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# **Environmental Sensitivities-Multiple Chemical Sensitivities Status Report**

**Advances in Knowledge, and Current Service Gaps**

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**Environmental Sensitivities-Multiple Chemical Sensitivities (ES-MCS) Status Report  
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# **Environmental Sensitivities-Multiple Chemical Sensitivities (ES-MCS) Status Report Advances in Knowledge, and Current Service Gaps**

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## **Executive Summary:**

There have been many advances in understanding of ES-MCS since the mid-1990's, including validation of consensus case criteria and refinement thereof, funded by the Ontario Ministry of Health; proposal and evolution of testing of etiological hypotheses; prevalence, co-morbidity and disability data from the U.S. and Canada; and development of diagnostic, therapeutic, education and health promotion strategies. Academically-affiliated, Ministry of Health-funded referral clinics have been established in Ontario and Nova Scotia, and a Paediatric Environmental Health Specialty Unit integrated into academically-affiliated paediatric services in Alberta. MCS has been recognized as a disability requiring accommodation by the Ontario (2000) and Canadian (2007) Human Rights Commissions.

While the causes and underlying mechanisms of MCS are still not fully understood, there has been increased recognition of the large number of ubiquitous chemicals to which we are all exposed in varying amounts and combinations. Their potential impacts on body defence mechanisms and the contributions of genetic and epigenetic susceptibility factors and metabolic consequences have been hypothesized and are slowly being tested. The science of toxicology has evolved substantially and there is a move away from "physical" versus "psychological" models of disease/illness to the multiple determinants of health model utilized by the World Health Organization (WHO). There is also increasing understanding of unique responses to low doses.

Prevalence surveys have now been conducted in several of the United States for both physician-diagnosed and self-reported MCS. The Canadian Community Health Survey has reported health professional-diagnosed MCS in those over the age of twelve in Canada (2.4% in adults, 3.4% in women and in those with the lowest household income), and has shed light on demographics, functional impacts, and the influence of poverty as well as of co-morbid conditions. In spite of high prevalence and morbidity, there are significant gaps in health, social and housing services.

Diagnosis of MCS in both the provincial Environmental Health Clinic in Ontario and the Nova Scotia Environmental Health Centre is accomplished by ruling out or carefully treating other conditions that could account for or contribute to the presenting symptoms, by assessing each individual's exposures, and by determining whether or not the person's pattern of symptoms fits validated consensus criteria. A few objective tests are helpful in assessing body burden of various chemicals, functional status, co-morbid allergies, and diminished blood flow to the brain.

There being a duty to provide care and not abandon patients with newly reported complex clinical conditions to their own devices, treatment for ES-MCS has evolved based upon approximately 50 years of international clinical case reports and case series, supported by treatment surveys. It is empirically evidence-informed best practice; individualized, holistic and person-centred. It focuses on assisting patients at the earliest possible opportunity to reduce their exposures to their unique symptom triggers and known hazardous chemicals, optimizing their internal processing and elimination of such chemicals through nutrition and dietary fibre, and reducing body burdens when necessary and possible. If co-morbid allergies are not relieved by environmental controls, ventilation or filtration at home or in the workplace, they may be helped by individualized desensitization or medications to relieve symptoms. Dysbiosis (imbalanced microflora in the gastrointestinal tract) may be helped by probiotics and stabilization of pH. Patients are encouraged and supported to take control and self-manage, instituting and nurturing elements of good health. While early diagnosis and prompt treatment can significantly improve individual functioning/quality of life and reduce healthcare utilization, primary prevention through partnering and health promotion is the ultimate goal.

## **Background:**

In response to the Environmental Health Association of Ontario's request for more information on the available scientific evidence underpinning current assessment and management of ES-MCS, this Status Report was developed by the provincial Environmental Health Clinic (EHC) physicians as an explanatory review of the evolution of knowledge of ES-MCS. Although EHC physicians have previously participated in systematic literature reviews on environmental health topics, the financial resources were not available to conduct such a review on ES-MCS at this time. None of the contributors to this report received any remuneration.

Ongoing input on issues included in this report has been provided by members of the Environmental Health Association of Ontario, Myalgic Encephalomyelitis Association of Ontario, and the National ME-FM Action Network, as well as our partners in the Canadian Coalition for Green Health Care, Canadian Partnership for Children's Health and the Environment, and Toronto Cancer Prevention Coalition. Consumer advisors to the EHC, Eleanor Johnston, Varda Burstyn and Lin Grist, as well as EHC Manager Lynn Carter and researcher Dr. Margaret Sears, were consulted and their suggestions to improve structure and clarity of language were gratefully received.

## **Overview of Efforts with regard to ES-MCS:**

With emerging conditions such as ES-MCS, there are many research questions to be answered, including about description, definition, etiological contributors/mechanisms, assessment, diagnosis, prevalence, functional status, and health care utilization, while providing increasingly targeted treatments as evidence evolves. There have been advances in validation of consensus ES-MCS case criteria and in assembling pieces of the etiological puzzle in Ontario Ministry of Health-funded research, in compilation of prevalence data by Statistics Canada via Canadian Community Health Surveys, and in determining functional status and healthcare utilization while providing clinical care in government-funded clinics in Ontario and Nova Scotia. ES-MCS has now been recognized as a disability requiring accommodation through avoidance of symptom-triggering exposures and toxin reduction by the Canadian and Ontario Human Rights Commissions, but there remain many gaps in primary care and specialty health services, income/other social supports, and safe, affordable housing.

In order for multi-centre research to provide the most useful ever-developing picture of a condition, it is important that there be agreement on the definition/case criteria for what is being studied, as outlined below. Patients' needs cannot ethically be ignored while answers to the many research questions slowly accrue, with some uncertainty almost always remaining. Health, social, and housing services need to continually improve, not only to meet immediate patient needs, but also to protect all citizens from health impacts of known or suspected environmental hazards. An ounce of protection can truly prevent a pound of costs- to individuals, the health/social service systems, and the economy.

## ***Case Criteria Development***

- In the 1980s and 90s various criteria had been proposed for defining a case of MCS, also called environmental sensitivities, hypersensitivities, illness, intolerances, or toxicant-induced loss of tolerance, names which were inclusive of a broader range of environmental agents. Based on the previous work of Nethercott et al ([Nethercott JR, Davidoff LL, Curbow B, et al. Multiple chemical sensitivities syndrome: toward a working case definition. Arch Environ Health 1993;48:19-26](#)), a list of criteria that reflected an internationally *consistently observed pattern* of symptom presentation was agreed upon by 34 North American clinicians and researchers who collectively had experience with thousands of MCS patients ([Bartha et al. Multiple Chemical Sensitivity: a 1999 consensus. Archives of Environmental Health, May/June 1999; 54\(3\): 147-9](#)).

- Part of the definitional challenge was, and is, related to the fact that symptoms and signs triggered by low level exposures to environmental agents vary among affected individuals and within individuals depending on inciting agents as well as the doses, timing, and combinations of exposures. Also, while there can be abnormal physical and laboratory findings, the same findings are not *consistently* abnormal in all patients or in individual patients all the time (Thomson GM, Day JH, Evers S, et al. Report of the Ad Hoc Committee on Environmental Hypersensitivity Disorders. Ontario Ministry of Health, 1985:17-18).
- The 1999 consensus criteria were subsequently validated using a reproducible questionnaire (McKeown-Eyssen Gail E., Sokoloff Ellen R., Jazmaji Vartouhi, Marshall Lynn M., Baines Cornelia J. Reproducibility of the University of Toronto self-administered questionnaire used to assess Environmental Sensitivity, American J. of Epidemiology, 2000; 151 (12): 1216-22). In addition, four *specific* neurological symptoms were found to discriminate between most patients and controls in a study by the Ministry of Health-funded Environmental Hypersensitivity Research Unit at the University of Toronto (McKeown-Eyssen GE, Baines CJ, Marshall LM, et al. Multiple Chemical Sensitivity: Discriminant validity of case definitions; Arch Environ Health, 2001; 56(5):406–12) (Table 1). A checklist of the criteria is posted on the Ontario College of Family Physicians website for use by practising clinicians (<http://www.ocfp.on.ca>, → Environmental Health Committee).

**Table 1:**

**Multiple Chemical Sensitivity Case Criteria**

<b>Multiple Chemical Sensitivity: A 1999 Consensus</b>	
Bartha et al. Archives of Environmental Health, May/June 1999; 54(3): 147-9; Based on: Nethercott JR, Davidoff LL, Curbow B, et al. Multiple chemical sensitivities syndrome: toward a working case definition. Arch Environ Health 1993;48:19-26	
<ul style="list-style-type: none"> <li>▪ The symptoms are reproducible with [repeated chemical] exposure.</li> <li>▪ The condition is chronic.</li> <li>▪ Low levels of exposure [lower than previously or commonly tolerated] result in manifestations of the syndrome.</li> <li>▪ The symptoms improve or resolve when the incitants are removed.</li> <li>▪ Responses occur to multiple chemically unrelated substances.</li> <li>▪ [Added in 1999]: Symptoms involve multiple organ systems.</li> </ul>	
<b>Multiple Chemical Sensitivity: Discriminant Validity of Case Definitions</b>	
McKeown-Eyssen GE, Baines CJ, Marshall LM, et al. Arch Environ Health, 2001; 56(5):406–12	
<ul style="list-style-type: none"> <li>▪ Having a stronger sense of smell than most people</li> <li>▪ Feeling spacey</li> <li>▪ Feeling dull or groggy</li> <li>▪ Having difficulty concentrating</li> </ul>	

- Lacour et al suggested adding non-discriminating non-specific complaints of the central nervous system and functional disturbances in other organ systems to the case definition, but this would decrease discriminative ability. (Lacour M, Zunder T, Schmidtke K, Vaith P, Scheidt C. Multiple chemical sensitivity syndrome (MCS)- suggestions for an extension of the US MCS-case definition, Int J. Hyg. Environ. Health, 2005; 203:141-51).

- Since the validated combined MCS case criteria do not distinguish mild, moderate and severe MCS, functional status measures have been employed clinically as well. Further clarity in research on MCS of varying degrees of severity may be possible using six evaluated domains of questionnaire-based criteria for MCS (Kutsogiannis DJ, Davidoff AL. *A multiple center study of multiple chemical sensitivity syndrome*, Arch Environ Health, May/June 2001; 56(3):196-207- funded by Ontario Ministry of Health).
- The validated combined 1999 MCS consensus criteria and four specific neurological symptoms were used to select cases in subsequent case control studies funded by the MOH/MOHLTC at the University of Toronto (McKeown-Eyssen G, Baines C, Cole DEC, Riley N, Tyndale RF, Marshall L, Jazmaji V. Case-control study of genotypes in multiple chemical sensitivity: CYP2D6, NAT1, NAT2, PON1, PON2 and MTHFR, Int. J. Epidemiol. July 15, 2004; 33: 1-8; Baines CJ, McKeown-Eyssen GE, Riley N, Cole DE, Marshall L, Loescher B, Jazmaji V. Case-control study of multiple chemical sensitivity, comparing haematology, biochemistry, vitamins, and serum volatile organic compound measures, September 2004; 54 (6):408-18; Baines CJ, McKeown-Eyssen GE, Riley N, Marshall L, Jazmaji V. University of Toronto case-control study of multiple chemical sensitivity-3: intra-erythrocytic mineral levels, Occupational Medicine, published online October 17, 2006).

#### ✚ *Initial Steps toward Addressing Patients' Needs*

- Those with ES-MCS have long complained about lack of availability of knowledgeable healthcare professionals and effective health services for their condition, borne out by Gibson et al's finding in a U.S. cross-sectional survey of 917 members of MCS support groups that participants had consulted a mean of twelve health care providers, but only found a mean of three helpful (Gibson PR, Elms AN-M, Ruding LA. *Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity*, Environmental Health Perspectives, September 2003; 111(12):1499).
- In Ontario, after carefully reviewing the available evidence on ES-MCS in 1984, both published and revealed in interviews and focus groups, the Ad Hoc Committee on Environmental Hypersensitivity Disorders, appointed by the then Ontario Minister of Health, Keith Norton, and chaired by Judge George M. Thomson ([http://www.lsuc.on.ca/media/june1209\\_georgebio.pdf](http://www.lsuc.on.ca/media/june1209_georgebio.pdf)), concluded that there was sufficient evidence that environmental hypersensitivity was a health problem that needed to be addressed, and recommended funding of a collaborating university research program and academically-affiliated provincial clinic to fill the scientific and service gaps (Thomson GM, Chair. *Report of the Ad Hoc Committee on Environmental Hypersensitivity Disorders to the Ontario Ministry of Health, 1985*). Health Minister Elinor Caplan appointed a liaison committee, arranged for interested researchers and clinicians to meet to discuss priorities, and funded several research initiatives.
- In the early 1990's, when Ontario Health Minister Frances Lankin learned that there had been other reports (Ashford NA, Miller CS. *Chemical sensitivity: A report to the New Jersey State Department of Health, December, 1989*; Health Canada. *Environmental Sensitivities Workshop, Chronic Diseases in Canada, Supplement, January, 1991*) that had very similar findings and had made similar recommendations as the Thomson Committee, she ordered funding, and the subsequent Health Minister Ruth Grier instituted the Environmental Hypersensitivity Research Unit (EHRU) at the University of Toronto (for a total of \$1,500, 000) (McKeown-Eyssen G, Marshall L, Baines C, Rodin G).

