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20/4/99

GULF WAR ILLNESSES/SYNDROME INFORMATION FOR CLINICIANS

Introduction

In September 1997 I was asked by a small group of Gulf War Veterans, GWVs, who went on to form the Gulf Veterans Association, GVA, if I would be their Scientific Advisor. This I agreed to and subsequently I was nominated by them to serve on the 'Independent Panel to assess Government research into the Possible Interactions between Vaccines and NAPS' (Nerve Agent Protection Sets - which contained pyridostigmine bromide tablets 30 mg three times per day). This Panel was established by the Ministry of Defence, MOD, following appeals to John Reid who was then Secretary of Defence. Later the GVA became the Gulf Veterans Branch of the Royal British Legion and I was invited to join the Gulf Support Group which brings together Parliamentarians, GWVs, Military Leaders and representatives of the forces Welfare Organisations.

Since then I have attended a major conference in the USA organised by the National Gulf Veterans Resource Centre, Sept. 1998, and the MOD conference on the Epidemiology of Gulf War Illness/Syndrome, December 10th, 1998, Royal Society of Medicine. Recently, October 2-6, 2000 I visited Washington DC as part of an official delegation from the Royal British Legion. I have also developed extensive contacts with GWVs through meetings organised in the UK by the GVA and NGV&FA (National Gulf Veterans and Families Association). The latter is the second organisation concerned with the welfare of GWVs in this country. Through these contacts and extensive correspondence over the Internet with many people concerned about the health of Gulf Veterans, through published literature, including numerous declassified documents from the Pentagon, Veterans Administration, Department of Defence, and the Food and Drug Administration, I have come to an understanding of Gulf War Illness/Syndrome and the possibilities for diagnosis and treatment.
The latest figures from the Veterans' Administration (VA) in the USA show that 183,037 - or 26% - of the troops in Operation Desert Storm now receive disability compensation from the VA. this is, at least, two and half time more than the disabilities found in any previous conflicts. 36,782 further claims are under adjudication. No figures are available for UK veterans.

A major concern of many Gulf Veterans is the lack of any meaningful diagnostic techniques and effective therapy that addresses their conditions. I have compiled the following in order to provide useful information for clinicians faced with diagnosing and treating Gulf Veterans and their families.

Definitions- WHAT IS GULF WAR ILLNESS/SYNDROME

1. CDC Definition - This was constructed out of a major self-reported epidemiological study in the States.

   'We defined a case as having one or more chronic symptoms (longer than 6 months) from at least two of three categories (fatigue, mood-cognition, and musculo-skeletal).

   They concluded that 'a chronic multi-symptom condition was significantly associated with deployment to the Gulf War.'

   Fukuda *et al. JAMA* 1998, **280**, 981-988.

This definition has been used by other research workers, notably Simon Wessley *et al.* in the recent paper in the *Lancet,* 1999, **153,** 169-178. A major omission from the analysis behind this definition is the failure to recognise the extensive reporting of gastrointestinal symptoms by the Veterans. In Fukuda's preliminary paper 41% of the veterans reported such symptoms, *MMWR,* 1995,**44**,443-7

2. Mucocutaneous Intestinal Rheumatoid Desert Sand, MIRDS.

This definition was proposed by Katherine Murray Leisure *et al, Intern. J. Med.,* 1997, **1**, 47-72. Rheumatoid includes neuromuscular and arthritic conditions. They saw the illness as affecting principally these sites and arising from some unusual organism associated with sand in that part of the desert which formed the theatre of war. .

This definition encompasses the major symptoms reported and the results of careful clinical examination of a significant number of Veterans. No novel organism has been identified - but see below on mycoplasmas.

3. Brain Stem-Limbic Immune Dysregulation is a definition put forward by W. Baumzweiger, *Int. J. Med.* 1998, **1**, 129-143.

This encompasses severe encephalitis with damage to the central, peripheral and autonomic nervous systems and agrees with the conclusions of Haley *et al., JAMA*, 1997, **277**, 223-230 and Goran Jamal, *Adverse Drug React. Toxicol. Rev.,* 1998, **17**, 1-17. It attaches no significance to the extensive reporting of gastrointestinal symptoms.

