

# GULF WAR ILLNESS

- *Is there a Gulf War Syndrome?*
- *Will research answer all the questions?*

Since the Gulf War in 1991, many Gulf War veterans have complained of a range of physical symptoms which they attribute to the after-effects of service in the Gulf. This has led to a substantial research effort on both sides of the Atlantic to try and determine the extents of such illnesses, and whether they can be related to service in the Gulf.

**POST reviewed current knowledge on Gulf War illnesses, the research underway, and implications for the policy debate. This note summarises the full report<sup>1</sup> and findings.**

## BACKGROUND

Some 12 to 18 months after the 1991 Gulf War, reports of various illnesses among Gulf War veterans started to surface - initially in the USA, but subsequently in the UK. This set in train a number of medical investigation programmes and much research into the epidemiology of the illnesses, and possible causes. The full report describes the programmes involved of which some of the key ones are:

In the USA, the Department of Veteran's Affairs (DVA) **Persian Gulf Health Registry Examination Program** (PGHREP) was set up in 1992, for the benefit of ex-service personnel, and this has now enrolled some 62,000 veterans. This was followed by the **Comprehensive Clinical Evaluation Program** (CCEP), set up by the Department of Defense (DoD) in June 1994, to gather more detailed and systematic information on personnel still serving; this has 34,000 enrolled. Research has been pursued in the USA under the general direction of a Persian Gulf Veterans Coordinating Board, and President Clinton established the **Presidential Advisory Committee** on Gulf War Veteran's Illnesses (PAC), in May 1995, to "ensure an independent, open and comprehensive examination of health concerns related to Gulf War service". This Committee reported in January 1997. Other relevant inquiries include that by the US General Accounting Office (GAO), an office of the US Congress.

In the UK, the Ministry of Defence (MoD) operates the **Medical Assessment Programme** (MAP) - initially at Princess Alexandra's RAF Hospital, Wroughton, but recently relocated to St. Thomas's Hospital (London). The MAP has now examined over 1,400 UK veterans.

1. The full report "Gulf War Illnesses - Dealing with the Uncertainties" (55 pp) is available from POST, 7 Millbank, London SW1P 3JA - free to Parliamentarians. (External sales: £12 from the Parliamentary Bookshop on 0171-219-3890).



**POST**  
REPORT  
SUMMARY

**107**  
December  
1997

*This is a summary of a 55-page report available from the PARLIAMENTARY OFFICE OF SCIENCE AND TECHNOLOGY (extension 2840).*

**Table 1 SYMPTOMS REPORTED BY CCEP, PGHREP AND MAP PARTICIPANTS**

<i>Symptom</i>	<i>US CCEP % as main symptom</i>	<i>US CCEP % as any symptom</i>	<i>US PGHREP % as one of top 3 symp.</i>	<i>UK MAP % as any 3 symp.</i>
Pain in the joints	11%	49%	17%	35%
Fatigue	10%	47%	20%	55%
Headache	7%	39%	18%	
Memory loss	4%	34%	14%	22%
Sleep disturbance	2%	32%	6%	24%
Skin problems	7%	31%	18%	16%
Difficulty concentrating	<1%	27%		
Depression	1%	23%		
Muscle pain	1%	21%		
Irritability				29%
Breathlessness		16%		21%
Tingling limbs				11%
<i>Number</i>		<i>18,075</i>	<i>52,216</i>	<i>284</i>

## THE SCALE OF THE PROBLEM

Around 96,000 veterans have enrolled in one of the two US evaluation programs - this represents nearly 14% of the total US deployment in the Gulf. Not all are necessarily ill - over 10% had no significant health complaint and some 20% have yet to be examined. In contrast, much smaller proportions of UK (4%) and Canadian (3%) veterans have registered in their respective evaluation programs. Making comparisons between these levels of complaints is complicated by national differences - particularly in the availability of free public health care.

The most detailed information to date comes from the DoD's CCEP, where results of the first 18,075 medical examinations were published in 1996. Around ten general symptoms were commonly reported (**Table 1**), and on average, veterans suffer from five different complaints. Joint pains and fatigue were most common; headache, memory loss, sleep disturbance, skin problems (rash/dermatitis), concentration difficulties, depression and muscle pain were also common; while other symptoms were reported less often, including gastrointestinal complaints (diarrhoea, abdominal pain), breathlessness, hair loss and weight loss.

