Clinical

Chronic Fatigue Syndrome in the UK Armed Forces

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Abstract

Chronic Fatigue Syndrome (CFS) is a debilitating condition that can have a significant impact on the lives of patients and those who care for them. In the UK Armed Forces this condition can also have a marked impact on a patient’s career and their ability to function in the deployed environment. In this article the recognition and management of CFS will be discussed, as well as the occupational considerations within the UK Armed Forces.

Case Study

Musculoskeletal pain is a common primary care presentation. A 35-year-old male JNCO became physically unwell and initially presented to his medical officer with lymphadenopathy and night sweats. He cited a number of infections he believed he had encountered in Iraq as a perceived trigger. The patient was medically restricted from full duties and referred to a haematologist. Lymph node biopsy showed minor, non-specific, reactive changes with no evidence of underlying lymphoma. Blood tests were performed, and the only abnormal finding proved to be a raised white cell count that returned to normal on repeat testing. Erythrocyte Sedimentation Rate was persistently normal, and cytomegalovirus, HIV-1 and HIV-2 titres were negative.

Following further assessment at a Tropical Diseases Centre, he was found to be positive for previous infection with Epstein-Barr virus (EBV), and a diagnosis of post-viral fatigue was made by the medical team. The patient was informed that he should expect a gradual improvement over time. He also underwent rheumatological investigation and the screen was normal including rheumatoid factor, protein electrophoresis, ferritin, folate, B12, thyroid function and immunoglobulin bone markers. After exhaustive physical investigation, the diagnosis of Chronic Fatigue Syndrome (CFS) was suggested.

He was referred for psychiatric assessment and treatment after displaying low mood and hopelessness. Over 12 months he was given a trial of both Amitriptyline and Mirtazapine with no apparent benefit. However, an improvement was demonstrated on Escitalopram and this was continued long-term. A residential rehabilitation course with occupational therapy was undertaken, and the patient reported a return to 70% of pre-morbid functioning levels. He managed to pass his fitness test and return to work. On returning to work he found that his night sweats and inability to concentrate became intolerable. Over the next 18 months deteriorating flu-like symptoms with multiple joint pains and muscle spasms were reported. Rebound fatigue was reported after each period of increased activity. He described struggling to spend more than 5 hours out of his bed daily. He was unable to carry out the requirements of his reduced employment category at work and was placed on sick leave at home. In the end he was medically retired from the UK Armed Forces 6 years after his initial presentation with the condition.

Definition

Chronic Fatigue Syndrome (CFS) is characterised by severe, disabling fatigue or fatigue not substantially relieved by rest, commonly associated with other symptoms that cannot be explained by a medical or psychiatric cause. Most research utilises one of two diagnostic criteria: namely, the US Centres for Disease Control and Prevention diagnostic criteria (1,2) and the Oxford criteria (3). A comparison of these diagnostic criteria can be found in Box 1. The National Institute for Clinical Excellence (NICE) Guidelines of 2007 (4) combined these criteria (Box 2).

Epidemiology

Fatigue affects 11.3% of patients attending primary care. However, the point prevalence of CFS is 0.1 to 2.6%, dependent on diagnostic criteria used (5). CFS appears to be significantly more common in women (6). The prevalence in the United Kingdom’s Armed Forces is not known. However, research has been carried out in the veteran population, the majority in relation to Gulf War veterans (7). A 2005 study comparing the health of deployed Gulf War veterans compared to non-deployed veterans stated that CFS affected 1.6% of deployed veterans.
Centres for Disease Control, 1994 (1)  
Oxford (3)

### Diagnostic Criteria

**Clinically evaluated, medically unexplained fatigue of at least six months duration that is:**
- of new onset
- not a result of ongoing exercise
- not substantially alleviated by rest
- a substantial reduction in previous levels of activity

