

Assessment and Treatment of Depression and Anxiety in patients with ME/CFS: A Psychiatric Perspective

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This paper outlines a conceptualization of and approach to the treatment of psychological symptoms in people with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) especially symptoms of depression and anxiety. This paper was written due to a perceived need to articulate an approach is under-represented in the medical literature. There are many psychological symptoms not represented in this paper. Only the most common are considered, however the approach discussed may serve as a template for other symptoms.

The sources are: a thorough review of the medical literature, the author's experience in a psychiatric practice restricted to patients with ME/CFS, Fibromyalgia and Multiple Chemical Sensitivity and the input of several experienced clinicians and persons suffering from ME/CFS. This topic remains controversial and there are other approaches. However this approach is recommended by being both evidence based and well accepted by patients. The author has given permission for this paper to be posted on the web sites of FM-CFS Canada (<http://www.fm-cfs.ca/index.html>) and the ME-FM Action Network of Canada (<http://www.mefmaction.net>) with the goal of increasing discussion and debate and improved outcome for patients.

1. Contents

This paper will

- Define ME/CFS
- Explain why ME/CFS is not a psychiatric disorder despite that a significant subgroup of patients have psychological symptoms.
- Outline how to differentiate the symptoms of ME/CFS from those of depression and anxiety
- Suggest a treatment approach for common psychiatric symptoms in patients with ME/CFS
- Summarize psychological treatment issues in patients with ME/CFS
- Summarize issues relevant to children and adolescents with ME/CFS
- Discuss the treatment issues of drug sensitivity and the utility of Cognitive Behavior Therapy and Graded Exercise in patients with ME/CFS

2. What is ME/CFS?

Myalgic Encephalomyelitis (ME) was first defined by Acheson in 1959 based on 14 documented outbreaks in several countries and hundreds of sporadic cases of illness characterized by: headache, myalgia, paresis, mental symptoms, low or absent fever and no mortality (Acheson, 1959). This was in contrast to polio and other paralyzing conditions prevalent at the time. The disorder was later operationalized by Ramsay to include the triad of: muscle weakness and fatigability, CNS involvement and symptom fluctuation. In early reports, lability of emotions was an almost constant feature ranging from slight irritability to violent manifestations.

In 1988 after an outbreak of illness at Incline Village Nevada, the CDC formed a committee that named the disorder "Chronic Fatigue Syndrome" and suggested criteria for a research definition (Holmes *et al*, 1988). These criteria were found clinically problematic and in 1994 the CDC revised their definition publishing what is commonly referred to as the "Fukuda criteria" (Fukuda *et al*, 1994). The 1994 definition requires fewer physical signs than the 1988 definition and therefore selects for less severely ill patients (De Becker *et al*, 2001). The Fukuda criteria require only one mandatory symptom: disabling fatigue of greater than 6 months duration. In addition there must be at least 4 of: impaired memory/concentration, sore throat, tender lymph nodes, muscle pain, multi-joint pain, new headache, unrefreshing sleep and post-exertional fatigue. The Fukuda criteria have been criticized for not requiring post exertional symptom exacerbation as mandatory. It is increasingly accepted that this is the core symptom of ME/CFS.

Cooperation between the National ME-FM Action Network of Canada and Health Canada resulted in the 2003 publication of what is referred to as the "Canadian Consensus Guidelines for ME/CFS" (Carruthers *et al*, 2003). The Guidelines describe a clinical case definition, clinical evaluation, prognosis, occupational disability and treatment protocol for patients with ME/CFS. The full document may be viewed at: <http://www.mefmaction.net/documents/journal.pdf>. The Canadian Consensus definition requires the concurrent presence for at least 6 months of five major criteria: disabling fatigue, post exertional malaise and/or fatigue, sleep dysfunction, pain and two or more neurological/cognitive symptoms. In addition there must be two of: autonomic, neuroendocrine and immune manifestations (Carruthers *et al*, 2003). The inclusion of autonomic, neuroendocrine and immune symptoms as minor criteria seems to increase specificity as this definition selects fewer patients with psychiatric disorder and more patients with severe physical symptoms than the Fukuda criteria (Jason *et al*, 2005).

There are two other definitions in the literature: the Oxford Criteria (Sharpe *et al*, 1991) and the Australian Criteria (Lloyd *et al*, 1990). Both of these are so broad as to make it impossible to ensure a homogeneous group. Both fail to exclude patients with primary psychiatric diagnoses in the absence of physical symptoms. Neither is recommended for either clinical or research use.

