FEATURES

Chronic Fatigue Syndrome: Implications for Women and their Health Care Providers During the Childbearing Years

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Chronic fatigue syndrome is a complex debilitating medical disorder that affects approximately 4 million persons in the United States, predominantly women. There has been little scientific exploration about the experience of pregnancy, childbirth, and the postpartum period for women with this disorder. A review of the literature and current research findings addressing the epidemiology, diagnosis, symptoms, and treatment of chronic fatigue syndrome are presented, as well as the currently available data regarding the experience of women with chronic fatigue syndrome anticipating or experiencing pregnancy and the postpartum period. Expert opinion is presented along with current evidence to provide guidelines for the care of women with chronic fatigue syndrome during pregnancy, labor and birth, lactation, and the postpartum period.

INTRODUCTION

Chronic fatigue syndrome (CFS) is a serious, complex, often debilitating medical disorder that predominantly affects women. Women of childbearing age with CFS are commonly concerned about the potential consequences of pregnancy on their health and the health of their children. Misperceptions about CFS as being “all in your head,” limited resources, and the lack of education among health care providers have not only been barriers to effective diagnosis and treatment of CFS but also have created a social context of illness that adds a significant burden for affected individuals and their families. As increased awareness and better diagnostic tools for CFS emerge, health care providers are likely to encounter more women with CFS.

Many health care providers are not aware of the current evidence regarding CFS. Therefore, this article provides a literature review of the epidemiology, diagnosis, symptoms, and treatment of the disorder. The literature review revealed a dearth of information addressing the experience of pregnancy, childbirth, and the postpartum period in women with CFS. Therefore, expert opinion is presented along with current evidence to provide guidelines for clinical practice in the care of women with CFS who are anticipating or experiencing pregnancy and the postpartum period.

EPIDEMIOLOGY OF CHRONIC FATIGUE SYNDROME

Epidemiologic estimates indicate that up to 4 million people in the United States meet the Centers for Disease Control and Prevention (CDC) criteria for the diagnosis of CFS, and that 85% of US citizens with CFS remain undiagnosed. The disorder affects individuals of all racial, ethnic, and socioeconomic backgrounds with no difference in prevalence between rural, urban, or metropolitan populations. It is at least as common among African Americans and Hispanics as in whites. CFS strikes 3 to 5 times more women than men, with incidence in females peaking between the ages of 40 and 59 years. Children and adolescents can be afflicted with the disorder, but incidence in younger populations is less common.

A recent CDC-sponsored, population-based study in Georgia provides evidence that CFS is 6 to 10 times more common than previously estimated and is a significant public health problem in the United States. Evidence-based estimates by the CDC also indicate that CFS has severe economic impact in the United States. The disorder results in a $9 billion annual loss in productivity, not including medical costs or disability benefits, and results in a $20,000 annual loss in wages and income per family.

The nature of CFS is that it “waxes and wanes,” following a cyclical pattern of improvement alternating with unpredictable relapses of variable severity. The percentage of people who recover from CFS is unknown, although preliminary estimates are that at least partial recovery is possible in 40% to 60% of patients. Delays in CFS diagnosis and treatment may lead to a more complicated course of illness and poorer prognosis for recovery.

Complications related to CFS may have serious health implications beyond those currently known. Nancy Klimas, MD, an immunologist and internationally recognized CFS and HIV researcher, cautions that although the...
long-term consequences of CFS are unknown, loss in the function and number of natural killer (NK) cells in persons with CFS may increase the risk for certain types of malignancies in women, particularly cancers related to viral reactivation such as human papillomavirus (HPV)-induced cervical cancer (personal communication, May 5, 2007). A DePaul University study of causes of death among persons with CFS echoes Klimas’ concern that women with CFS may have an increased incidence and younger onset of cancer from abnormalities in immune function. Also in support of Klimas’ concern, preliminary studies indicate that the expression of CD26 activation marker, which acts as a costimulatory molecule for T and NK cell activity, is significantly depleted in persons with CFS compared to healthy controls. Furthermore, host susceptibility to HPV-induced cervical cancer and resistance to chemotherapy in advanced cases may be increased by a loss in function and number of NK cells and depleted T-lymphocyte levels.

**DEFINITION AND ETIOLOGY OF CHRONIC FATIGUE SYNDROME**

“Recent research from scientists around the world demonstrates multiple abnormalities of the brain and autonomic nervous system, a state of chronic immune system activation, a strong hereditary component, characteristic gene and gene expression patterns, and various abnormalities of energy metabolism in people with chronic fatigue syndrome.”

—Anthony Komaroff

Historically, CFS has been misunderstood and trivialized to the extent that even health care providers have doubted whether it really exists. Although the causes of CFS remain elusive, scientific evidence from more than 3000 internationally based research studies have shown unequivocally that CFS is a real physiologic medical condition and not a manifestation of depression or some other somatoform disorder. Studies also indicate that many persons afflicted with CFS do not have any diagnosable psychiatric disorder. The majority of people with CFS have not experienced depression before the onset of CFS but may become depressed from the profound impact of a chronic disabling illness on their lives. This impact may be compounded by the manner in which a person with CFS is regarded by the health care provider. In a meta-ethnographic analysis of 20 qualitative studies of the experience of persons with CFS and doctors caring for them, the investigators found that the skepticism with which CFS is regarded can negatively impact an affected individual’s self-identity and increase social withdrawal and isolation.

