbers of GWI patients (15). In some patients infections by *Leishmania tropica*, spread by the sandfly *Phlebotomus papatasi*, can result in viscerotropic Leishmaniasis and elevated temperature, lymphadenopathy and hepatosplenomegaly (21). However, most of the common signs and symptoms of GWI do not fit with this explanation, and diagnosis of Leishmaniasis is relatively uncommon (estimated at less than one hundred) in Gulf War veterans.

Biological toxins were also present (15). The Iraqi Army had ample stores of aflatoxin (*Aspergillus flavus* toxin), ricin (from *Ricinus communis* beans), *Clostridium botulinum* toxin and possibly other toxins. They also had tricothecene mycotoxins produced by various species of fungi that can act quickly by direct cutanous contact and cause erythema accompanied by blisters, wheezing, pain and burning sensations. Some of these toxins can be fatal in very low doses (inhaled ricin in extremely small doses can cause inflammation of the respiratory mucosa with hemorrhage into the lungs or edema, hemorrhage of the GI tract and death within 8-72 hours) or cause delayed carcinogenic or immunosuppressive effects (aflatoxin). The preferred method of delivery of these toxins was by BW sprayer onto the sand or by aircraft (12, 15). Over 50 Italian-made BW sprayers were found fully deployed in Southern Iraq and Western Kuwait, and aircraft fitted with BW sprayers were captured at airfields in Southern Iraq.

In one subset of GWI patients Murray-Leisure et al. (4) have described an association with cutaneous sand exposure. This is most likely caused by a chronic transmittable infection found in sand that is endemic to the region, such as *Bacillus anthracis* or *Brucella* species. The risk for sand-associated illness appeared to be highest in the fall. Although no infections were ever identified, the slow appearance of the same signs and symptoms in spouses and children of veterans with GWI suggested that a slow-growing microorganism was being transferred (4). Anthrax, caused by the Gram-positive *Bacillus anthracis*, a commonly used BW agent, is found in soil. It can gain entrance through skin wounds but also by inhalation or ingestion. Anthrax infection does not result in a chronic illness, because its signs and symptoms, such as malaise, fever, fatigue, headache, respiratory distress and other more severe signs and symptoms, usually appear within 1-6 days of exposure. That anthrax exposure caused a subset of GWI is unlikely since the usual signs and symptoms of anthrax exposure were not reported in ODS veterans (15).

There is evidence for the presence of transmittable infectious agents in GWI patients. In many cases, the veterans' immediate family members appear to have the same or similar signs and symptoms (7, 22, 23). One estimate derived from inquiries of >1,200 GWI families indicated that approximately 77% of spouses and 65% of children born after the war now have the signs and symptoms of GWI (24). When immediate family members presented with the same or similar illness, the onset of their GWI signs and symptoms usually occurred from 6 months to one year or more after the onset of the veteran's illness, and not every family member developed GWI signs and symptoms. Because of the apparent slow rate of transmission to immediate family members, the general public is probably not at high risk for contracting GWI from casual contact with GWI patients (4, 7).

Veterans with transmittable biological exposures could have received these through natural contact (soil, water, etc.) or from other types of exposures (15). Infectious agents have been found in GWI patients' urine (6) and blood (7, 22, 23). Using a microscopic technique for determining bacterial infections in urine, Hyman (25) has found evidence of bacterial infections in GWI patients that can be successfully treated with several courses of broad spectrum antibiotics. We found that most of the signs and symptoms in subsets of GWI patients can be explained by chronic pathogenic bacterial infections, such as mycoplasmal infections (7, 15, 22, 23). Mycoplasmal infections usually produce relatively benign diseases limited to particular tissue sites or organs, such as urinary tract or respiratory infections (26). However, the types of mycoplasmas that we have detected in ODS veterans, such as *Mycoplasma fermentans*, are very pathogenic, colonize a variety of organs and tissues, and are difficult to treat (16, 17). In studies of over 300 patients, including both U. S. and British veterans with GWI and their symptomatic family members, evidence of mycoplasmal infections has been found in just under one-half of the GWI patients' blood (22, 23, 27, 28). The incidence of mycoplasmal infections in nondeployed, healthy subjects was found to be approximately 6-9% (reviewed in 28). The appearance of mycoplasmas in the leukocytes of some controls could indicate that these individuals are in a very early stage of the illness or that they are nonsymptomatic carriers of the infection.

