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Poorly understood chronic health conditions are challenging because they are usually complex and multifactorial, likely arising from the combined action of many genetic and environmental factors. Three of these conditions—chronic fatigue syndrome (CFS), fibromyalgia (FM), and multiple chemical sensitivity (MCS)—are not only often profoundly life-altering for the patient, but also may provoke a feeling of helplessness in physicians.

What do CFS, FM, and MCS have in common?

Numerous authors have noted that patients often concurrently meet the case criteria for more than one of these three conditions. They are all more prevalent in females and have many multi-system symptoms in common (see page 32, question 1).^{1,2} However, the predominant complaint in each condition differs (see page 32, question 2). There is a broad spectrum of

In this article:

- 1. What do chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity have in common?
- 2. How are these conditions diagnosed?
- 3. How do I help my patients manage these conditions?

morbidity, ranging from minor inconvenience to total disability.

The search is on for commonalities in etiologic factors and/or pathophysiologic mechanisms, with several theories in need of further testing.²⁻⁴ Given the etiologic and mechanistic uncertainties, it may be useful to view these conditions as multifactorial, with a failure of adaptation, whereby each patient's maximum tolerance for combined stressors, no matter what their source, has been exceeded. An advantage of this framework is that it fits with a patient-centred, biological, psychological, social, and spiritual approach.

For a case discussion on CFS, FM, and MCS, go to page 39.

Table 1

Things to rule out when considering CFS, FM, or MCS diagnosis

- Acute or chronic viral, bacterial, fungal, or parasitic infections
- Cancer
- · Connective tissue disorders
- · Endocrine/metabolic disorders
- · Heavy metal poisoning
- Immune deficiency
- · Neurologic disorders
- · Nutritional disorders
- · Primary psychiatric disorders
- Sleep apnea
- Substance abuse

Table 2

Basic laboratory tests

- · Complete blood cell count with differential
- Erythrocyte sedimentation rate
- Alanine aminotransferase
- Total protein
- Alkaline phosphatase
- · Calcium, phosphorous
- Glucose
- Electrolytes
- Creatinine
- Thyroid-stimulating hormone
- Urinalysis

Additional tests should be done if indicated from history, physical, and basic lab results.

Table 3

Clinical case definitions

CFS

- New onset, unexplained, persistent fatigue that substantially reduces activity
- Post-exertional malaise or fatigue
- Sleep dysfunction
- · Pain in muscles and joints
- Neurologic/cognitive manifestations
- At least one symptom in two categories: autonomic, neuroendocrine, and immune manifestations (page 32, question 1)
- The illness persists at least six months; onset is usually distinct, but can be gradual

FM

- More than three months of widespread pain (bilateral, upper and lower body, and axial)
- Report of pain by patient in 11 or more of 18 tender points, palpated with thumb or first and/or second finger at 4 kg of pressure (nail blanches)

MCS

- Symptoms are reproducible with exposure
- Chronic
- Low levels of exposure result in manifestations
- Symptoms improve or resolve when triggers are removed
- Responses occur to multiple, chemically-unrelated substances
- Symptoms involve multiple organ systems

How are CFS, FM, and MCS diagnosed?

Not only do these three conditions have many symptoms in common, but the symptoms are also common to many other conditions. For example, in general practice, up to 25% of patients present with

a symptom of unexplained fatigue.⁵ When making a differential diagnosis, consider the conditions listed in Table 1. Then, take the steps outlined on page 32, question 3. If you discover conditions other than

CFS, FM, and/or MCS, treat them and re-assess the patient.

When taking exposure history use the mnemonic CH²OPD² (Community, Home and Hobby, Occupation, Personal [exposures or stresses1. Diet and Drugs) (Download history forms from Web site at end of article).6 Note that when diagnosing CFS, and/or MCS there will usually be some physical signs. but there are no consistently abnormal physical findings. The basic laboratory testing that should be done is outlined in Table 2. There consistently no abnormal laboratory tests. You may download case criteria check*CELEBREX.
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lists from the Web site mentioned at the end of the

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article, and, if the case criteria for CFS, FM, and/or MCS are met (Table 3), you may copy these checklists and send then to insurers, as required.