Research Initiatives at the University of Toronto Environmental Hypersensitivity Research Unit, Regulatory Toxicology and Pharmacology, 1996; 24: S126-S128). A collaborating Environmental Health Clinic was also established for the province at Women's College Hospital, Toronto. Decisions regarding priorities for clinical services and research studies were effectively guided by a Clinical and Research Advisory Board (CRAB) appointed by the Ontario Ministry of Health in the 1990's.

- Pioneering research was done in the EHRU that validated published MCS case criteria and refined them (McKeown-Eyssen GE, Baines CJ, Marshall LM, et al. *Multiple Chemical Sensitivity: Discriminant validity of case definitions*; Arch Environ Health, 2001; 56(5):406–12), and that pointed to potential genetic susceptibility factors (McKeown-Eyssen G, Baines C, Cole DEC, Riley N, Tyndale RF, Marshall L, Jazmaji V. *Case-control study of genotypes in multiple chemical sensitivity: CYP2D6, NAT1, NAT2, PON1, PON2 and MTHFR*, Int. J. Epidemiol. July 15, 2004; 33: 1-8), as well as investigating other potential etiological factors and diagnostic test possibilities. However, the EHRU funding ended before further studies on etiology, diagnosis and treatment could be mounted.
- The enduring provincial Environmental Health Clinic (EHC) at Women's College Hospital, with a total annual budget of \$408,000, essentially static since 1998, employs 0.9 of a full time equivalent (FTE) physician, shared among 5 physicians, supplemented somewhat for clinical work by the Ontario Health Insurance Plan and recently for teaching by a hospital family practice group alternate funding plan. It also employs one full time Nurse Educator, 0.8 FTE Community Outreach Coordinator, 0.8 FTE receptionist/dictatypist, and approximately 0.3 FTE shared manager. The clinic provides comprehensive assessments and treatment advice to ongoing care physicians, and self management advice to physician-referred patients from a provincial population base of over 13 million ([http://www.ontario.ca/en/about\\_ontario/EC001035](http://www.ontario.ca/en/about_ontario/EC001035) - accessed August 13, 2010-website last modified May 5, 2010). The EHC has a virtually perpetual six to eight month waiting list, is unable to offer urgent or ongoing treatment, and generally cannot provide consultations for children or out-of-province residents.
- Canada has one paediatric environmental health consulting clinic integrated into a regular multi-function paediatric clinic in Edmonton, Alberta, affiliated with the University of Alberta and a group of Paediatric Environmental Health Specialty Units in the U.S.
- The Nova Scotia Environmental Health Centre (NSEHC) is located in Fall River just outside Halifax, Nova Scotia. The NSEHC is funded by the Capital District Health Authority and is affiliated with Dalhousie University. The NSEHC has been able to offer assessments and ongoing multi-faceted, individualized treatment and psychosocial support to both adults and children in Nova Scotia, with a provincial population of 938,183 (<http://www.gov.ns.ca/finance/statistics/agency/default.asp>, July 1, 2009), as well as to some out-of-province residents. The NSEHC has an annual budget of \$1,410,000 and employs two physicians, two nurses, one licensed practical nurse, one dietician, one psychologist, one psychotherapist, one occupational therapist, one rehabilitation counsellor, one manager/researcher, and five administrative staff (Merritt C, NSEHC. *Personal communication with Drs. A. Bested, R. Bray and L. Marshall by telephone and e-mail, October 2010*). The average waiting time for referred patients in Nova Scotia is approximately four months, but eight months if from out of province.

- It has been extremely challenging to assist EHC patients in Ontario to obtain adequate ongoing care in their communities when primary care physicians, specialists, and other local healthcare/homecare professionals have had little training in environmental health. The provincial EHC in Ontario has leveraged its resources by collaborating with multiple partners (**Table 6**) for education/training, research, community support, and health promotion with regard to ES-MCS and other environment-associated conditions.
- There is currently no Ontario Health Insurance Plan diagnostic code for ES-MCS, and no time-based complex case code to pay physicians for the extra time required for them to assess and treat those with ES-MCS. Hence, although Ontarians' needs are great, it is difficult to attract new physicians, given this reality.

#### **Cost Implications and Recognition of the Need to Accommodate**

- Health care utilization costs for patients referred to the Nova Scotia Environmental Health Centre between 1998 and 2000, who were diagnosed with MCS by NSEHC physicians, were almost twice the provincial average. However, a NSEHC cohort study combining chart review and medical insurance records revealed reduced healthcare utilization by NSEHC patients subsequent to treatment, resulting in significant health care system savings. The largest reduction in health system utilization occurred in those who were initially most severely ill (Fox RA, Joffres MR, Sampalli T, Casey J. [The impact of a multidisciplinary, holistic approach to management of patients diagnosed with multiple chemical sensitivity on health care utilization costs: An observational study, The Journal of Alternative and Complementary Medicine, 2007; 13\(2\):223-9.](#))
- A chart review study in the provincial Environmental Health Clinic in Ontario of 128 consecutive patients diagnosed with one or more of MCS, chronic fatigue syndrome, or fibromyalgia revealed that the mean number of visits to a family physician in the twelve months before completion of the intake questionnaire was 10.7 (SD 8.7; n=123), and to other physicians was 13.7 (SD 18.2; n=123). This was far higher than for the general population in Canada where the mean numbers of visits were 2.9 (SD 4.3) and 0.79 (SD 2.0) respectively. Furthermore, most (68.8%) had stopped work, on average about three years after symptom onset, and had “markedly lower functional scores than population average values” (Lavergne MR, Cole DC, Kerr K, Marshall LM. [Functional impairment in chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity, Canadian Family Physician, February 2010; 56: e60-1.](#))
- Although some of the basic steps to fill scientific and service gaps have been taken as suggested by Thomson et al (Thomson GM, Chair. [Report of the Ad Hoc Committee on Environmental Hypersensitivity Disorders to the Ontario Ministry of Health, 1985](#)), there is unfortunately still a disturbing lack of recognition of the many challenges for those with ES-MCS in accessing knowledgeable health care (both urgent and ongoing) in safe facilities, adequate nutrition, supportive dietetic and community services, workplace accommodation, and safe healthy housing (Canada Mortgage and Housing Corporation. [Research House for the environmentally sensitive, 1994, reprinted 1995, 1998, 2002, Cat. No. NH15-90/1994E; http://journals.lww.com/jphmp/toc/2010/09001#-1750774083; Building materials for the environmentally hypersensitive 61089, 1995, revised 2005, \[www.cmhc-schl.gc.ca/\]\(#\); http://journals.lww.com/jphmp/toc/2010/09001#-1750774083 J of Public Health Management and Practice, September/October 2010 16 \(E-Supplement 5\): S1-S93\).](#)



- In 2006, having received many complaints from Canadians with ES-MCS about the lack of health and financial support services and dismissal or trivialization of their health problems, the Canadian Human Rights Commission (CHRC) ordered a scientific literature review on environmental sensitivities (Sears M. *The Medical Perspective on Environmental Sensitivities*. Canadian Human Rights Commission, 2007, [http://www.chrc-ccdp.ca/pdf/envsensitivity\\_en.pdf](http://www.chrc-ccdp.ca/pdf/envsensitivity_en.pdf)). The CHRC subsequently declared the condition to be a disability requiring accommodation under the *Canadian Human Rights Act* (the policy is posted at: [http://www.chrc-ccdp.ca/legislation\\_policies/policy\\_environ\\_politique-en.asp](http://www.chrc-ccdp.ca/legislation_policies/policy_environ_politique-en.asp)).
- The Department for Transport Energy and Infrastructure in South Australia has also specified a detailed disability accommodation policy for those with MCS in government buildings: [http://www.sacfs.asn.au/download/SA%20Gov%20Access%20Assement%20%20guide%20version%20SBF%20final%20DTEI%202007\\_30\\_11.pdf](http://www.sacfs.asn.au/download/SA%20Gov%20Access%20Assement%20%20guide%20version%20SBF%20final%20DTEI%202007_30_11.pdf)
- Environmental sensitivities were included as “non-evident disabilities” in the Ontario Human Rights Commission’s *Policy and Guidelines on the Duty to Accommodate* in 2000, and are also specifically mentioned when defining disabilities that must be accommodated under the Ontario *Human Rights Code* <http://www.ohrc.on.ca/en/issues/disability>.
- The Ontario Accessible Built Environment Standards Development Committee under the *Accessibility for Ontarians with Disabilities Act, 2005* has appointed the Environmental Health Clinic’s Community Outreach Coordinator to represent those with environmental sensitivities.
- The Public Service Alliance of Canada (PSAC) has a policy statement on scent-free environments (Chemical Sensitivities - Environmental Disabilities) on their website that includes the PSAC Awareness Kit on Scent-Free Environments, January 2006 <http://psac.com/documents/what/scent-free-kit-feb2006-e.pdf>.
- The Canadian Centre for Occupational Health and Safety has information on its website on how to establish a “Scent-Free Policy for the Workplace” ([www.ccohs.ca/oshanswers/hsprograms/scent\\_free.html](http://www.ccohs.ca/oshanswers/hsprograms/scent_free.html)), as does National Defence and the Canadian Forces. (Environmental sensitivities, *Safety Digest*, Edition 6/2010, reproduced from the Safety, Emergency and Security Management Division of Treasury Board; retrieved August 27, 2010. <http://www.vcds-vcemd.forces.gc.ca/dsafeg-dsg/pi/sd-dsg/6-10/article-07-eng.asp>.)
- The Ontario provincial Environmental Health Clinic team, other Women’s College Hospital staff and consumer support groups have collaborated with the Canadian Society for Environmental Medicine on information for hospital staff to enable accommodation of those with allergies or sensitivities (Marshall LM, Maclellan JG. *Environmental health in hospital: A practical guide for hospital staff. Part I Pollution prevention, Part II Environment-sensitive care*, Canadian Society for Environmental Medicine, 1993, revised editions 2001, [www.mcscanadian.org/hospital.html](http://www.mcscanadian.org/hospital.html))

- Through participation in the Canadian Coalition for Green Health Care ([www.greenhealthcare.ca](http://www.greenhealthcare.ca)), the provincial Environmental Health Clinic in Ontario has been a leader in promoting fragrance/scent-free programs and policies in health care facilities across the country, with the assistance of an Ontario Trillium Foundation grant.

### **Etiology:**

While the causes and underlying mechanisms of ES-MCS are still not fully understood, progress has been made over the past 15 or so years. There has been increased recognition of the large number of ubiquitous chemicals to which we are all exposed in varying amounts and combinations. Their potential impacts on body defence mechanisms and the contributions of genetic and epigenetic susceptibility factors and metabolic consequences have been hypothesized and are slowly being tested. The science of toxicology has evolved substantially and there is a move away from “physical” versus “psychological” dualistic models of disease/illness to the multiple determinants of health model utilized by the World Health Organization (WHO).