A model of CFS pathogenesis that is gaining acceptance by scientists and CFS experts is that when genetically vulnerable individuals are exposed to a triggering event, such as infection, traumatic injury, emotional trauma, hormonal changes, environmental conditions and/or chemical exposure, the usual hypothalamic-pituitary-adrenal (HPA) axis and sympathetic response to such physiologic stress is dysregulated. This abnormal stress response plus the cumulative wear and tear on the body from these triggering factors results in what is termed a high allostatic load. The clinical manifestation of the high allostatic load may be CFS with its multisystem effects.

Although symptom severity varies between individuals, all people with CFS are functionally impaired. Studies by the CDC indicate that the level of disability experienced by persons with CFS can be equal to disability experienced by persons undergoing chemotherapy or with other disabling chronic conditions, such as multiple sclerosis, end-stage renal disease, and heart disease.

Now that science has accepted that CFS is a legitimate medical disorder, research efforts are focusing on defining the physiologic mechanisms of the disorder and discovering causes and effective treatments. Ongoing genetic studies at the University of Utah from a large population database have identified “high-risk” CFS pedigrees. Genomic CFS research is revealing the involvement of genes connected to HPA axis activity, the sympathetic nervous system, and immune function. Other genomic studies have revealed that persons with CFS have a disordered expression of genes that are important in energy metabolism.

A number of studies suggest that the severity of CFS symptoms is positively related to the degree of immune system activation, as is similarly found in autoimmune disorders like multiple sclerosis and lupus. A recently published study investigated the role in CFS of nuclear factor-kappa beta (NF-κB), the major intracellular mechanism in white blood cells that regulates inflammation and oxidative stress. In a comparison of the production of NF-κB in unstimulated, tumor necrosis factor-α (TNF-α) and phorbolmyristate acetate (PMA)-stimulated peripheral blood lymphocytes of 18 persons with CFS and 18 age-sex matched controls, the researchers found that the production of NF-κB is significantly higher in persons with CFS.

In addition, factors that increase produc-
tion of NF-κB, such as viral and bacterial infections, physical exhaustion, and psychologic stress, may also be the causes of CFS.12 Similarly, a blinded study of immune function in CFS showed that persons with CFS (n = 57) have abnormalities in the ribonuclease L (RNase L) pathway, an enzyme-mediated mechanism in the body that fights infection, when compared to controls (healthy subjects, n = 28; persons with depression or fibromyalgia, n = 25).18 The results of this study indicated that the presence of a higher level of smaller molecular weight RNase L found in persons with CFS (88%) versus controls (28%) may help to ultimately identify a biomarker for CFS.18

Significant advances have been made in identifying a subset of persons with postinfective onset of CFS, with herpesviruses, enteroviruses, Ross River virus, and Q fever being among the suspected causative agents.19–21 In a prospective cohort study of 253 individuals with Epstein–Barr virus (EBV), Ross River virus, and Q fever infection, investigators found that approximately 12% of all the study subjects later developed postinfection fatigue syndrome and CFS, regardless of the original infectious agent, supporting the idea that viruses may trigger CFS in at least a subset of affected individuals.21

In another recent study using endoscopy and stomach biopsy of CFS individuals with prominent gastrointestinal symptoms, investigators found evidence of enteroviral infection in 80% of 165 subjects with CFS compared to only 20% of 34 controls (P < .001).20 These findings provide further evidence that infections may trigger or perpetuate CFS in a subset of affected individuals.

Research is beginning to investigate the symptom of “brain fog,” a term sometimes used by persons with CFS to describe memory and concentration problems. In a population-based study of 43 patients with CFS and 53 matched non-fatigued controls, the relationship between subjective report of mental fatigue and cognitive dysfunction in CFS was measured by a battery of computerized tests. The investigators found a strong correlation among persons with CFS in subjective reports of mental fatigue and objective measurement of cognitive impairment in sustained attention and spatial working memory, suggesting that mental fatigue is an important component of cognitive dysfunction in CFS.22 Other studies have examined fatigue and cognitive problems with chronic fatigue on a biochemical level.25 In an effort to elucidate the neurobiologic effects of CFS and identify potential biomarkers for the illness, Nestadt et al.23 used magnetic resonance imaging technology called proton magnetic resonance spectroscopic imagining (H MRSI) in a cross-sectional study of 16 persons with CFS, 16 healthy controls, and 16 persons with generalized anxiety disorder (GAD). The investigators found that ventricular lactate levels were significantly elevated in patients with CFS compared to persons with GAD and healthy controls (297% and 348% higher, respectively; P < .001). Additional chemical variations could be found in the occipito-hippocampal and other regions of the brain in individuals with CFS. In all 3 groups, lactate levels positively correlated to level of fatigue (P < .001). Elevated ventricular lactate levels suggest mitochondrial dysfunction and/or anaerobic energy conversion in the brain of individuals with CFS as cells utilize glucose for energy in the absence of adequate oxygenation.23

DIAGNOSIS, SYMPTOMS, AND COMORBID CONDITIONS

The diagnosis of CFS is challenging for a variety of reasons: CFS lacks a diagnostic laboratory test or biomarker; many people with CFS do not look sick despite profound disability; symptoms may vary from person to person and even day to day in an individual; and fatigue and other CFS symptoms are common in many other illnesses. Thus, CFS is a diagnosis of exclusion.4

