

Chronic Fatigue Syndrome: The fibromyalgic approach



Curriculum Vitae

Prof Helgard Meyer qualified with and MBChB (cum laude) from the University of Pretoria in 1976. He received the M Prax Med from the University of Pretoria in 1982 and attained the MFGP(SA) in 1983 being awarded the Claude Leon Harris Medal. Helgard practiced as a family practitioner in Ermelo from 1981 to 1989 and was then appointed as professor and clinical head, Department of Family Medicine, University of Pretoria in 1990. His main interest lies in the chronic fatigue/fibromyalgia group of disorders and he has presented more than 70 papers, posters and lectures at local and international congresses, symposiums and seminars. He is married to Katinka and they have three children.

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Summary

Chronic fatigue syndrome (CFS) is a chronic illness characterised by at least six months of debilitating fatigue and associated non-specific symptoms. Depression is seen in many of the patients, although the features often differ from other patients with depression. Many efforts have been made to identify a chronic virus infection as cause of the syndrome – however, no unequivocal evidence exists for persistent virus infection. The prominence of muscle pain led many to conclude that CFS is a muscle disorder, but various studies have disproved this hypothesis. A hypothalamic dysfunction, particularly involving 5-hydroxy tryptamine metabolism, is postulated. A study was undertaken to determine the prevalence of the fibromyalgia syndrome (FMS) and major depression in patients who fulfil the CDC criteria for CFS. It was found that CFS has a high prevalence among young patients and is frequently a long standing problem. Doctors should be aware of the high prevalence of depression in these patients. None of the FMS patients were previously correctly diagnosed, confirming an alarming lack of knowledge of this common condition among doctors. Trigger points cause referred pain in many different anatomical areas – these patients undergo numerous unnecessary investigations and procedures. This could have been managed at primary care level with the emphasis on compassionate holistic care. The recognition of FMS in CFS patients has important economic implications. CFS, FMS and major depression probably share a similar neurochemical background, although there are clinical and therapeutic differences.

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Physicians, family;
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Depression.

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INTRODUCTION

Chronic Fatigue Syndrome (CFS) is a chronic heterogeneous disorder of uncertain etiology characterised by at least six months of debilitating fatigue and associated non-specific symptoms, eg, fatigue and myalgia. Some of these symptoms are also seen in psychiatric illness and CFS is often associated with marked impairment of functional health status. To reduce the diagnostic confusion surrounding the syndrome of chronic fatigue and to produce a rational basis for evaluation of patients, the United States Centres for Disease Control (CDC) developed a consensus case definition which focused on fatigue as an essential feature of the syndrome (Table 1) (Holmes et al, 1988).

The CDC criteria (Holmes et al, 1988) exclude all patients with a history of or present psychiatric illness and were not developed for clinical practice but for research purposes.^{1,2}

The International Chronic Fatigue Syndrome Study Group has recently published a revised case definition of the CFS as well as guidelines for the clinical evaluation of fatigued persons.³ In this revised model all physical signs were dropped from the inclusion criteria because it was agreed that their presence had been unreliably documented in past studies. The required number of symptoms was decreased from 11 to eight. The following psychiatric conditions presently exclude the diagnosis of CFS: Past or current major depressive disorder with psychotic or

Chronic symptoms often develop after an acute pyrexial illness.

TABLE 1: Diagnostic criteria for CFS
(Adapted from Holmes et al, 1988)

Major criteria (both required for diagnosis)

- New onset of fatigue causing 50% reduction in activity for at least six months.
- Exclusion of physical and all psychiatric conditions producing similar symptoms.

Minor criteria

Presence of eight of the 11 symptoms listed, or six of the 11 symptoms and two of the three signs listed.

Symptoms

1. Muscle discomfort or myalgia.
2. Migratory arthralgia.
3. Generalised headaches.
4. Generalised muscle weakness.
5. Sleep disturbances.
6. Neuropsychiatric symptoms.
7. Prolonged fatigue after previously easily tolerated exercise.
8. Mild fever or chills.
9. Recurrent sore throat.
10. Painful cervical or axillary lymph nodes.
11. Rapid onset of symptom complex.

