The Independent Medical Expert Group (IMEG)

Report and recommendations on medical and scientific aspects of the Armed Forces Compensation Scheme

March 2015

Topic 1 – Infectious diseases and sequelae in recent deployed service

1. Following several claims for deployment related febrile illness and their sequelae, IMEG was asked by Minister to investigate and report on the AFCS approach to these disorders, with a particular focus on Q fever and post Q fever fatigue syndrome (QFS). Our short report was informed by a literature search and discussion with relevant military and civilian experts.

2. Despite a significant body of published scientific and medical literature on fatiguing illness, there remain many uncertainties and gaps in the evidence, particularly on post–infective fatiguing illness and QFS. While a Dutch group has recently published a protocol for a prospective cohort study on the health impact of Q fever up to four years from clinical onset of the acute illness (1), there is currently no planned cohort study reported with follow-up beyond about 26 months (2). These evidential limitations constrain IMEG's findings and recommendations.

Deployed service and infectious disease

3. Undifferentiated febrile illnesses (known as "Helmand Fever" when occurring in Afghanistan), meningitis, encephalitis and gastroenteritis seem to be the commonest infectious causes of long-term symptoms following deployments. To-day, most deployment-related febrile illness is self-limiting, lasting at most a few weeks with low rates of morbidity and mortality in the acute phase. In 2008 a small study identified 26 cases of "Helmand Fever" diagnosed clinically over six months and, to identify their cause, applied a standard protocol which included acute and convalescent serology (3). In about 10% of cases no firm diagnosis was made. 52% of the remaining cases were viral due to sand fly fever; 22% due to rickettsial infections, commonly typhus, and 26% were bacterial due to Q fever. Of these, only Q fever is known to be associated with significant disabling illness and sequelae.

Q fever

4. Q fever was first described in Queensland, Australia in 1937. Notable outbreaks have since occurred in Birmingham in 1989 and in Holland between 2007 and 2010. It is a zoonosis caused by Coxiella burnetii infection, transmitted especially from parturient animals. It is highly infectious and spread by inhalation from wind borne spores (4). Q fever occurs around the world with slightly different clinical symptoms and patterns. The Public Health Laboratory Service reports about 100 sporadic cases per annum in the UK.

5. In the current Afghanistan deployment, 3.4% of troops have serological evidence of new Coxiella burnetii infection each year with about half (340 per year) being asymptomatic or having very mild symptoms. The other half have a flu like illness with fever, myalgia, arthralgia, tiredness or atypical pneumonia. The acute phase is not usually life threatening and the majority of cases make a good recovery in a few weeks. About 10-15% have varying degrees of persisting fatigue and functional limitation - post Q fever fatigue syndrome (QFS). This occurs most commonly where fatigue is a prominent symptom at the beginning of the illness. These symptoms may be accompanied by muscle pain with fasciculation and night sweats. Some 16% of military cases of acute Q fever are unable to pass a military fitness test at a year after the acute illness. Chronic Q

fever, a discrete entity, diagnosed serologically, which affects between 1 and 5% of those infected usually presents as endocarditis. No military cases have been reported from Afghanistan. In Australia, where the disorder occurs particularly amongst stockmen and abattoir workers, a Q fever vaccination programme was introduced in 2001. No vaccine is yet licensed for use in the UK. UK military clinical management of Q fever includes empirical use of doxycycline for two weeks. Clinically this seems to reduce the severity of the acute illness and to lower the risk of QFS. In different Q fever outbreaks there are core symptoms / features with variations. Most reported outbreaks include patients with fatigue during both the acute illness and longer term. While variation in bacterial strain may be relevant, there is at present no clear explanation for the different clinical patterns. It is also unclear whether persistent fatigue in QFS is a long term manifestation of Q fever or a specific consequential disorder.

6. In the 1989 Birmingham Q fever outbreak in which 147 cases occurred in a month, the infection source was birth by-products from ewes lambing in the fields south of the M42. Spores were spread due to unusual weather conditions with, on one April day, southerly gales up to 80 mph. The acute disease was severe, often requiring hospitalization. Symptoms included dramatic weight loss of up to one stone in a week. Chest symptoms were prominent, with a range of radiographic change which included lobar pneumonia. Neurological symptoms were also common, with headache and visual problems. At six month follow-up, a third of patients were still symptomatic and complaining of fatigue. Of the 147 cases seen in the acute phase, two had myocarditis and two subsequently developed chronic Q fever with endocarditis (5).