**The occurrence of four or more of the following symptoms:**
- Subjective memory impairment
- Tender lymph nodes
- Muscle pain
- Joint pain
- Headache
- Post-exertion malaise
- Non-refreshing sleep

**Exclusion Criteria**
- Active, unresolved or suspected disease to cause fatigue
- Psychotic, melancholic or bipolar depression (but not accompanied major depression)
- Psychotic disorders
- Dementia
- Anorexia or bulimia nervosa
- Alcohol misuse or other substance misuse
- Severe obesity

### Oxford (3) Diagnostic Criteria

**Severe, disabling fatigue of at least 6 months duration that:**
- affects both physical and mental functioning
- is present for more than 50% of the time

**The occurrence of four or more of the following symptoms:**
- Myalgia,
- Sleep and mood disturbance may be present.

**Exclusion Criteria**
- Active, unresolved, or suspected disease likely to cause fatigue
- Psychotic, melancholic or bipolar depression (but not uncomplicated major depression)
- Psychotic disorders
- Dementia
- Anorexia or bulimia nervosa

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Box 1: Comparison of widely used diagnostic criteria

### Consider the possibility of CFS/ME if a person has:

**Fatigue with all of the following features:**
- New or had a specific onset (that is, it is not lifelong)
- Persistent and/or recurrent
- Unexplained by other conditions
- Has resulted in a substantial reduction in activity level characterized by post-exertional malaise and/or fatigue (typically delayed, for example by at least 24 hours, with slow recovery over several days)

**And one or more of the following symptoms:**
- Difficulty with sleeping, such as insomnia, hypersomnia, non-refreshing sleep, a disturbed sleep-wake cycle
- Muscle and/or joint pain that is multi-site and without evidence of inflammation
- Headaches
- Painful lymph nodes without pathological enlargement
- Sore throat
- Cognitive dysfunction, such as difficulty thinking, inability to concentrate, impairment of short-term memory, and difficulties with word-finding, planning/organising thoughts and information processing
- Physical or mental exertion makes symptoms worse
- General malaise or ‘flu-like’ symptoms
- Dizziness and/or nausea
- Palpitation in the absence of identified cardiac pathology

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Box 2: Definition of chronic fatigue (NICE Guidelines 2007) (4)

of deployed and 0.1% of non-deployed veterans (8). Box 3 summarises the studies involving Gulf War veterans.

**Aetiology**
The identification of a single cause of CFS remains elusive. Up to 75% of patients report a viral illness as a precipitating factor; however, this figure does not account for recall bias. Hope of an identified cause was kindled when xenotropic MLV-related virus (XMRV) was identified in the mononuclear cells of CFS patients (14). However, a paper released in 2012 (15), refuted this concept, with no link being found between CFS and the retrovirus. The Centres for Disease Control
and Prevention lists a selection of infectious agents currently being researched, including EBV, Human Papilloma Virus 6, enterovirus, rubella and candida albicans (16).

Currently a multi-factorial approach to the aetiology is employed, addressing biological, social, and psychological factors (17). Consideration of predisposing, precipitating and perpetuating factors can be helpful when considering the patient’s diagnosis and management (4). These factors are listed in Box 4. In addition to these factors, there is a strong association between CFS and chronic widespread pain (CWP), irritable bowel syndrome (IBS) and major depressive disorder (21).

Clinical features
The core symptom in patients with CFS is overwhelming exhaustion not relieved, or only partially relieved, by rest. The fatigue is often accompanied by other symptoms not explained by an alternate diagnosis, including difficulty sleeping, muscle/joint pain and painful lymph nodes without pathological enlargement. A comprehensive list can be found in Boxes 1 and 2. A patient may have had multiple investigations related to their symptoms, following which no firm diagnosis for their collection of disparate symptoms could be made, as demonstrated in the case study.

The nature of impairment caused by CFS can affect a patient’s physical, psychological, cognitive, social, and occupational wellbeing. The level of disability experienced by patients is variable. Some patients may manage to maintain their pre-morbid activities, whereas others find themselves housebound. This change in function and social circumstances can often affect the patient’s mental wellbeing and self esteem (21).