Signs

1. Low grade fever (37.6-38.6°C).
2. Non-exudative pharyngitis.
3. Palpable or tender cervical or axillary lymph nodes (<2cm).

Viral infection may act as a trigger.

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melancholic features; bipolar affective disorders; schizophrenia; delusional disorders; dementia; substance abuse. Patients with 'milder forms' of psychopathology, eg, generalised anxiety and panic disorder, somatoform disorder, etc, are included in the definition of CFS.

Many of the patients develop their chronic symptoms after an acute pyrexial illness and it has also been called post-viral fatigue syndrome. Many efforts have been made to identify a chronic virus infection as cause of the syndrome – however, in well controlled studies no unequivocal evidence exists for persistent viral infection in this disorder.¹ Acute viral infections may act as a trigger in some patients but it is not true for all patients, and the term 'post-viral fatigue syndrome' is best avoided. Immune activation has been reported in patients.⁴ Abnormalities in both humeral and cellular immunity have been demonstrated and reduced natural killer cell function is perhaps the most consistently reproducible immunological abnormality.⁵

CFS is by no means a new condition and the first well documented 'epidemic' of this disorder occurred in Iceland in the 1930s at which time it became known as Icelandic Disease. In the mid-1950s a large number of healthcare workers employed in the Royal Free Hospital, London, developed an acute flu-like illness which was followed by a prolonged period of fatigue and muscle pain.⁴

The prominence of muscle pain led many to conclude that CFS is a muscle disorder, but studies by Edwards et al have firmly established that patients have central subjective fatigue and not a myopathic disorder.⁶ A hypothalamic dysfunction, involving 5-hydroxy-tryptamine metabolism, is postulated and results of objective laboratory studies have shown possible upregulation (increased sensitivity) of central 5-hydroxy-tryptamine receptors in CFS patients.⁵

Most psychiatric studies on CFS patients have reported a greater level of psychiatric morbidity in CFS patients than controls with a high prevalence of major depression as well as a past history of psychiatric disorder, in particular mood disorders.⁷ Such findings do not necessarily imply psychological aetiology and patients themselves are mostly less willing to associate their condition with psychological disorders. Although psychiatric disorders may confer some susceptibility to the development of CFS, depression is associated with many chronic diseases and is often missed in physically ill patients.⁵

However, there exists a subset of patients with CFS with no psychiatric diagnosis and nearly 25% of patients in a series reported by Wesseley and Powell had no other features of depression or other psychiatric disorder.⁸ There may also be pathophysiological differences between CFS and primary depression and the evidence suggestive of possible upregulation of hypothalamic serotonin receptors in CFS patients, was not found in a control group of patients with primary depression.⁹

Fibromyalgia syndrome (FS) has symptoms similar to CFS, especially myalgia, fatigue and neuropsychiatric symptoms, and may share a common pathophysiology.⁹ FS has been established as a distinctive diagnosis in the World Health Organisation's disease classification, ICD-10 and is supposed to be the most common cause of widespread musculoskeletal pain.¹⁰ A recent prevalence study indicated that it affected 3,4% of women and 0,5% of men.

FS is described by the American College of Rheumatology in its classification criteria of 1990 and the core features are generalised pain with evidence of a widespread local tenderness.¹¹ Pain is considered widespread when all of the following are present: pain in both sides of the body and pain above and below the waist. In addition,

Certain doctors are more likely to recognise depression.

Sadly, none of the patients in this study had been correctly diagnosed previously.

axial skeletal pain must be present (cervical spine, anterior chest, thoracic spine, low back). Widespread local tenderness is manifested in pain at a minimum of 11 anatomically defined tender points. These criteria have a diagnostic sensitivity of 88,4% and specificity of 81,1%.¹¹ See Figure 1.