Translating such general symptoms into medical diagnoses is problematic, and a potential source of contention - particularly in the balance between psychological and physiological origins; **Table 2** shows the primary

Table 2 MAIN DIAGNOSTIC CATEGORIES IN GULF WAR VETERANS

Category	US CCEP primary diagnosis	US PGHREP any of top 3 diagnoses	UK MAP primary diagnosis
Psychological conditions	18.4%	15.1%	35%
Musculoskeletal diseases	18.3%	25.3%	6%
Ill defined conditions	17.9%	19.9%	15%
Respiratory diseases	6.8%	14.4%	9%
Digestive diseases	6.3%	11.4%	7%
Skin diseases	6.2%	13.5%	8%
Nervous system diseases	5.7%	8.3%	6%
Infectious diseases	2.6%	7.1%	1%
Circulatory system diseases	2.2%	7.1%	3%
Endocrine conditions / disorders	2%		1%
Genito-urinary diseases	1.3%	3.4%	2%
Cancer	0.8%	0.4%	1%

diagnoses made to date in the USA and UK. Around 1 in 5 US veterans were diagnosed as having a psychological condition of some kind, and similar sized groups received a primary diagnosis of musculoskeletal diseases or displayed 'signs, symptoms and ill-defined conditions' that did not fall conveniently into any other diagnostic category. In comparison, UK veterans were diagnosed with higher rates of psychological conditions (35% overall) and lower rates of musculoskeletal diseases (6%) than their American contemporaries.

The full report also looks at the studies on the health of veterans' families, where only limited data are available. Mortality studies show however that, in the 2.4 years following the war, there were proportionally more deaths (9% more) among some US Gulf veterans relative to control groups, but that this increase in mortality was entirely due to 'external causes' such as accidents (particularly motor accidents) rather than to diseases, suicides, etc. Similar findings have followed other wars such as Vietnam.

The full report looks at the difficulty of answering the question "Is there a Gulf War Syndrome?" First, it is sometimes suggested that there is nothing unique about the illnesses exhibited by Gulf war veterans *per se*, since similar signs and symptoms have been noted among veterans of other wars, from the US Civil War, through both World Wars to Vietnam. This proposition cannot be confirmed or rejected because the data to allow a quantitative comparison with earlier conflicts are lacking. Consequently, the essential answer will have to come from further research (including epidemiological studies - see below). Here some recent work from a small but properly designed cross-sectional telephone survey of nearly 3,700 randomly selected military personnel in Iowa (USA) did find that the personnel serving in the Gulf reported **significantly higher rates (often double) of medical and psychiatric conditions<sup>2</sup>** than their contemporaries who were not

deployed in the War. The larger epidemiological studies currently underway in the US and UK have been designed to tell us whether the illnesses are specific to service in the Gulf, or represent just another manifestation of previous 'war syndrome' phenomena. The primary question - "is there a Gulf War Syndrome?" - should thus be resolved one way or another when the studies report over the next 2-3 years.

## THE GULF RISK FACTORS

Many possible 'risk factors' have been put forward as possible causes of illnesses among veterans:

- exposure to biological and/or chemical warfare (CW) agents;
- exposure to pesticides;
- exposure to the vaccines and drugs used to protect the troops;
- infectious disease (e.g. leishmaniasis);
- psychological and physical stress;
- environmental factors (smoke from oil well fires, petroleum fuels, depleted uranium)

The full report looks at the evidence that significant numbers of personnel were exposed to these factors during and after the war, and also what health effects might be expected in the light of current scientific knowledge. On **CW agents**, it is now accepted that low levels of sarin were released after the war when US troops destroyed the munitions dump at Khamisiyah. Atmospheric modelling originally led DoD to the conclusion that some 20,000 troops within a 50 km radius of the munitions dump between March 4-15th 1991 might have been exposed to very low levels of chemical agents, but more recent estimates have increased this to as many as 100,000. As far as UK troops are concerned, only one person was present within the original 50 km radius fallout 'footprint'. With the latest reassessment, MoD estimate that some 10-15,000 troops **might** have been in the enlarged 'footprint'. However, the levels involved are extremely low - DoD estimates that the levels of Sarin to which US troops may have been exposed were around 1/80th of the dose needed to cause immediate noticeable effects in humans.

Another risk factor to have received much scrutiny is the use of **pesticides**. The full report describes the types taken to the Gulf, which included organophosphates (OPs), methyl carbamates, pyrethroids and various other chemicals. Much attention has been given to this by the Defence Committee (among others) and investigations showed use of OP pesticides to have been greater than at first alleged (see full report for details). The official position remains however that provided they were handled and applied by trained environmental health personnel, the risk of widespread exposure should have been small.