What is CFS?

In 2001, an International Expert Medical Consensus Panel of Health Canada established a detailed clinical working case definition of CFS (Table 3) with a checklist (Web site at end of article) and practical diagnostic and treatment protocols.²

In a large, population-based sample of 28,000 adults, 0.5% of women and 0.3% of men suffered from CFS.⁷ Patients commonly report a severe infection as an initiating event, although there is no conclusive support for any one pathogen.

What is FM?

The American College of Rheumatology defined FM (Table 3) after carefully mapping the most common tender points (Download checklist with location of tender points from Web site at end of article). The prevalence of FM is

Table 4

Medication treatment options

Sleep

- Low-dose tricyclic (e.g., amitriptyline, 5-50 mg, doxepin HCl, 10-50 mg at bedtime)
- Try symptom-relieving medications with hypnotic effects at bedtime (e.g., diphenhydramine HCl, 25-50 mg if rhinitis or itching; dimenhydrinate, 50-100 mg orally, or by suppository if nauseated)

Pain

- Acetaminophen, 325-650 mg every four hours as needed; add codeine, 8, 15, or 30 mg, as needed (no more than 12 tablets/day)
- Amitriptyline, 5-100 mg, at bedtime, especially for FM
- Cylclobenzaprine, 10 mg three times daily for no longer than two to three weeks at a time.
- Trial: Magnesium citrate, 300 mg, twice or three times daily (reduce dose if diarrhea develops)

- Nonsteroidal anti-inflammatories sometimes help for breakthrough pain, but commonly cause gastrointestinal side-effects
- If need to progress to other narcotics, follow professional guidelines endorsed by regulatory bodies

Depression

- Selective serotonin reuptake inhibitors are the first choice, but are not effective in treating fatigue in CFS. Side-effect potential needs to be considered for each patient individually
- With tricyclic antidepressants, start low and go slow to avoid sedation and anticholinergic side-effects
- St. John's Wort, 300-600 mg three times daily with food, has a mild antidepressant effect

Infection

 If antibiotics are needed, always maintain gut flora with one cup/day of live culture yogurt or refrigerated acidophilus and bifidus culture

0.5% to 1.2% worldwide, but it is 3.4% among U.S. women.⁸ Patients often report the onset of FM after an accident.

What is MCS?

In the '70s, an apparently mild form of MCS, dubbed "sick building syndrome" (SBS), came into prominence after a Middle East oil crisis led to tightening of buildings and lowering of ventilation rates to save energy. At the same time, new off-gassing synthetic products were increasingly being used indoors. The World Health Organization described SBS as a set of multi-system symptoms, occurring with increased frequency in buildings with indoor climate problems, that improved or resolved on leaving the buildings. Some poeple began to experience similar symptoms in other locations and noted that they were sensitive to multiple commonly-encountered chemicals.

Eventually, a consensus was reached on the clinical definition of MCS (Table 3).¹⁰ A large survey confirmed that this definition distinguishes between populations of patients most and least likely to have the condition.¹¹

Population-based studies in New Mexico¹² and California¹³ revealed 2% to 6% of participants, respectively, had been diagnosed with MCS. In the California study, 16% reported they were "unusually sensitive to everyday chemicals." MCS does not appear to be an uncommon problem.

How can I help my patients?

1. Establish/enhance a therapeutic alliance by acknowledging the patient has a real illness. Avoid discrediting the patient's reported experiences and attributed causes. Validate and work with the patient

to explore different potential illness contributors. 2. Educate the patient and family about the course of the illness:

• *CFS*—The illness course can be a repeated "crash and burn" experience if the patient overextends beyond

the limitations imposed by the illness. Suggest the patient practice energy conservation and pacing.