Patients who suffer from symptoms consistent with CFS dislike the name because it trivializes the severe, incapacitating mental and muscle fatigue that is experienced. Though ME and CFS differ in definition, many groups including the group of international researchers who published the Canadian Guidelines refer to the disorder as: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) encompassing patients with both epidemic and sporadic onsets and patients with mild to extremely severe symptoms. The term ME/CFS will be used in this paper.

Clinical Variability

The clinical profile of ME/CFS is of unremitting and fluctuating mental and physical fatigue, non restorative sleep, cognitive dysfunction and other symptoms. The severity can be

- mild - still able to work/study full time though with effort and rest on weekends
- moderate - able to work or study part time with effort,
- severe - unable to work/study and requires assistance to live independently
- extreme – unable to live independently, virtually house and sometimes bedbound

The course of ME/CFS is variable. A hallmark feature of the disease is prolonged reactive exacerbations following activities with recovery time of greater than 24 hours.

Comorbidity

In the largest epidemiological study to date, it was shown by Jason and colleagues in Chicago that only 40% of the community CFS cohort had CFS in the absence of other disorders (Jason *et al*, 1999). Sixteen percent of the cohort also had Fibromyalgia Syndrome (FM), a disorder of chronic generalized muscle pain and joint stiffness with the presence on physical exam of at least 11/18 designated tender points. Forty-one percent had Multiple Chemical Sensitivity (MCS), a disorder defined as a chronic condition with symptoms that recur reproducibly in response to low levels of exposure to multiple unrelated chemicals. The symptoms improve or resolve when the incitants are removed. The symptoms of ME/CFS occur in multiple organ systems and no other disorder can account for the symptoms (1999). The disability found in patients with ME/CFS is often aggravated by the comorbidity of ME/CFS with FM and MCS as well as other medical and psychiatric disorders if present. A full history must be taken to identify all of the symptoms which impact on function and health.

Prevalence

The prevalence of CFS in population based epidemiological studies using the Fukuda criteria is 0.24 - 0.42% (Reyes *et al*, 2003; Jason *et al*, 1999). This means that in Canada there are approximately 125,000 people meeting the CDC criteria for CFS. American estimates of annual lost productivity is \$20,000 per person. In Canada annual lost productivity is estimated at \$2.5 billion (Reynolds *et al*, 2004). This is a huge burden on the economy and suggests that more

research funding should be directed towards understanding the prevention, diagnosis and management of ME/CFS.

Etiology

Despite 20 years of research and over 3000 published peer reviewed papers, the etiology of ME/CFS remains unclear. It is now generally accepted that ME/CFS is an umbrella term for a heterogeneous group of disorders and that one etiology or mechanism may not be found. This has led for a call for careful subtyping using known correlates if future research (Jason *et al*, 2005).

Never the less, certain abnormalities are consistently reported. These include: autonomic nervous system dysfunction using the objective measure of heart rate variability (Cordero *et al*, 1996) or tilt table testing (Rowe & Calkins, 1998). Several studies have shown deficiency in natural killer cell function (Whiteside & Friberg, 1998; Ogawa *et al*, 1998) in ME/CFS. Studies of cytokine profiles have generally suggested a Th1 to Th2 shift. Th1 is the aspect of the immune system that controls intracellular infection. An intriguing finding is that of increased levels of 37 kDa RNase L in patients with ME/CFS but not in healthy controls or patients with depression (Suhadolnik *et al*, 2004; Suhadolnik *et al*, 1994). This is an abnormal variant of the enzyme normally produced by cells to kill RNA viruses. This variant is not found in healthy people and is not subject to the normal cellular control mechanisms. Further supporting relevance to clinical presentation is that 37 kDa Rnase L levels correlate with exercise capacity in patients with ME/CFS (Snell *et al*, 2002).