A case definition of CFS was internationally accepted and published in 1994 and continues to provide the standard for diagnosis of CFS in adults.24 The International Chronic Fatigue Study Group, a committee of CFS experts, advocates revisions in the application of the current case definition to research because aspects of the case definition are ambiguous and have contributed to the heterogeneity and difficulty in studying the CFS population.25 In 2006, a pediatric CFS case definition and a reliable assessment instrument to aid clinicians in the diagnosis of CFS in young people was published.26

To be diagnosed with CFS, a person must experience a significant reduction in their previous ability to perform one or more aspects of daily life in work, school, household, or recreation. All people suffering from CFS experience severe, all-consuming mental and physical fatigue that is not relieved by rest. The fatigue can be worsened by minimal physical or mental exertion. Although the formal diagnosis of CFS requires fatigue of at least 6 months’ duration in adults and 3 months in children, the entire symptom complex must be considered rather than fatigue alone in making a diagnosis.4,26

According to the CDC, a thorough medical history, physical examination, mental status examination, and laboratory tests must be conducted to identify any underlying or contributing conditions that require treatment. Figure 1 shows an algorithm for the diagnosis of CFS in adults, while Table 1 shows some exclusionary laboratory tests.

Orthostatic intolerance, an umbrella term that includes the conditions of neurally mediated hypotension and postural orthostatic tachycardia syndrome, commonly occurs with CFS, particularly among adolescents.27–30 Neurally mediated hypotension occurs when the autonomic nervous system, which controls heart rate and blood pressure response, misinterprets what the body needs during an upright posture and sends a message to the heart to slow down and lower the blood pressure, the
opposite of what the body needs. Postural orthostatic tachycardia syndrome is defined by an increase in heart rate of more than 30 beats per minute or an increase in heart rate exceeding 120 beats per minute within 5 to 10 minutes when changing from a supine to upright position. The symptoms of orthostatic intolerance are listed in Table 2.

Factors that cause orthostatic intolerance in CFS are poorly understood and may include complex interactions between adrenal hormones, HPA-axis dysregulation, and autonomic dysfunction of heart rate, heart muscle contraction and relaxation, peripheral vasodilation and constriction, reduced cerebral perfusion, and volume deple-

### Table 1. Laboratory Tests Used in the Diagnosis of Chronic Fatigue Syndrome*

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Reprinted from the Centers for Disease Control and Prevention Web site (<a href="http://www.cdc.gov/cfs">www.cdc.gov/cfs</a>).</th>
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<tr>
<td>Urinalysis</td>
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<td>Complete blood count (CBC)</td>
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<td>Leukocyte differential</td>
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<td>Erythrocyte sedimentation rate (ESR)</td>
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<td>Total protein</td>
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<td>C-reactive protein</td>
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<td>Alanine aminotransferase (ALT)</td>
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<td>Aspartate transaminase serum level (AST)</td>
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<td>Alkaline phosphatase (ALP)</td>
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<td>Blood urea nitrogen (BUN)</td>
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<tr>
<td>Electrolytes</td>
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<td>Creatinine</td>
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<td>Albumin</td>
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<td>Globulin</td>
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<td>Glucose</td>
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<td>Calcium</td>
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<td>Phosphorus</td>
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<td>Thyroid function tests: Thyroid-stimulating hormone (TSH) and free T4</td>
<td>Reprinted with permission from Stewart.</td>
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*Chronic fatigue syndrome is a diagnosis of exclusion; these tests are done to rule out another etiology for symptoms.

### Table 2. Symptoms of Orthostatic Intolerance

<table>
<thead>
<tr>
<th>Symptom Description</th>
<th>Reprinted with permission from Stewart.29</th>
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<tbody>
<tr>
<td>Lightheadedness</td>
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<tr>
<td>Headache</td>
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<tr>
<td>Fatigue</td>
<td></td>
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<tr>
<td>Weakness</td>
<td></td>
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<tr>
<td>Exercise intolerance</td>
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<td>Hyperpnea/dyspnea</td>
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<tr>
<td>Nausea</td>
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<td>Abdominal pain</td>
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<tr>
<td>Anxiety/palpitations</td>
<td></td>
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<tr>
<td>Sweating</td>
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<tr>
<td>Tremulousness</td>
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Cardiology testing with the tilt-table test can aid in the diagnosis of orthostatic intolerance with CFS.27,28,30

Many comorbid conditions with CFS have US Food and Drug Administration (FDA)-approved drugs or evidence-based treatment options. In addition to the orthostatic syndromes of neurally mediated hypotension and postural orthostatic tachycardia syndrome, these conditions include metabolic syndrome, hormone imbalances or dysregulation, vitamin D and vitamin B12 deficiencies, irritable bowel syndrome (IBS), gastroesophageal reflux disease (GERD), and celiac disease.31

**TREATMENT**

**Current Status and Future Directions**

Because there is no known cure, CFS treatment evolves around supportive management. Few therapies thought to be helpful for CFS have been tested for efficacy in double-blind, placebo-controlled trials. A meta-analysis of 59 randomized controlled trials and 11 non-randomized controlled trials of interventions for CFS found that graded exercise therapy and cognitive behavioral therapy have the clearest evidence of benefit.32 The four randomized controlled trials that assessed the effectiveness of pharmacologic treatment had inconclusive results.32 Furthermore, there are no drugs approved by the FDA for the treatment of CFS; therefore, most drugs used to treat CFS are done so “off-label.” Although there are no evidence-based standards established in the pharmacologic treatment of CFS, the CDC includes pharmacologic therapy as an important option in providing the “aggressive” symptom management many persons with CFS need to increase functional ability and quality of life.4 Therefore, expert opinion is included in the following summaries as the currently best-available guide for pharmacologic and other treatments for CFS.