#### **✦ Increased Chemical Exposure**

- More than 80,000 potentially toxic chemicals have been introduced into commerce in North America mostly since World War II (Grossman E. What the EPA’s “Chemicals of Concern” plans really mean, *Scientific American*, January 11, 2010), and 23,000 in Canada (Health Canada. *Assessing Chemicals in Canada for Risk: Protecting the Health of Canadians and their Environment*. Health Canada. Dec. 15, 2006. March 27, 2009 <http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/brochure/index-eng.php>), to which Canadians are virtually all regularly exposed (Genius SJ. Nowhere to hide: chemical toxicants and the unborn child, *Reprod Toxicology*, 2009; 28:115-6).
- Some patients began reporting a variety of symptoms linked with intermittent exposure to synthetic chemicals in the 1950’s and 60’s, and their physicians reported the phenomenon to colleagues (e.g. Randolph T.G. *Human ecology and susceptibility to the chemical environment*. Springfield, IL: Charles C Thomas, 1962), but little notice seemed to be taken initially- perhaps not surprising since the effects of chemical sensitivities are usually not visible to others, and it can be hard to believe that chemicals at levels not bothering most people could be adversely affecting some.
- In the 1970’s, in the wake of an oil embargo in the Middle East, buildings were “tightened” to prevent heat loss, trapping chemicals indoors, at the same time as regulated ventilation rates were lowered to save energy. Reports of symptoms in multiple body systems occurring “with increased frequency in buildings with indoor climate problems” were recognized by the World Health Organization as a clinical phenomenon called “Sick Building Syndrome” (WHO, *Indoor Air Quality Research. Euro-Reports and Studies*. Copenhagen, No. 103. 1984).
- ES-MCS was reported more in the 1980’s and 90’s - a similar phenomenon to Sick Building Syndrome occurring in a broader range of locations and circumstances. Symptoms were triggered by ‘everyday’ exposures, often after a recognizable initiating event, usually of a pronounced chemical exposure, such as a chemical spill at work, pesticide application or building renovation, or by a combination of chemical exposures in the stressful context of war (Cullen, MR. *The worker with multiple chemical sensitivities: an overview*. *Occup. Med.* 1987; 2:655-661; Ashford NA, Miller CS. *Chemical sensitivity: a report to the New Jersey State Department of Health*, December, 1989; Ashford NA, Miller CS. *Chemical exposures, low levels and high stakes*, Van

Nostrand Reinhold, New York, 1991, and 2<sup>nd</sup> Edition, John Wiley & Sons Inc., 1998; Ross GH. History and clinical presentation of the chemically sensitive patient. *Toxicol. Ind. Health.* 1992; 8, 21-28; Miller CS, Mitzel HC. Chemical sensitivity attributed to pesticide exposure versus remodeling. *Arch. Environ. Health,* 1995; 50, 119-129; Haley RW, Billecke S, La Du BN. Association of low PON1 type Q (type A) arylesterase activity with neurologic symptom complexes in Gulf War veterans, *Toxicol Appl Pharmacol* 1999;157:227-233; *Gulf War and Health, Vol. 8: Health Effects of Serving in the Gulf War Update 2009* , National Academies Press, 2010, <http://www.nap.edu>).

- Early on, the most common symptom-triggering agents, reported by occupants of sick buildings and those with ES-MCS, were usually not recognized as containing potentially harmful ingredients (e.g. the unlabeled volatile organic compounds (VOC's) being emitted from many common building and furnishing materials, cleaning, laundry, and personal care products), or exposures were considered to be at levels too low to be harmful. While reports of chronic conditions in children, such as asthma and neurocognitive difficulties, were increasing, they were not necessarily seen as related (McKeown D. *Toronto Public Health. Environmental threats to children: Understanding the risks, enabling prevention, September 2005*; Grandjean P, Landrigan JP. *Developmental neurotoxicity of industrial chemicals*, doi:10.1016/S0140-6736(06)69665-7, 2006).
- In the first decade of the 21<sup>st</sup> century, as uses of electrical appliances/equipment and radiofrequency telecommunications have expanded, there have been reports of a condition with a pattern like MCS of multisystem symptoms occurring in relation to exposures to everyday levels of electromagnetic radiation (Huss A, Roosli M. *Consultations in primary care for symptoms attributed to electromagnetic fields- a survey among general practitioners, BMC Public Health, Oct. 30 2006;6:267*). An international committee of scientists have examined and reported on the evidence to date (The Bioinitiative Working Group. *Bioinitiative report: A rationale for a biologically-based public exposure standard for electromagnetic fields, 2006, last updated 24 May 2010; www.bioinitiative.org*). Although there is still much uncertainty, in response to public enquiries, Toronto Public Health has developed fact sheets (Toronto Public Health. *Electromagnetic fields-Fact sheet, <http://www.toronto.ca/health/emfs.htm>, last updated 12 June 2008*; Toronto Public Health, *Children and safe cell phone use, [http://www.toronto.ca/health/hphelpdf/factsheet\\_children\\_safecellphone.pdf](http://www.toronto.ca/health/hphelpdf/factsheet_children_safecellphone.pdf), July 2008*). The latter fact sheet discusses precautionary advice from the World Health Organization about increasing distance from the radiofrequency-emitting handset through use of hands-free devices like headsets or earphones.
- It may be that people in many industrialized nations reporting the pattern of ES-MCS from the 1950s on are the ‘canaries’ for the general population with respect to responses to the multitude of chemicals introduced into our air, food, water, soil, and consumer products since World War II, as well as to increasing exposure to electromagnetic radiation.

#### **Overwhelmed Body Defence Mechanisms**

- Fortunately, the body may normally utilize many mechanisms and combinations thereof to defend against foreign biological, chemical or physical agents, or rapidly dividing cancer cells. However, defence mechanisms can become overwhelmed and individuals may become more sensitive to a variety of chemicals at everyday dosages, for example patients with cirrhosis of the liver, or undergoing chemotherapy for cancer.

- Primary body defence mechanisms include the following (simplified):
  - Surface barriers: Inhaled particles and chemicals may be breathed out or trapped in mucus in the nose and sneezed out, or in the bronchi and lungs and coughed out. The gastrointestinal tract wall and mucus can block absorption of ingested hazardous substances. Substances may be brushed or washed off the skin before they are absorbed.
  - Cellular Immune Responses: immune cells, including neutrophils, monocytes and lymphocytes e.g. B cells, T cells and Natural Killer cells, are found in the blood and throughout the body in organs such as the lungs, liver, spleen and brain. When viruses, bacteria or other foreign proteins enter the body, the immune cells become activated to release chemical mediators to ‘chew’ them up (Klaasen CD. Casarett and Doull’s Toxicology, the basic science of poisons, 7<sup>th</sup> Edition, 2008, McGraw-Hill Inc.; Guyton AC, Hall JE. Textbook of Medical Physiology, 11<sup>th</sup> Edition, Saunders, July 2005).

Immune responses are powerful mechanisms in the body, with potential to cause harm (e.g. anaphylaxis or autoimmune disease). Danish researchers have demonstrated dose response-related increased histamine release from the basophils of patients with asthma and perfume contact allergy, in comparison with controls, on exposure to perfume (Elberling J, Skov PS, Mosbech H, Holst H, Dirksen A, Johansen JD. Increased release of histamine in patients with respiratory symptoms related to perfume, Clin and Experim Allergy, 2007; 37:1676-1680).

- Humoral Non-Cellular Immunity: there are many different humoral immune pathways where the body produces or reacts with large complicated proteins such as immunoglobulins (antibodies), complex proteins and enzymes for the coagulation or clotting system and the complement system, or reactive proteins such as cytokines or other chemicals that are produced in response to what the body identifies as foreign: bacteria, viruses, fungi, cancer cells, radiation and chemicals. The proteins and chemicals travel through Phase I and Phase II biotransformation pathways that occur mainly in the liver (Klaasen CD. Casarett and Doull’s Toxicology, the basic science of poisons, 7<sup>th</sup> Edition, 2008, McGraw-Hill Inc.; Guyton AC, Hall JE. Textbook of Medical Physiology, 11<sup>th</sup> Edition, Saunders, July 2005, 1152 pgs).
- Phase I and Phase II Biotransformation: the Phase I (Cytochrome P-450) enzyme system prepares (bioactivates) the parent substance via various mechanisms, so that it can connect (conjugate) with another substance in a Phase II pathway to make the compound water soluble in order that it may be excreted more easily. The rate at which Phase I produces activated intermediates must be balanced by the rate at which Phase II conjugates and excretes toxins in the urine via the kidneys, in the bile and stool via the bowel, and to some degree in sweat. Otherwise, there can be a build up of the parent substance and its active intermediate metabolites, which, in some cases can be more toxic than the parent.

Many drugs are P-450 enzyme inhibitors which may result in accumulation of medications and foreign chemicals (xenobiotics) with increased side effects and toxicity. Examples are cimetidine, ciprofloxacin, diltiazem, erythromycin, ketoconazole, verapamil, and a number of selective serotonin reuptake inhibitors (SSRIs).

There are essentially six Phase II conjugation pathways:

- Glutathione conjugation
- Amino acid conjugation
- Methylation
- Sulfation
- Acetylation
- Glucuronidation

There must be adequate nutrients available for efficient operation of Phase I and II biotransformation pathways, in particular, high intake of highly-coloured vegetables, ascorbate, anti-oxidants, glutathione precursors provided by adequate protein, niacin and cobalamin, as well as balanced essential fatty acid intake and phosphatidyl choline, along with high fibre to enhance GI transit function in Phase III (excretion) (Burford-Mason A. What foods need to deliver, Nutrition for Docs, Dalla Lana School of Public Health, University of Toronto, Syllabus, April 17-18, 2010).

#### ✦ **Genetic Susceptibility Factors**

- From 1990-2003, the human genome was categorized ([http://www.ornl.gov/sci/techresources/Human\\_Genome/project/about.shtml](http://www.ornl.gov/sci/techresources/Human_Genome/project/about.shtml)). Genetic polymorphisms have been found in those with ES-MCS in comparison with controls that seem to indicate that people with ES-MCS may have more difficulty than the majority of the population metabolizing and excreting commonly encountered environmental chemicals and medications (La Du BN, Billecke S, Hsu C, Haley RW, Broomfield CA. Serum paraoxonase (PON1) isozymes: the quantitative analysis of isozymes affecting individual sensitivity to environmental chemicals. *Drug Metab Dispos.* 2001;29:566-9; McKeown-Eyssen G, Baines C, Cole DEC, Riley N, Tyndale RF, Marshall L, Jazmaji V. Case-control study of genotypes in multiple chemical sensitivity: CYP2D6, NAT1, NAT2, PON1, PON2 and MTHFR, *International Journal of Epidemiology* 2004; 33:1-8 [funded by the Ontario Ministry of Health]; Furlong CE, Cole TB, Jarvik GP et al. Role of paraoxonase (PON1) status in pesticide sensitivity: genetic and temporal determinants, *Neurotoxicology* 2005;26:651-9; Schnakenberg E, Fabig KR, Stanulla M et al. A cross-sectional study of self-reported chemical-related sensitivity is associated with gene variants of drug metabolizing enzymes. *Environ Health.* 2007; 6:6 ; Muller KE, Schnakenberg E. Die Bedeutung der Glukuronidierung bei umweltmedizinischen Erkrankungen am Beispiel der UDP-Glukuronosyltransferase 1A1. *Umwelt Medizin Gesellschaft*, 2008; 21(4): 295-300).
- The science of epigenetics and how environmental stimuli influence genes to turn on and off their expression of metabolic enzymes is in its infancy and is evolving rapidly (Anway MD, Skinner MK. Epigenetic transgenerational actions of endocrine disruptors, *Endocrinology* 2006, Vol. 147, No. 6 s43-s49; Crews D, McLachlan JA. Epigenetics, evolution, endocrine disruption, health and disease, *Endocrinology*, 2006, Vol. 147, No. 6 s43-s49; Korkina L, Scordo MG, Deeva T, Cesareo E, De Luca C. The chemical defensive system in the pathobiology of idiopathic environment-associated diseases, *Current Drug Metabolism*, 2008; 10:914-31). Genuis noted “Just as a loaded gun needs to be triggered to unload destruction, epigenetic research confirms that disease is often the result of vulnerable genes being triggered by specific determinants. Mounting evidence suggests that without activation, some disease processes will not develop, and removal of the initiating trigger may allow developing illness to abate or subside.”

(Genius SJ. Medical practice and community health care in the 21<sup>st</sup> century: A time of change, Public Health, 2008; 122:671-80).

- In a recent Italian study comparing diagnosed or suspected MCS patients with healthy controls, even though some measured genes were not noted to be different in the combined 'case' population, it was found that several key metabolizing enzymes were. The authors concluded, "Altered redox and cytokine patterns suggest inhibition of expression/activity of metabolizing and antioxidant enzymes in MCS. Metabolic parameters indicating accelerated lipid oxidation, increased nitric oxide production, and glutathione depletion in combination with increased plasma inflammatory cytokines should be considered in biological definition and diagnosis of MCS" (De Luca C, Scordo MG, Cesareo E, Pastore S, et al. Biological definition of multiple chemical sensitivity from redox state and cytokine profiling and not from polymorphisms of xenobiotic-metabolizing enzymes, Toxicology and Applied Pharmacology, 2010, doi:10.1016/j.taap.2010.04.017).