7. Five years after the Birmingham outbreak, amid evidence of continuing poor health, 142 of the original 147 patients were traced and asked to complete a postal questionnaire. The controls, who had not complained of symptoms during the outbreak, were matched on age, sex and geographical location. The study investigated 71 patients and 142 matched controls. Symptoms such as fatigue, sweating, breathlessness, blurring of vision were more common in cases than controls although there was a high symptom prevalence in the controls. No serology was available for the controls, so it is possible that they may have included some mild or asymptomatic cases of Q fever (6).

8. Further follow-up of this cohort at ten years post-infection included hospital interview, clinical examination and a standard battery of tests including serology. Controls matched for age, sex and smoking habit were selected from GP lists. The protocol included the administration of the Chalder fatigue questionnaire and psychological symptoms were measured by the General Health Questionnaire (GHQ). Fatigue symptoms were again more common in cases than controls with GHQ case criteria met in 47% of cases and 23% controls (7). 10% of cases had persisting fatigue and functional limitation. It should be appreciated that the infected population in Birmingham was not of similar age or gender as the military population, with the average age at the time of infection in this outbreak being in the forties.

9. Between 2007 and 2010 the Netherlands had the largest outbreak of Q fever yet reported, with 3,523 notified cases of infection (8). Study of the Dutch patients show that, as with the Birmingham outbreak, following acute Q fever many patients had disabling symptoms, most commonly QFS, 12 to 26 months after initial infection (2).

10. Other infectious agents associated with post-infectious fatigue relevant to military populations include infectious mononucleosis (glandular fever), viral hepatitis, viral meningitis, parvovirus and non-viral diseases including Lyme disease. In post-infective fatigue states in addition to generic symptoms, specific infections can be associated with particular symptoms such as nausea and fatty food intolerance in hepatitis, sore throat and painful cervical lymphadenopathy in

infectious mononucleosis. Research findings suggest that some 10 to 13% of cases of these infections go on to develop post infective fatiguing state (9). Factors which have been suggested to increase the risk of developing these symptoms include:

i) pre-morbid fatigue and depression.

ii) severe initial infection.

iii) the patient's belief that the illness will be prolonged with difficult recovery, so (s)he needs to rest, with resultant physical deconditioning.

In addition there may be possible links to:

iii) abnormal autonomic nervous system function, e.g. low heart rate beat to beat variability.

iv) down-regulation of the hypothalamic-pituitary-adrenal axis (low cortisol levels may be a factor in some types of Chronic Fatigue Syndrome (CFS), but have not been shown in post infective states).

v) immune abnormality (findings in post-infective fatigue states are inconsistent).

vii) host genetic factors.

Are post infective fatiguing illnesses including QFS the same disorder as chronic fatigue of spontaneous onset?

11. Cases with QFS usually meet the general case definition for spontaneous Chronic Fatigue Syndrome (CFS) (10). However, information on the natural course, average duration and prognosis of QFS, whether treated or untreated, is sparse. It is not known whether chronic fatigue following infection is the same entity or different from CFS of spontaneous onset.

12. The large majority of patients in most studies of chronic fatiguing illness of spontaneous onset are women. In contrast, while the UK Afghanistan military and Australian abattoir studies of QFS are occupationally based, and therefore with men predominantly affected; there was also a clear preponderance of working age men in the Birmingham outbreak, where no links to occupation were identified. Three quarters of those affected were employed working aged males. Just one child was infected and only three non-white people.

13. CFS is usually a diagnosis of exclusion. Of patients referred to secondary care CFS clinics, with six months or more of abnormal fatigue, poor concentration and sleep, myalgia and arthralgia of unknown aetiology, about half do not have CFS but other diagnoses such as depression and sleep apnoea. CFS is often associated with other disorders such as fibromyalgia, migraine and irritable bowel syndrome. These associations are considerably less common with post-infectious fatigue syndrome. Some patients with spontaneous CFS also have comorbid psychiatric disorders, but there is no evidence that post-infectious fatigue states are particularly associated with specific psychiatric diagnoses.

14. Although, as referenced above, overall study numbers are small with inconsistent results which are difficult to interpret in terms of cause or consequence, a number of studies on the mechanism of fatiguing illness suggest that post-infectious CFS may be different from spontaneous onset CFS (11). Studies from Australia and Birmingham have shown that in QFS, following Q fever, persistent symptoms are associated with either antigen or organism DNA retained in tissues, particularly the bone marrow of these patients (12). Potential immunological mechanisms and host genetic influences are emerging as research topics which may in the future provide improved understanding of chronic fatigue following acute infection (13).

