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Gulf War Syndrome and Pregnancy

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Between August 1990 and March 1991, the United States deployed 697,000 troops to the Persian Gulf in support of a United Nations' resolution to aid in the release of Kuwait from Iraqi forces. This immediate response by the United States is known as Operation Desert Shield. More than 5 months later Operation Desert Storm began on January 16, 1991 with an air war followed by a ground war. The medical preparations by UN troops were extensive due to the threat of chemical and biological warfare and included immunizations and nerve-gas protectors.

Since the Gulf War the media has reported on thousands of veterans who are afflicted with illnesses of unknown etiology. More recently, the lay press has also detailed the stories of the health of children born to Gulf War veterans after their return. This issue of RISK||NEWSLETTER will contrast lay media reports with available scientific data and address the risk for morbidity and congenital malformations in the children of Gulf War veterans.

GULF WAR SYNDROME

17,248 individuals from the Desert Storm troops have been evaluated in the Veterans Administration Persian Gulf Health Registry. All but 3,000 patients have a diagnosable condition. Those veterans having unexplained illnesses report a range of symptoms commonly referred to as Gulf War syndrome. There have also been reports of undiagnosed illness from Gulf War veterans in Canada and Great Britain. The unexplained complaints have included chronic fatigue, rash, headaches, muscle and joint pains, difficulty concentrating, forgetfulness, gastrointestinal and respiratory symptoms and irritability among others. These symptoms have not been localized to any one organ system and there has been no consistent physical sign or laboratory abnormality that indicates a single specific condition.

Studies have been conducted to define a specific disease or a single cause that could account for these findings. These studies are complicated by unknown health histories of individuals who served, unknown specific substances to which each individual was exposed, and that actual exposure often differed from that which was documented. The Naval Health Research Center in San Diego studied more than 1.2 million veterans and found that those individuals who served in the Gulf have about the same hospitalization rate as those who did not. Other studies on mortality rate, cancer rates, reproductive health and work days lost to illness show no significant differences between the two groups. An advisory panel to the US National Institutes of Health concluded in April, 1994 that Persian Gulf syndrome does not exist; however, they did acknowledge that these people were suffering real illnesses. Presently, the government has recommitted itself to investigating this issue.

POSSIBLE EXPOSURES IN THE PERSIAN GULF

There have been no distinctive demographic, exposure, or geographic risk factors among veterans with unexplained illness except that nearly half of these veterans have been reservists/National Guard personnel. Similar unexplained medical problems have not been reported among local inhabitants of Saudi Arabia and Kuwait or among many of the non-US coalition forces (Saudi, French, Egyptian, Syrian and Moroccan troops). There are numerous possible explanations and the following factors are important to consider.

Chemical and Biological Warfare:

The Pentagon stated that thousands of US troops may have been exposed to nerve gas when Iraqi arms depots were destroyed. During the war detection equipment sounded hundreds of alarms indicating the possible presence of poison gas. Most were false, but some are still being investigated. Reproductive hazards of chemical and biological agents used in war are unknown.

Nerve Agent Prophylaxis and Immunizations:

All US and British troops were provided with tablets of pyridostigmine bromide (PB; 3-dimethylaminocarbonyloxy-N-methyl pyridinium bromide), a cholinesterase inhibitor, to help prevent lethal effects of chemical warfare nerve agents. This drug has been used since the 1950s in anesthesia and for the treatment of myasthenia gravis without any known long-term effects. Numerous studies of this drug in low doses have not revealed any serious side effects nor has any association with PB treatment in pregnant women and adverse pregnancy outcome been found.

Two non-live vaccines given to the coalition forces, botulinum toxoid and anthrax, also have been postulated to be causes of unexplained illnesses. The botulinum vaccine is an unlikely factor because it was given to only 8000 troops, and these troops, which are being closely followed up, have not reported problems with unexplained illnesses. Anthrax vaccine was given to a much larger number of troops, approximately 150,000, but no association has been found between this vaccine and Gulf War syndrome. There have been no epidemiological studies on the effects of these two vaccines on reproduction.

Infectious Diseases:

The US troops were exposed to a number of infectious diseases, including leishmaniasis, Q fever and brucellosis, which can cause chronic disease. However, those veterans with unexplained illnesses have not had any of the symptoms associated with these infections. Other viral diseases carried by insects found in the Persian Gulf are not known to cause chronic infection and disease. Some reports have described family members that have contracted symptoms much like those of Gulf War syndrome. Potential infectious disease threats and likely infectious biological agents are rarely, if ever, transmitted by casual personal contact or sexual contact. No studies on the reproductive effects of many of these infectious agents could be found with the exception of leishmaniasis where congenital infection of the newborn has been reported.

Environmental Hazards:

Desert Storm troops were exposed to several potentially harmful environmental hazards in the Persian Gulf. These hazards include smoke from oil well fires, chemicals from petrochemical plants, depleted uranium and pesticides. There has been no indication of unexplained illnesses among the US civilian firefighters who were extensively exposed to combustible and noncombustible products of damaged oil wells. There have also been no accounts of increased health problems among local workers or inhabitants of the cities around petrochemical plants. There is no detailed information available on the possible reproductive effects of the components of petroleum. One study, however, found a higher frequency of cytogenetic abnormalities in a group of petroleum industry workers (Simeonova et al., 1986). Desert Storm troops were tested to identify an increased level of uranium in their urine and none

was found. Those troops most likely to have been exposed to depleted uranium from munitions stores are being closely followed. Uranium has been found to reduce the number of offspring of male mice, but no human studies have been reported.