Until the causes of CFS are better defined, Lucinda Bateman, MD, one of the few clinicians in the United States who specializes in the treatment of CFS and fibromyalgia, recommends following these general principles of supportive management: diagnose and treat comorbid conditions; prioritize and treat the major disabling symptoms, but revisit diagnosis and economize medications; and encourage patients to “pace” activity to prevent deconditioning without precipitating relapse.31 Furthermore, Dr. Bateman considers pacing as the most effective way to reduce global CFS symptoms and minimize “flares” or relapse. A randomized controlled trial to evaluate the effectiveness of adaptive pacing therapy as treatment for CFS is currently underway in the United Kingdom.32

Treatment will eventually be directed more at the cause of illness as subsets of persons with CFS from specific etiologies are identified.31 For example, a randomized, double-blind, placebo-controlled clinical trial is currently underway at Stanford University to further investigate the effectiveness of the antiviral drug valganciclovir (Valcyte; Roche Pharmaceuticals, Nutley, NJ), in the treatment of CFS. In a previous open-label study, 9 out of 12 (75%) persons with chronic debilitating fatigue with central nervous system dysfunction and high IgG antibody titers against EBV and human herpesvirus-6 (HHV-6) experienced near total resolution in symptoms with a significant decrease in EBV viral capsid antigen IgG titer and a decrease, although not statistically significant, in HHV-6 IgG titers after a 6-month treatment with valganciclovir.33

**Medication Options**

Dr. Bateman tailors treatment to focus on the most bothersome symptoms in her patients, which can include fatigue, sleep disturbance, pain, orthostatic intolerance, and/or mood. The presence of a symptom does not necessitate treatment if the symptom is not significantly bothersome.31 Dr. Bateman and other CFS experts recommend economizing the use of medications by using one drug to target several symptoms. For example, anticonvulsant drugs like gabapentin (Neurontin; Pfizer, Inc., New York, NY) can be used effectively to treat sleep, mood, and pain in some CFS patients. Selective serotonin reuptake inhibitors (e.g., sertraline HCL and fluoxetine HCL) and serotonin and norepinephrine reuptake inhibitors (e.g., venlafaxine and duloxetine) can be used to improve cognition as well as to treat mood, pain, and sleep.31,34

Fatigue is best managed by reduction in activity and lifestyle adaptations, but medications such as modafinil (Provigil; Cephalon, Inc., Frazer, PA), adderall (Dexedrine; GlaxoSmithKline, Philadelphia, PA), and methylphenidate HCL (Ritalin; Novartis Pharmaceuticals, New York, NY) may also be considered.31,34 Buproprion XL (Wellbutrin XL; GlaxoSmithKline, Philadelphia, PA) may be helpful with concentration and attention difficulties related to mental fatigue.31,34

Sleep disturbance may be minimized with simple sleep hygiene measures (Table 3). However, these measures may be inadequate, and medication to initiate or sustain sleep may become necessary. Sleep “initiators” used for CFS includes zolpidem (Ambien; Sanofi-Aventis, Bridgewater, NJ), eszopiclone (Lunesta; Sepracor Inc., Marlborough, MA), and ramelteon (Rozerem; Takeda Pharmaceuticals, Deerfield, IL). Sleep “sustainers” include trazodone (Desyrel; Bristol-Myers Squibb, Princeton, NJ), tricyclic antidepressants, benzodiazepines, and muscle relaxants.31,34

**Medications for Orthostatic Intolerance**

Pharmacologic options to minimize orthostatic intolerance include the drugs midodrine (ProAmatine; Shire Pharmaceuticals, Wayne, PA), fludrocortisone (Flori-
nef; Bristol-Myers Squibb, Princeton, NJ), and propranolol XL (Inderal; Wyeth Pharmaceuticals, Madison, NJ), although a randomized drug trial indicated fludrocortisone as monotherapy for orthostatic intolerance can be ineffective. Additional treatment options may also be considered. Administration of an intravenous (IV) infusion of 1 L of normal saline for several consecutive days to weeks to improve orthostatic intolerance and fatigue with CFS has been used successfully by Dr. David Bell, an internationally recognized expert on adult and pediatric CFS, as well as by other CFS clinicians. The mechanism by which this intervention is effective is unknown and warrants scientific inquiry. There is some evidence in cardiology literature that increasing intravascular volume with intravenous normal saline can alter the autonomic response that triggers neurally mediated syncope, a potential endpoint of neurally mediated hypotension with CFS. A case report in the literature cites improved performance during graded exercise testing in a woman with CFS after daily treatment with 1 L of 0.9% saline via a central venous line over a period of 417 days. Improvement in a variety of cardiopulmonary measures as well as subjective report by the study participant of improved activity tolerance, reduced muscle fatigue and pain, and improved orthostatic tolerance were cited. Although double-blind studies for efficacy are lacking, the use of intravascular volume expansion for relief of fatigue in CFS patients with orthostatic intolerance is regarded as a “reasonable option” in the scientific literature.

Nonpharmacologic interventions for orthostatic intolerance include increasing oral fluids; increasing dietary salt or salt tablet supplementation up to 2000 mg/day as tolerated; avoiding overheating and prolonged standing; wearing support hose; and, if able to tolerate exercise, performing physical activity in a supine or seated position, or in water.