#### ✚ **Metabolic Vicious Cycle**

- Human metabolic systems, identical in all cells, are responsible for conversion of matter into the energy of adenosine triphosphate (ATP) to perform life- and health-necessary functions. Humans are equipped with alternate pathways to maintain or restore normal levels of bio-energetic potential, even with genetic and environmental insult (Strohman R. Manoeuvring in the complex path from genotype to phenotype, Science, 26 April 2002;296(5568):701-3). A comprehensive catalogue of human metabolic pathways is now readily accessible (<http://www.genome.jp/kegg/pathway.html>).
- Plausible biochemical vicious cycle mechanisms (the nitric oxide-peroxynitrite or NO-ONOO cycle) in MCS and other commonly overlapping complex chronic conditions such as myalgic encephalomyelitis/chronic fatigue syndrome have been proposed and partially tested (Pall ML, Satterlee J. Elevated nitric oxide/peroxynitrite mechanism for the common etiology of multiple chemical sensitivity, chronic fatigue syndrome, and post traumatic stress disorder, Ann NY Acad Sci 2001; 933:323-9; Pall ML. Elevated Nitric Oxide/Peroxynitrite theory of Multiple Chemical Sensitivity: Central role of N-Methyl-D-Aspartate Receptors in the Sensitivity Mechanism, EHP, September 2003; 111(12):1461-4; Pall ML, Anderson JH. The vanilloid receptor as a putative target of diverse chemicals in multiple chemical sensitivity, Arch Environ Health, July 2004; 59(7):363-75; Pall ML. Multiple Chemical Sensitivity: Toxicological Questions and Mechanisms, Part 8, Environmental and Ecotoxicology, 92, in General and Applied Toxicology, 6 volume set, 3rd Edition. Editors: Ballantyne B, Marrs T, and Syversen T. November 2009, John Wiley & Sons Inc., 3940 pages).
- Pall proposed that cases of Multiple Chemical Sensitivity may be initiated by seven classes of chemicals, each acting along a specific pathway in the body, stimulating the N-Methyl-D-Aspartate (NMDA) cell membrane receptors. The chemical stimulation produces increased NMDA cell membrane receptor activity in mammals that can be measured, and toxic effects, which are diminished by giving NMDA antagonists. The NMDA receptors are found on the surface of cell membranes throughout the body including in the brain, the peripheral nervous system, the bronchi and the gut. Hence, the NMDA cell membrane receptors can become sensitized by chemical contaminants, become over-active and trigger sensitivity responses in MCS patients. Further support for these metabolic mechanisms has come recently from an Italian study (De Luca C, Scordo

MG, Cesareo E, Pastore S, et al. Biological definition of multiple chemical sensitivity from redox state and cytokine profiling and not from polymorphisms of xenobiotic-metabolizing enzymes, *Toxicology and Applied Pharmacology*, 2010, doi:10.1016/j.taap.2010.04.017).

- Pall has been able to relate the NO-ONOO vicious cycle to previously published MCS etiological hypotheses (Bell I, Miller C, Schwartz G. An olfactory limbic model of multiple chemical sensitivity syndrome: possible relationships to kindling and affective spectrum disorders, *Biol Psychiatry*, 1992;32:218-42; Meggs WJ. Neurogenic inflammation and sensitivity to environmental chemicals, *Environ Health Perspect*, 1993; 101:234-38; Meggs WJ. Neurogenic switching: A hypothesis for a mechanism for shifting the site of inflammation in allergy and chemical sensitivity, *Environ Health Perspect*, 1995; 103(1):54-56; Miller CS. Toxicant-induced loss of tolerance- an emerging theory of disease? *Environ Health Perspect* March 1997; 105S:445-53).

#### ✚ *Sensory Hypersensitivity*

- Capsaicin is the heat producing ingredient in hot peppers and is a well known cough inducer when inhaled, by stimulating vanilloid-sensitive receptors in the bronchial tubes. There are several double-blind capsaicin inhalation challenge studies which demonstrate hypersensitivity in those with MCS when compared to controls, even when asthma has been ruled out (Terneston-Hasseus E. Increased capsaicin cough sensitivity in patients with multiple chemical sensitivity. *J Occup Environ Med*. 2002 Nov; 44(11):1012-7; Nogami H. Capsaicin provocation test as a diagnostic method for determining multiple chemical sensitivity. *Allergology Int* 2004 53(2):153-157(155).
- Challenge studies in those with atopy, and upper and lower airway symptoms have produced the same results, demonstrating neural receptor hypersensitivity to chemicals (Millqvist E. Cough provocation with capsaicin is an objective way to test sensory hyperreactivity in patients with asthma-like symptoms, *Allergy*, June 2000; 55(6):546-50; Millqvist E. Relationship of airway symptoms from chemicals to capsaicin cough sensitivity in atopic subjects, *Clin Exp Allergy*, April 2004; 34(4):619-23; Millqvist E. Changes in levels of nerve growth factor in nasal secretions after capsaicin inhalation in patients with airway symptoms from scents and chemicals, *Environ Health Perspective*, July 2005; 113(7):849-52).
- Patients with capsaicin sensitivity have faster CNS processing of other chemosomatosensory substances as well (Andersson L. On the relation between capsaicin sensitivity and responsiveness to CO<sub>2</sub>: detection sensitivity and event-related brain potentials. *Arch Environ Health*, February 2009; 82(3):285-90).
- Given that vanilloid receptors are involved in pain perception, it is perhaps not surprising that MCS patients are also more likely to have fibromyalgia (Ziem G. Profile of patients with chemical injury and sensitivity, *Environ Health Perspect*, March 1997; 105 Suppl 2:417-36; Rainville P. Representation of acute and persistent pain in the human CNS: potential implications for chemical intolerance, *Ann NY Acad Sci*, March 2001; 933:130-41; Black DW. The Iowa follow-up of chemically sensitive persons. *Ann NY Acad Sci*, March 2001; 933:48-56).

### ✚ *Evolving Toxicology*

- The science of toxicology has only recently evolved to understand concepts such as quasi-persistence and chronic toxicity of substances to which there is frequent or continuous exposure, even at low levels ([Genuis SJ. Elimination of persistent toxicants from the human body, Hum Exp Toxicol Online First, April 16, 2010; doi:10.1177/0960327110368417](#)) (particularly relevant for those with MCS who may not be able to metabolize and excrete xenobiotics as readily as most adults and for vulnerable fetuses and children whose metabolic capacities are still under development ([Furlong CE, Cole TB, Jarvik GP et al. Role of paraoxonase \(PON1\) status in pesticide sensitivity: genetic and temporal determinants. Neurotoxicology. 2005; 26:651-659; McKeown D. Environmental threats to children: Understanding the risks, enabling prevention, Toronto Public Health, September, 2005](#)).
- It was also not until recently considered that dose response curves could be non-monotonic, and that some substances encountered at exceedingly low levels could adversely affect the endocrine and immune systems ([American Chemical Society. \[http://portal.acs.org/portal/PublicWebSite/policy/publicpolicies/promote/endocrinedisruptors/CNBP\\\_023441\]\(http://portal.acs.org/portal/PublicWebSite/policy/publicpolicies/promote/endocrinedisruptors/CNBP\_023441\)](#); [Martin OV, Lester JN, Voulvoulis N, Boobis AR. Human health and endocrine disruption: A simple multicriteria framework for the qualitative assessment of end point-specific risks in a context of scientific uncertainty, Toxicological Sciences, 2007; 98\(2\):332-48; \[www.ourstolenfuture.org\]\(http://www.ourstolenfuture.org\) -->Does the dose make the poison?; Vogel SA. The politics of plastics: The making and unmaking of Bisphenol A “safety”, Amer J Pub Health, 2009 99\(S3\):S559-66; American Chemical Society. Testing for Endocrine Disruption. Public Policy Statement 2009-2010. \[http://portal.acs.org/portal/PublicWebSite/policy/publicpolicies/promote/endocrinedisruptors/CNBP\\\_023441\]\(http://portal.acs.org/portal/PublicWebSite/policy/publicpolicies/promote/endocrinedisruptors/CNBP\_023441\)\).](#)
- It has recently been realized that there might be no safe threshold of exposure below which there would be no adverse health effects for some substances, such as lead ([American Academy of Pediatrics, Committee on Environmental Health. Lead exposure, including: prevention, detection and management, Pediatrics, Oct. 2005,116\(4\):1036-46; Abelsohn AR, Sanborn M. Lead and children, clinical management for family physicians, Canadian Family Physician, June 2010:531-5](#)). High dose laboratory animal experimental “no observable adverse effect levels” (NOAELs) are typically relied upon to estimate regulatory exposure limits, with somewhat arbitrary ‘safety’ factors applied to protect those more vulnerable.

### ✚ *Central Nervous System Hypoperfusion*

- Baseline and post-chemical challenge brain perfusion decreases have been noted in MCS patients compared with controls on single photon emission computed tomography (SPECT) brain scans. Decreased perfusion correlated with psychometric test results of decreased quality of life and neurocognitive function in cases at baseline, and neurocognitive worsening after chemical exposure “at non-toxic concentrations” ([Orriols R, Costa R, Cuberas G, Jacas C, Castell J, Sunyer J. Brain dysfunction in multiple chemical sensitivity, Journal of the Neurological Sciences, 2009; 287:72-8](#)).

### ✚ *‘Physical’ vs ‘Psychological’ and Consequences, or Multiple Determinants*

- Since the time of French philosopher Rene Descartes (1596-1650), the mechanistic concept of separation of mind and body has persisted in medicine ([Gold J. Cartesian dualism and the current crisis in medicine- a plea for a philosophical approach: discussion paper, J of](#)



the Royal Soc of Med, August 1985; 78: 663-6), in spite of ongoing evidence of mutual influence of each on the other (e.g. Choi J, Fauce SR, Effros RB. [Reduced telomerase activity in human T lymphocytes exposed to cortisol, Brain, Behavior and Immunity, May, 2008; 22\(4\): 600-605](#)). There has correspondingly been a tendency to categorize ES-MCS etiological factors as *either* physical *or* psychological. This reductionist dichotomous view and ensuing discordant medial debate about ‘physical’ versus ‘psychological’ origins for ES-MCS has lead to public confusion and misunderstandings, since society looks to the medical community for information and guidance. The Thomson Committee commented “We believe that confidence in the health care system is eroded when productive dialogue between different medical specialties disappears or is replaced by acrimonious debate before a confused public” (Thomson GM, Day JH, Evers S, et al. [Report of the Ad Hoc Committee on Environmental Hypersensitivity Disorders. Ontario Ministry of Health, 1985:266-70](#)).

- Since consistently abnormal objective physical findings and laboratory test results are presently not established to ‘prove’ a physical origin for ES-MCS, the dichotomous view can lead to an assumption of psychogenic etiology, with a tendency for this assumption to be favoured by industry, insurers and government agencies, as discussed by Ziem and Spencer and Schur ([Ziem G. Multiple chemical sensitivity: Treatment and follow up with avoidance and control of chemical exposures, Toxicol Ind Health July 1, 1992; 8\(4\):73-86](#); [Spencer TR, Schur PM. The challenge of multiple chemical sensitivity. J Environ Health 2008, 70\(10\):24-7](#)).
- Although there is no objective evidence of psychogenesis, some people disbelieve patients reporting ES-MCS, diminish the significance of symptoms and experiences, and dismiss even the possibility of the condition. Also, Genuis has noted the tendency of some authors to have “disregard for recent laboratory and animal evidence” and to categorize sensitivity-related illness as a “psychogenic confabulation” ([Genuis SJ. Sensitivity-related illness: The escalating pandemic of allergy, food intolerance and chemical sensitivity, Science of the Total Environment, 2010; 408: 6047-61; 6057](#)). For instance, Staudenmayer et al concluded that “idiopathic environmental intolerance” “is a belief characterised by an over-valued idea of toxic attribution of symptoms and disability, fulfilling criteria for a somatoform disorder and a functional somatic syndrome” ([Staudenmayer H, Binkley KE, Leznoff A, Phillips S. Idiopathic Environmental Intolerance, Toxicol Rev 2003;22\(4\):247-61](#)). Even psychiatrists can tend to hold patients responsible for “psychological” illnesses ([Miresco MJ, Kirmayer LJ. The persistence of mind-brain dualism in psychiatric reasoning about clinical scenarios, Am J Psychiatry, May, 2006, 163:913-18](#)).
- Studies supporting MCS psychogenesis, when critically reviewed, had various methodological problems and were often subject to selection biases ([Davidoff AL, Fogarty L. Psychogenic origins of multiple chemical sensitivities syndrome: a critical review of the research literature, Archives of Environmental Health, 1994; 49\(5\):316-25](#)).
- In contrast, in a 2001 multi-center cross-sectional survey of 1,166 patients who visited outpatient occupational, otolaryngology, allergy and clinical ecological/environmental clinics, the authors found that the majority (60-79%) of those who met the criteria for MCS did not report treatment for anxiety, depression, or distress/adjustment problems, and 73% reported “good” or “excellent” health during their first 30 years of life which