4. Autoimmune-Neurological Disease with Connective Tissue disorders. R. Schuster posted this definition on the Internet in 1997. This acknowledges the very wide extent of autoimmune diseases amongst many Gulf Veterans - including lupus, (SLE), Sjorgren's syndrome, multiple sclerosis-like symptoms, and autoimmune diseases affecting various organs, thyroid, parathyroid, heart, lungs (asthma, pulmonary fibrosis), and others.

Other Important Identifications

a. **The Cholinergic System** -despite initial denials by the DOD, and VA it is now clear that the cholinergic system suffered a 'triple whammy' from pyridostigmine tablet taken prophyllactically, exposure to large doses of organophosphate and carbamates used as insecticides, and low level exposure to nerve agents such as sarin, VX, and possibly tabun and soman. This repeated and extensive inhibition of acetylcholinesterases affected the classical and non-classical actions of this key enzyme system and can produce both acute and chronic effects in the central, peripheral and autonomic nervous systems. A summary of the changes in the cholinergic system,at the genetic, and post synaptic levels, following robust stimulation is given by ; Chaudhri and Behan, *CNS*, 1998,**1**,16-20.

b. **Depleted Uranium (DU)-** this was incorporated in the modern munitions fired by tanks, aircraft, and tomohawk cruise missiles. It has been admitted by the DOD, Pentagon and MOD that at least 300 metric tonnes of DU dust was distributed over the battlefield and target areas some/much in <10 micron hazardous particles which can be respired. DU has been unequivocally identified in the urine of a number of UK, 14 out of 14 fully examined, and USA Veterans. DU is principally an α- emitter (although the $\beta-$ and $\gamma-$ emissions cannot be ignored) which although of low toxicity and radiological danger outside the body becomes a powerful **internal** radiological poison when ingested and/or inhaled, particularly as insoluble oxides. Neurological and cognitive defects, endocrine disruption, and increased cancer risks are associated with exposure, Encyclopaedia of Occupational Health, Vol. 2.
   It is becoming clear that the arms/industrial/and military lobby area unwilling to investigate the DU question beyond where it is absolutely necessary. A report on the consequences of friendly fire exposure by USA troops identified DU in the sperm of 5/22 veterans excreting excessive levels of uranium (isotope ratios were not investigated thus avoiding any specific conclusions about DU). Neurocognitive deficits were reported in this cohort and changes in the levels of FSH and LH hormones correlated with uranium levels in the urine. One of the cohort had a large tumour on his arm.
   Birth defects in children born to Gulf War Veterans are a cause for concern, one cohort from Mississippi has a 67% incidence of birth defects- a fact denied by the Pentagon on a spurious study on a tiny cohort of Gulf Veterans.
   Reports from Iraq indicate a 5-7 fold increase in childhood leukaemias and gross birth defects consistent with radation and toxin exposures, Horst Gunther, 1996 and 2000.

c. **Oil and Smoke from Oil Well Fires** - some service personnel were exposed to drenching with crude oil and the dense smoke from the oil well fires - a cocktail of known injurious chemicals with a variety of damaging effects, particularly on the respiratory, skin, and immune systems.

d. **The Mycoplasma Story** -Garth Nicolson, *Intern. J.Occupational Medicine,Immunology, and Toxicology*, 1996, **1**, 69-78, identified *Mycoplasma fermentans incognitus, MFI,* in 45% of GWVs he examined. He used advanced gene-

tracking techniques to identify fragments of mycoplasma DNA associated with the nuclei of lymphocytes. The work has been hotly disputed and Nicolson much maligned in some quarters. He treated these unusual infections effectively with doxycycline in high dose and in repeat cycles. A DOD study has just been announced in which 1000 Veterans will receive doxycycline therapy for their Gulf Illnesses. Details at http://www.immed.org/