In terms of the hazards of pesticides, no cases of acute pesticide poisoning are known to have occurred during Operations Desert Shield/Storm. No adverse reproductive effects were found in pilots who spray insecticides (Roan et al., 1984). It is possible, however, that there was a synergistic effect between pesticides and anti-nerve gas agents. One study conducted at Duke University (funded by Ross Perot) found that hens exposed to three times the human dose of PB, DEET (or N,N-diethyl-m-toluamide — a common insect repellent), or permethrin (or 3-(2,2-dichloro-ethynyl)-2,2-dimethylcyclo-propane-carboxylic acid (3-phenoxyphenyl) methyl ester — a pesticide) displayed no neurotoxic symptoms (Pennisi, 1996). However, when there was concurrent exposure, problems similar to those reported in individuals with Gulf War syndrome were found. The authors hypothesized that blood and liver esterases are competed for by these compounds which in turn leads to their decreased breakdown and increased transport to nervous tissues. This hypothesis suggests that those individuals with lower plasma esterase activity may be predisposed to neurologic problems.

PATERNAL EXPOSURES

The majority of individuals who served in the Gulf War were men. It is not likely that preconceptional non-genetic effects on the sperm could affect fetal development. The presence of these agents in the semen have not been associated with an increased rate of congenital anomalies. If a chemical was found to be detrimental to the sperm, it would likely result in decreased motility or abnormal morphology rather than an anomaly in the offspring.

THE LAY PRESS

Numerous reports and personal stories of Gulf War veterans' illnesses and the health of their offspring have appeared in the lay press. Nightline, People Magazine, Life, Ladies' Home Journal, Redbook and Family Circle have each had at least one segment or article that featured the children of Gulf War veterans. These reports suggested that the numerous exposures of the veterans increased the incidence of birth defects among their children. The articles were entitled "What's Wrong with Our Children" (Ladies' Home Journal, June, 1994), "Legacy of Worry" (Los Angeles Times, 10/22/95), "Still No Answers" (Life, January, 1996), and "An Enemy Within" (People, 1/30/95). "Though the parents themselves have shown no symptoms of what has come to be known as Gulf War syndrome, they have had children with profound afflictions and nearly surrealistic deformities" (People, 1/30/95).

Some of the children highlighted in these stories have genetically-determined conditions which must be inherited from both parents (autosomal recessive) not just the veteran. Two of the children cited in these articles had thrombocytopenia-absent radius syndrome and Seckel syndrome. Other disorders found include Goldenhar syndrome, congenital heart defect, hyaline membrane disease, and an "umbilical-cord disorder" (single umbilical artery). The founder of the Association of Birth Defect Children (or ABDC) stated on Nightline that they were beginning to see clusters of specific birth defects that seemed to be more frequent in children born to parents who served in the Gulf. She reported that three cases out of thirteen of Goldenhar syndrome in the ABDC database were "Gulf War Children". A clustering of children with "immune problems" were reported along with a report stating that 13 out of 15 children born to veterans had serious health problems (Ladies' Home Journal, June, 1994).

SCIENTIFIC DATA

The hypothetical cause for an increase in the number of birth defects in these children include exposure to teratogens that caused gene or chromosomal mutations in the germ cells or that the agents

themselves were carried in the semen. Many investigations have discounted a connection between the reported disorders and the exposures. Those exposures that are known are unlikely to have caused the birth defects reported. Also, no clustering of a specific defect has been consistently found. No connection between Gulf War syndrome in an adult and congenital malformations in a child has been noted to date. Presently there are only two small epidemiological studies available (Kirkpatrick and Currier, 1996; Penman and Tarver, 1996); however, the Department of Defense, the Department of Veterans Affairs, the Institute of Medicine and the Department of Health and Human Services are attempting their own evaluations.

Risk for Congenital Malformation:

There has been no increase in major or minor birth defects found in a sample population of veterans' children when compared to that of the general population (Kirkpatrick & Currier 1996; Penman & Tarver, 1996). Although both studies found a variety of anomalies, no clustering of any one type or of an affected system was observed. Furthermore, no known genetic or chromosomal abnormality or teratogen is common to the various defects. The frequency of premature birth and low birth weight were similar to the general population (Penman & Tarver, 1996). These findings must be interpreted with caution due to the small size of the study populations and the few occurrences of birth defects.

Risk for Morbidity:

The amount of morbidity in children (including respiratory infections, otitis media, gastroenteritis, jaundice, and skin problems) born to veterans of the Gulf War does not seem to be increased over that of the general population (Penman and Tarver, 1996). It is difficult to determine if the rate of such health problems is higher than normal because comparative data in appropriate population groups is lacking. Many of these illnesses are common in childhood, however, and the frequency of their occurrences among this group of children did not appear higher than among all children in the United States.

SUMMARY

Much attention has been paid to Gulf War syndrome. At this time there does not seem to be a link between any specific exposure and any specific symptom associated with this syndrome. There also does not appear to be an increase in the number of major or minor birth defects found among the children of veterans of the Gulf War.