Many intracellular infections have been shown to be more prevalent in people with ME/CFS compared with healthy controls. These include the Human Herpes viruses: EBV (Lerner *et al*, 2004), CMV (Lerner *et al*, 2004), HHV6 (Ablashi *et al*, 2000) and HHV7. Other intracellular pathogens including: Mycoplasma (Choppa *et al*, 1998), Chlamydia (Nicolson *et al*, 2003) and Coxiella (Wildman *et al*, 2002) (Ayres *et al*, 1998) have consistently been found in high proportions. The post Q fever fatigue syndrome caused by Coxiella sp. may prove to be a close clinical model for CFS (Ayres *et al*, 1998). Finding so many intracellular infections suggests that the infections are secondary to an immune dysfunction. Cognitive function (DeLuca *et al*, 1997; Michiels *et al*, 1999; Tiersky *et al*, 2003), brain blood flow on SPECT (Ichise *et al*, 1992; Costa *et al*, 1995; Fischler *et al*, 1996) and quantitative EEG are all abnormal (Flor-Henry *et al*, 2003). Hormonal studies show hypo-function at the level of the hypothalamus. It has recently been suggested that this may be secondary to chronic illness rather than causative of ME/CFS (Cleare, 2004).

3. ME/CFS is NOT a psychiatric disorder

The first question in the minds of many psychiatrists will be whether ME/CFS is a psychiatric disorder. If so why isn't it in the DSM? If not why are guidelines being written for psychiatrists?

In the early 90's there were a spate of papers proposing that CFS was a psychosocial condition. This view is summarized by the following quote from Abbey and Garfinkle: "majority of its (CFS) sufferers are experiencing primary psychiatric disorders or psychophysiological reactions and the disorder is often a culturally sanctioned form of illness behavior" (Abbey & Garfinkel, 1991). The research does not support that view. It is increasingly clear that CFS is **not** a primary psychiatric disorder though psychological symptoms may be prominent, The World Health Organization has classified ME/CFS as a neurological disorder.

Rates of psychiatric disorder in CFS are similar to rates in other chronic medical conditions. If ME/CFS were a psychiatric disorder, psychiatric symptoms should be universal. However when the specific criteria are used for patient selection, and when community samples are surveyed, the prevalence of known psychiatric disorders among patients with ME/CFS is similar to the rates in patients with other chronic, disabling medical conditions such as rheumatoid arthritis; approximately 30 - 40% (Thieme *et al*, 2004; Hickie *et al*, 1990; Fiedler *et al*, 1996). By comparing groups of patients using different definitions of the disorder, it is shown that the definition has a clear effect on who is considered to have the disorder (Jason *et al*,

2004). Studies which have reported higher prevalence rates of psychiatric disorder have had sampling biases eg. selecting those who seek treatment at specialty centers or inappropriate use of survey instruments (Thieme *et al*, 2004). Furthermore, the type of questionnaire used in a study can significantly affect the prevalence (50% using the DIS vs 25% using the SCID) of psychiatric disorders reported in ME/CFS populations (Jason *et al*, 2003). For research purposes the Structured Clinical Interview for DSMIV developed by Spitzer *et al* is recommended in ME/CFS studies (Spitzer *et al*, 1992;Williams *et al*, 1992).

Rates of personality disorder in ME/CFS are not elevated

If ME/CFS were a psychiatric disorder one would expect that rates of personality disorder would be elevated. However people with CFS have similar rates of personality disorder (approx 10%) as the general population and lower rates than that found in depression (Thieme *et al*, 2004;Pepper *et al*, 1993;Saltzstein *et al*, 1998;Chubb *et al*, 1999). There are studies which report higher rates of psychological distress using the MMPI (Blakely *et al*, 1991) in CFS as compared with healthy controls. However the MMPI assumes a normal state of physical health and subjects with chronic illness tend to load high to the "hyperchondriasis" and "hysteria" scales resulting in false positives (Pincus *et al*, 1986;Goldenberg, 1989). It has been argued therefore, that the MMPI is not an accurate assessment in people with chronic medical conditions.

There is a group of psychiatrists who write that ME/CFS is caused and exacerbated by faulty self-perception and avoidance behavior. The faulty beliefs are described as: "the belief that one has a serious disease; the expectation that one's condition is likely to worsen; the "sick role," including the effects of litigation and compensation; and the alarming portrayal of the condition as catastrophic and disabling" (Barsky & Borus, 1999). It should be noted that neither this paper written by Barsky nor any of the others with similar views are evidence based, they are the personal opinions of the authors.

The genetics of depression and ME/CFS are independent

The genetics of CFS vary independently from those of depression suggesting that the two disorders do not have a similar genetic risk (Thieme *et al*, 2004) (Hickie *et al*, 1999).