Treatment and prognosis of fatiguing illness

15. A variety of treatments, ranging from steroids to anti-microbial treatment has been provided for fatiguing illness following infection, but as yet there is no consistent evidence to support their use. In general, for all types of persistent fatigue state, optimal management is based on: i) accurate diagnosis of all disorders including co-morbid sleep problems, depression and pain; ii) treatment of co-morbid conditions; iii) focus on the fatiguing illness with active rehabilitation therapies. Research findings show that individually (not group) delivered Cognitive Behavioural Therapy (CBT) and Graded Exercise Therapy (GET), when compared to specialist medical care alone, are moderately effective with effect sizes of 0.5 to 0.8, when added to specialist medical care and delivered in courses of suitable intensity and duration by appropriately qualified, trained and supervised therapists (14). Cochrane reviews generally support the efficacy and safety of these therapies (15) (16).

16. The published literature on the natural course, duration, prognosis and effective interventions for fatiguing illness of all types is limited. Disability, functional outcomes and employability have not been a major focus of studies and comparison of studies and interpretation is hindered by different case definitions and whether patients are drawn from primary or specialist care settings, the latter usually being the more severe cases. The prognosis for patients receiving specialist care for persisting fatiguing illness without specific treatment is poor. A 2005 meta-analysis of 14 studies, with sample sizes of between 20 to 3,201, with defined entry criteria, published between 1991 and 2002, followed for between one and five years showed in untreated cases, a median full recovery rate of 5% (with a range across the studies of 0 to 31%), with symptomatic improvement at follow-up in a median of 39.5% cases (range 8 to 63%). Better outcomes were associated with less severe fatigue at the onset, patients having a sense of control over their symptoms, absence of past or comorbid mood disorders, and not attributing illnesses to a physical cause (17). The limited literature on mortality associated with CFS suggests there is no increased risk (17) (18) (19).

17. In contrast to CFS, the prognosis of post-infectious fatigue states is better (18). There have been a number of follow up studies of cohorts of confirmed infectious cases, which all suggest the longer the follow up period the greater the reduction in prevalence of both symptoms and disability (9) (19) (20) (21). Following up the outcome of three different infections, one of which was Q fever, Hickie and colleagues found the prevalence of an established post-infectious fatigue syndrome was 27% at three months after the onset of infection, 12% at six months and 9% at 12 months, with no significant differences between infections (9). A recent follow up study of Q fever found the prevalence of abnormal symptomatic fatigue, rather than an established fatigue syndrome, fell from 73% at three months, to 60% at twelve months and to 37% by 24 months (22).

AFCS approach to infections and their sequelae

18. The armed forces population is on average younger and fitter, with a higher proportion of men, than the general employed population and AFCS claims for physical disorders are unusual. It was anticipated that infections might be an issue for the Scheme and the legislation sets out the circumstances, where benefit may be payable for an exogenous infection. These are first deployed service in a temperate region, where there has been an outbreak of the infection in service accommodation / workplace.

Table 4 – Physical disorders including infectious diseases*

Column (a) Level	Column (b Level
6	Physical disorder causing severe functional limitation or restriction where life expectancy is less than five years.
7	Physical disorder causing severe functional limitation or restriction where life expectancy is reduced, but is more than 5 years.
9	Physical disorder causing permanent severe functional limitation or restriction.
11	Physical disorder which has caused, or is expected to cause severe functional limitation or restriction at 26 weeks from which the claimant has made, or is expected to make, a substantial recovery beyond that date.
11	Physical disorder causing permanent moderate functional limitation and restriction.
12	Permanent physical disorder where symptoms and functional effects are well controlled by regular medication.
13	Physical disorder which has caused, or is expected to cause, moderate functional limitation or restriction at 26 weeks, from which the claimant has made, or is expected to make, a substantial recovery beyond that date.
14	Physical disorder which has caused, or is expected to cause, severe functional limitation or restriction at 6 weeks, from which the claimant has made, or is expected to make, a substantial recovery within 13 weeks.
14	Physical disorder which has caused, or is expected to cause, moderate functional limitation or restriction at 13 weeks, from which the claimant has made, or is expected to make, a substantial recovery within 26 weeks.
15	Physical disorder which has caused, or is expected to cause, moderate functional limitation or restriction at 6 weeks, from which the claimant has made, or is expected to make, a substantial recovery within 13 weeks.

*Any reference to duration of effects in column (b) is from date of injury or onset of illness.

*Awards for injuries in this Table include compensation for any associated psychological effects short of a distinct diagnosable disorder.