**Physical Activity**

Graded activity and exercise are advisable to avoid deconditioning without causing relapse. With graded exercise, an individual is instructed to start any activity slowly and to gradually increase the level and duration of the activity. Persons with CFS should be taught that all exercise must be followed with rest in a ratio of 1:3 (1 minute of exercise followed by 3 minutes of rest). Some individuals cannot tolerate longer than 2 to 5 minutes of exercise without risking a relapse. A systematic Cochrane review of five randomized controlled trials investigating the effect of exercise on CFS found that exercise therapy can lessen fatigue and improve physical functioning, but persons with CFS had a higher dropout rate than controls. The authors conclude that exercise therapy may benefit some persons with CFS, that rest and pacing may be more acceptable than exercise therapy to individuals with the disorder, and that additional randomized studies are needed to measure outcomes such as adverse effects and quality of life over time. Caution in prescribing exercise therapy to persons with CFS is supported by research findings that indicate the functional capacity of individuals with CFS, as measured by cardiopulmonary exercise testing, can range from no impairment to severe impairment, and that relapse in physical symptoms of CFS may be delayed by as much as 5 days after exercise.

**Alternative Therapies**

Alternative therapies, such as acupuncture, meditation, and biofeedback, have been helpful to some persons with CFS, although scientific evidence to support these treatments is lacking. Yoga and tai chi may be effective for individuals with CFS who can tolerate more activity. Few clinical trials address the efficacy of nutritional and herbal supplements in the treatments of CFS. The meta-
analysis of interventions for CFS previously cited in this paper indicated that one or two trials showed that essential fatty acid and magnesium supplementation had beneficial effects in the reduction of symptoms.  

**Psychosocial Considerations**

Persons with CFS and their families face numerous challenges. Variable and unpredictable symptoms cause difficulty in day-to-day planning; limited stamina interferes with activities of daily living; memory and concentration problems seriously impact work or school performance; and uncertain prognosis, loss of independence, loss of economic security, and alterations in relationships with family and friends oftentimes complicate the illness experience. Validation of the illness experience and support for how disabling symptoms can be paramount in establishing a therapeutic relationship between the health care provider and individuals with CFS. A therapist can be helpful for persons with CFS struggling with the grief, anger, guilt, depression and anxiety that commonly accompany any chronic illness. The use of cognitive behavioral therapy has been helpful for some with CFS, but evidence indicates results are inconsistent.

Because employment and schooling may be profoundly affected for persons with CFS, it is important to realize that the disorder is a disabling condition for which affected individuals may be protected under the Americans with Disabilities Act. Primary health care providers are usually needed to participate in the disability application process for people with CFS and careful documentation of clinical care is paramount to facilitate the benefit process.

**CHRONIC FATIGUE SYNDROME DURING PREGNANCY, CHILDBIRTH, AND THE POSTPARTUM PERIOD**

“We still have no definitive idea of the risks involved in pregnancy for women with chronic fatigue syndrome. The suggestion that it’s okay to be pregnant is not yet substantiated by science. I will not tell my chronic fatigue syndrome patients to postpone pregnancy. But I must tell them that we don’t know enough about the dangers.”

—R.C.W. Vermeulen, MD, PhD, endocrinologist and gynecologist at the Chronic Fatigue Syndrome Research Center in Amsterdam

Minimal research addresses reproductive issues in women with CFS. Whether or not the course of CFS changes during or as a result of pregnancy, or whether or not the experience of pregnancy and childbirth is different for women with CFS, remains mostly unexplored. Current pregnancy-related recommendations are mostly based on the opinions and observations of CFS experts and will likely remain anecdotal until more interest in reproductive issues in women with CFS is generated among women’s health researchers and clinicians. Nevertheless, women of childbearing age with CFS are commonly concerned about the potential consequences of pregnancy on their health and the health of their children. These issues are very relevant to women’s health care providers.

Women with CFS and their providers need information and guidelines for care during pregnancy, childbirth, and the postpartum period, yet the scant scientific evidence currently available is integrated with expert opinion to provide the following summaries. Expert opinion is shared from CFS experts Dr. Nancy Klimas (personal communication, May 5, 2007), Dr. Lucinda Bateman (personal communication, June 14, 2007), and Dr. Charles Lapp.

**Effects of Pregnancy on Chronic Fatigue Syndrome**

M.T. is a 27-year-old married gravida 2 para 1001 who established care with the author at 12 weeks’ gestation. She has been ill with CFS since the age of 18. She described her experience of normal pregnancy fatigue compared to fatigue with CFS as follows: “If it’s normal pregnancy fatigue, I might feel too tired to get up and brush my teeth, but I can make myself do it. If I’m fatigued from CFS, my body feels heavy like I can’t move and I really cannot make myself get up to brush my teeth.” Throughout the current pregnancy, she described less severe relapses in terms of frequency and duration as compared to her pre-pregnancy norm, but never achieved the feeling of complete wellness that she had experienced with her first pregnancy.

The most comprehensive study to date investigating the reciprocal relationship between CFS and pregnancy was published by Schacterle and Komaroff in 2004. Through a retrospective self-reported questionnaire, the investigators compared outcomes for 86 women with a cumulative total of 252 pregnancies that occurred before or after the onset of CFS. In “many cases,” pregnancy predated the time of data collection “by several years.” The investigators found that 41% of women experienced no change in CFS symptoms during pregnancy, 30% noted improvement of symptoms, and 29% experienced a worsening of CFS symptoms during pregnancy. The researchers were unable to identify factors that may influence whether an individual woman with CFS will improve or worsen during pregnancy.