Physiological measures differ between ME/CFS and Depression

In depression the hypothalamic-pituitary-adrenal axis is stimulated and difficult to suppress with dexamethasone, whereas the opposite is true in ME/CFS. In group data, urinary cortisol levels are low and serum cortisol levels decrease sharply and for long periods of time with oral dexamethasone (Scott & Dinan, 1998). It is unclear whether these changes in hypothalamic-pituitary-adrenal axis function are primary or secondary (Cleare, 2004). Electrodermal skin response and digital skin temperature are different in ME/CFS than in depression (Pazderka-Robinson *et al*, 2004). Quantitative EEG profiles discriminate between ME/CFS, depression and healthy controls (Flor-Henry *et al*, 2003).

Illness severity and not psychological factors predict outcome

If ME/CFS were a psychiatric disorder, one would expect psychological symptoms to predict outcome. However this is not the case. Studies consistently show that symptom severity at onset and whether one meets full criteria for CFS predict prognosis in ME/CFS (Darbishire *et al*, 2005) but psychological symptoms and cognitive beliefs do not (Deale *et al*, 1998;Jones *et al*, 2004a) (Darbishire *et al*, 2005).(White *et al*, 1998)

As the research data builds that ME/CFS is in fact a serious, often disabling condition, the abandonment of the psychological model of causation is understandable. In this author's conceptualization, psychological symptoms and psychiatric disorder in ME/CFS is most often secondary to the loss of health, lifestyle, social role and financial means as well as the social stigma of having a serious disabling but poorly understood illness.

4. Diagnosing and Treating Depression

Four types of depressive disorder commonly seen in ME/CFS

1. Reactive grief due to loss of health, social connections, family support, financial capability, career and uncertainty regarding all of these
2. Biological change in mood/cognition as part of the disorder of ME/CFS (similar to mood change in MS or Parkinson's disease and as reported in epidemic ME)
3. Comorbid depressive disorder
4. Mood change due to medication or food or withdrawal from either

The following chart identifies some of the clinical keys in differentiating ME/CFS from Depression. Of course none of these are always true. There are always exceptions.

Clinical Presentation	
CFS	Depression
Infectious onset in > 80% of cases	Rarely follows infectious illness
Fatigue is necessary for diagnosis	Mood change is necessary for diagnosis
Muscle and/or joint pain and significant headaches	Not usually associated with pain symptoms
Diurnal variation with pm the worst time of day	Diurnal variation with am the worst time of day
Orthostatic intolerance, tachycardia and other autonomic dysfunctions are common (Rowe & Calkins, 1998)	No association with autonomic symptoms
Immune manifestations including tender lymph nodes, sore throat, chemical and food sensitivities	No association with immune symptoms
Loss of body thermostatic stability, intolerance to extremes of temperature	No association with thermostatic instability
Fatigue worsened by physical or mental exertion (Blackwood <i>et al</i> , 1998)	Fatigue and mood improve with exercise
Decreased positive affect (energy, enthusiasm, happiness)	Increased negative affect (apathy, hopelessness, suicidal ideation, self reproach)
Children have a better prognosis than adults	Children have a worse prognosis than adults

Consider a diagnosis of comorbid depression when:

- The depressive symptoms precede the physical disorder.
- Pessimism is generalized beyond health and illness related issues.
- The patient is stuck in depression and it is having a negative effect on treatment.

Teaching the patient careful self observation skills and using daily ratings of mood and other symptoms can help distinguish patients whose mood problems are biological and associated with ME/CFS from other types of mood changes. Biological mood changes which are part of the illness vary in parallel with physical symptoms, while other types of mood problems are more independent. Ask the patient: "does it ever happen that you are having a good day with respect to energy but a bad day with respect to mood". If the patient says "yes" then the mood disorder is independent of the ME/CFS and may be secondary to illness or other life events. If the answer is "no", the depression is likely a concomitant of ME/CFS

**Diagnosing Major Depression in the presence of ME/CFS
(Must tick all four boxes for diagnosis)**

Does the subject currently have:

5 or more of following symptoms:

1. depressed mood (sad or empty) most of the day nearly every day
2. decreased interest or pleasure in most activities nearly all the time
3. significant (>5% change) weight loss or weight gain not due to dieting and/or change in appetite (up or down)
4. insomnia or hypersomnia nearly every day
5. objective (notable by others) psychomotor agitation/retardation nearly all the time
6. fatigue or loss of energy nearly every day
7. feelings of worthlessness or excessive guilt nearly every day
8. decreased ability to think or concentrate or indecisiveness nearly every day

Duration of > 2 weeks

Level of functioning decreased from before

Must have either depressed mood or loss of interest or pleasure

The last point should prevent patients with physical symptoms only being classified as depressed. According to DSM IV if the subject has physical symptoms only i.e. items 3,4,5,6,8 only the diagnosis of depression cannot be made. If the subject has symptoms 3,4,5,6,8 AND has items 1,2 or 7 then the criteria are met.