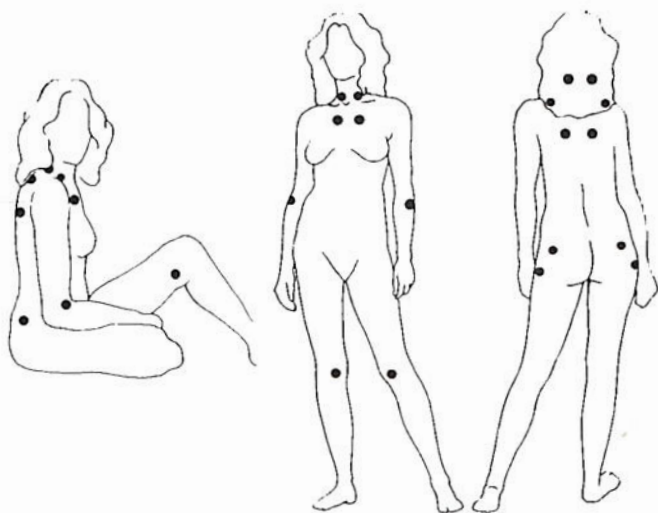
Apart from the core features, a number of other characteristic features are present in the majority of patients: fatigue, non-refreshing or disturbed sleep, headaches, cold sensitivity, restless legs, paraesthesiae, irritable bowel syndrome, irritable bladder, etc.¹² The syndrome thus encompasses a heterogeneous number of symptoms and no laboratory data are of any diagnostic significance. Although the aetiology and pathophysiology is unknown, the majority of patients shows a non-REM stage 4 sleep anomaly.¹² This abnormality may be related to the lower levels of the serotonin metabolite, 5-hydroxy-indole acetic acid, in the cerebrospinal fluid of patients with FS.^{12, 13}

The non-REM sleep abnormality described in patients with FS has also been reported in patients with CFS and patients complain of unrefreshing sleep ('non-restorative'), being sleepy during day time and having muscle aches.¹⁴

Depression is very common in the general population. The present classification includes the syndrome of 'major depression' – namely presence of depressed mood or loss of interest and pleasure with four or more of seven concomitant symptoms, namely loss or increase of appetite and weight, insomnia or hypersomnia, retardation or agitation, fatigue, feelings of inappropriate guilt or worthlessness, impaired concentration, thoughts of suicide.¹⁵ The minimum duration of the disorder should be two weeks.

Other forms of depression include depressive episodes which do not reach the thresholds for major depression and lifelong mild fluctuating depression (dysthymia).¹⁶

**FIGURE 1: American College of Rheumatology Criteria
18 tender point sites**



The **purpose** of this study was to determine the prevalence of the *fibromyalgia syndrome* (FS) and *major depression* in patients who fulfil the CDC criteria for chronic fatigue syndrome (CFS).

METHODS

One hundred and two referred patients who fulfilled the CDC criteria for CFS were included in the study. Patients with a history of the following psychiatric disorders were excluded from the study: psychotic depressive disorder, bipolar affective disorder, schizophrenia, and substance abuse.

A thorough physical examination and urine-analysis was done on every patient to exclude physical conditions which may cause similar symptoms. Laboratory screening included full blood count, erythrocyte sedimentation rate, liver enzymes, calcium, glucose, blood urea and electrolytes, thyroid-stimulating hormone. Routine performance of other screening tests is of no proven value.³ The study was done on mainly referred patients and most of them had received extensive laboratory testing in the preceding months – the tests were then not repeated.

Recognition of depression is very important – it, for example, changes management.

High prevalence amongst young people.

Patients had to fulfil both major and eight of the 11 minor symptom criteria of CFS (See Table 1). The minor physical criteria ('signs', Table 1) were not used in this study, as these criteria have to be documented on at least two occasions at least one month apart and are impractical in a study with referred patients. These criteria are also subjective and low in prevalence.³

The 102 patients were seen over an 11 month period (November 1992 to September 1993) by the same examiner and were evaluated for:

1. Current major depression according to the DSM III (R) criteria.

The diagnosis was based on a direct interview for the main specific symptoms of depression which has been described as the best method for the family practitioner to diagnose depression.¹⁵

2. Current FS according to the 1990 American College of Rheumatology Criteria.

For a tender point to be considered positive, the patient had to state that digital palpation with a pressure of $\pm 4\text{kg/cm}^2$ at the mentioned anatomical sites, was painful. This is approximately the pressure required to blanch the blood from the thumbnail. The control areas used in this study were the patients' forehead and thumbnail.