CFS experts Nancy Klimas, Lucinda Bateman, and Charles Lapp report slightly different findings in clinical practice. Their reports are based on relatively small numbers of women with CFS whom they have followed throughout pregnancy, accentuating the current scarcity of evidence-based information. In the approximately 20 women Dr. Klimas followed throughout pregnancy, improvement in CFS symptoms during pregnancy was almost universal, in some cases to the point of total remission, despite typically more severe early pregnancy
nausea and vomiting requiring antiemetics used during chemotherapy. In Dr. Bateman’s clinical observations of the approximately 6 women she followed throughout pregnancy, women commonly report feeling less ill with CFS symptoms during pregnancy despite experiencing typical pregnancy discomforts. Dr. Lapp reports that 25 out of 27 patients in his practice who became pregnant while they had CFS felt better during pregnancy. Dr. Lapp proposes that lessening in severity of CFS symptoms during pregnancy may be related to immune system and hormonal changes of pregnancy.

Effects of Chronic Fatigue Syndrome on Pregnancy

The presence of illness with CFS impacted the decision of whether or not to bear children in 21% of Schacterle and Komaroff’s survey respondents, in either choosing not to parent or not to have additional children. The most common reason for the decision to remain childless or limit family size was concern that disability caused by CFS would impair parenting ability. CFS may adversely affect fertility, although research findings addressing this area are very preliminary. Polycystic ovarian syndrome and related anovulatory cycles are reported more often in women with CFS compared to controls. Additionally, dysmenorrhea is almost universal in women with CFS. Dysmenorrhea is a common symptom of endometriosis and preliminary studies are indicating that endometriosis, with a well-known potential for adverse effects on fertility, may be more common in women with CFS.

Schacterle and Komaroff found that the rate of first trimester spontaneous miscarriage was 4 times higher than normal in women with CFS. The authors acknowledge that this higher rate may be caused by confounding variables and that further investigation is needed to validate this finding. The authors found no significant difference in the rate of other pregnancy complications, such as preeclampsia, gestational diabetes, preterm labor, or low birth weight infants, in women who became pregnant after the onset of CFS. While there is compelling scientific evidence for a genetic predisposition to CFS, there is no evidence that a pregnant woman can directly transmit CFS to her fetus. Schacterle and Komaroff found that developmental delays were reported more often in offspring of women who became pregnant after as compared to before the onset of CFS. The hypocortisolism that occurs with CFS and the role of maternal cortisol secretion in fetal growth and development has been hypothesized as an explanation for this increased rate of developmental delays, although Schacterle and Komaroff are careful to note that their finding needs validation by larger, prospective studies with control populations.

Reciprocal Effects of Chronic Fatigue Syndrome and Labor and Birth

There are no scientific studies that directly address whether CFS directly affects labor and birth, or whether labor and birth affect CFS. In the absence of evidence-based reviews, one could infer from the well-documented abnormal physiologic response to stress in persons with CFS that a prolonged and more painful labor increases risk of relapse for a woman with CFS, an inference supported by the opinion of all three CFS experts cited in this paper.

The importance of adequate hydration during labor for normal progress and overall maternal and fetal well-being may be amplified in the laboring woman with CFS. According to Dr. Bateman, stress and exhaustion cause the autonomic nervous system in a CFS patient to become more dysregulated and “almost chaotic,” precipitating the likelihood of relapse. Bateman advises measures like maintaining vascular volume with intravenous fluid and pain and stress reduction techniques during childbirth to help prevent or moderate this response. The use of epidural anesthesia may be considered to conserve energy and prevent relapse, especially in the case of prolonged labor. A case report of a woman with severe CFS whose 9-hour labor culminated in a low forceps delivery because of maternal exhaustion is noted in the British literature; this intervention is used with declining frequency in the United States.

Postpartum Recovery with Chronic Fatigue Syndrome

Again, there is no scientific evidence that comprehensively defines the relationship between CFS and a woman’s experience during the postpartum period. Schacterle and Komaroff found that 50% of patients surveyed reported worsening of CFS symptoms, 30% reported no change, and 20% reported improvement during the postpartum period. Dr. Klimas observed that her patients with CFS typically do well postpartum until 3 to 6 months after delivery, at which time a relapse in CFS symptoms typically occurs, and is oftentimes severe. Dr. Klimas hypothesizes that relapse at this time may be related to physiologic reduction in red cell mass and blood volume that increased in pregnancy, and/or to the cumulative stress of interrupted sleep and demands of caring for an infant. Dr. Lapp reports a similar incidence in worsening of CFS symptoms in one-third of his patients who had given birth.

Dr. Bateman considers the potential for a severe postpartum CFS relapse to be the biggest issue to address with prospective parents. Similar to Dr. Klimas, Dr. Bateman hypothesizes that hormonal changes combined with the physical and emotional demands of caring for an infant, particularly nocturnal sleep disruption, magnify.
the risk of relapse during the postpartum period for women with CFS. The rate of postpartum CFS relapse in mothers who are breastfeeding as compared to bottle-feeding has not been examined, nor have there been any studies to explore any influence CFS may have on initiation and maintenance of milk supply. Considering that CFS impacts multiple body systems and that pituitary function has been implicated, lactation effects of CFS seem possible. Lapp raises the question of whether or not a woman with the subset of post-infective viral-induced CFS can transmit the offending virus to her infant through breast milk. Although this possibility seems remote, it warrants scientific inquiry.