Additional Pointers

- The sine qua non of clinical depression is a persistent low or irritable mood and anhedonia, guilt or self blame
- The sine qua non of CFS is severe, prolonged fatigue post-exertional malaise, sleep dysfunction, pain, neurological/cognitive, autonomic, neuroendocrine and immune manifestations.
- Ask which activities the patient enjoys when s/he feels well or better. If s/he can't think of anything, consider depression.
- Those who think of ME/CFS as "fatigue" and forget the importance of the other symptoms will be risk of misdiagnosing patients with depression leading to inappropriate treatment recommendations.

Management of depressive reactions to ME/CFS and its effects

- The best antidepressant for patients with ME/CFS is improved physical health & quality of life.
- Validation by physician of life circumstances is NB.
- Ask about suicidal ideation. Anecdotally, suicide is the #1 cause of death in CFS
- Supportive counseling/therapy regarding career, peer group and family issues. Lack of social support is reported in patients with ME/CFS and lack of social support is correlated with poorer quality of life (Schoofs *et al*, 2004).
- Active support of patient obtaining sustainable school/work conditions or leave of absence from school or work, disability insurance, etc.

Treatment of comorbid depression in CFS

- Treat similarly to depression in the absence of CFS.
- No antidepressant has been shown to improve the core symptoms of ME/CFS (White & Cleary, 1997), (Vercoulen *et al*, 1996)
- Low dose tricyclics are often useful for sleep rehabilitation and pain management but rarely have antidepressant effect at tolerable doses.
- Psychotropic medication may be tried if symptoms are interfering with sleep and rehabilitation.
- Antidepressant doses usually need to be lower than in other patients. Some patients will be unable to tolerate any antidepressant
- CBT to help a patient overcome unrealistic assumptions is generally helpful as it is in other depressed patients.

- CBT to convince a patient that s/he does not have a physical disorder is disrespectful and inappropriate.

5. Diagnosing and Treating Anxiety

Four types of anxiety are commonly seen in ME/CFS

1. Anxiety about health e.g. prognosis, cause of symptoms or unpredictability of symptoms.
2. Anxiety as a result of the impact of having ME/CFS e.g. loss of social connections, loss of family support, financial hardship, loss of career. Anxiety about being denied disability payments is common.
3. Biological anxiety as part of the physical disorder of ME/CFS.
4. Comorbid anxiety disorder; GAD and social anxiety being the most common.
5. In the proportion of patients with ME/CFS who also have Multiple Chemical Sensitivity, anxiety can be in reaction to drug or volatile organic exposure or fear of such exposures.

Consider comorbid anxiety disorder when:

1. Anxiety preceded the physical disorder
2. Anxiety is generalized and not limited to health and health care related issues
3. Patient is unable to cope with or resolve anxiety over the long term

Diagnosing Generalized Anxiety Disorder in the presence of ME/CFS (must tick all 6 boxes for diagnosis)

Does the subject have:

Excessive worry on most days (about many things, not just illness)

Duration > 6 months

Difficulty controlling worry

Must have 3 or more of the following symptoms:

- feeling restless or keyed up
- easily fatigued
- difficulty concentrating/mind going blank
- irritability
- muscle tension
- sleep disturbance (difficulty falling asleep or unrefreshing sleep)

Symptoms cause clinically significant distress/impairment

Symptoms are NOT due to direct physiological effects of a medical condition (eg. ME/CFS)

Most subjects with ME/CFS will have 3 or more of the physical symptoms of GAD and many are worried about their health and related problems. However most will not be excessively worried about life every day and/or have difficulty controlling their worry. Therefore the necessary inclusion of items 1, 3 and 6 differentiates ME/CFS patients from psychiatric cases.