e. **Squalene** -this has been widely investigated as an adjuvant for experimental vaccines, particularly for HIV, influenza, and anthrax. Very recently the identification of specific antibodies to squalene was announced in studies by Robert Garry and Pam Asa at Tulane University Medical School. Although the work has been peer reviewed the first accounts to date, have appeared in Vanity Fair, May 1999, written by Gary Matsumoto, in New Scientist, April 10th 1999 - by Debora Mackenzie, and in Insight Magazine, Volume 15, April 19th 1999, written by Paul Rodriguez. The definitive paper has now appeared, Asa P, Yan C, Garry RF. Antibodies to Squalene in Gulf War Syndrome. *Experimental and Molecular Pathology*, 2000, **68**, 55-64. These studies indicate that 95% of USA Veterans suffering from GWI/S tested positive whilst 100% of non-deployed but vaccinated personnel were also positive. The most common autoimmune disease is lupus, SLE. Lupus is predominantly a disease of women, female/male ratio *circa* 14/1, but amongst GWVs it is found mostly amongst men. Women made up only 6.8% of the USA Gulf force of 697,000. Four out of five UK GWVs tested were also positive. Squalene has never been licensed as an adjuvant but has been used in a number of experimental vaccine preparations including HIV.

f. Several research groups have drawn attention to the many close similarities between GWI/S, CFIDS (Chronic Fatigue Immune Dysregulation Syndrome-aka ME, CFS) and Fibromyalgia -see *inter alia* Nicolson, *Intern. J. Med.*, 1997, **1**, 42-46; Amato *et al.,Neurology,*1997, **48**, 4-13; Chaudhri and Behan, *CNS,* 1998,**1**,16-20. Factors common to these disorders need special attention. Despite earlier controversies CFIDS is now recognised by the WHO, USA and UK authorities. Some military personnel are beginning to call Gulf War Syndrome the ME of the military- Colonel John Graham. ME belongs with Gulf War Syndrome to "Syndromes of Uncertain Origin", Merck Manual 1999 (Millennium Edition) where it is made clear that, "considering the extent of the patient's complaints and disability, the results of ROUTINE laboratory tests were strikingly NORMAL", S Straus.

g. There are growing reports of the transmissibility of GWI/S from husband to wife and children, and in some cases household pets! There are various speculations about how GWI/S could be transmitted.

My judgement is that the massive vaccination programme that all Gulf personnel received involved the administration, usually by injection, of a large number of vaccines, of different types (live organisms, dead organisms, extracts from organisms, immunoglobulins). In defiance of established protocols vaccines were given too close together and mixed unacceptably, eg. immunoglobulins with live vaccines. Such procedures could lead to immune dysregulation with marked suppression of the Th1, cell-mediated immune response, and enhancement of the Th2 arm of the immune system, see Rook and Zumla , *Lancet*, 1997, **347**,1831-1833. Such extensive dysregulation provides a basis for the development of various diseases associated with immune malfunction. In addition it is well known that the genetic halotype has a significant role in determining the type of immune/autoimmune response exhibited by individuals. There are both positive and negative control groups to substantiate this statement. The positive groups are those military personnel who received all their injections but who were not deployed to the Gulf- some of these have GWI/S. Some civilians also received the full course of injections and were deployed to the Gulf - some of these have become ill. The negative groups are the press corps whose injections were already maintained at an appropriate level and who did not receive vaccines to protect against biological agents. And French troops who were supplied with medicines to counteract any biological threat but may not have been vaccinated on the scale of USA and UK troops. However, it now appears that French Troops are suffering from Gulf War Syndrome. My comments about vaccines are substantiated by GWVs as eye witnesses and by some surviving records. Most field records were destroyed in accordance with MOD policy.
Further evidence of an association of Gulf Illnesses with vaccines among UK troops has appeared recently, Unwin et al *Lancet* 1999, **353**, 169-178; Hotopf et al *BMJ*, 2000, **320**, 1363-67, Shaheen *BMJ* 2000, **320**, 1351-2.

It is clear that both diagnosis and treatment of GWVs pose a formidable challenge to clinicians. What follows is culled from the literature and provides suggestions for making a diagnosis and providing treatment for GWVs. The first requirement is a thorough and detailed history taking. Followed by tests drawn from those outlined below in the light of the clinical assessment. Some of the tests and procedures are straightforward and could be done in a GP's surgery but others will require biochemical and specialised laboratories to obtain and interpret the data. Treatment can then be

determined from the results of the diagnostic investigations. I offer this information in the hope that it will stimulate clinicians to consider other tests that might elucidate GWI/S and suggest additional ways of treatment.

The following are among the most commonly reported symptoms of GWI/S.