Since the subgroup of mycoplasma-positive patients may be more symptomatic than the average GWI patient, it is likely that the final incidence of mycoplasmal infections in GWI will be lower than the incidence rate reported above (28). Over 80% of mycoplasma-positive GWI patients had *Mycoplasma fermentans* infections, and this has now been confirmed in a large VA study. Interestingly, when civilian patients with CSF/ME or FMS were examined for systemic mycoplasmal infections, high frequencies of mycoplasmal infections were also found (approximately 60%), indicating another link between these disorders, but in addition to *M. fermentans* several other species of mycoplasmas were found in CSF/ME and FMS (27-29). The types of assays performed in these studies were molecular tests of active infections, using polymerase chain reaction (26-29), and not antibody tests (11), because the latter do not usually detect intracellular mycoplasmas that do not elicit a strong antibody response (7, 26). The presence of mycoplasmal infections could also explain the recent observation of activation of the coagulation system in GWI patients (30), since mycoplasmal infections can cause these changes.

Other chronic infections have also been found in GWI patients. For example, in contrast to official reports (31), there is some preliminary evidence for *Brucella* infections (Unpublished observations). Inhalation of *Brucella spp.* (*Brucella melitensis* strains predominantly) can cause the slow onset of brucellosis, a chronic illness that shares many but not all of the signs and symptoms of GWI. Other possible infections include Q Fever (32), caused by *Coxiella burnetii,* anthrax caused by *Bacillus anthracis,* botulism caused by the botulinum toxin released from *Clostridium botulinum*, *Yersinia pestis*, a gram-negative, non-spore forming bacillus obtained from the bite of insects (fleas), Malaria, caused by *P. falciparum* or *P. vivax* from the bite of infected *Anopheline* mosquitos and other possible infectious agents. The prevalence of these infections has not been determined in GWI patients but it is likely to be low.

One possible source for chronic bacterial infections is the multiple vaccines that were used in ODS. Unwin et al. (33) found an association of GWI with the multiple vaccines received during deployment. In the U.S. there have been GWI signs and symptoms in personnel who recently received the anthrax vaccine. In some cases this has resulted in chronic illnesses in as many as 7-10% of personnel receiving the vaccine (34). Some of the chronic signs and symptoms associated with anthrax vaccination are very similar to those found in GWI patients, suggesting that at least some of the chronic illnesses suffered by veterans of the 1991 Gulf War may have been caused by multiple vaccines in combination with other exposures (33, 34). Relatively minor microorganism contaminants in vaccines could have resulted in illness in chemically exposed, immune depressed individuals. The French forces deployed to ODS did not receive multiple vaccines to protect against biological warfare agents, and this may turn out to be one of the most important reasons

why the French reported few if any GWI cases. The other possible reasons were the locations of French forces and the types of protective suits used in ODS.

TREATMENT OF GWI

The treatment of chemically exposed patients usually involves removal of offending chemicals from the patients' environment, depletion of chemicals from the patients' system and treatment of the signs and symptoms caused by chemical exposures (15, 24). Chemically exposed patients are often extremely sensitive to a variety of commonly encountered chemicals, including perfumes and air freshners, petrochemical fumes, chlorine, cleaning solutions and solvents, among others. They are also very sensitive to certain foods, and special diets are often necessary, and in some cases direct skin contact with certain substances can cause strong cutaneous reactions. An important part of treatment for chemical exposures requires limiting future exposures to a variety of common chemicals and removal of toxic chemicals (15, 35).

Patients with MCS or OPIDN benefit from procedures that slowly remove offending chemicals from their bodies. We recommend dry saunas for help in chemical removal, as well as magnesium sulfate-hydrogen peroxide baths (35). Some GWI patients may have irreversible nerve damage due to organophosphate exposure or low level nerve agent exposure potentiated by the effects of the antinerve agent pyridostigmine bromide, and it may be difficult to reverse their condition. Chemicals can be reduced through a program of heat depuration, physical therapy and nutritional supplementation in a special environment (35). In addition to heat, exercise and diet, a variety of medications may alleviate some of the signs and symptoms of chemical exposures in GWI patients. Many patients have benefited from anti-anxiety, anti-depressant and anti-inflammatory drugs (5), but this may not be beneficial for some GWI patients, especially those with biological exposures.