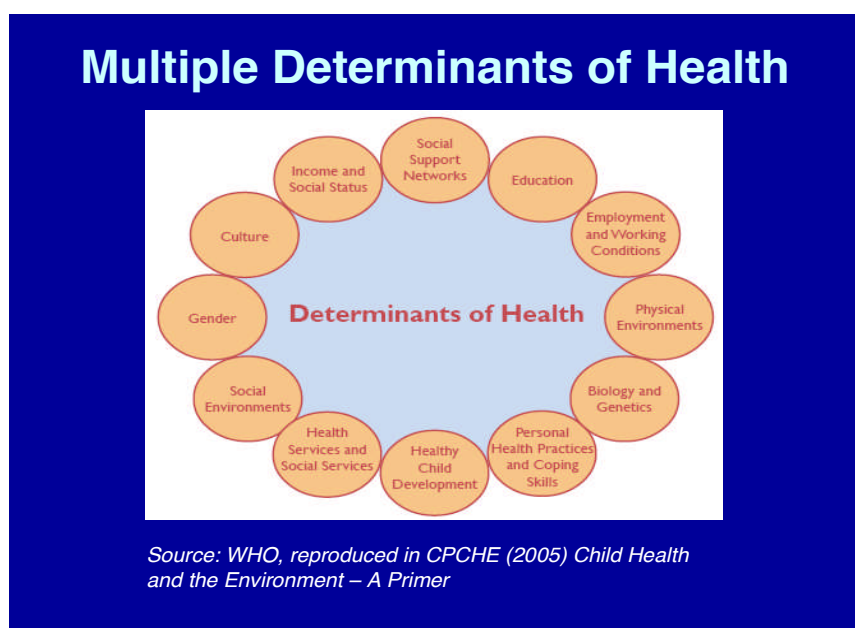
they thought was “not supportive of the idea that MCS syndrome is primarily a psychiatric or psychosomatic condition”. However, they reported that MCS patients were 5-6 times more likely than controls to seek treatment for psychological concerns secondary to chemical sensitivity “congruent with the hypothesis that much of the psychopathology seen in MCS syndrome is secondary to feeling ill” (Kutsogiannis DJ, Davidoff AL. [A multiple center study of multiple chemical sensitivity syndrome, Arch Environ Health, May/June 2001, 56\(3\):196-207](#)).

- Also, a 2003 population-based survey (N=1582) revealed that few of 199 individuals reporting MCS (1.4%) had a history of prior emotional problems, whereas a substantial number (37.7%) developed such problems after the onset of physical symptoms associated with chemical exposures (Caress SM, Steinemann AC [A review of a two-phase study of multiple chemical sensitivities, Environ. Health Perspect. 2003, 111\(12\), 1490](#)).
- Furthermore, Gibson et al found that the 917 persons with self-reported MCS who participated in their treatment survey reported a higher help-harm ratio for “psychotherapy to cope with MCS” and “support group” than for “psychotherapy to cure MCS”. Psychotropic medications were consistently rated more likely to harm than to help (Gibson PR, Elms AN-M, Ruding LA. [Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity, Environmental Health Perspectives, September 2003; 111\(12\):1501-2](#)).
- Disbelief, diminishment and/or dismissal lead to stigmatization and a lack of appropriate emergency or ongoing medical care for sufferers, as well as barriers to obtaining workplace and housing accommodation and income support. Being marginalized and impoverished can in turn lead to increased illness and disability (Lipson JG. [Multiple chemical sensitivities: Stigma and social experiences, Medical Anthropology Quarterly, 2004;18\(2\):200–213](#)). Das-Munshi et al noted that those with MCS were frequently refused Workers’ Compensation “on the grounds it is psychological” (Das-Munshi J, Rubin GJ, Wessely S. [Multiple chemical sensitivity: Review, Current Opinion in Otolaryngology Head Neck Surgery, 2007; 15:274-80](#)).
- Delegitimizing those with ES-MCS, who may be the ‘*canaries*’ warning us all of the need for toxics reduction, also tends to impede development of practical, precautionary, potentially preventive and cost-saving public health strategies.
- Trivialization and disparagement of ES-MCS as a legitimate medical condition, and of ES-MCS patients, has also extended to their physicians, prompting the Thomson Committee’s Recommendation 8: “We recommend that the fee schedule permit an enlargement of the fee to be charged if added time is required to obtain good histories, to counsel a patient on avoidance procedures and to monitor the patient’s performance” (Thomson GM, Day JH, Evers S, et al. [Report of the Ad Hoc Committee on Environmental Hypersensitivity Disorders. Ontario Ministry of Health, 1985:280](#)). Recommendation 33 of a May 24, 1990 Health and Welfare Canada Workshop on environmental sensitivities stated: “Physicians who show interest in the field should not be stigmatized and should be adequately compensated for the time they spend with patients with complicated illnesses” (Health and Welfare Canada. [Environmental sensitivities workshop, Chronic Diseases in Canada, Supplement, January 1991, ISSN-0228-8699](#)). Unfortunately, the

situations leading to these recommendations have not changed, and so few physicians are attracted to the field of environmental health, and research progress is hampered.

- The World Health Organization (WHO) describes multiple determinants of health (**Figure 1**), which may be addressed for each ill individual, allowing many more treatment options. A “multifactorial model” for MCS was suggested by Das-Munshi et al, although psychological-behavioural treatment approaches were, perhaps not surprisingly, favoured by the psychiatrist and psychologist authors (Das–Munshi J, Rubin GJ, Wessely S. [Multiple chemical sensitivities: review, Curr Opin Otolaryngol Head Neck Surg 2007, 15\(4\): 274-80](#)).

**Figure 1: World Health Organization’s Multiple Determinants of Health**  
(Child Health and the Environment- A Primer, Canadian Partnership for Children’s Health and the Environment, August 2005, [www.healthyenvironmentforkids.ca](http://www.healthyenvironmentforkids.ca))



### **Prevalence:**

Prevalence surveys have now been conducted in several of the United States for both physician-diagnosed and self-reported MCS. The Canadian Community Health Survey has reported health professional-diagnosed MCS in those over the age of twelve in Canada, and has shed light on demographics, functional impacts, influence of poverty and co-morbid conditions. There is no available incidence data nor are there prevalence statistics for children under twelve.

### **✚ Diagnosis by a Health Professional**

- In a study funded by the Ontario Ministry of Health, Kutsogiannis and Davidoff noted that several statewide surveys in the U.S. found that 3.1-6.3 percent of the American population reported diagnosis of MCS by a physician (Kutsogiannis DJ, Davidoff AL. [A multiple center study of multiple chemical sensitivity syndrome, Arch Environ Health, May/June 2001, 56\(3\):196-207](#)). Also, the 2002 and 2003 Canadian Community Health Surveys (CCHS) revealed that 2-3 % of Canadians reported being diagnosed with MCS

by a health professional (Park J, Knudson s. Medically unexplained physical symptoms, Health Reports, Statistics Canada Catalogue 82-003, February 2007, 18(1):43-7).

- We believe it is important to recognize the significant reporting of MCS compared with a few other well known “long term conditions” in the Canadian Community Health Survey (2000-2003) that are “expected to last or have already lasted 6 months or more and that have been diagnosed by a health professional” (**Table 2**).

**Table 2:**

**Prevalence of Multiple Chemical Sensitivity and Other Long Term Conditions**

(From online Statistics Canada-based prevalence reports, 13/08/2010, compiled by L. Marshall)

<b>Long Term Health Condition</b>	<b>Prevalence over age 12 or 15 (CCHS, 2000-2003)</b>
Multiple Sclerosis	0.24%
AIDS	0.4%
Breast Cancer	1%
All cancers	2.6%
<b>Multiple Chemical Sensitivity</b>	<b>2.4% (1.4% men, 3.4 % women)</b>
Type 2 Diabetes	3-4%
Heart Disease	5.4% men, 4.6% women
Arthritis/Rheumatism	16% (2/3 women)

- In the 2005 Canadian Community Health Survey, 2.5% of adult Ontarians had been diagnosed by a health professional with MCS, with prevalence increasing with age, peaking at 5.8% in women between the ages of 60 and 64 years (**Table 3**).
- The provincial Environmental Health Clinic in Ontario recently reported considerably decreased functional status of our MCS patients relative to the Canadian population on the eight functional status scales of the well-validated Short Form-36 (Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). 1. Conceptual framework and item selection, Med Care 1992, 30(6):473-83), and markedly increased health care utilization rates (Lavergne MR, Cole DC, Kerr K, Marshall LM. Functional impairment in chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity, Canadian Family Physician, February 2010; 56: e57-65).

**Table 3:****Prevalence of Multiple Chemical Sensitivity (MCS) by Age and Gender in a Target Population\***

(From the 2005 Public Use Microdata File of the Canadian Community Health Survey, Statistics Canada.10-10-2007, compiled by Margaret Parlor, BA, LLB, Statistical Analyst)

	<b>% of population* with MCS</b>	<b>% of males with MCS</b>	<b>% of females with MCS</b>
<b>Total age 12 y and over</b>	2.2	1.2%	3.1%
<b>12 to 14 years</b>	0.8	0.6	1.0
<b>15 to 17 years</b>	0.7	0.4	1.0
<b>18 to 19 years</b>	0.9	0.8	0.9
<b>20 to 24 years</b>	0.9	0.5	1.2
<b>25 to 29 years</b>	1.4	1.1	1.7
<b>30 to 34 years</b>	1.6	1.0	2.1
<b>35 to 39 years</b>	1.7	1.2	2.2
<b>40 to 44 years</b>	2.4	1.7	3.0
<b>45 to 49 years</b>	2.9	1.3	4.4
<b>50 to 54 years</b>	3.3	1.7	4.9
<b>55 to 59 years</b>	3.6	1.7	5.5
<b>60 to 64 years</b>	3.6	1.4	5.8
<b>65 to 69 years</b>	3.3	1.8	4.6
<b>70 to 74 years</b>	2.9	1.9	3.8
<b>75 to 79 years</b>	3.2	1.6	4.5
<b>80 years plus</b>	1.9	1.1	2.3

\*Target population: citizens aged 12 and over, excluding Canadians living in institutions, native Canadians living on reserves, full time members of the armed forces, and Canadians living in remote regions

#### **Self-reported MCS**

- Like almost any medical condition, people may be mildly, moderately or severely affected, and those more mildly affected may not present for medical care. Also, it takes time for educational programs for healthcare professionals to be developed after a relatively newly observed illness has been reported, and so diagnoses may be less frequently made and the condition under-reported. Researchers in three U.S. states therefore also asked randomly selected adults if they thought themselves to be “unusually” or “especially” sensitive and if they felt ill on exposure to low-level everyday chemicals. In California and New Mexico, 16% said yes ([Kreutzer R, Neutra RR, Lashuay N. Prevalence of people reporting sensitivities to chemicals in a population-based survey. Am J Epidemiol 1999, 150:1-12; Voorhees RE. Memorandum from New](#)

Mexico Deputy State Epidemiologist to Joe Thompson, Special counsel, Office of the Governor, 13 March 1998). In North Carolina, 33 % of randomly selected adults, and in Arizona, 33 % of college students answered affirmatively (Meggs WJ, Dunn KA, Bloch Rm et al. Prevalence and nature of allergy and chemical sensitivity in a general population, Arch Environ Health, 1996, 51:275-82; Bell IR, Schwartz Ge, Peterson JM et al. Self-reported illness from chemical odors in young adults without clinical syndromes or occupational exposures, Arch Environ Health, 1993, 48:6-13). High prevalence rates found in workers studied after occupational overexposures were cited in a study funded by the Ontario Ministry of Health (Kutsogiannis DJ, Davidoff AL. A multiple center study of multiple chemical sensitivity syndrome, Arch Environ Health, May/June 2001, 56(3):196-207).

- The 2005 National Survey of the Work and Health of Nurses revealed that 3.6% of all Canadian nurses, predominantly women, experienced chemical sensitivities (N=18,676). Of nurses younger than 35 years, 1.4% reported chemical sensitivities, which increased to 3.7% in nurses 35-44 years old, and 4.3% and 4.8% in successive decades (Statistics Canada [www.statcan.ca](http://www.statcan.ca) → Publications, electronic format catalogue no. 83-003-XIE; print version 83-003-XPE)..