Fatigue
Musculo-skeletal problems joint stiffness, weakness, pain -Muscular atrophies
Gastrointestinal problems
Cardiac and Cardiovascular problems
Headache
Mood swings
Irritability
Depression
Memory loss/malfunction
Loss of executive functions
Speech problems
Susceptibility to infections - catch anything that's going -difficulty in shaking off an infection
Sleep problems - unrefreshing, disturbed,
Temperature control problems -excessive bouts of hot and cold sensations
Shortness of breath, asthmatic coditions
Skin problems
Sexual problems- includes 'burning semen syndrome', loss of libido, birth defects in offspring

TESTING PROCEDURES

Brain Stem Encephalitis
Balance
Focus
Sound-spatial awareness

Specialised scans - such as SPECT scans which provide information about brain perfusion are useful in investigating CFIDS. The brain stem is commonly affected. Thallium-201 scans for heart perfusion deficiencies. Whole body potassium and water determinations indicative of chronic fatigue.

Very recently the results were reported of MRS (magnetic resonance spectroscopy) scans in a group of Gulf War Veterans in the States, Haley, Fleckenstein and collaborators, 85th Scientific Assembly and Annual Meeting of the Radiological Society of North America (RNSA)-November 1999. They found up to 25% lower than normal levels of NAA (N-acetylaspartate) in brain stem and basal ganglia which suggests loss of neurones in those areas- now published in *Radiology* 2000, **215**, 807-817. Professor Graham Whitehouse at Liverpool University is using the same technique to look at ME-CFS patients in the UK.

A detailed paper on Vestibular Dysfunction in Gulf War Syndrome has recently been published, Roland et al. *Otolarynology- Head and Neck Surgery* 2000, **122**, 319-330.

Hypothalamic-Pituitary Axis
Excessive micturation is not uncommon and may indicate loss of pituitary function or damage to local autonomic control mechanisms.
Levels of Hypothalamic Releasing hormones and Anterior pituitary hormones can be measured by immuno-assay. Reduced levels of Gonadotrophin Releasing Hormone and Gonadotrophins offer grounds for reduced libido and some sexual disorders.
Loss of central control of thyroid and adrenal function can arise from disturbances of the HPA.

Peripheral Nerve Damage
Pinprick tests for glove and stocking anaesthesia
Manipulation tests picking up small objects etc

Specialised tests on nerve conduction and function described by Goran Jamal, Central Middlesex Hospital, London.

A Note on Muscular Dystrophies
These include-
Amyotrophic Lateral Sclerosis, ALS, Lou Gehrig's disease, is a rare motor neurone disease which occurs at 10 times the normal level (~ 1 in 100,000) in USA Veterans-there is debate about whether this is an autoimmune disease. I am not aware of any cases among the 53,000 UK veterans.
Guillaine Barre syndrome has been reported as a reaction to anthrax vaccination.
Endocrine myopathies involve loss of thyroid, adrenal, and parathyroid function.
Myopathies associated with the neuromuscular junction - acetylcholinesterase is a key enzyme at this site.

Cardiovascular and Blood Tests

Heart Rates
Baumzweiger noticed a much greater change in GWV'S heart rates when sitting and standing compared with matched controls.
'The 60 Gulf War veterans demonstrated an average increase in heart rates of 22.09 beats per minute upon standing. Sitting the heart rates averaged 77.69 beat per minute. While standing, their heart rates were on average 99.78 beats per minute for the first fifteen to sixteen seconds. This contrasts with the 38 'normal' neurological patients who showed an average increase in heart rate of 3.89 beats per minute. The normal patients' sitting heart rates were on average 81 beats per minute and on standing on averaged 84.9 beats per minute. The "T" value for this is 10.51 ……smaller than 1 in a million.' [Examination of the changes following medication with dihydropyridine calcium blockers showed a reduction in heart rate changes from standing to sitting to 11.26 beats per minute.]
Further studies using Doppler and computerised EEG studies indicated abnormal vascular spasm and abnormal EEG patterns.

