Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): Implications for Women and their Health Care Providers During the Childbearing Years

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Objectives

- Increase awareness of ME/CFS through selected “fast facts” re: history, epidemiology, symptoms, and current evidence re: cause(s)
- Provide overview of current evidence re: the experience of women with ME/CFS experiencing or anticipating pregnancy and the postpartum period, and highlight guidelines for practice.

Stigma of Illness

Social Context of Illness and Barriers to Effective Diagnosis and Treatment

- Misperceptions about ME/CFS as being “all in your head”
- Lack of education among health care providers
- Limited resources

“Fatigue is what we experience, but it is what a match is to an atomic bomb.” —Laura Hillenbrand, author of Seabiscuit and Unbroken (NYT, “An Author Escapes From Chronic Fatigue Syndrome”, February 4, 2011)

State of Evidence

Good News:

Scientific literature of over 4500 published research articles from around the world defines a number of distinct physical or biological abnormalities in ME/CFS. Research has validated that this is a real physical disorder, not a manifestation of depression or some other somatiform disorder.

XMRV debate has raised the profile of international interest in ME/CFS research.

Bad News:

- ME/CFS is a complex disease involving profound dysregulation of the CNS and immune system, dysfunction of cellular energy metabolism and ion transport, and cardiovascular abnormalities.
- Multisystem and complex disease with predominantly debilitating physical and cognitive symptoms
- Lack of consensus persists on many issues:
  - What to call it (ME, CFS, CFIDS, ME/CFS)
  - How to define illness
  - Case definitions: Holmes (1988); Fukuda (1994); Canadian (2003); International Consensus Criteria (2011)
  - No known cause or cure

CDC ME/CFS Epidemiology

- Affects at least 1 million Americans
- More common in women (3-5X), but impacts men, adolescents, and children
- More common yet less recognized in racial/ethnic minorities (incidence highest among Latinos) and in socioeconomically disadvantaged
- Majority of individuals with CFS do not have any psychiatric disorder.
- Level of disability comparable to MS, AIDS, heart disease, and stage renal failure.
- Triggering events of illness may include infections (viruses/bacteria), traumatic injury, emotional trauma (HPA axis dysregulation), hormonal changes, exposure to chemical or environmental toxins.
- Recovery rates unclear: 30% improvement in 5 yrs; 48% in first 10 yrs.
- "Recovered" individuals still had some CFS symptoms
- Prognosis improves with early diagnosis and treatment.

Symptoms

- Vary from day to day, even during course of same day, unpredictable duration/severity, follow cyclic pattern of relapse and remission.
- Individual may look well despite significant disability. “Invisible Illness”
- Post-exertional neuroimmune exhaustion is considered the cardinal symptom of illness

To meet ME criteria, an individual must have:

1. Energy production/transport symptom
2. Neurological symptoms in 3 of 4 categories
3. Immunological symptoms in 3 of 5 categories

Post-exertional neuroimmune exhaustion

1. Marked rapid physical or cognitive fatigue in response to exertion
2. Post-exertional symptom exacerbation of flu-like and other symptoms
3. May occur immediately or be delayed by hours or days
4. Prolonged recovery period of 24 hours or longer
5. Low threshold of physical or mental fatigue results in at least 50% reduction in pre-illness activity

Neurological Impairments

1. Neurocognitive: difficulty processing information (slowed thought, impaired concentration) and/or short-term memory loss
2. Pain: headaches and/or pain in muscles, muscle-tendon junctions, joints, abdomen or chest
3. Sleep disturbance: Disturbed sleep patterns and/or unrefreshed sleep
4. Neurosensory, perceptual and motor disturbances: inability to focus vision, sensitivity to light/noise, muscle weakness, etc.

Immunological Impairments

1. Flu-like symptoms (recurrent, chronic, worsen with exertion)
2. Susceptibility to viral infections with prolonged recovery
3. GI tract: nausea, abdominal pain, bloating, IBS
4. Genitourinary: urinary urgency or frequency, nocturia
5. Sensitivities to food, medications, odors or chemicals
Energy Production/Transport Impairments

1. Cardiovascular: inability to tolerate upright position
2. Respiratory: air hunger, labored breathing, fatigue of chest wall muscles
3. Loss of thermoregulatory stability: subnormal body temp., sweating episodes, feelings of cold extremities
4. Intolerance of extremes of temperature

Selected research

“Putting patients through some sort of challenge – whether it is an exercise test, a psychological stress, tilt table test – whatever – is becoming more and more a requirement than an option for CFS researchers because lab tests involving CFS patients often seem normal until a stressor is involved.”