When considering patients with a diagnosis of CFS in the Armed Forces, the effects on their ability to continue in their role must be closely examined. Armed Forces personnel are required to meet minimum fitness standards, tested every 6 to 12 months. Being unable to carry out physical training on a regular basis would greatly impact on an individual’s ability to perform and achieve the required levels in the fitness tests, and to meet the day-to-day physical demands of service.

<table>
<thead>
<tr>
<th>Study</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Iowa Persian Study Group (9)</td>
<td>Statistically significant increased prevalence rate difference between deployed and non-deployed veterans was 1.4 after adjustment for age, sex, race, branch, and rank.</td>
</tr>
<tr>
<td>Goss Gilroy Inc. 1998 (10)</td>
<td>Canadian survey based on questions used by Iowa Persian Study Group. Suggested that deployed veterans were more than five times as likely as non-deployed veterans to report symptoms of CFS. Veterans who had served in land units had a slightly higher risk than those who served in the sea or air.</td>
</tr>
<tr>
<td>Unwin et al (1999) (11)</td>
<td>Self-reported CFS was strongly associated with deployment to the Gulf compared with deployment to Bosnia or no deployment. The prevalence of CFS was low in all cohorts: Gulf 3.3%; Bosnia 0.8%; Era 0.8%</td>
</tr>
<tr>
<td>Reid et al (2001) (12)</td>
<td>Health Survey of UK Military Personnel revealed CFS to be three times greater in Gulf War veterans (2.1%), compared with Bosnia (0.7%) and Era (1.8%)</td>
</tr>
<tr>
<td>Ismail K., et al (2008) (13)</td>
<td>Disabled Gulf War veterans were found to be more likely than similarly disabled Bosnia-Era veterans to meet CFS criteria, whereas rates for other medically unexplained conditions were not significantly increased.</td>
</tr>
</tbody>
</table>

Box 3: CFS In Gulf War veterans (9, 10, 11, 12, 13)

<table>
<thead>
<tr>
<th>Predisposing factor</th>
<th>Precipitating</th>
<th>Perpetuating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>Occupational stress</td>
<td>Excessive rest</td>
</tr>
<tr>
<td>Pre-morbid psychopathology</td>
<td>Serious life events</td>
<td>Fear of exercise</td>
</tr>
<tr>
<td>Neurotic and perfectionist personality traits</td>
<td>Poor sleep</td>
<td></td>
</tr>
<tr>
<td>Race: African American and Native American (19)</td>
<td></td>
<td>Irregular patterns of activity</td>
</tr>
<tr>
<td>Age 40-59 (20)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Box 4: Suggested predisposing, precipitating and perpetuating factors (18)
<table>
<thead>
<tr>
<th>System</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Occupational stress. Excessive rest</td>
</tr>
<tr>
<td>Neurological</td>
<td>Serious life events. Fear of exercise</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Poor sleep</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Irregular patterns of activity</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Ischaemic heart disease, cardiac insufficiency</td>
</tr>
<tr>
<td>Respiratory</td>
<td>COPD, sleep apnoea</td>
</tr>
<tr>
<td>Renal</td>
<td>Chronic renal failure</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Liver disease, coeliac disease</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Depression, anxiety disorders, eating disorders, somatoform disorders, negative symptoms of schizophrenia</td>
</tr>
<tr>
<td>Substance misuse</td>
<td>Alcohol misuse, drug dependency</td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>Antihistamines, antipsychotics, beta-blockers, corticosteroids, other sedative drugs</td>
</tr>
</tbody>
</table>

Box 5: Differential diagnosis of CFS

Beyond minimum fitness requirements, the effect on training and operational roles must be addressed. A common feature of CFS is the rebound tiredness experienced after prolonged or increased activity. The challenge of carrying heavy loads and moving around in physically challenging environments can exhaust patients. In the Royal Navy specifically, moving around a ship on a day to day basis can in itself activate severe exhaustion, without considering more arduous activities such as fire fighting and casualty exercises. This can have a profound effect on the patient’s ability to function on deployments or exercises, and any significant degree of CFS usually involves employment restrictions that are unlikely to be compatible with the deployed environment.