2. These included depression, PTSD, chronic fatigue, cognitive dysfunction, bronchitis, asthma, alcohol abuse, and anxiety.

The third main risk factor reviewed in the full report is the **vaccines and the drugs used as counter measures** against the threat of CBW agents. Particular attention now focuses on the combined anthrax and pertussis inoculations in view of a warning (in December 1990) from the Department of Health (DH) that tests showed serious loss of weight and condition in animals exposed to this combination. In addition to the vaccines, all US and UK troops were issued with Nerve Agent Pretreatment Sets (NAPS), which contain the drug pyridostigmine bromide (PB) as a precautionary measure against nerve agents, with troops self-administering doses every 8 hours.

Much of the research into **possible health effects** has focused on the various agents capable of acting on the nervous system (nerve gas, OP pesticide and PB), and the full report examines the scientific evidence - particularly on the health effects at low exposure levels. The US PAC concluded that there was no evidence that low level exposures to nerve agents caused long-term health effects in humans and that long-term/delayed effects of OP pesticides would only be expected at doses large enough to cause symptoms of immediate and severe poisoning. Despite the short-term side-effects of PB, studies suggest that such side-effects disappear when individuals stop taking the drug, and follow-up studies fail to show any evidence of long-term health effects. **PAC thus concluded that none of these agents provided a likely cause of Gulf War illnesses.**

The role of these agents as a potential cause of Gulf War illnesses has however continued to come under scrutiny and there are challenges to the PAC conclusion. Some investigations using various measures of neurological damage/dysfunction have linked signs of neurological damage to self-reported exposure to agents which can act on the nervous system. Similarities have also been found between symptoms among farmers exposed to low levels of OP pesticides over long periods and those seen in small numbers of Gulf War veterans. Given the lack of scientific consensus, however, over what measurements are appropriate in this field (e.g. in the balance between physiological and psychological indicators) and uncertainty over their precision, the jury is still out on whether the low levels of exposure likely to have been encountered in the Gulf can be expected to give rise to long term problems in the absence of evidence at the time of acute poisoning.

## ISSUES

The full report pulls together the certainties and uncertainties remaining on this complex issue. On the side of knowledge, there is now:

- a comprehensive record (particularly in the USA) of

the state of health of a large number of veterans, and an initial assignment into diagnostic categories for approaching 100,000 people;

- the product of a large number of reviews, including a number which have been deliberately constituted as expert and independent into the existence and possible causes of Gulf War illnesses.

Despite this, fundamental uncertainties remain:

- While there is no dispute that numbers of Gulf War veterans are ill, there is no consensus over whether there is an excess of illness over what might be expected. None of the large epidemiological studies comparing illness among those serving in the Gulf with scientifically selected control groups have yet reported. The Iowa study however found that self-reported illness among Gulf War veterans was higher than in comparable groups.
- Previous conflicts have been associated with various war syndromes which appear to have certain features in common with Gulf War illnesses. However, there are no reliable data which allow a detailed comparison with these previous conflicts.
- While no proof of cause and effect has appeared, some potential risk factors are attracting more attention than others as possible causes of increased rates of illness (if such enhanced rates exist);
  - exposure to low levels of CW agents as a result of destruction of Iraqi stockpiles;
  - synergistic effects of combinations of agents acting on the nervous system (e.g. PB, OP and possibly other pesticides, nerve agents);
  - effects arising from administering large numbers of vaccines simultaneously (possibly in combination with PB);
  - psychological and physical stress.

The USA has embarked on a series of major research projects to try and reduce some of the above uncertainties and to reach conclusions on the extent and causality of Gulf War illnesses, as reviewed in the full report. The UK has also initiated in the last year a number of research projects, also described in the full report and summarised in the **Box** (next page). Many will report over the next 2-3 years, but some of the US studies will not be complete for up to 10 years. However, it can be reliably stated now that there are fundamental limits to the information available which will limit the ability of any of these to reach firm conclusions at any point in the future. Thus, while the epidemiological studies are large enough to reveal general increases in the rates of illness, they will not reveal higher rates of illness among a few individuals with specific exposure histories not shared by significant numbers of other troops. Neither do these studies provide conclusive evidence of cause and effect, even if they may provide a useful steer towards likely causes.