Management of anxiety reactions to ME/CFS and its effects

- Validation of ME/CFS diagnosis by physician is therapeutic.
- Spend time listening to patient's worries and explaining why certain diagnoses may or may not be relevant.
- Undertake appropriate investigation and referral to rule out feared diagnoses such as cancer, MS or heart disease.
- The best antidote to anxiety is improvement in physical health.
- Institute appropriate management e.g. ensuring adequate sleep, adequate diet, adequate rest, treatment of other syndrome components such as postural hypotension, tachycardia, reactive hypoglycemia, irritable bladder and bowel which can be very anxiety provoking.
- Offer supportive counseling/therapy regarding career, peer group and family issues.
- Offer active support of patient obtaining sustainable school/work conditions or leave of absence from school or work, disability, insurance etc.

Treatment of comorbid anxiety disorder in CFS

- Treat similarly to anxiety in the absence of CFS.
- CBT to help patient cope with and face unrealistic fears is generally helpful as in other anxiety patients.
- CBT to convince patient that s/he does not have a physical disorder is disrespectful and inappropriate.
- Patient's energy level, cognitive dysfunction and sensitivity to medication must be taken into account.
- Psychotropic medication may be required to ensure sleep and prevent excess energy drain.
- Use low doses of SSRI's and avoid benzodiazepines if possible.
- Benzodiazepines are useful in patients who have anxiety as well as movement disorders such as restless legs syndrome.

6. Psychological issues

Grief → Acceptance

Grief is a universal issue for people with ME/CFS. The losses are numerous and individual. People should be asked about how their lives have changed since becoming ill and be given a chance to describe the process of adjustment. Primary losses are of financial independence, in some cases physical independence, role in family, role as a worker and bread winner, loss of support from family and friends who do not understand the illness and loss of self esteem from all of the above. Allowing grief opens the possibility for acceptance. Acceptance of chronic illness and limitations does not mean giving up hope for improvement or even total recovery. Rather it is acceptance of current circumstances so that one can cope with them realistically rather than remaining in anger, denial and depression.

Coping

Patricia Fennell MSW describes four phases of coping with chronic illness: Her model borrowing heavily from the Kubler-Ross model of coping with death is used widely by therapists working with patients with ME/CFS. Fennell stresses that the four phases are not followed in linear fashion and that people move between phases and aspects of more than one phase may be evident at one time. Given the fluctuant and unpredictable nature of ME/CFS, there are always new challenges. Maintaining an integrated, "phase 4" position is not a realistic goal. The goal is to be flexible enough to adapt to the significant changes imposed by chronic illness with ME/CFS as they occur.

Phase 1 Crisis – This occurs whether onset is sudden or gradual. Crisis develops when one's values, self concept, and life goals are called into question i.e. you are too sick to function as you used to. The action goal of phase 1 is to batten down the hatches, take stock of resources, adjust expenditure and try to minimize immediate pain. A tool of phase 1 is to begin a personal narrative. The spiritual goal of phase one is to learn to allow one's suffering.

Phase 2 Stabilization – One reaches phase two when one's physical condition has stabilized somewhat due to the adjustments one has made in phase 1. However people in phase 2 continue to think they can function as they used to and continue to overestimate their personal resources. They have relapses as a result. The action goal of phase 2 is to focus on what one really needs. The tools of phase two are learning, restructuring and educating others. The spiritual goal of phase 2 is to learn to regard one's suffering with compassion.

Phase 3 Resolution – The work of Phase 3 is grief work, the challenge to obtain insight and develop meaning in the face of huge losses. In phase 3 patients are becoming more self reliant and self trusting with regard to health decisions. Humor and play become possible again. The action goal of phase three is to stand for oneself without apology. The spiritual goal of phase three is to meet one's suffering with respect.

Phase 4 Integration - Becoming more than one's illness frees up emotional energy for other meaningful tasks and interactions. One begins to connect the personal to the world view and

embrace the mystery and unknown of life. The spiritual goal of phase 4 is to integrate your suffering into a whole life.

Empowerment

As in all chronic medical conditions, long term health status for patients with ME/CFS depends upon patients learning to observe and trust their body's reactions to psychological and physical stressors, experiment to see what works best for them and then make changes accordingly. Self management is accepted as the most cost effective and successful approach to chronic illness (Lorig *et al*, 2000) and the Stanford model of self management developed by Lorig is widely used. From a psychotherapeutic perspective one can observe a change in emotional status when a patient has the moment of realization that his/her actions do make an impact on physical and psychological health. With that sense of self empowerment, the ability to change one's circumstances, people cope better even if their physical condition or life circumstances do not improve.