Assessment
If a patient presents with symptoms consistent with CFS diagnostic criteria, a step-wise approach should be employed.

Step 1: Initial Assessment
It is essential that a full history be taken from the patient. Ask them if they have any theories as to the trigger for their symptoms. Discuss any factors they have noticed that exacerbate or alleviate their symptoms, including sleep disturbance and current stressors. It is important to explore any history of CFS-associated co-morbidities e.g. IBS, CWP and depressive disorder. A full examination of the patient should be carried out, with possible differential diagnoses in mind. Lymph node examination should be a standard part of the physical examination. A full assessment of the patient’s psychological wellbeing is essential, and using the Patient Health Questionnaire (PHQ-9) may be useful (22). The differential diagnosis of CFS is listed in Box 5.

Step 2: Investigation
There is no definitive investigation to confirm or refute a diagnosis of CFS, and so the diagnosis is one of exclusion. NICE guidelines (4) indicate ‘red flag’ features that must be investigated to exclude serious conditions (Box 6). ‘Red flag’ symptoms should be investigated as per appropriate NICE guidelines. Blood tests should also be requested (Box 7).

Serological testing should only be carried out if there is a history of infection, for example chronic bacterial infections, chronic viral infections (HIV, Hepatitis B/C), acute viral infections (mononucleosis) or latent infections (EBV).

Red Flag Symptoms
- Localising/focal neurological signs
- Signs and symptoms of inflammatory arthritis or connective tissue disease
- Signs and symptoms of cardio-respiratory disease
- Significant weight loss
- Sleep apnoea
- Clinically significant lymphadenopathy

Appropriate pathology investigations
- Urinalysis
- Full blood count
- Liver function
- Thyroid function
- Erythrocyte sedimentation rate or plasma viscosity
- C-reactive protein
- Serum creatinine
- Screening blood tests for gluten sensitivity
- Serum calcium, creatine kinase
- Assessment of serum ferritin levels in children and young women only
Management

Many patients with CFS can be managed in the Primary Care setting. A shared-decision-making approach should be utilised, allowing the patient to engage in their care. NICE recognises the reality and impact of the condition and symptoms, and the importance of keeping the patient well informed with regards to their diagnosis and the stage of their condition, encouraging cautious optimism. Symptoms should be managed as they would usually be managed in any other condition. Some patients do find that exclusion diets aid associated bowel symptoms, but care should be taken to ensure that the selected diet does not put the patient at risk of malnutrition and is not incompatible with realistic nutrition in the deployed environment at sea or on land. If malnutrition is a concern it is prudent to involve a dietician in the patient’s care.

Advice on function and quality of life management is important in order to establish a plan to limit ‘boom and bust’ activity by encouraging steady, incremental increases in physical activity, and identifying other perpetuating factors. Discuss sleep hygiene, and introduce any change to sleep patterns gradually. Daytime napping should be discouraged in order to improve the sleep-wake cycle. If sleep and rest do not improve with sensible alterations, consider an underlying sleep disorder. Rest periods are also important, and building these into the day can be beneficial. However, rest periods should never last longer than 30 minutes. Relaxation techniques can be introduced to these rest periods, for example guided visualisation or breathing techniques. The concept of setbacks/relapses should also be explored with patients, looking at how to identify them, as well as some coping mechanisms for difficult periods and tasks to avoid/encourage according to their experiences of perpetuating and remitting factors.