Other questions raised in the full report include: -

- Why UK veterans are much more likely to receive a psychological diagnosis than their US counter-parts. Here a factor may be that UK diagnoses reported so far have been the result of a single physician's assessment, whereas those in the USA are the result of many doctor's separate judgements (including referral/advice involving specialists). There is also the possibility that the rate (based on the first 284 patients) may not be representative of the 1,400 now completed, but not yet published.
- Why appropriate research was not carried out to demonstrate the safety or otherwise of the pertussis/anthrax combination before being applied in theatre. Here, there was certainly no time to act between the advice provided by DH and the preparations for hostilities (3 weeks). However, the question remains whether prudent anticipation could have foreseen the need for the combination, and submitted it to the same health and safety safeguards as the civilian population would expect.
- How far UK (and US) epidemiological work suffers an inherent weakness when it comes to exposure assessment, since primary emphasis remains on self-reports with their inherent unreliability, especially so long after the event.

The interfaces between uncertainties and policy can be grouped into three areas:

There are **lessons to be learnt for the future** - these include the need for better record keeping (much of the current uncertainties stem from inadequate records of who received what vaccines and when, who self-administered what doses of PB, the types of pesticides used, where they were used and by whom, records of deployment and hospitalisation, etc.). Another lesson to emerge from the Gulf War is that military personnel expect a similar degree of care over routine health and safety issues to that enjoyed by those in other employment. This underlines the need to ensure that all countermeasures are checked for safety **before** being given to troops.

Then there is the key effort to **resolve the scientific uncertainties** where, over the next three years, the combined output of work on both sides of the Atlantic promises to shed considerable new light on the issue of Gulf War illnesses and potential origins. One issue that is relevant here is **the arrangements by which the UK keeps up to date with emerging research in the USA**, and the full report suggests that a more systematic review process could be put in place to supplement current *ad hoc* arrangements.

Even when the results are in however, there are **inherent limitations which will restrict our ability to detect** certain kinds of effect or, where effects are established,

#### Box THE UK STRATEGY

The UK strategy for dealing with Gulf War illnesses has evolved considerably over the last year. Since the MAP was established in 1993, its capacity has been expanded and more than 1,800 veterans have since been referred to the MAP of which 1,435 have consulted a MAP physician (who then writes to the veteran's doctor providing information and advice regarding diagnosis and treatment). The MAP recently moved into new premises at St Thomas's Hospital, London, which should prove to be a more accessible location than Wroughton previously. Currently, only the results of the first 284 examinations have been made public, but results of the other examinations to date are expected to be published early in 1998.

There has also been progress in the last year in the area of research. For some time, a full scale epidemiological study was seen as the highest priority, to establish the prevalence of signs and symptoms among UK Gulf War veterans, and to determine whether these are higher or lower than expected. Although the Defence Committee recommended this in 1995, the relevant work only got off the ground in July 1997. Other priorities include research into the health of veteran's children and into the possible effects of the 'cocktail' of vaccines and drugs given to troops. The detailed programme is described in the full report and includes:

- Three epidemiological studies looking at signs and symptoms in UK Gulf War veterans and their children. Two of these are funded by the MoD (at a total cost of £1.59M), and one by the US DoD. All three started in July 1997, are projected to run for 3 years and are being co-ordinated by the MRC.
- Research into the possible health effects of the combination of vaccines and PB tablets given to UK troops in the Gulf to protect them from BW and CW agents. Particular attention will focus on the effects of simultaneous administration of anthrax and pertussis vaccine. The overall cost of this new research programme is estimated to be at least £2.5M, and it is expected to take some 2.5 years to complete (although initial results may be available in 1998).
- Crosslinkage between MAFF-funded research to investigate the effects on farmworkers of low level exposure to OP pesticides may also be relevant to Gulf War illnesses.

to definitively assign their cause - primarily because of the lack of objective information on exposures. This has implications for the debate over **compensation** schemes, and debate on the adequacy and nature of the various current compensation schemes may need to be pursued independently of the current research programmes and their outcome - firstly because of the relatively long timescales remaining for the research, and secondly because of the difficulty of proving cause and effect, especially in individual cases.

This issue will remain on Parliament's agenda for some time. The Defence Committee is keeping developments in Gulf War illnesses under review, and the results of the 1400 UK veterans in the MAP are due to be published early in 1998. This review is intended to assist Parliamentarians in their considerations of the issues involved.

*Parliamentary Copyright, 1997. (Enquiries to POST, House of Commons, 7, Millbank, London SW1P3JA. Internet <http://www.parliament.uk/post/home.htm>)*