#### **Poverty Influence**

- In the 2002 and 2003 CCHS, MCS prevalence was higher in those of the lowest socioeconomic status, who are known to have higher exposures to hazardous environmental agents, generally poorer nutrition, and more psychosocial stress, all known vulnerability factors for chronic health problems. In addition, these surveys found that 22% of those with MCS were “dependent in instrumental activities of daily living” (Statistics Canada. Canadian Community Health Survey 2003, reported by Park J, Knudson S, Health Reports, Catalogue 82-003, February 2007, 18(1):45).
- Of a random sample of 1,582 individuals from Atlanta, Georgia, 12.6% reported hypersensitivity to common chemicals, and 13.5 % of these (1.8% of the entire sample) reported loss of employment due to their hypersensitivity (Caress SM, Steinemann AC. A review of a two-phase population study of multiple chemical sensitivities, Environ Health Perspect. 2003, 111:1490-7).
- **Prevalence in Childhood and Incidence**  
The prevalence of MCS in children under age 12 has never been studied, but we at the EHC think there is cause for concern, given that fetuses and children are known to be the most vulnerable to health impacts from exposure to environmental toxins, and exposure during key developmental stages can have lifelong consequences (McKeown D, Toronto Public Health, Environmental Threats to Children, Understanding the Risks, Enabling Prevention, September 2005). Certainly, the rapid rise in childhood asthma, learning and neurobehavioural disorders and disabilities has been linked with increased exposure to various environmental chemicals (Canadian Partnership for Children’s Health and the Environment. Child health and the environment-A primer, August 2005:33-40; [www.healthyenvironmentforkids.ca](http://www.healthyenvironmentforkids.ca)).
- To our knowledge, no studies of incidence of MCS at any age have yet been published, and so it is unknown if the condition is increasing or not.

- ***Co-morbid Conditions***

Much overlap has been noted in the U.S. between prevalence of allergies and chemical sensitivities (Meggs WJ, Dunn KA, Bloch RM, Goodman PE, Davidoff AL. Prevalence and nature of allergy and chemical sensitivity in a general population, *Arch Environ Health*, 1996, 51:275-82), and between asthma and chemical sensitivities (Caress SM, Steinemann AC. National prevalence of asthma and chemical hypersensitivity: an examination of potential overlap, *J Occup Environ Med*, 2005, 47:518-22).
  
- Allergies and asthma commonly overlap with MCS in Canada too, and the prevalence of several other underlying or co-morbid chronic conditions affecting multiple body systems is greater in the MCS population compared to the general Canadian ‘target population’ (Statistics Canada, CCHS, 2005) (Table 4) Medical care for many of the listed chronic conditions on their own is provided in medical specialty clinics, although patients with myalgic encephalomyelitis/chronic fatigue syndrome and some with fibromyalgia are chronically underserved by specialty clinics in Ontario and are commonly referred to the provincial Environmental Health Clinic by their primary care physicians. If specialists are not knowledgeable about how chemical sensitivity reactions can mimic or trigger many of the problems that they treat, patients with ES-MCS who go to such specialists are not likely to receive effective treatment/support, and may even have treatments recommended that are harmful for them, such as non-tolerated medications. Because of stigmatization of ES-MCS, specialists have not been encouraged to study how the condition impacts their specialty scope.

**Table 4:**

**Frequencies of MCS Co-diagnoses for Canadian Target Population\***

(From the 2005 Public Use Microdata File of the Canadian Community Health Survey, Statistics Canada.10-10-2007, compiled by Margaret Parlor, BA, LLB, Statistical Analyst)

<b>Chronic condition</b>	<b>% of people with MCS having this additional diagnosis...</b>	<b>% of target population having this diagnosis...</b>
<b>Other allergies (not food)</b>	61.1	26.6
<b>Other back problems (not arthritis or fibromyalgia)</b>	39.7	18.8
<b>Arthritis/rheumatism</b>	38.5	16.4
<b>Food Allergies</b>	27.3	7.2
<b>Migraine headache</b>	26.3	10.5
<b>Asthma</b>	25.7	8.3
<b>High blood pressure</b>	24.5	14.9
<b>Mood disorder</b>	15.9	5.6
<b>Anxiety Disorder</b>	14.5	4.4
<b>Thyroid condition</b>	13.8	5.6
<b>Bowel disorder</b>	13.1	3.9
<b>Bronchitis</b>	11.4	2.5
<b>Fibromyalgia</b>	10.0	1.4
<b>Chronic Fatigue Syndrome</b>	9.9	1.2
<b>Heart disease</b>	9.8	4.7
<b>Cataracts</b>	9.1	4.2
<b>Stomach/Intestinal ulcers</b>	8.9	3.1
<b>Diabetes</b>	6.9	4.9
<b>Glaucoma</b>	3.9	1.5
<b>Effects of stroke</b>	2.5	1.1
<b>Cancer</b>	2.3	1.4
<b>Epilepsy</b>	1.3	0.6

\* Target Population: citizens aged 12 and over, excluding Canadians living in institutions, native Canadians living on reserves, full time members of the armed forces, and Canadians living in remote regions.

**Diagnosis:**

Diagnosis of ES-MCS is accomplished by ruling out or treating other conditions that could account for, or contribute to the presenting symptoms, by assessing each individual's exposures, and determining whether or not the person's pattern of symptoms fits validated clinical consensus criteria. A few tests are helpful in assessing body burden of various chemicals, functional status, co-morbid allergies, and brain hypoperfusion.

**✚ Ruling Out Other Conditions**

- Given that there are no definitive objective diagnostic tests for ES-MCS, a practical strategy of 'ruling out' other conditions or factors that could be contributing to each patient's symptoms is used initially via comprehensive clinical history, physical examination, and readily available laboratory tests ([Sears M. The Medical Perspective on Environmental Sensitivities. Canadian Human Rights Commission, 2007](#),



[http://www.chrc-ccdp.ca/pdf/envsensitivity\\_en.pdf](http://www.chrc-ccdp.ca/pdf/envsensitivity_en.pdf)). If ES-MCS is suspected, but other conditions or potential contributors are found, they are treated, cautiously, with tolerated treatments, often at lower doses than usual, and the patient's symptoms are re-assessed (Marshall Lynn M., Bested Alison C., Bray Riina I. Poorly understood conditions of the 21<sup>st</sup> century- Chronic Fatigue Syndrome, Fibromyalgia, and Multiple Chemical Sensitivity, invited paper, Canadian Journal of Diagnosis, July 2003: 65-71, based on a presentation for Family Medicine Forum 2002, Montreal, College of Family Physicians of Canada.

<http://www.stacommunications.com/journals/pdfs/diagnosis/dxjuly03/drmarshallsyndromes%20pd.pdf> and Frequently Asked questions, Poorly understood conditions of the 21<sup>st</sup> century: Chronic Fatigue syndrome (CFS), Fibromyalgia (FM), and Multiple Chemical Sensitivity:32, and Why do I feel so tired? : 39-42

<http://www.stacommunications.com/journals/pdfs/diagnosis/dxjuly03/wydx.pdf>). If a patient has both ES-MCS and one or more co-morbid conditions, it can be challenging to find tolerable treatments, and medication side effects can obscure links between symptoms and exposure to other environmental agents.

#### ✚ **Exposure Assessment**

- A systematic method of taking a comprehensive exposure history using a handy mnemonic has been developed (Marshall Lynn, Weir Erica, Abelsohn Alan, Sanborn Margaret D. Identifying and managing adverse environmental health effects: 1. Taking an exposure history. CMAJ Apr. 16, 2002; 166 (8): 1049-55 and Occupational and environmental exposure, response to letter to the editor by Michael Schweigert, CMAJ, Oct. 1, 2002; 167 (7): 744, 746), as well as exposure history forms utilizing this method, which may be downloaded from the Ontario College of Family Physicians website (Marshall Lynn. Taking an Exposure History, 2002, updated 2004 and 2005 after peer review by the provincial Environmental Health Clinic physicians and Ontario College of Family Physicians Environmental Health Committee Members, [www.ocfp.ca](http://www.ocfp.ca) → Environmental Health Committee and scroll).
- Blood and 24-hour urine tests for some toxic metals are accessible in Ontario and, for the most part, are funded by the Ontario Health Insurance Plan. However, blood or urine tests or fat biopsies for other retained chemicals must be obtained in the United States at patients' expense. Some of these tests are currently being used in Canada in biomonitoring studies (Canadian Health Measures Survey, Maternal-Infant Research on Environmental Chemicals, accessed August 15, 2010, <http://www.chemicalsubstanceschimiques.gc.ca/plan/surveil/bio-initiatives-enquetes-eng.php>)

#### ✚ **Ruling In MCS**

- If no other explanation is found for a patient's presenting illness, and their symptom pattern follows that specified in the consensus case criteria (Bartha et al. Multiple Chemical Sensitivity: a 1999 consensus. Archives of Environmental Health, May/June 1999; 54(3): 147-9), and if the patient reports having a stronger sense of smell than most people and two of three discriminating neurological symptoms (McKeown-Eyssen GE, Baines CJ, Marshall LM, et al. "Multiple Chemical Sensitivity: Discriminant Validity of Case Definitions." Arch Environ Health, 2001; 56(5):406-12), this is considered to 'rule in' MCS. The Environmental Health Clinic physicians have created a checklist of these criteria and posted them online for the use of practising physicians ([www.ocfp.on.ca](http://www.ocfp.on.ca) → Environmental Health Committee and scroll).

### **Functional Status**

- Blood test indicators of various organ functions as well as nutritional status, along with pulmonary function tests and sleep studies are employed to gauge various functions of ES-MCS patients along the severity continuum.
- The physicians in the provincial Environmental Health Clinic in Ontario also assess functional status of patients referred by Ontario physicians using the Short Form-36 questionnaire (Ware JE, Sherbourne CD. *The MOS 36-item short-form health survey (SF-36). 1. Conceptual framework and item selection*, *Med Care* 1992, 30(6):473-83). A chart review of 128 consecutive patients diagnosed by an EHC physician with one or more of MCS, chronic fatigue syndrome or fibromyalgia revealed substantial functional impairment (Lavergne MR, Cole DC, Kerr K, Marshall LM. *Functional impairment in chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity*, *Canadian Family Physician*, February 2010; 56: e57-65). The results supported findings in the United States (Black DW, Doebbeling BN, Voelker MD, Carke WR, Woolson RF, Barrett DH et al. *Quality of life and health services utilization in a population-based sample of military personnel reporting multiple chemical sensitivities*, *J Occup Environ Med*, 1999;41(10):928-33; Jason LA, Taylor RR, Kennedy CL. *Chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities in a community-based sample of persons with chronic fatigue syndrome-like symptoms*, *Psychosom Med*, 2000; 62(5):655-63).
- EHC physicians in Ontario have developed an Activity Log and Functional Capacity Scale that may be downloaded from the Ontario College of Family Physicians website (Bested AC, Marshall LM. *Activity Log and Functional Capacity Scale*, [www.ocfp.on.ca](http://www.ocfp.on.ca) → Environmental Health Committee).

### **Chemical Provocation Tests**

- In our view, there are ethical concerns with chemical provocation inhalation challenges because in a vulnerable population it is hard to determine challenge dosages without potential for harm.
- Das-Munshi et al reviewed heterogeneous studies of chemical provocation, in that various chemicals were used in various doses, sometimes with or without nasal clips or face masks, and sometimes with or without chemical masking agents/placebos that were acknowledged to be potentially active (Das-Munshi J., Rubin G.J., and Wessely S. *Multiple chemical sensitivities: A systematic review of provocation studies*, *J Allergy Clin Immunol*, December 2006; 118(6):1257-64). In addition, there was an apparent lack of understanding of, and accounting for the confusing impacts on provocation results of habitual versus intermittent exposure to test agents. Coupled with lack of consistent, objective, easily measurable outcomes, it is not surprising to us that results of these studies were inconsistent.

### **Allergy Tests**

- As noted previously (Meggs WJ, Dunn KA, Bloch RM, Goodman PE, Davidoff AL. *Prevalence and nature of allergy and chemical sensitivity in a general population*, *Arch Environ Health*, 1996, 51:275-82; Parlor M. *Frequencies of MCS Co-diagnoses for Canadian Target Population*, CCHS Public Use Microdata File, Statistics Canada, 2005), there is a strong overlap of allergies, to both foods and biological inhalants, such as dust mites, animal danders, pollens and moulds. While blood radioallergosorbent (RAST) tests

may be used to identify antibodies to such allergens, the results do not correlate well with symptoms. Skin prick tests may be helpful to screen for inhalant allergens, less so for foods, but, empirically, can provoke significant exacerbation of symptoms for some patients with ES-MCS.