The occupational impact of CFS should also be addressed, especially when considering military patients. A good history from the patient about their role and how they are coping is important. If the patient consents, more information can be requested from their workplace. The patient’s ability to manage their role will depend on the severity of their condition. Advice from Occupational Health should be sought where available. During periods in which symptoms worsen, rest periods should be arranged in the workplace where applicable. The medical category should be reviewed if the patient poses a risk to themselves or others in the workplace, or cannot fulfil their role. For example, if a patient’s cognitive function is decreased, the risk of them making a mistake whilst weapon handling could be fatal. Medical employment restrictions protects patients and those around them, and also allow continued care, protected medical appointments, and the opportunity to address future role prospects. More severe cases may require specialist referral and intervention. In the UK Armed Forces, as a rule of thumb, those diagnosed with functionally impairing CFS should be placed in a non-deployable medical category.

Specialist management

Specialist management requires an individualised, person-centred programme with the aim to ‘sustain or gradually extend...the person’s physical, emotional and cognitive capacity and manage the physical and emotional impact of their symptoms’ (4). Specialist units provide both Cognitive Behavioural Therapy (CBT) and Graduated Exercise Therapy (GET) by trained practitioners experienced in managing CFS to treat more complex cases. Inpatient care is only advised in cases where multiple and frequent trips to the hospital are required for severe CFS. Examples include frequent investigations where the travelling in itself may exacerbate the CFS. In the current UK Armed Forces provision, CBT can be accessed through regional Departments of Community Mental Health (DCMH), and specialist occupational therapy and inpatient treatment at the Defence Medical Rehabilitation Centre.

CBT

CBT explores the relationship between thoughts, feelings, behaviours and symptoms. Sessions address areas including: adjustment to diagnosis; addressing any symptom hypervigilance; building on existing assertion and communication skills, and managing set-backs/relapses.

GET

GET should be delivered by GET therapists with experience in treating CFS patients. The first step is to assess the current activity levels of the patient, beginning with low intensity activities e.g. brushing hair or a short walk, and subsequently use this assessment to formulate short, medium and long term goals. Low-intensity exercises are initiated and their frequency and intensity slowly increased.

Pacing

Pacing is a technique favoured by some patients and patient organisations. Pacing involves limiting activities according to fatigue, and balancing activities and rest. However, pacing is not recommended by NICE and a recent randomised trial did not find it an effective treatment (19).

During any period of psychotherapy military patients should be medically restricted for the duration of their treatment.

Medication

Although psychotropic medication is not recommended as first-line treatment for those with CFS, it is important to treat any mental-health co-morbidities, such as anxiety and depression, appropriately.

Prognosis

Full, spontaneous recovery is rare but improvement in milder cases, especially those managed in Primary Care, is not uncommon. Reliable data on milder cases is limited, with the majority of prognostic studies displaying a bias towards severe cases. The median recovery rate has been estimated at 5% (range 0 – 31%) and the median improvement rate at 39.5%
(8 – 63%) in both Primary Care patients and those managed by specialist units. Approximately 40% improve with CBT or GET (23). The rate of medical discharge from the UK Armed Forces for moderate to severe cases is likely to be high due to the functional limitations conferred by their symptoms.

**Conclusion**

It is important where symptoms of fatigue are more severe or persist longer than would be expected that a diagnosis of CFS should be considered. Investigation of severe fatigue should be undertaken. Pain, depression and anxiety disorders should be treated as per clinical norm. Acknowledgement of patient’s symptoms and how they impact on their life is essential. A collaborative management plan should be developed between the doctor and the patient. In the UK Armed Forces an occupational assessment should be conducted and the appropriate restrictions considered. Referral should be considered to a regional DCMH.

**References**


15. Alter HJ, Mikovits JA, Switzer WM Ruscetti FW et al. A multicentre blinded analysis indicates no association between chronic fatigue syndrome/ME and either xenotropic murine leukemia virus-related virus or polytropic murine leukemia virus. *J Biol.* 2012 Sep 18;3(5)


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