-Dr. Jose Montoya, Harvard infectious disease expert & ME/CFS researcher

“Moderate exercise increases expression for sensory, adrenergic, and immune genes in Chronic Fatigue Syndrome patients but not in normal subjects.”


“Gene expression alterations at baseline and following moderate exercise in patients with Chronic Fatigue Syndrome, and Fibromyalgia Syndrome.”


Genetic Predisposition

“Study of a large Utah Population Database identified high risk CFS pedigrees among first, second, and third degree relatives

Found strong support for heritable contribution to predisposition to CFS.”

Albright, F., Light, K., Bissett, L., Cannon Albright, LA. Evidence for a heritable predisposition to chronic fatigue syndrome. BMC Neurol 2011; 11:62

Basics of Treatment Strategies

Per Dr. Lucinda Bateman, local ME/CFS researcher & clinician

- Pacing was the most effective tool to reduce global symptoms of ME/CFS and to prevent flares
- Diagnosis and treat comorbid conditions: Orthostatic intolerance/NMH, IBS, chronic thyroid disorders, dyslipidemia, musculoskeletal problems
- Prioritize and treat major disabling symptoms
- Revisit diagnosis and economize medications

Treatment will be directed more at the cause of illness as subsets of individuals with specific etiologies are identified. Rituximab research findings (B cell depleting chemotherapy agent used to treat lymphoma) *

Information accessed through CFIDS www.research1st.com/2011/10/19/rituximab-

Considerations for Childbearing

Women of childbearing age with ME/CFS are commonly concerned about potential consequences of pregnancy on their own health and that of their children

Whether or not the course of ME/CFS changes during or as a result of pregnancy, or whether or not the experience of pregnancy and childbirth is different for women with ME/CFS remains mostly unexplored by research.

- Current pregnancy related recommendations mostly based on opinion & observations of ME/CFS experts generated from relatively small numbers of women they have followed in practice
- Recommendations will likely remain anecdotal until more interest in reproductive issues in women with ME/CFS is generated among women’s health care researchers and clinicians

"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 Vermulen, MD, PhD, Chronic Fatigue Syndrome Research Center, Amsterdam


Effects of Pregnancy on ME/CFS
consensus of expert opinion/Schacterle and Komaroff study 2

- ME/CFS symptoms should either improve or remain unchanged during pregnancy for most women with ME/CFS. The need for ME/CFS treatment during pregnancy should be lessened or similar to pre-pregnancy norms.


Schacterle and Komaroff findings, based on retrospective self-reported questionnaire that compared outcomes for 86 women with cumulative of 252 pregnancies that occurred before or after the onset of ME/CFS:

- 41% women reported no change in ME/CFS symptoms during pregnancy
- 30% noted improvement
- 29% experienced a worsening of ME/CFS symptoms during pregnancy

Findings of ME/CFS Experts

- KLIMAS - of approx 20 women followed through pregnancy, improvement in ME/CFS symptoms during pregnancy almost universal, in some cases to the point of almost total remission despite typically more severe early pregnancy nausea/vomiting
- BATEMAN - of approx 6 women followed, women reported feeling less ill with ME/CFS symptoms during pregnancy despite experiencing typical pregnancy discomforts
- LAPP - 25 out of 27 patients with ME/CFS felt better during pregnancy

Effects of ME/CFS on Pregnancy

- 24% survey respondents stated illness with CSS impacted decision of whether or not to bear children
- Most common reason for decision to remain childless or limit family size was concern that disability from CSS would impair parenting ability
- Very preliminary studies suggest fertility impairment—PCOS, endometriosis
- Incidence rate of first trimester spontaneous miscarriage 4 times higher. Coupling BMI to result in statistical significance
- No significant difference in rate of other pregnancy complications like preeclampsia, gestational diabetes, preterm labor, or low birth weight babies
- Possible increased incidence of developmental delays in offspring of women who became pregnant after onset of CFS—related to effect of lower maternal cortisol levels on fetal growth & development
- No current evidence that CFS can be directly transmitted to fetus despite scientific evidence of genetic predisposition

References for above findings:
Reciprocal Effects of ME/CFS and Labor and Birth

Does ME/CFS directly affect labor and birth, or does labor and birth affect ME/CFS?