The scoring system for grading the severity of tender points (Tender Point Index)¹¹ was not used in this study because changes in the patients' condition and response to therapy were not recorded.

RESULTS

Thirty males and 72 females were included in the study. The mean age of the study population was just less than 40 years (Figure 2).

**TABLE 2: Major depression
DSM III (R) criteria (adapted by Paykel¹⁵)**

At least five of the following of which one is depressed mood or loss of interest > 2 weeks.

- Depressed mood
- Loss of interest or pleasure
- Change in appetite and weight
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue
- Inappropriate guilt, worthlessness
- Impaired concentration
- Suicidal thoughts

**TABLE 3: Fibromyalgia Syndrome
American College of Rheumatology Criteria (1990)**

1. A history of widespread pain (>3 months)
 - Above and below the waist
 - Both sides of the body
 - Axial skeletal pain
2. Pain to be present in at least 11 of the following 18 (bilateral) tender point sites.
 - Occiput (suboccipital muscle insertions).
 - Low cervical (anterior aspects of the intertransverse spaces at C5-C7).
 - Trapezius (midpoint of the upper border).
 - Supraspinatus (at origin above the spine of the scapula).
 - Second rib (at the second costo-chondral junction).
 - Lateral epicondyle (2cm distal to the epicondyles).
 - Gluteal (upper outer quadrants of buttocks in anterior fold of muscle).
 - Greater trochanter (posterior to the prominence).
 - Knee (at the medial fat pad proximal to the joint line).

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The mean duration of symptoms was more than three years, varying from six months to a maximum of 22 years (Figure 3).

A high prevalence of current major depression was found, particularly in the male group (Figure 4).

A significant finding was that 92% of the patients fulfilled the criteria for FS – this was particularly prevalent in the female group (Figure 5).

In the FS patients as a group, just less than 40% also fulfilled criteria for current major depression (Figure 6).

DISCUSSION

The mean age of the patients in this study (males 39,7 years; females 39,1 years) confirms the high prevalence of CFS among young patients.

The female:male ratio in this study with referred patients was 2,4:1. In a study with unselected patients the ratio was 1,8:1.¹⁸

The mean duration of symptoms was more than three years, illustrating the chronic nature of this problem. The tenacity of the fatigue can be very severe and in a study by Komaroff, the mean duration of symptoms was nearly six years.¹⁹

Current major depression was diagnosed in 44% of the patients. The diagnosis of major depression is often overlooked and many of the patients are treated for physical complaints. The possible co-morbidity of depression in CFS patients should always be explored, because it alters the management. Accurate recognition of depression in general practice depends primarily on the skill of the doctor as interviewer.¹⁵ Recognition of depression can be achieved within routine consultations, but it is often necessary to set aside additional time.