Differential Monocyte Counts
Rosalie Bertell has developed this test as a blood marker for DU poisoning. I obtained the details following correspondence with Dr. Bertell, as follows

BLOOD TEST FOR BIOMARKER OF RADIONUCLIDES INCORPORATED INTO BONE

Please hand count the white blood cell differential, using at least 500 cells. It is acceptable to also give the Coulter Counter estimates, but the Coulter is not as accurate for the monocyte count as for the more frequent white cells.
Please report the Differential count in absolute number, rather than in a percentage of a hundred cells. (The absolute number is the percentage times the total number of white cells, for example, if the patient has 4,000 white blood cells per microlitre of blood, and in a sample of 500 cells 12 are monocytes, the percent monocytes is 2.4% and the absolute count is 96 per microlitre).
A normal healthy community has an average monocyte count of 350 monocytes per microlitre, with a range of 200-800 monocytes per microlitre. Children's counts would be higher.
This technique is designed to detect a shift to the left in monocyte counts for a population. When used on an individual. It is good to have three consecutive blood tests about one week apart.

Notes from Rosalie Bertell
My concerns about monocytes rest on two of their functions in the body: they release a material which triggers the lymphocytes (the cellular immune system) and they recycle the iron into new red blood cells when the old cells die. The first property makes the immune system dysfunctional, even though the lymphocytes may be intact. This leaves the person open to opportunistic infections and tumours. The second function can cause iron deficient anaemia since the recycling accounts for close to 40% of the iron in the red blood cells. Diet accounts for the other 60%. It is not easy to keep up the iron content without the recycling.
The above test protocol is the property of Dr. Rosalie Bertell, Ph D, GNSH, President ACS (1998-2000), 710-264 Queens Quay West, Toronto, ONTARIO, M5J 1B5, CANADA.
Phone 00 1 416 260 0575: Fax 00 1 416 260 3404
e-mail IICPH@compuserve.com

Red Blood Cells Structure and Function
Dr. Bertell further writes, in relation to RBCs, tests for anti-cholinesterase and organophosphate may also be helpful.
A recent paper, Gong JK, Glomski CA, Guo Y. A Lifelong, Wide-Range Radiation Biodosimeter: Erythrocytes with Transferrin Receptors. *Health Physics* 1999, **77**, 713-718, describes the Transferrin Receptor Red Cell Assay that identifies

mutations arising from low-level radiation or exposures to some chemicals. The test provides a way to measure the damage before the first signs of cancer appear.
The current debate about 'safe ' levels of radiation and the competing paradigms of high level acute exposure to soluble radioactive materials or persistent low-level internal radiation from insoluble radioactive materials has been explored in Iyer R and Lehnert BE. *Science and Medicine* 2000, Jan/Feb, 54-63. See also McDiarmid MA et al. *Environmental Research* Section A 2000, **82**, 168-180- for a report on the American Veterans who survived a friendly fire incident. Contrast with Hooper M. Depleted Uranium Munitions: New weapons of Indiscriminate and Mutually Assured Destruction, United Nations peace Celebrations, Helsinki, Oct. 23rd 1999. Available at www.kaapeli.fi/~tep/vipu/00-1

Dr L.O. Simpson has suggested that the shape of RBCs may play a crucial role in restricting capillary blood flow and reducing oxygenation of tissues in CFS, CFIDS, ME and FM, *New Jersey Medicine,* 1992, **89**, 211-216. More recently he has begun to investigate such changes in GWI/S. Essentially the procedure requires red cell shape analysis. The proportion of normal discoid cells to crenated (cells with altered margins), cells with surface changes, and cup forms are counted from 5 different blood samples. A typical result would be in a well patient - RBCs discoid 87.8%, surface changes 4.7%, cup forms 0.6%, altered margins 6.9%. The same patient when suffering from fatigue and headache - discoid 55.6%, surface changes 7.0%, cup forms 0.0%, altered margins 37.3%.
Red Blood Cell Research Limited Director: Dr. L.O. Simpson Technical Manager: D.J. O'Neill, 31, Bath Street Dunedin, New Zealand 9001 > Telephone: 64 3 471-8540. Fax: 64 3 471-8530 email: rbc.research.limited@xtra.co.nz

Immunopathology
A number of major teaching hospitals provide Immunopathology Services which will provide detailed analysis of auto antibodies, immune complexes, differential lymphocyte marker counts etc. I have a copy of
the Immunopathology Services Tayside Handbook which provides autoantibody tests for diseases of the thyroid, TSH, liver, adrenal, parathyroid etc. anti-Acetylcholine Receptor Antibodies, a range of anti-nuclear antibodies associated with lupus, Sjorgren's syndrome. Myelin basic protein antibodies are of particular interest where there are progressive neurological defects. Differential CD4 AND CD8 counts are also important- see Rook and Zumla. Such specialised services provide advice about the tests and help with the interpretation of the data.
Very recently an important paper has appeared- Abou-Donia MB and Garrettson LK. Detection of neurofilament autoantibodies in human serum following chemically induced neurologic disorder: a case report. *Environmental Epidemiology and Toxicology* 2000, **2**, 37-41.