-No Evidence-Based Reviews

Stress and exhaustion cause ANS in person with ME/CFS to become more dysregulated and almost "chaotic", precipitating relapse (Bateman).

Inference supported by expert opinion:

- Prolonged, more painful labor increases risk of relapse for a woman with ME/CFS (abnormal physiologic response to stress in persons with ME/CFS)
- Poor exercise tolerance and propensity for relapse in response to stress that is well-documented in ME/CFS predicts greater fatigue ability during and after childbirth in a woman with ME/CFS

NO SCIENTIFIC EVIDENCE TO VALIDATE

Measures to Moderate Physiologic Stress Response

1. Hydration: Maintain vascular volume with IVF*
   - Volume expander intrapartum (Lactated Ringers or Normal Saline)
   - Continue for approximately 6 hours after delivery
   - Aims to maintain high of volume and cardiovascular function
3. Balance energy conservation with usual recommendations of ambulation and frequent position changes
4. Consider avoidance of/limits to overly heated or prolonged showers, baths, or jaccuzis (vasodilation) for women in labor with ME/CFS who also have OI


Other Measures to Moderate Physiologic Stress Response to Childbirth

5. Consider epidural anesthesia, esp. if prolonged labor
6. Advisability of elective cesarean (mentioned in lay literature) highly debatable
7. Case report in British literature of woman with severe ME/CFS whose 9-hour labor culminated in forceps delivery due to maternal exhaustion

IV Hydrocortisone

- "Stress Dose"(s) IV hydrocortisone during labor and possibly once post-delivery (suggested 25mg-50mg IV each dose)
- Experimental, considered safe and reasonable option
- Idea is that IV hydrocortisone may help prevent ME/CFS "crash" from physiologic stress of childbirth
- No scientific data on efficacy for individuals with ME/CFS

Postpartum Recovery with ME/CFS

- No scientific evidence that comprehensively defines relationship between ME/CFS and a woman's experience of postpartum period

Schachter and Komaroff
- 50% patients surveyed reported worsening of CFS symptoms
- 50% reported no change
- 25% reported improvement
Observations of ME/CFS Experts
Postpartum recovery with ME/CFS

- KLIMAS: Women typically do well until 3-6 mos postpartum at which time relapse in ME/CFS symptoms typically occurs, oftentimes severe.
- LAPP: Reports similar incidence in worsening of ME/CFS symptoms in 1/3 of his patients who had given birth.
- BATEMAN: Considers potential for postpartum ME/CFS relapse to be biggest issue to address with prospective parents.

Why is risk potential of ME/CFS relapse magnified postpartum?
- Physiologic reduction in red cell mass and blood volume that increased in pregnancy, and/or cumulative stress of interrupted sleep and demands of caring for infant (Klimas)
- Hormonal changes combined with physical and emotional demands of infant care, particularly nocturnal sleep disruption (Bateman)

Risk of ME/CFS Relapse in Mothers who Breastfeed Compared to Bottle-feed

- Not examined
- Nor are there any studies that explore any influence ME/CFS may have on initiation and maintenance of milk supply

Can women with subset of post-infective viral-induced ME/CFS transmit offending virus to infant through breast milk? (Lapp)

Medications for ME/CFS during Pregnancy and Lactation

- Medications commonly used for ME/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 risk-to-benefit ratio

- Midodrine contraindicated during pregnancy and lactation.
- Endro cortisone not studied for use during human pregnancy, but considered theoretically safe. Compatible with breastfeeding in doses of 0.1-0.4 mg/day

Conclusion

- Very little scientific information that addresses reciprocal relationship between ME/CFS & pregnancy
- Whether or not to parent is a common concern of women of childbearing age with ME/CFS
- Personal choice, based on careful consideration
- Be prepared for possible need to discontinue certain medications during pregnancy and lactation.
- Minimize stressors
- Strong network of support, especially for the early months postpartum.
“Empathy and caring have tremendous capacity to facilitate healing in a patient with an illness for which there is no cure”

-Stuart Dreschler, PhD

Resources
The Chronic Fatigue Immune Deficiency Syndrome Association of America: www.cfids.org
US Center for Disease Control and Prevention: www.cdc.gov/cfs
International Association for Chronic Fatigue Syndrome (IACFS): www.iacfs.net
Organization for Fatigue and Fibromyalgia Education and Research (OFFER): www.offerrtah.org
ME/CFS Parents: www.mecfparents.org.uk
National CFIDS Foundation, Inc: www.ncf-net.org