Certain doctors are more likely to

Figure 2

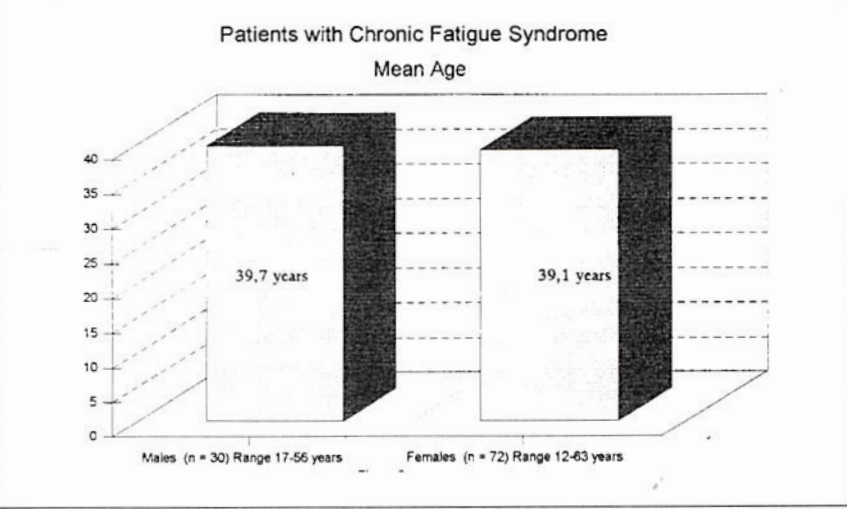


Figure 3

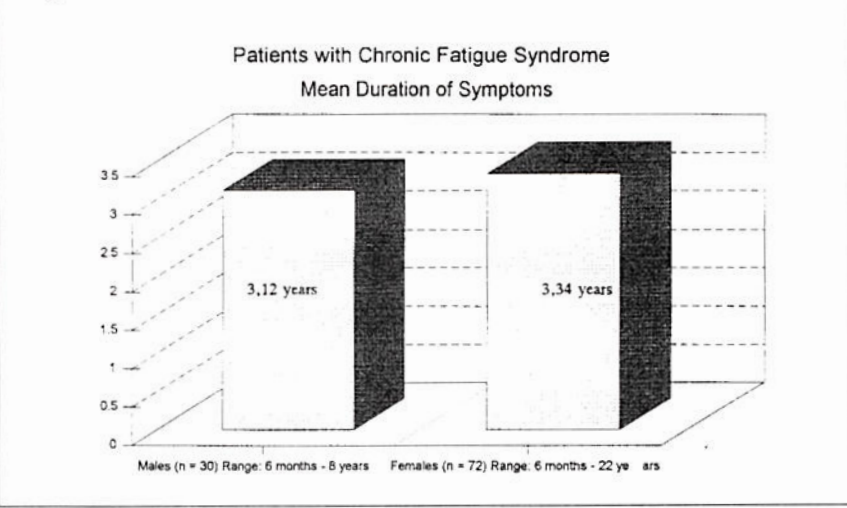
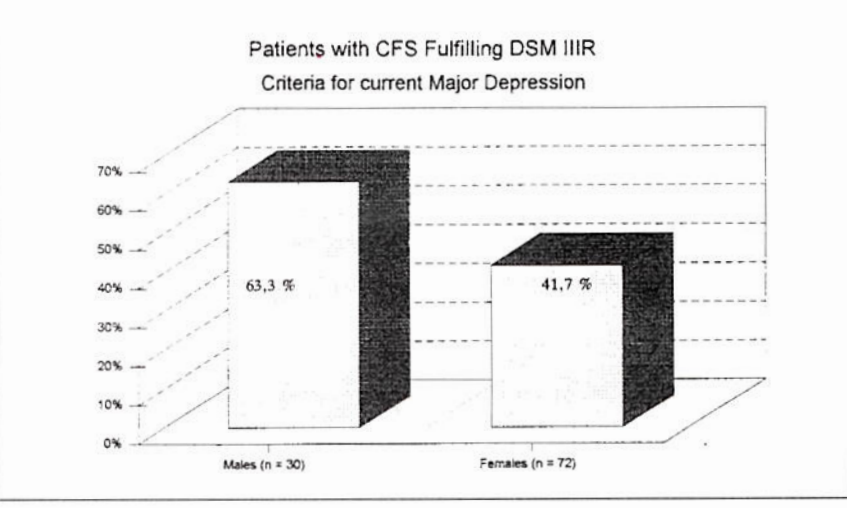


Figure 4



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recognise depression – those who make more eye contact with the patient, who don't interrupt the patient and are good listeners.^{15, 17} The teaching of interviewing skills should concentrate on showing empathy, how to tolerate and use silence and to notice non-verbal behaviour.¹⁷

Of the patients in this study, 92% fulfilled the criteria for FS. No other study could be found in the literature where this specific relationship was investigated with the same diagnostic criteria. None of the patients in this study was previously correctly diagnosed as FS, illustrating a severe lack of knowledge of this condition among doctors.