Stress management

One neuroendocrine manifestation of ME/CFS is "loss of adaptability and worsening of symptoms with stress". This indicates that homeostatic failures occur among patients with ME/CFS. Small physical stressors such as walking up a flight of stairs or being in a cold room can cause exhaustion, pain and other symptoms. Psychological stressors such as interpersonal issues which were easily managed before becoming ill can feel monumental. In part this reaction may be due to the stress of altered lifestyle, occupational, and financial circumstances over which the patient has little control and which may not be easily resolved. Many problems in life can be solved by more effort or more money. However, patients with ME/CFS often do not have sufficient reserve of energy or money to cope with small increases in ordinary stressors. The need for basic stress management skills becomes greater as reserve is depleted. Some useful suggestions are:

- Prioritize energy for solving problems that are solvable and put aside worries about things that cannot be changed.
- Use written reminders for tasks and messages to avoid confusion and errors.
- Listen to your body and pace activities according to the body's feedback rather than a predetermined schedule or activity goal.
- Plan rest days between appointments and visits if necessary.
- Enlist the support of friends and family.
- Believe in oneself and use self talk to get through hard times.
- Note and address thought patterns which are counterproductive.

7. Special Cases: Children and Adolescents

Children and adolescents do get ME/CFS though the prevalence is lower than in adults (Jones *et al*, 2004b; Patel *et al*, 2003; Bell *et al*, 2001). In young people the onset is typically acute and infectious and the symptoms severe. However, as in adults, the onset can also be gradual and difficult to diagnose. If managed carefully, the outcome is better for young people with ME/CFS than for adults. The reason for this is unclear.

Children are less able than adults to describe their symptoms and reactions to trials and are more vulnerable to outside pressures. In the absence of obvious secondary gain, children and adolescents with ME/CFS should be encouraged to develop self management skills as appropriate for their developmental age. It is important to remember that as of yet there are no objective tests to prove severity of fatigue or pain. An extreme adverse consequence of disbelief by health care professionals is that supportive parents are thought to be facilitating the child's avoidance and children have been removed from their families due to assumed medical neglect (Hammond, 1999). This iatrogenic trauma should be avoided.

Many young patients with ME/CFS are too ill to attend school full time or even part time. Some are limited by mental and physical fatigue, some by pain, some by cognitive dysfunction, some by sensory overload, many by a combination of these. Pushing through the symptoms often leads

to worsening of symptoms and a longer recovery time. In general, if a child is not able to recover from a day's activity by the next day that level of activity will not be sustainable. Just as adults may need work accommodation, children and adolescents may need accommodation at school such as reduced school hours, a quiet place to work and extended time to finish courses and exams.

8. Treatment issues

Drug dosage and Drug sensitivity

It is widely accepted that some patients with ME/CFS are more sensitive to the adverse effects of medication than most healthy people. They share this trait with chronic pain and fibromyalgia patients. Tricyclic antidepressants for example are useful for sleep maintenance and to decrease central pain sensitivity. However many patients with ME/CFS benefit from and tolerate only very low doses, an average of 10 – 40 mg qhs. Some patients benefit from as little as 2 – 4 mg per dose. SSRIs which are generally well tolerated for the treatment of depression and anxiety are not tolerated by a subgroup of ME/CFS patients. The mechanism of these reactions is unknown. However to push the dose higher in the face of adverse effects in these patients is to court disaster and to weaken the therapeutic relationship. In the case of severe and/or persistent adverse effects one must lower the dose, add a low dose of a second agent or change drug class. In some cases drug sensitivity can severely hamper the treatment of the subset of these patients who have psychiatric disorders.

Utility of CBT/Graded Exercise in ME/CFS

Although Cognitive Behavior Therapy (CBT) is widely recommended for patients with ME/CFS, it is far from clear whether cognitive behavior therapy is helpful for most patients. The rationale for using CBT in ME/CFS is that inaccurate beliefs (that etiology is physical) and ineffective coping (activity avoidance) maintain and perpetuate CFS morbidity (Deale *et al*, 1997;Sharpe *et al*, 1996). However, it has never been proven that these illness beliefs contribute to morbidity in CFS. Where correlations do exist it is possible, even likely, that beliefs in physical etiology are correct and that activity avoidance is necessary for the more severely ill (Lloyd *et al*, 1993;Ray *et al*, 1995).