- Serially diluted intradermal or sublingual tests for inhalants with individual formulation of hyposensitization treatments have been empirically helpful in ES-MCS cases with concomitant allergies ([Wright ST. Diagnosis and management of inhalant allergens, http://www.utmb.edu/otoref/grnds/Inhalant-allergens-2003-0611/Inhalant-allergens-2003-0611.doc](#)) in Canada, the U.S. and U.K. They were not included in Gibson's U.S. survey. Moreover, since the treatment is unique for each individual, and individuals with ES-MCS are heterogeneous in many respects, they are not amenable to group trials.
- Since skin prick test results for food allergens do not correlate well with symptoms, elimination and re-ingestion challenge tests may be used, except of course if there is a history of known or suspected life-threatening (anaphylactic) reactions. If many foods are suspected to be problematic, rotation of a broader range of foods can help to ferret out intolerances, and then, once discovered, the patient may be able to limit exposure to those foods. In contrast to Das-Munshi et al's interpretation that rotation of foods has "iatrogenic effects" ([Das-Munshi J, Rubin GJ, Wessely S. Multiple chemical sensitivities: review, Current Opinion in Otolaryngology & Head and Neck Surgery, 2007; 15:277](#)), Taylor et al found that the more the diet was adhered to, the better the nutritional intake and the fewer and less severe the symptoms ([Taylor JP, Krondl MM, Spidel M, Csima AC. Dietary adequacy of the rotary diversified diet as a treatment for 'environmental illness', Canadian Journal of Dietetic Practice and Research, Winter 2002; 63\(4\):198-201](#)).

#### **SPECT Scans**

- Physicians of the internationally consulted Dallas, Texas Environmental Health Center described specific abnormalities of metabolism in the brains of those with MCS with neurocognitive impairment when imaged with single photon emission computed tomography (SPECT). The recurrent patterns consistent with neurotoxicity included a mismatch in tracer uptake between early- and late-phase imaging, multiple hot and cold foci throughout the cortex, temporal asymmetry and increased tracer uptake into the soft tissues and sometimes the basal ganglia. They had previously noted a similar pattern in patients with acute neurotoxic chemical exposures and breast implants, and indicated: "Affective processes such as depression do not, alone, show this pattern". Further they found that controlled challenges to ambient chemicals induced the same specific changes on SPECT imaging in chemically sensitive patients, and that significant improvement on SPECT brain imaging frequently followed detoxification treatment in these patients. ([Ross GH, Rea W, Johnson AR, Hickey DC, Simon TR. Neurotoxicity in single photon emission computed tomography brain scans of patients reporting chemical sensitivities, Toxicology and Industrial Health, 1999 April/May;15\(3-4\):415-20](#)).
- However, controlled studies have been difficult to mount due to challenges in finding controls, ethical issues regarding chemical challenges, and cost. Nevertheless, a recent, well-designed and executed study has confirmed empirical reports and the authors concluded, "Chemical exposure caused neurocognitive impairment and SPECT brain dysfunction, particularly in odour processing areas, thereby suggesting a neurogenic origin

of MCS” (Orriols R, Costa R, Cuberas G, Jacas C, Castell J, Sunyer J. Brain dysfunction in multiple chemical sensitivity, *Journal of the Neurological Sciences*, 2009; 287:72-8).

- SPECT scans are very expensive and, while they do provide some objective evidence in MCS, they do not generally impact management more than a careful exposure history. They have been used to bolster legal efforts to obtain benefits or accommodation for those seriously ill with MCS.

#### ✚ *Etiological Understanding and Diagnosis*

- As understanding of etiological mechanisms improves, it will hopefully become possible to design readily available and affordable objective diagnostic tests for those with ES-MCS, and any subset populations that are discovered that have unique features. Such tests would aid earlier diagnosis and treatment and likely save much cost for the health care system.

### **Treatment:**

Treatment for ES-MCS is based on evidence-informed principles, is individualized, holistic and person-centred. It focuses on assisting patients to reduce their exposures to their unique symptom triggers and hazardous chemicals, optimizing their internal processing and elimination of chemicals, and reducing chemical body burdens when necessary and achievable. If co-morbid allergies are not relieved by environmental controls at home and in the workplace, they may be helped by increased ventilation, filtration, individualized desensitization or symptom-relieving medications. Dysbiosis (imbalanced microflora in the gastrointestinal tract) may be helped by probiotics and stabilization of pH. Patients are encouraged to take control and self-manage their health, planting a “health garden” using a “weed, SEEDS and feed approach”. With the support of their health care professionals, patients learn how to weed out aggravators, and then to institute and nurture elements of good health. [SEEDS is an acronym for Sleep, Exercise (and pacing), Environment, Diet (nutrition), and Support.]

Patients who do not have adequate economic resources to achieve the above measures early in the course of their illnesses, and/or cannot access knowledgeable physicians in safe facilities, and/or who are severely chemically sensitive, and/or have co-morbid infections/other conditions are greatly challenged. For such people, it can be risky to their already compromised health to undertake necessary activities such as shopping in a supermarket or consulting with a physician in an unsafe office, and lack of physician awareness can increase the risk of inappropriate treatment and further deterioration.

#### ✚ *Duty to Provide Care*

- In the 21<sup>st</sup> century, physicians and other healthcare professionals are frequently consulted by patients suffering with complex conditions such as ES-MCS, who need immediate and ongoing medical assistance. Despite imperfect knowledge of etiology and mechanisms of conditions, and in the absence of definitive laboratory tests, healthcare professionals nevertheless have a responsibility to provide care. Even if there is a dearth of randomized clinical trial evidence for therapies, physicians are duty bound to “Consider first the well-being of the patient” (Canadian Medical Association. Code of ethics, Update 2004, <http://policybase.cma.ca/PolicyPDF/PD04-06.pdf>). They need to listen to patients’ feedback about their observations and pay attention to their own, and then take the time to advise patients using the *available* evidence and their best clinical judgment, so that patients may make informed choices about the lowest risk, highest potential benefit modalities likely to apply to their individual situations. Such a collaborative working relationship avoids abandoning patients to their own devices.

✦ **Patient-centred Trend in Health Care**

- There has been a shift by Canadian healthcare professionals and policymakers towards “patient centredness” in care, which “may be most commonly understood for what it is not- technology centred, doctor centred, hospital centred, disease centred” (Stewart M. Towards a global definition of patient centred care: The patient should be the judge of patient centred care, *BMJ*, February 24, 2001; 322, 444-5; Stewart M, Brown JB, Weston WW, McWhinney IR, McWilliam CL, Freeman TR. Patient-centred medicine: Transforming the clinical method, 2<sup>nd</sup> Edition, 2003, Radcliffe Medical Press Ltd, U.K.).
- In an observational cohort study of 315 patients seen by 39 randomly selected family physicians, patient-centred communication/practice was found to improve health status outcome and decrease health care costs by decreasing diagnostic tests and referrals (Stewart M, Brown JB, Donner A, McWhinney IR, Oates J, Weston WW, Jordan J. The impact of patient-centred care on outcomes, *The Journal of Family Practice*, July 4, 2000, <http://www.jfponline.com/Pages.asp?AID=2601>).
- An observational study of 865 consecutive patients in the offices of three doctors revealed the key components to patients of a patient-centred model of care (**Table 5**) (Little P, Everitt, H, Williamson I, Warner G, Moore M, Gould C, Ferrier K, Payne S. Preferences of patients for patient centred approach to consultation in primary care: observational study, *BMJ*, 24 February, 2001; 322:1-7).

**Table 5:**

**Key Components of a Patient Centred Model of Care According to Patients**

(Little P, Everitt, H, Williamson I, Warner G, Moore M, Gould C, Ferrier K, Payne S. Preferences of patients for patient centred approach to consultation in primary care: observational study, *BMJ*, 24 February, 2001; 322:1-7)

<i>“Main domains of model of patient centredness”</i>
“Exploring the experience of disease and illness: patients' ideas about the problem, feelings, expectations for the visit, and effects on function
Understanding the whole person: personal and developmental issues (for example, feeling emotionally understood) and the context (the family and how life has been affected)
Finding common ground (partnership): problems, priorities, goals of treatment, and roles of doctor and patient
Health promotion: health enhancement, risk reduction, early detection of disease
Enhancing the doctor-patient relationship: sharing power, the caring and healing relationship”

- However, as Ball has pointed out, “Politics and power drive the system and the fact is: consumers have no power” (Ball T. *Disruptive innovation: Patient/family-focused care, Managing Change, Summer 2010:1-16*). He cited Glover: “the principle of individuality creates an interesting problem: a patient-centred system must be inclusive enough to support 34 million personalized health systems that are unique to each Canadian and ultimately managed by him or her”. Glover and the Canadian Association for People-centred Health envision that patients

should be able to select and access the most appropriate providers/coaches and support services they need, and that they are collectively willing to pay for in the Canadian health care system (Glover V. [Journey to wellness: Designing a people-centred health system](#); available at [www.caph.ca](http://www.caph.ca)).

- For ES-MCS sufferers the ideal of ‘patient-centred care’ is currently in stark contrast to realities within the health care system. Knowledgeable healthcare professionals and support workers are so few as to be virtually inaccessible most of the time. For moderately or severely chemically sensitive persons, physicians’ offices, clinics and hospitals commonly are unsafe places to wait, consult, or undergo procedures because patients can be exposed to many symptom triggers emitted from furnishings, cleaning and laundry products, disinfectants, and personal care products on staff or other patients, making their conditions worse. Fragrance/scent-free hospital, home care and rehabilitation services are very rarely available, and there are no chemically safe emergency shelters. Consequently, patients with severe chemical sensitivities may avoid seeking care, risking further deterioration and chronicity, thereby being “caught between a rock and a hard place.”
- In this time of health professional shortages and increasing demand by an aging population, it is also difficult to get knowledgeable ongoing medical or surgical care for complex multi-system health problems such as ES-MCS, and patients may still be disbelieved and ignored. The results include poor health outcomes and higher health care costs, both for the patient and for the health care system.
- In addition to aspiring towards truly person-centred individual care, the Environmental Health Clinic team consults with consumer representatives from patient support groups on EHC programs. These representatives attend several EHC staff meetings each year, keep the leaders of relevant support groups informed, and consult them for their opinions on environmental health service issues. The EHC team is constantly hearing from the consumer support organizations how Ontarians with ES-MCS are underserved, and how their ongoing care physicians from across the province find it extremely challenging and time-consuming to address the needs of the population of patients with ES-MCS in their own communities. Clearly, with the current level of funding and staffing, the support that the Ontario EHC team has been able to offer to Ontarians with ES-MCS is inadequate.

#### ***Empirical Evidence-informed Approaches***

- The team at the provincial Environmental Health Clinic in Ontario believes, as does the staff at the Nova Scotia Environmental Health Centre (NSEHC), “that there is no need to wait for a full understanding of the pathophysiology of these conditions before we should manage them” (Fox RA, Joffres MR, Sampalli T, Casey J. [The impact of a multidisciplinary, holistic approach to management of patients diagnosed with multiple chemical sensitivity on health care utilization costs: An observational study](#), *The Journal of Alternative and Complementary Medicine*, 2007; 13(2):223-9). Both clinics assess potential biological, physical environmental, nutritional, psychosocial, and other potential contributors to illness for each patient, and, whenever possible, assist the individual to self manage these factors with their primary care physician's medical support. Our clinical impression, consistent with that of other clinicians, is that generally the earlier actions are taken to address illness factors, the faster and more satisfactory the recovery- and thus the lower the utilization of the health care system.
- In Gibson et al’s study, subjects commented that it was only the combination of treatments that helped them improve. Many reported that it was necessary to do environmental controls, a

correctly tailored program of nutritional supplements, and a number of other interventions that addressed their own unique constellation of symptoms” (Gibson PR, Elms AN-M, Ruding LA. [Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity, Environmental Health Perspectives, September 2003; 111\(12\):1503](#)).