General Biochemical Testing

There are batteries of tests available which provide a useful assessment of a range of functions and deficiencies. These tests can be carried out by Biolab Medical Unit, on referral, who also provide advice on interpretation and possible therapy. It may well be that Hospital Laboratory Services in your area can carry out some or all of these tests.

Biolab Medical Unit, 9, Weymouth Street, LONDON W1N 3FF
Phone 0171 636 5959/5905
Fax 0171 580 3910
E-mail lab@biolab.demon.co
Internet http://www.biolab.co.uk

This laboratory specialises in Nutritional and Environmental Medicine.

Summary of Tests
Trace and Toxic Elements incl. Mg, Zn, Fe, Ca, Mn, Se, etc.
Vitamin Profiles - Direct measurements, Functional Tests etc.
Profiles -incl. Gut Fermentation, Gut Permeability, Red Cell Fatty acids, Plasma essential fatty acids, Antioxidant status, Pesticide Screens incl. blood, serum, fat needle aspirates, Isoenzyme profiles eg. Glutathione sulphur transferases, Metal sensitivity tests, osteoporosis screen, etc.
Individual tests on Serum, Red cells, White cells, Urine, challenge tests.
Special tests incl. Gastrogram, myothermogram, non-invasive vascular screen, reproductive function tests etc.
At Biolab there are doctors familiar with all the tests who are available for consultation. A Nutritionist is also available for consultation.

Several Gulf War Veterans, organophosphate poisoned farmers, and pesticide-poisoned patients have been examined in a battery of tests proposed by Biolab Medical. The results have helped to direct the course of treatment.

Paraoxonase- a key enzyme, with four genotypes, in the metabolism of organophosphate insecticides has recently been shown to be at low levels in some seriously ill Gulf War veterans, Haley et al. *Toxicology and Applied Pharmaciology* 1999, **157**, 227-233: Machness B, Durrington PN, Mackness MI. Low Paraoxonase in Persian Gulf War Veterans Self Reporting Gulf War Syndrome. *Biochemical and Biophysical Research Communications* 2000, **276**, 729-733. The paraoxonase test can be carried out at the Department of Medicine, University of Manchester by Dr M. Mackness the UK expert in this field.

Other less well established Diagnostic Procedures

The following groups have developed tests which have been found to identify important aspects of GWI/S

IAG, Indolylacroylglycine, is a urinary metabolite found in the small and intermediate peptide fraction which first came to prominence in the search for diagnostic markers in autism. It has since been found that this molecule is in excess in organophosphate farmers, 100%, GWVs, 95%, and ME patients, ~90%. The significance of this molecule is being investigated but it appears to indicate severe disturbance of tryptophan and 5-hydroxytryphan metabolism in the gut and is associated with marked permeability of the gut. See also ; Chaudhri and Behan, *CNS*, 1998,**1**,16-20 and references therein. It is now incorporated in the opioid theory of autism which led to the use of naltrexone and gluten/casein free diets to treat autism. This work has been published in peer reviewed journals. See Paul Shattock, Autism Research Unit, University of Sunderland- for details visit the web site http:/osiris.sunderland.ac.uk/autism or phone 0191 515 2481 or 0191 510 8922.

Several Gulf War Veterans and some of their children have found considerable improvements in mood and behaviour when using such a diet.

Plasma Cysteine/Sulphate Ratios. This test was also developed in the search for diagnostic biochemical markers for autism. The very low sulphate levels leading to high cysteine/sulphate ratios is thought to be indicative of low sulphation levels in mucosal membranes and offers an explanation of membrane failure in the 'leaky gut' of many autistic children. Low sulphate levels are also found in GWVs. This is consistent with the extensive gastrointestinal disorders found in many GWVs. Inflammatory bowel disease is known to be associated with abnormal sulphated glycosaminoglycans. This work has been published in peer reviewed journals. The test was developed by Rosemary Waring, School of Biochemistry, University of Birmingham, UK. Other laboratories might be able to carry out this test.