M.T. had a normal spontaneous vaginal hospital-based delivery at term after a relatively rapid 5.5-hour labor using hypnobirthing techniques, with her husband and midwife in attendance. M.T. was able to consume oral fluids throughout labor and requested that intravenous fluids be deferred until after delivery. Immediately thereafter, she was given an intravenous bolus of 1 L of lactated ringers followed by an infusion of normal saline that was arbitrarily continued at 150 mL/hr for the first 6 hours postpartum, at the advice of her chronic fatigue specialist. M.T. was discharged home with her infant at 36 hours postpartum after an uncomplicated hospital stay. M.T. breastfed her infant until 2 weeks postpartum, at which time she weaned because of a concern that the rigors of nighttime feedings would trigger a CFS relapse. After weaning, she resumed taking the medications fludrocortisone and midodrine that she had stopped with the pregnancy. (During the first 2 years of illness with CFS, M.T. was diagnosed with orthostatic intolerance after a positive tilt table test revealed an intake BP 110/61 HR 81 and after 34 minutes, presyncopal symptoms with an upright BP of 55/45 P77.) By 12 weeks postpartum, M.T. began to experience an increase in chronic fatigue syndrome symptoms, which developed into a severe relapse by 14 weeks postpartum. She retrospectively identified a similar relapse that had occurred at 6 months postpartum following her first birth.

**Medications for Chronic Fatigue Syndrome During Pregnancy and Lactation**

Women with CFS who become pregnant and breastfeed their infants should be prepared to discontinue some of the medications commonly prescribed for CFS symptom relief. Midodrine (Proamatine; Shire Pharmaceuticals, Wayne, PA), an α-agonist commonly prescribed for women with CFS-related orthostatic intolerance, has not been studied in human pregnancy or lactation. Midodrine is not recommended, because it has the potential to interfere with uteroplacental circulation, and since it is concentrated in fat cells in breast milk, could potentially cause hypertension in a breastfed infant. Fludrocortisone (Florinef; Bristol-Myers Squibb, Victoria, Australia), a fluorinated corticosteroid, is also commonly prescribed for CFS-associated neurally mediated hypotension either alone or in combination with midodrine and also has not been studied for use during human pregnancy. However, fludrocortisone is considered theoretically safe during pregnancy because of its similarity to cortisone, which has not been associated with an increased risk of birth defects aside from the 3% to 5% background risk of birth defects that can occur with any pregnancy. Fludrocortisone is compatible with breastfeeding in doses of 0.1 to 0.4 mg/day. Other medications commonly used for CFS to treat sleep disturbances, memory, cognition, pain, and mood may or may not be continued safely during pregnancy and lactation and should be addressed on a case by case basis with usual consideration for the risk-to-benefit ratio.

**IMPLICATIONS FOR CLINICAL PRACTICE**

Health care providers are likely to encounter more women in practice with CFS as awareness, education, and diagnostic tools for the illness improve. Although the complexities of establishing initial diagnosis and treatment of CFS are beyond the usual scope of midwifery practice, it is prudent as providers of women’s health care to increase awareness and knowledge of this disorder that affects a preponderance of women and so profoundly impacts their lives and the lives of their families. Midwives can initiate initial diagnostic testing in women presenting with symptoms suggestive of CFS with follow-up by internal medicine or other specialists as indicated. Midwives are well-qualified to provide gynecologic and obstetric care to women with CFS with consultation, collaboration, or referral to specialists according to usual guidelines for practice. Collaboration with or referral to the woman’s primary care physician for medication adjustment or treatment related to CFS may be necessary.

**Preconception**

Preconception counseling for a woman with CFS should include explanation of the paucity of evidence regarding the reciprocal effect of pregnancy and CFS. The woman should be encouraged to discuss her plans for pregnancy with her primary care provider and make any adjustments in medications that could have potential adverse effect on pregnancy and lactation. She should be cautioned regarding the potential for a severe CFS relapse postpartum.

**Pregnancy**

If further study validates the findings of Schacterle and Komaroff and the observations of CFS experts described in this paper, symptoms should either improve or remain unchanged during pregnancy for most women with CFS. The need for CFS treatment should be lessened or similar to pre-pregnancy norms. Referral to physical therapy for muscle and joint pain can be provided, although referral to a physical therapist famil-
iar with the limited exercise tolerance of CFS is important as inappropriate therapy can trigger relapse. Intra-
venous hydration with normal saline can be considered. While this treatment carries little risk, its indication and benefit for women with CFS during pregnancy is not known. For women with orthostatic intolerance, continuing to wear compression stockings and pushing daily oral fluids may be beneficial in minimizing CFS symptoms as well as pregnancy-related discomforts. Although scientific study documenting the effects of pregnancy on orthostatic intolerance with CFS is lacking, it seems intuitive that physiologic changes of pregnancy including expanded blood volume may improve this symptom.

During pregnancy, the clinician should assess a woman’s physical and psychosocial adjustment to pregnancy. As stress from any source, physical or emotional, can exacerbate illness in a person with CFS, measures should be taken to minimize stressors. Increased assistance from a partner or other family and friends with household responsibilities, childcare, or a decrease in employment responsibilities may be especially indicated for women with CFS during pregnancy. Anticipatory guidance for building a strong network of support for the early months postpartum is paramount.