The above Table applies from 9 May 2011

19. AFCS descriptors assess severity of injuries and disorders in terms of the associated functional restriction or limitation and their duration. When choosing a descriptor it is useful to consider first the likely impact of the accepted condition on civilian employability, whether or not a Guaranteed Income Payment (GIP) is appropriate, and at what level. This allows narrowing of Tariff range and finally individual Tariff selection. Awards should be consistent, providing horizontal

equity i.e. across the range of disorders and Tariff Tables, and vertical equity i.e. through the degrees of severity of an injury /disorder category in a single Table. To provide financial certainty for claimants when they leave service, the Scheme aims to make full and final awards as early as possible. Ideally, this is when the injury or disorder is in a steady state of maximum medical improvement, following an adequate course of best practice treatment. When the disorder is not in a steady state, an interim award may be paid for up to four years after initial notification. Functional limitation or restriction is considered permanent where an injury has reached a steady state of maximum medical improvement with no further improvement expected.

20. Tables 3 and 4 of the Tariff relate to Mental Disorders and Physical Disorders – including infectious diseases. The Tables do not list specific diagnoses but are generic. Table 3 has previously been reviewed by IMEG and Table 4 descriptors and Tariff Levels were informed by civil awards where currently (2013) a highly malignant life-limiting disease such as mesothelioma would attract a general damages award of about £100,000. This compares with AFCS Tariff Level 8 which is £60,000; Level 7 £90,000 and Level 6, £140,000. Items 1 and 2 of Table 4 apply to disorders with reduced life expectancy, which is not an issue with post–infective fatiguing illness. Where Table 4 Items 1 and 2 are paid, death and dependents' benefits will also apply. For both Tables 3 and 4 the highest GIP band is Band B based on 75% service salary at service termination. Injuries attracting AFCS band A i.e. 100% salary base include full thickness burns affecting 70% or more body area; several categories of severe polytrauma and amputations; severe brain and spinal injuries and loss of senses. The descriptors aim to reflect injuries and disorders relevant to the military population and potentially attributable to AFCS service. The most severe and enduring mental health disorders in terms of very severe functional compromise and employability are the psychotic disorders which, in line with contemporary medical understanding are not on the balance of probabilities due to AFCS service.

21. As discussed, for post infective fatiguing illness of all types, including QFS, there remain uncertainties, which include best practice treatment and prognosis, but recent research suggest that prognosis is better than for CFS which does not follow an identified infection. It should be remembered that end points and outcomes used in the few published studies are variable, often expressed as self-reported symptoms, and not using an objective functional measure. The available evidence indicates that the majority of people with corroborated post-infectious fatigue states do recover in time, and without treatment. Treatments appropriate for CFS may also help to improve prognosis in post-infectious states.

Suggested descriptors for Q fever and QFS

22. As listed above the Table 4 descriptors applicable from May 2011 do not sufficiently reflect the range of QFS functional limitation or restriction and the following additions are suggested:

- Physical disorder causing permanent very severe functional limitation or restriction Level 6
- Physical disorder causing permanent severe functional limitation or restriction Level 8

The existing Item 5 Level 11 should remain

- Physical disorder causing permanent moderate functional limitation or restriction Level 11

In the footnote to Table 4 in respect of physical disorders

> **"very severe"** Permanent functional limitation or restriction is very severe when the claimant is unable to undertake work appropriate to experience, qualifications and skills, following best practice treatment and at best thereafter is able only to undertake work sporadically and in physically undemanding jobs.
>
> **"severe"** Permanent functional limitation or restriction is severe where the claimant is unable to undertake work appropriate to experience, qualifications or skills at the time of onset of the disorder and over time able to work only in physically less demanding jobs.
>
> **"moderate"** Permanent functional limitation or restriction is moderate where the claimant is unable to undertake work appropriate to qualifications skills and experience at the time of onset of the illness but in time able to work regularly in a less physically demanding job.

23. To maintain coherence the Table 4 descriptors and definitions have a similar format to those in Table 3, Mental disorders. Awards for Physical disorders include psychological symptoms but do not include primary cognitive, mood or behavioural symptoms and are generally paid lower awards than equivalent mental disorders. Factors taken into account in valuing awards for mental disorders include the associated vulnerability and compromised relationships with family, friends and at work. In AFCS terms the current epidemiological findings on the likely better prognosis where a fatiguing illness follows a confirmed infection are not robust enough to allow different descriptors for fatiguing states that post date a confirmed infection compared with spontaneous illness. In addition the descriptors proposed above for Q fever and its sequelae will also apply to other disorders, including infections and primary physical disorders and their sequelae:

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