A simple alternative is to test for urinary sulphite. Normally no sulphite is present in urine. About one-third of autistic children show significant improvements with molybdenum supplementation. Molybdenum is a crucial component of sulphite and nitrite oxidase.

ME/CFIDS/FM Two diagnostic tests of proven value in these newly recognised conditions are the SPECT scan which provides evidence of perfusion of various regions of the brain. The brain stem is frequently affected and has low perfusion rates. The buspirone-prolactin test has also proved useful in the diagnosis of these illnesses. See Relationship between SPECT Scans and Buspirone Tests in patients with ME/CFS. Richardson J et al. *J. Chronic Fatigue Syndrome,* 1998, **4**, 23-38.

POSSIBLE TREATMENTS

Clearly the chosen treatment option will depend upon the history taking and diagnosis. What follows are treatments that have proved useful for significant numbers of GWVs and people with allied diseases, There may well be other treatments that you might want to consider.

Standard Drugs and Medicines

Baumzweiger tailored a therapeutic regimen to match the needs of individual GWVs. A major part of the treatment is the use of Calcium Blockers of the dihydropyridine class. He used either **nisoldipine, felodipine,** or **nimodipine** as major components of his therapeutic regimen and titrated the dose for each individual. Sometimes a drug was needed to support blood pressure during the titration of the calcium blocker. He advocates the use of intravenous **Pooled Human Immunoglobulins** in the light of the known depressed state of the immune system and evidence of both viral and

bacterial damage/infections. He claims that demyelination was reversed by this treatment. For hypertension he used **Phentolamine** an alpha-blocker with a positive inotropic action. As antidepressants he used **trazadone** or **bupropion**. The latter is a none-specific, weak, unselective uptake inhibitor of all the major biogenic amines. In many ways similar to amitriptyline.
Where there was evidence of viral, bacterial, or mycoplasma infections he chose from the following- **famcyclovir, acyclovir, amantadine, doxycycline**. Amantadine was also useful where Parkinson-like symptoms were evident. It is also proving useful in the treatment of MS patients as a glutamate inhibitor.
Ibuprofen or **naprosyn** were used where necessary as non-steroidal anti-inflammatory drugs.

Dietary changes, which require the elimination of wheat and/or milk from the diet, in line with the opioid hypothesis for autism have proved helpful for some GWVs but a major factor is the cost of dietary items which can be supplied on prescription.

Epsom salt baths might help where sulphate levels are low and some parents of autistic children have found some help from them. Hydrogen peroxide used in the baths has also proved beneficial.

Identifiable vitamin and metals and metalloid supplements, Mg, Zn, Fe, Se would be helpful, and anti-oxidants such as vitamin C and E either from dietary sources or in a purified form would also be justified in some cases.

The importance of ω–3 and ω–6 polyunsaturated fatty acids is of growing significance, particularly the former. Lipid analyses of RBC membranes provides the necessary information. Supplementation with fish oils is the appropriate treatment.

A major area of treatment is that offered by different detoxification regimens. Bill Rea in California successfully treated one UK GWV. Details of his regimen which is tailored to individual needs can be found at http://www.ehcd.com/index.html

Diagnostic Testing

1.Skin challenge test for sensitivities to moulds, pollens, dust, danders, terpenes, intestinal peptide, plant phenoline, food and chemicals. Preservative free, standard and customized antigens are used. Cell mediated immunity -- test delayed 48 hour function.
2.Oral challenge tests for foods and chemicals.
3.Inhaled ambient dose chemical challenges.
4.Evaluation of the autonomic nervous system through the binocular iris corder.
5.Computerized Balance Tests for - inner ear and brain toxicity.
6.Neurometer - for peripheral neuropathy - sensory loss.
7.Psychological - brain function evaluation.
8.Exercise Stress Testing - the EHC-D is the only site in the world that provides environmentally controlled conditions for heart and lung evaluation.
9.Pulmonary function testing for arrhythmia, respiratory restrictive deficit.
10.Blood analysis for:
Immune function - immunoglobulins, T&B lympocytes, T-cell functions, cell cycles, phagocytic indexes for (recent vaccines), and autoimmune tests.
Blood Toxins
HSST - pentanes, hexanes, heptane, etc., for solvents.
GVST - benzene, xylene, toluene, trimethylbenzene, etc., dichloromethane, dichlorobenzene, chloroform, trichloroethylene, trichloroethane, tetrachloroethylene, etc., for solvents. Pesticide - PCB pentachlorophenol, chloradene, DDT, BHC, lindane.
Vitamin, Mineral, Amino Acids, Lipids.
11.Air Analysis Indoor - bacteria and mould testing.
12.Nutrition - dietary analysis.
13.Acupuncture evaluation.
14.Homeopathic evaluation.
15.General medical evaluation.
16.Surgical evaluations.