**Intrapartum**

One could extrapolate that the poor exercise tolerance and propensity for relapse in response to stress that is well documented in CFS predicts greater fatigue ability during and after childbirth in a woman with CFS, although there is no scientific evidence to validate this. The usual recommendations of ambulation and frequent position changes to facilitate labor progress may need to be moderated to conserve energy and prevent relapse in the laboring woman with CFS. Additionally, consideration may need to be given to avoid the vasodilatation effect of overly heated or prolonged showers, baths, or jacuzzis for women in labor with CFS who also have orthostatic intolerance. Continuous intravenous fluid with a volume expander like normal saline or lactated ringers solution seems advisable to maintain hydration and avoid fatigue in the laboring woman with CFS, especially if she is unable to consume much oral fluid.

Although the primary care needs of women with CFS are complex and usually warrant referral or comanagement, midwives are ideally suited to provide care related to pregnancy, childbirth, and postpartum to women with CFS. The “with woman” midwifery philosophy and care practices can result in an increase in a woman’s sense of empowerment and satisfaction with her care. In addition, this type of supportive care decreases pain and the associated emotional and physical stress of labor, and decreases the rate of childbirth complications. One could easily postulate that all of these benefits of midwifery care in childbirth can decrease the incidence or severity of CFS relapse after childbirth. Epidural anesthesia may also be advisable for women with CFS who have a more prolonged labor. The benefit of elective cesarean for women with CFS to avoid the physical stress of labor has been mentioned in self-help literature, but the advisability of this recommendation is highly debatable.

**Postpartum**

Whether the woman with CFS chooses to breastfeed or bottle-feed her infant, strong support with nighttime feedings as well as daytime meal preparation, grocery shopping, childcare, and household responsibilities is especially important during the postpartum period. Home health nursing referral may be indicated at hospital or birth center discharge to assess the level of support and adjustment of a woman with CFS once home. Anticipatory guidance for increase in energy conservation measures to avoid the 3- to 6-month postpartum relapse observed by Dr. Klimas may also be helpful.

**CONCLUSION**

“Empathy and caring have tremendous capacity to facilitate healing in a patient with an illness for which there is no cure.”

—Stuart Dreschler

CFS is a complex debilitating physiologic illness with a poorly understood etiology and no known cure. Providers of women’s health care have a responsibility to increase awareness and sensitivity regarding this disorder, which affects a preponderance of women with profound effects on the individual and her family. Providers of women’s health care have a responsibility to increase awareness and sensitivity regarding this disorder, which affects a preponderance of women with profound effects on the individual and her family. Evidence indicates that the midwife is ideally suited to provide the type of perinatal care that is most conducive to a positive childbirth experience for women with CFS. Empathy and caring, in addition to high standards for quality, evidence-based care, are among the hallmarks of midwifery care. By virtue of who we are as health care providers, midwives can make a powerful and positive impact on the health and well-being of a woman with CFS, a benefit that can extend to her entire family.

**REFERENCES**


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Appendix

In an effort to meet the pressing need for increased awareness and education among medical and lay communities regarding chronic fatigue syndrome, the Centers for Disease Control and Prevention (CDC) and Chronic Fatigue Immune Deficiency Syndrome Association of America (CFIDS) have collaborated in sponsoring the Chronic Fatigue Syndrome Provider Education Project, a comprehensive medical education program designed to provide current evidence-based guidelines for providers in the detection, diagnosis, and management of this complex illness. In November 2006, the CDC and CFIDS jointly launched a public education campaign to increase chronic fatigue syndrome awareness and detection rates. Since then, information about chronic fatigue syndrome has appeared in media outlets like NBC Nightly News and in popular magazines such as Parade, US News and World Report, and Ladies Home Journal. Contact information for the CDC and CFIDS is included in this list of resources.
Chronic Fatigue Syndrome Resources

The Chronic Fatigue Immune Deficiency Syndrome Association of America (CFIDS): www.cfids.org/cfs

Provides resources and educational materials for patients, family members, caregivers, support groups, the general public, and health care professionals.

US Centers for Disease Control and Prevention: www.cdc.gov/cfs

Identifies treatment strategies for patients, caregivers, and health care professionals.

International Association for Chronic Fatigue Syndrome (IACFS): www.IACFS.net

Promotes and evaluates research relating to chronic fatigue syndrome, fibromyalgia research, patient care, and treatment.

ME/CFS Parents: www.mecfsparents.org.uk

Provides chronic fatigue syndrome patients with self-help information regarding pregnancy and parenting.

The National CFIDS Foundation, Inc.: www.ncf-net.org

An all volunteer organization that provides support and educational support to chronic fatigue syndrome patients and caregivers.

Organization for Fatigue and Fibromyalgia Education and Research (OFFER): www.offerutah.org

Provides information on chronic fatigue syndrome and fibromyalgia treatment options, education meetings, and a health provider directory.

Co-Cure: www.co-cure.org

Provides information on chronic fatigue syndrome and fibromyalgia syndrome, and is an information exchange forum on chronic fatigue syndrome and fibromyalgia.

Journal of Midwifery & Women’s Health 2008 Award Winners

We are pleased to announce the following awards given to authors published in 2007:

Best Article of the Year Award
Air Pollution: Impact on Maternal and Perinatal Health
by Barbara Hackley, CNM, MSN, Abigail Feinstein, CNM, MSN
and Jane Dixon, PhD

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Felicia Mancini, CNM, MPH, MSN
for the article entitled
Use of the Postpartum Depression Screening Scale in a Collaborative Obstetric Practice
co-authored by Cristina Carlson, APRN, BC
and Leah Albers, CNM, DrPH, FACNM, FAAN

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