Of the 6 reported studies using CBT in "ME/CFS" two selected patients as defined by the Oxford (Deale *et al*, 1997;Sharpe *et al*, 1996) one using the Australian criteria (Lloyd *et al*, 1993) and one using the Fukuda criteria "with the exception of the criterion requiring four of eight additional symptoms to be present" (Prins *et al*, 2001). These methods of patient selection allow for considerable heterogeneity and inclusion of psychiatrically ill patients with fatigue. Therefore, the results may not be applicable to the average Fukuda or Canadian defined patient. Of the remaining two studies using valid selection criteria, one found no benefit of CBT (Friedberg & Krupp, 1994). The only study reporting benefit (improved functional capacity and decreased fatigue) was conducted in adolescents (Stulemeijer *et al*, 2005).

It is important to note that no CBT study has reported that patients have been improved enough to return to work nor have they reported changes in the physical symptoms of CFS eg. muscle pain, fever, lymphadenopathy, headache or orthostatic intolerance. Furthermore, clinical experience suggests that trying to convince a patient with ME/CFS that s/he does not have a physical disorder and should not rest when tired leads to conflict in the doctor-patient relationship and poor outcome for the patients. Therefore it would be prudent to await further research before recommending this CBT approach.

Despite the fact that worsening of symptoms after exercise is a compulsory criteria for diagnosis of ME/CFS, graded exercise programs have often prescribed for such patients. Presumably these recommendations are made on the assumption that exercise will be accompanied by improved aerobic capacity, increased anaerobic threshold and improved exercise tolerance. However, in patients with ME/CFS, neither exercise tolerance nor fitness has been shown to improve with exercise programs. This may be connected with abnormal responses to exercise in people with ME/CFS. The resting heart rate of patients is elevated, and maximum oxygen uptake is reduced

compared with healthy sedentary controls (Riley *et al*, 1990;Farquhar *et al*, 2002;Fulcher & White, 1997;De Becker *et al*, 2000). SPECT scan brain analysis indicates worsening of hypoperfusion (Goldstein, 1993) and decreased cerebral blood flow (Peterson *et al*, 1994) after exercise. Decreased cognition (Blackwood *et al*, 1998;LaManca *et al*, 1998), decreased pain threshold (Whiteside *et al*, 2004;Whiteside *et al*, 2004) and reduced maximal muscle contraction (Paul *et al*, 1999) are also reported.

According to the recent Cochrane Collaboration metanalysis (Edmonds *et al*, 2004) there are five studies on exercise and ME/CFS that are methodologically sound. However three of these studies used the Oxford criteria for patient selection which requiring only fatigue of 6 months duration and no physical symptoms for diagnosis. One of the five studies excluded patients with sleep disrupted sleep (Fulcher & White, 1997) meaning that virtually all patients seen in clinical practice would be excluded. There are two studies using valid diagnostic criteria and both report improved fatigue by self report (Chalder Fatigue Scale) (Wallman *et al*, 2004;Moss-Morris *et al*, 2005). Neither of these report follow-ups past 12 weeks. Neither report on core physical symptoms of ME/CFS such as pain, unrefreshing sleep, infective, autonomic, neurological or endocrine symptoms. It is unclear whether these findings are applicable to severely ill patients as none of these patients are well enough to participate in studies. It will require more study on a broader group of patients, reporting all symptoms to discern if graded exercise affects the core symptoms of ME/CFS.

9. Conclusions

ME/CFS is a multi-systemic potentially disabling medical disorder. Although a gold standard diagnostic test is not available, the medical literature is clear that ME/CFS is not the same as depression or any other psychiatric disorder. It is important to discern whether a patient has ME/CFS, a psychiatric disorder or both. Using the Canadian Criteria (a clinical diagnostic tool), the signs and symptoms of ME/CFS can clearly be distinguished from psychiatric disorders in most cases. Being knowledgeable in both physical and psychological medicine, psychiatry plays an important role in the overall management of ME/CFS. Psychiatrists can offer accurate diagnosis and treatment of psychiatric disorders, assessment of the patients' phase of coping and adaptation and psychotherapeutic support. Comorbid psychological symptoms such as depression and anxiety occur in ME/CFS and are often secondary to loss of health, financial means and role in society. When present, psychiatric symptoms should be treated similarly to any other patient while paying attention to the increased incidence of drug side effects in this population and decreased energy available for therapy. Self management seems important in the long term outcome for patients with ME/CFS and empowerment facilitates self management. Research on psychosocial interventions is in its infancy. While awaiting further research it is important to first do no harm.

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