17.Peripheral Oxygen Status - Tissue oxygenation.
18.Eye and lens evaluations.
19.Electromagnetic challenge testing.

Treatment Modalities
1.General medical and surgical services.
2.Massive pollutant avoidance of substances in air, food, water.
3.Injection therapy for biological inhalants (moulds, food, water).
4.Nutrition - dietary manipulation - rotary diets, macrobiotic diets, caveman diets. oral individual vitamin, mineral and amino acids and lipid. parenteral nutrition for caloric and specific nutrient deficiency.
5.Heat depuration and physical therapy consisting of:
especially designed heat (sauna) chambers so that no toxics exposure will occur.
massage under environmentally controlled conditions.
exercise under environmentally controlled conditions.
physical therapy under environmentally controlled conditions.
6.Autogenous immune and non immune modulators, autogenous bacterial and fungal vaccines.
7.Surgery.
8.Homeopathy.
9.Acupuncture.
10.Optical manipulation.
11.Psychological counselling.
12.Oxygen therapy - this is a modification after the German technique of Professor Van Ardenne for treatment of the Chemically Sensitive, those with brain dysfunction and arteriosclerotic disease.
13.Osteopathic manipulation.

A similar extensive pattern of treatment is available in the UK through British Society for Allergy, Environmental, and Nutritional Medicine, BSAENM. www.bsaenm.org

1. Dr. Jean Monro, Breakspear Hospital, Belswains Lane, Hemel Hempstead, Herts HP3 9HP
Phone 01442 261333
Fax 01442 266388

2. The Airedale Allergy Centre- contact Dr Jonathan Mabereley, Airedale Allergy Centre, High Hall, Steeton, Keighley, W. Yorks BD20 6SB
Phone: 01535 656 013

Dr. David Freed, 14, Marston Road, SALFORD M7 4ER,
Phone: 0161 795 6225.
Gulf War Veterans have been successfully treated at both centres.

Institute for Functional Medicine
I recently attended a major international meeting on Applying Functional Medicine in Clinical Practice, April 2-7, 2001 at Gig Harbor, Seattle.
This impressive meeting was packed with information and examples about the use of the paradigm of Functional Medicine in the consideration and treatment of chronic diseases.
The principles of Functional Medicine are
Science Based
Biochemical Individuality
Patient centered not disease centered
Involve a Dynamic balance of internal and external factors
Health is a positive vitality not merely the absence of disease
Involve the promotion of organ reserve leading to a healthy life span

The Web of interacting Factors
Nutritional Status
Immune/Inflammation

GI function
Neuro-Endocrine Function
Detoxification
Oxidative Stress
Structural Factors
Body-Mind Factors

Among the major features to emerge was the widespread incidence of dysinsulinaemia which can be readily measured before frank diabetes is established- the measurement of **both** blood glucose and insulin levels- both are high and indicate insulin resistance that is often readily corrected by control of diet and nutritional factors.
There was an astonishing video of Parkinsonism patients receiving intravenous glutathione (a major detoxifying agent) that lead to an immediate improvement in their ability to walk and turn.
I shall be adding a more comprehensive update of this material in the near future.
Much more information is available at the IFM website www.fxmed.com

I am aware that there are many questions about what is offered here but at least it offers suggestions for diagnosis and therapy which has been singularly lacking in the debate about Gulf War Illness/Syndrome to date. To the best of my knowledge none of this kind of information has been disseminated to GPs who are the first point of contact for many GWVs. No treatment is offered by the MAP programme.

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Created 20th April 1999
Updated 15th May 2000
Updated 21st June 2000
Revised Version 2: 21 Dec 2000
2nd Revision 2a 19 April 2001