The successful treatment of patients exposed to DU depends on reducing the body burden of U-235. Such particles can remain inert in the lungs for extended periods of time, resulting primarily in local tissue alpha irradiation and the resulting radiation damage and immune suppression. In time the U-235 moves to the bones where it can be difficult to remove. Systemic U-235 can be slowly removed by chelation therapy, usually with ethylenediaminetetraacetic acid (EDTA) or penacillamine (15).

Infectious microorganisms can be treated with the appropriate antibiotics. Treatment with antibiotics can result in improvement and even recovery in patients exposed to bacteria or mycoplasmas such as *M. fermentans* (22, 23). The recommended treatments for systemic mycoplasmal infections require long-term antibiotic therapy, usually at least 6-12 months of doxycycline, ciprofloxacin, azithromycin or clarithromycin (36). Long-term treatments are required, because few patients recover after only a months treatment (23), possibly because of the intracellular locations of mycoplasmas, the slow-growing nature of these microorganisms and their inherent resistance to antibiotics (37). Once patients recovered and were able to return to active duty or normal activity, mycoplasma gene sequences could no longer be detected in their blood leukocytes. These clinical responses were not due to placebo effects, because administration of some antibiotics that are not effective against mycoplasmal infections, such as penicillins, resulted in patients becoming more not less symptomatic, and they are not due to immunosuppressive effects that can occur with some of the recommended antibiotics. Interestingly, CFS/ME, FMS and GWI patients with systemic infections that slowly recover on antibiotic therapy are generally less environmentally sensitive, suggesting that their immune systems may be returning to pre-illness states. If such patients had illnesses that were caused by psychological or psychiatric problems or solely by chemical exposures, they should not respond to the recommended antibiotics and slowly recover. In addition, if such treatments were just reducing autoimmune responses, then patients should have relapsed after the treatments were discontinued.

SUMMARY

Gulf War Illnesses (GWI) can produce complex signs and symptoms, such as polyarthralgia, chronic fatigue, short-term memory loss, sleep difficulties, headaches, intermittent fevers, skin rashes, diarrhea, vision problems, nausea, breathing and heart problems and other signs and symptoms. Although there is not yet a case definition for GWI, the chronic signs and symptoms loosely fit the clinical criteria for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis and/or Fibromyalgia Syndrome. Some patients have additionally what appears to be neurotoxicity and brainstem dysfunction that can result in autonomic, cranial and peripheral nerve demyelination, possibly from complex chemical exposures. Often these patients have been diagnosed with Multiple Chemical Sensitivity Syndrome (MCS) or Organophosphate-Induced Delayed Neurotoxicity (OPIDN). Chemically exposed patients can be treated by removal of offending chemicals from the patient's environment, depletion of chemicals from the patient's system and treatment of the neurotoxic signs and symptoms caused by chemical exposure(s). A rather large subset (~40%) of GWI patients have systemic infections, including mycoplasmal and other chronic bacterial infections, that are probably responsible for the appearance of GWI in immediate family members. These infections can be treated with antibiotics, vitamin and nutritional supplementation. It is likely that GWI patients owe their illnesses to a variety of exposures: (a) chemical mixtures, primarily organophosphates, anti-nerve agents and possibly nerve agents, (b) radiological sources, primarily depleted uranium and possibly fallout from destroyed nuclear reactors, and (c) biological sources, primarily bacteria, such as *M. fermentans*, and toxins, before, during and after the conflict. The multiple vaccines used in ODS are a prime suspect for chronic infections. The French did not use vaccines as a primary defense against Iraqi BW, and they did not use anti-nerve agents as a defense against Iraqi CW agents. They used prophylactic antibiotics to counter BW agents and protective suits to counter chemicals and thus had few GWI cases (33). The multiple, complex exposures during ODS resulted in poorly defined chronic illnesses, but subsets of GWI can be treated using appropriate procedures.

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FIGURE LEGENDS

Figure 1. Multiple exposures (chemical, radiological, biological) or multifactorial causes may have resulted in GWI in susceptible individuals (modified from reference 15).

ABOUT THE AUTHOR

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