- *FM*—The course is variable with stress. Exercising beyond tolerance exacerbates the illness.
- *MCS*—The link between exposures to each patient's triggers and his/her symptoms may be obscured if the patient has frequent, relatively low dose exposures. An addiction phenomenon may develop as the person's physiology struggles to adapt. The true trigger-symptom relationship will become apparent with

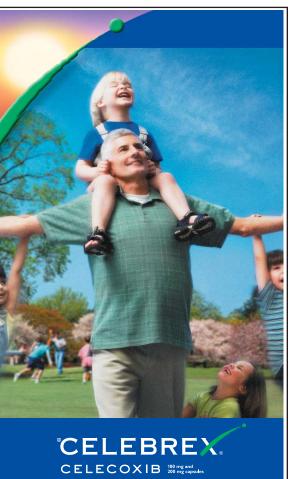
accidental or deliberate environmental changes. 14 Continued avoidance of identified triggers has been observed to help. 15

3. Point out that people have their own threshold of tolerance for a variety of illness contributors and successful treatment will entail a decrease of the patient's total body burden. Ask patients what they think the biggest contributors could be to

their ongoing ill health and which factors they think could be reduced most quickly and easily.

- 4. Relieve symptoms however possible (Tables 4, 5).
- 5. Suggest patients start or expand their own "health garden." Their health should gradually grow

as they plant and nurture the SEEDS (Sleep, Environment, Exercise, Diet/Drugs, Support) of health (Table 5).



How can I maintain my practice flow?

- Ask the patient to complete medical and exposure history forms at home rather than at the clinic.
- Complete insurance forms in the patient's presence.
- Schedule sufficient time for visits according to your and the patient's needs, at intervals the patient chooses, if possible. It may help initially to schedule short, fre-

quent visits (15 to 20 minutes), with the focus on one or two issues per visit. Have the patient write out the issues of the day to aid efficiency of the visit. Longer supportive mental health-care visits (20 to 50 minutes) may be scheduled as needed.

• Schedule visits at a time of day and/or on a day of the week when you are likely to be the least harried.

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Table 5

SEEDS of health

Sleep

- Regular bedtime in quiet, dark surroundings; relaxation tape; adequate pain relief
- Protect neck while sleeping by maintaining space between mandible and clavicle using a pillow

Environment

- Review CH²OPD² history with patient, looking for triggers or increased exposure to irritating, sensitizing, or toxic agents in various locations
- Minimize exposure to air-borne triggers and contaminants by excluding them at source, or the patient from the source, or removing them by ventilation and/or filtration
- Avoid/minimize ingestion of caffeine, alcohol, food colours, and additives
- To minimize health effects from exposure to food-borne contaminants, eat lots of fruit and vegetables, organic or local produce when possible
- When eating foods high on the food chain, organic and low-fat are best (e.g., meats, dairy products).
- Minimize intake of fish with high mercury (e.g., swordfish, shark, fresh or frozen tuna, some sportsfish)
- Drink six to eight glasses per day of filtered or spring water
- Store food and water in glass or ceramic containers

Exercise/pacing

- Use daily symptom and activity log to evaluate baseline. Develop a mobility program based on patient's tolerance. Repeatedly increase by 10% as energy improves (e.g., increase walking from 10 to 11 minutes)
- Start with stretching exercises in a.m., p.m., and after a shower, and walking with gradual buildup

Diet/drugs

- Daily multivitamin and mineral supplement (no iron if post-menopausal)
- Supplement other nutrients if low levels or if a clinical trial seems warranted
- Encourage eating at three- to four-hour intervals
- Suggest easily prepared/assimilated foods that can be frozen in individual servings

Support

Medical:

- Reframe symptoms as early warning signals
- Encourage self-care for relief of symptoms (e.g., epsom salt baths, local heat or cold applications, acupressure, massage.
- Follow available objective measurements and be vigilant for newly revealed conditions and/or new environmental contributors
- Refer carefully to sympathetic, knowledgeable professionals for specific therapeutic tasks, inform them of patient's special needs, and book followup appointment
- Ask staff not to wear scented products to work
- Offer patients with MCS the first appointment of the day, before other patients arrive wearing scented products

Self/spiritual:

- Encourage activities that help patient to feel better (e.g., yoga, Tai Chi, music, art, audio books, prayer, etc.)
- Teach progressive relaxation, deep breathing, and positive imagery for meditation
- Normalize grief over loss of former life
- Encourage search for new life meaning and purpose
- Explore avenues to achieve a sense of community (e.g., discuss connecting with supportive institutions of choice)

Family/social:

- Ask patient his/her needs, and meet with family
- Encourage brief, hands-free telephone contacts and/or e-mails with friends and relatives to relieve isolation

Occupational:

 Ask patient to obtain Material Safety Data Sheets (MSDS) if you suspect workplace contamination, and get signed consent to inform employer if any concerns; also ask patient to inform supervisor, health and safety committee, and union representative

References

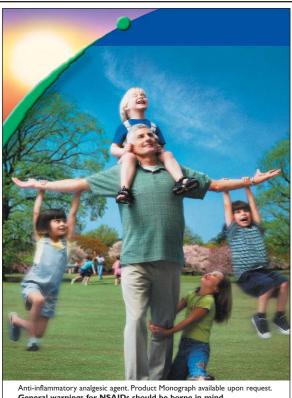
- Buchwald D, Garrity D. Comparison of patients with chronic fatigue syndrome, fibromyalgia and multiple chemical sensitivities. Arch Intern Med 1994; 154(18):2049-53.
- Carruthers BM, Jain AK, De Meirleir KL, et al: Myalgic encephalomyelitis/chronic fatigue syndrome: Clinical working case definition, diagnostic and treatment protocols. J of Chronic Fatigue Syndrome 2003; 11(1):7-115.
- Páll ML. NMDA sensitization and stimulation by peroxynitrite, nitric oxide, and organic solvents as the mechanism of chemical sensitivity in multiple chemical sensitivity. FASEB 2002;16(11):407-17.
- Bested AC, Saunders PR, Logan AC: Chronic fatigue syndrome: Neurological findings may be related to blood-brain barrier permeability. Medical Hypotheses 2001; 57(2):231-7.
- Komaroff AL, Fagioli LR, Doolittle TH, et al: Health status in patients with chronic fatigue syndrome and in general population and disease comparison groups. Am J of Med 1996; 101(3):281-90.
- Marshall LM, Weir E, Abelsohn A, e al: Identifying and managing adverse environmental health effects: Taking an exposure history. CMAJ 2002; 166(8):1049-55.
- Jason LA, Richman JA, Rademaker AW, et al: A community-based study of chronic fatigue syndrome. Arch Intern Med 1999; 159(18):2129-37.
- Wolfe F, Ross K, Anderson J, et al: The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995; 38(1):19-28.
- WHO: Indoor Air Quality Research. Euro-Reports and Studies No. 103. Copenhagen: WHO Regional Office for Europe, 1984.
- 10. 1999 Consensus on Multiple Chemical Sensitivity. Arch Env Health 1999; 54(3):147-9.
- McKeown-Eyssen GE, Baines CJ, Marshall LM, et al: Multiple chemical sensitivity: Discriminant validity of case definitions. Arch Env Health 2001; 56(5):406-12.
- Voorhees R: Results of analysis of multiple chemical sensitivities questions, 1997. Behavior Risk Surveillance System, New Mexico Department of Health, 1999.
- Kreutzer R, Neutra RR, Lashuay N, et al: Prevalence of people reporting sensitivities to chemicals in a population-based survey. Am J Epidemiol 1999; 150(1):1-12.
- Ashford NA, Miller CS: Chemical exposures, low levels and high stakes. Van Nostrand Reinhold, 1998:304.
- Lax MB, Henneberger PK: Patients with multiple chemical sensitivities in an occupational health clinic: Presentation and follow-up. Arch Env Health 1995; 50(6):425-31.

Web site

Exposure history forms and case criteria checklists can be downloaded from the Ontario College of Family Physicians Web site:

www.ocfp.on.ca

Use search bar to locate clinical tools.



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Table references available upon request—contact *The Canadian Journal of Diagnosis* at diagnosis@sta.ca.