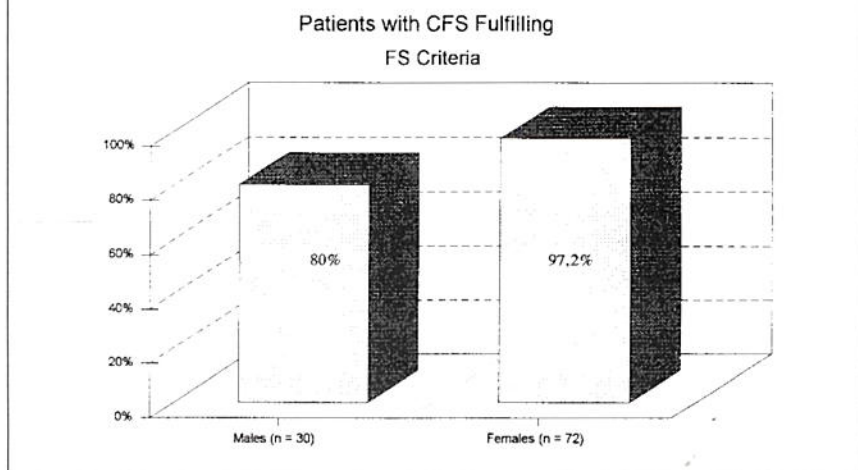
It was also found that 39,4% of the patients with FS also fulfilled the DSM IIR' criteria for current major depression. Despite the increased prevalence of depression in FS patients, the majority of patients did not meet criteria for major depression. Recent studies have demonstrated no differences between FS and rheumatoid arthritis patients concerning the prevalence of depression.²⁰ This data therefore does not support a psychopathology model as a primary explanation of the symptoms of FS. However, the presence of a psychiatric disorder is relevant in that patients with FS and a psychiatric history have significantly more somatic symptoms.²⁰ These data do not rule out the possibility that psychological factors are important in the development and maintenance of FS.

CONCLUSION

All the patients in this study fulfilled either the FS or major depression criteria or both. This finding has important implications as both these conditions can mostly be managed satisfactorily at a primary care level.

The recognition of depression and FS in patients with CFS is of great economic importance. This will eliminate unnecessary special investigations and

Figure 5



inappropriate therapy – both costly and frustrating to patients. The awareness of primary healthcare workers for FS and depression should be improved.

The chronic nature was clearly illustrated.

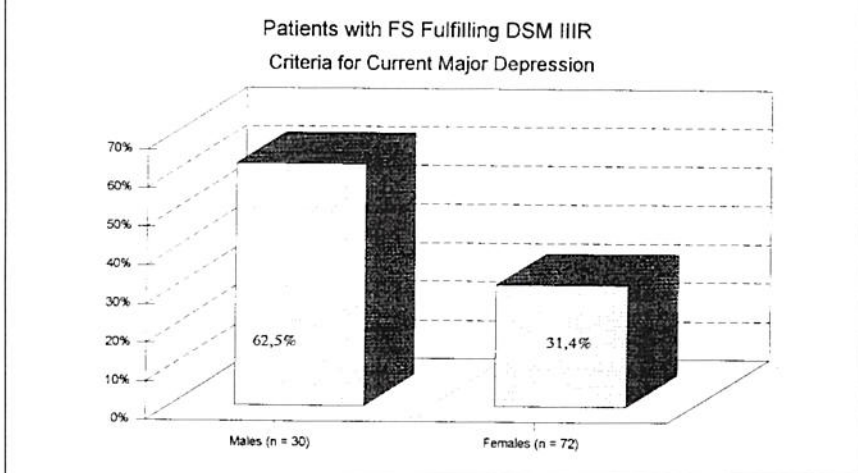
Both CFS and FS share some overlap of symptoms with major depression and may share a similar neurochemical background, but there are, however, also distinct clinical and therapeutic differences.

The great similarity of the clinical symptomatology of CFS and FS in this study suggests a closely related or perhaps identical pathophysiological mechanism.

Co-morbidity of depression should always be explored.

(The clinical presentation and manage-

Figure 6



ment of patients with Fibromyalgia syndrome will be reviewed in an article by the same author in a future edition of SA Family Practice.)

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Dr Gordon-Smith will, during his term of office, be supported by the following honorary officers and members of council:

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