- Such a multi-faceted, individualized approach to care of heterogeneous ES-MCS patients is not conducive to group randomized controlled trials, and so no specific treatment protocol has been assessed by that method.
- Just as ES-MCS patients have been disparaged, so have the practising physicians who first observed and reported ES-MCS, hypothesized pathological mechanisms, and clinically explored what they thought were rational therapeutic responses (Swoboda DA. [Negotiating the diagnostic uncertainty of contested illnesses: physician practices and paradigms, Health \(London\), October, 2008; 12\(4\):453-78](#)). Nevertheless, many of their ideas, including reduction of exposure to triggers and toxins, have stood the test of time. Physicians from family medicine and many medical specialties are now recognizing the importance of environment-health links and information about exposure reduction is being made available to the public (<http://www.newswire.ca/en/releases/archive/March2007/01/c4421.html>; Canadian Liver Foundation, [Liver health begins at home](#); The Lung Association, [http://www.lung.ca/protect-protegez/pollution-pollution/indoor-interieur/index\\_e.php](http://www.lung.ca/protect-protegez/pollution-pollution/indoor-interieur/index_e.php); Reuben SH for the President’s Cancer Panel. [Reducing environmental cancer risk- What we can do now](#). U.S. Department of Health and Human Services, April 2010; [http://deainfo.nci.nih.gov/advisory/pcp/annualReports/pcp08-09rpt/PCP\\_Report\\_08-09\\_508.pdf](http://deainfo.nci.nih.gov/advisory/pcp/annualReports/pcp08-09rpt/PCP_Report_08-09_508.pdf)).
- The cornerstones in clinical management of ES-MCS are:
  - reduction of exposure to each person’s unique environmental symptom triggers (e.g. some perfumes, cat dander) and toxins (e.g. formaldehyde emitted from particleboard, pesticides), once identified via exposure history and observation,
  - enhancement of internal processing and elimination of chemicals,
  - reduction in body burden of retained chemicals if necessary,
  - relief of suffering with symptomatic treatments as needed,
  - treatment of co-morbid conditions that can exacerbate or be exacerbated by ES-MCS, and
  - encouragement to make changes in habits that would be likely to prevent further illness and promote health.
- Unlike the provincial EHC in Ontario, the NSEHC provides ongoing treatment, and there is now evidence of reduced healthcare utilization by NSEHC patients after treatment, resulting in significant health care system savings from reduced physician visits both to general practitioners and specialists, as well as reduced emergency room visits and hospital admissions (Fox RA, Joffres MR, Sampalli T, Casey J. [The impact of a multidisciplinary, holistic approach to management of patients diagnosed with multiple chemical sensitivity on health care utilization costs: An observational study, The Journal of Alternative and Complementary Medicine, 2007; 13\(2\):223-9](#)).

#### ✚ **Reduction of Exposure to Triggers and Toxins**

- By definition, people with MCS have symptoms that “are reproducible with [repeated chemical] exposure” and that “improve or resolve when the incitants are removed” (Bartha et al. [Multiple Chemical Sensitivity: a 1999 consensus. Archives of](#)

[Environmental Health, May/June 1999; 54\(3\): 147-9](#)). Most patients who have noted a few such links between their symptoms and exposure to environmental triggers have already avoided them as best they can by the time they come to medical care, with some improvement in acute, intermittent symptoms. However, they may have chronic symptoms and may not have noticed the symptom-exposure links of substances to which they are exposed very frequently, which may be “masked” due to quasi-persistence in the body. It takes time and expertise for physicians to identify the most likely problematic chemicals via a detailed exposure history and observation, to educate patients about where these chemicals are likely to be encountered, and then how to avoid them or reduce exposures, for example by using less-toxic and/or better-tolerated substitutes.

- Since many of the same triggering agents (e.g. pesticides, paints, and perfumes) are repeatedly reported by those with MCS, it often helps to assist patients to focus on reducing their exposure to these substances as well as to their own unique symptom triggers as a precautionary measure if there is no undue hardship. Gibson et al’s finding of MCS sufferers’ almost universal use and the helpfulness of “chemical avoidance” and “chemical-free living space” is not surprising. Gibson et al also noted that these therapies are “fairly non-invasive and low risk”, as respectively these two strategies were rated to be 119 and 155 times more likely to be helpful than harmful. ([Gibson PR, Elms AN-M, Ruding LA. Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity, Environmental Health Perspectives, September 2003; 111\(12\):1498-1504](#)).
- Avoidance strategies have also been reported to be helpful for those with MCS by many other authors (e.g. [Ziem G. Multiple chemical sensitivity: Treatment and follow up with avoidance and control of chemical exposures, Toxicol Ind Health July 1, 1992; 8\(4\):73-86](#); [Lax, M., Henneberger, P. Patients with Multiple Chemical Sensitivities in an Occupational Health Clinic: Presentation and Follow-up, Archives of Environmental Health, 1995; 50\(6\):425-31](#)); [Ashford NA, Miller CS. Chemical exposures, low levels and high stakes, 2<sup>nd</sup> Edition, John Wiley & Sons Inc., 1998](#); [Canada Mortgage and Housing Corporation. Research House for the environmentally sensitive, 1994, reprinted 1995, 1998, 2002, Cat. No. NH15-90/1994E](#); [Caress S.M., Steinemann A.C. Prevalence of fragrance sensitivity in the American population. Journal of Environmental Health , 2009; 71\(7\): 46-50](#); [National Defence and the Canadian Forces. Environmental sensitivities, Safety Digest, Edition 6/2010, reproduced from the Safety, Emergency and Security Management Division of Treasury Board](#)).
- Sadly, treatment of severely ill patients is often less successful than of those identified in primary care and treated early, when often simple modifications such as avoiding pesticide applications and using low VOC (volatile organic compound) paints and unscented cleaning, laundry and personal care products, possibly with minor dietary changes, are enough to return the person to health. They may still experience symptoms when they encounter such substances elsewhere, but if they can keep away from them in their daily diet, home and work environments, the symptoms triggered elsewhere generally become much milder and shorter lasting. However, avoiding many symptom-triggering exposures in air, food, water, and consumer products is not easy, and much less so if the sufferer has limited financial means ([Gibson PR, Elms AN-M, Ruding LA. Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity, Environmental Health Perspectives, September 2003; 111\(12\):1503](#)).



- If people with ES-MCS are not successful in achieving accommodation in the workplace, it can directly impact their income-earning capacity and financial resources. Gibson et al found that the mean annual personal income for their sample of 917 people was \$20,000. 286 (31%) of the 917 had made a worker's compensation claim, 115 had been compensated and 54 were awaiting resolution. Only 211 (23%) were employed outside the home (Gibson PR, Elms AN-M, Ruding LA. Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity, *Environmental Health Perspectives*, September 2003; 111(12):1499).
- Finding or creating a safe living space, although medically desirable (Canada Mortgage and Housing Corporation. *Research house for the environmentally hypersensitive*, 1994, reprinted 1995, 1998, 2002, and *Building materials for the environmentally hypersensitive* 61089, 1995, revised 2005, [www.cmhc-schl.gc.ca/](http://www.cmhc-schl.gc.ca/); <http://journals.lww.com/jphmp/toc/2010/09001#-1750774083>, *J of Public Health Management and Practice*, September/October 2010 16 (E-Supplement 5): S1-S93) can be very challenging and can lead to considerable expenditures and possibly the need for stopgap measures. For example, in a 1996 survey, Gibson et al found that 66% of their sample of 305 people with MCS had lived in what they described as "unusual conditions", such as in their vehicles, on porches, or in tents at some time during their illness (Gibson PR, Cleavers J, Warren ML. Multiple chemical sensitivity/environmental illness and life disruption, *Women Ther*, 1996; 19:63-79). In the Canadian climate, such temporary measures are only tenable in mild weather.
- While relatively modest changes at home such as substituting non-fragranced cleaning, laundry and personal care products, de-cluttering, and removing carpets may make significant differences for many of those with ES-MCS, for others, making a truly safe home can involve remodelling/building anew with tolerated building materials or extensive mould remediation. Gibson et al. found that respondents in their 2003 survey had spent a mean of US \$57,000 on such expenses from the onset of their illnesses (Gibson PR, Elms AN-M, Ruding LA. Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity, *Environmental Health Perspectives*, September 2003; 111(12):1499).
- Homelessness is an extreme, sometimes life-threatening hardship for any person, but especially for someone who is ill. Ontario has no sufficiently environmentally safe emergency shelters, where a person with moderate to severe ES-MCS can get away from acute chemical exposures quickly enough and stay long enough to recover from them in order to avoid health deterioration. The necessary environmental accommodations are not available in the usual continuum of government-supported care and shelter for Ontarians, from urgent to acute to ongoing to assisted living to long term care. Sufficiently environmentally-safe government-supported housing for those with moderate to severe ES-MCS is also as yet virtually unavailable.
- With only a handful of Ontario ES-MCS-knowledgeable physicians, urgent care treatments that have rationales and a long history of empirical benefit, such as intravenous nutrient repletion (Rea W.J. *Chemical sensitivity*, Volume 4, Lewis Publishers, 1997:2438, 2653-66) and oxygen therapy (Rea WJ. *Chemical sensitivity*, Volume 4, CRC Lewis Publishers, 1997:2554-63), are generally not obtainable from hospital emergency rooms.

#### ✦ *Enhancing Internal Processing and Elimination of Chemicals*

- It will never be possible to eliminate all hazardous substances in communities, homes and workplaces. Hence, it is important to take steps to help MCS patients to metabolize and excrete the chemicals they inadvertently absorb, whenever possible.
- Poverty impacts on the ability of the body's defence systems to defend, both directly through increased exposure to environmental chemical and biological hazards, and indirectly through overloading and overwhelming of protective mechanisms. Both direct and indirect impacts can take effect for those with or susceptible to MCS over a prolonged period in poor housing, more so if they do not have access to protective devices such as air and water filters.
- Besides a highly nutritious, preferably organic, diet, which may be difficult and expensive to maintain, if there are many food intolerances, nutritional supplements are often required by sensitive people in order to be able to metabolize and eliminate toxic chemicals to which they are unavoidably exposed ([Burford-Mason A. Nutrition for Docs: Using nutritional supplements in clinical practice, a practical, evidence-based approach, Dalla Lana School of Public Health, University of Toronto, Syllabus, April 17-18, 2010](#)).
- Tolerated targeted supplements may be cost prohibitive, but if patients do not have adequate nutrition, they may accumulate more and more body burden of hazardous substances and become so overloaded that encountering even minute quantities of avoided chemical triggers will initiate severe symptoms which can be debilitating and last for days or longer. In such circumstances, their symptoms often spread to other body systems and the number of triggering substances expands as well. If they are being continually exposed to triggering agents, they may have chronic "masked" symptoms that affect their ability to function and to defend against infectious organisms ([Miller CS. The compelling anomaly of chemical intolerance, Annals of the New York Academy of Sciences, 2001; 933:1-23](#)).
- A high fibre diet is also a well-accepted and common sense method to enhance bowel transit function and elimination of toxins ([Mayo Clinic Staff. Dietary fiber: Essential for a healthy diet, <http://www.mayoclinic.com/health/fiber/NU00033>, updated July 8, 2010; accessed August 17, 2010](#)).
- Since thyroid and other hormonal functioning can be disrupted by many commonly encountered environmental chemicals, sometimes at exceedingly low levels ([Diamanti-Kandarakis E et al \(2009\) Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement. \*Endocrine Reviews\* 30\(4\):293-342](#)), vigilance for deficiencies or imbalances and swift correction with the tolerated medication and dosage is important.
- As noted in the Canadian Community Health Survey 2005 (**Table 4**), there is a strong overlap of MCS and gastrointestinal disorders. Gut inflammation could be related to direct effects on the gut mucosa from ingestion of toxic substances, or altered immune resistance to pathological organisms. "Probiotic therapies have attempted to modify disease expression by favourably altering bacterial composition, immune status and inflammation" ([Tamboli CP, Neut C., Desreumaux P, Colombel JF. Dysbiosis in irritable bowel disorder, \*Gut\*, January 2004; 53\(1\):1-4; Rao AV, Bsted AC, Beaulne TM, Katzman MA, Iorio C, Berardi JM, Logan AC. A randomized, double-blind, placebo-](#)

controlled pilot study of a probiotic in emotional symptoms of chronic fatigue syndrome, *Gut Pathogens* 2009, 1:6, Biomed Central). The Dallas Environmental Health Center has long found that intravenous nutrient repletion has been useful in bypassing inflamed GI tracts with impaired nutrient absorption (Rea W.J. *Chemical sensitivity*, Volume 4, Lewis Publishers, 1997:2438, 2594, 2653-66).

#### ***Decreasing Body Burden***

- If avoidance of symptom triggers and toxics reduction, along with described enhancement of metabolism and elimination of chemicals are insufficient to provide relief, and there are retained substances that may be prolonging a patient's illness, it is important to assess what could be done to decrease that body burden- e.g. by removing mercury amalgam fillings (Health Canada. *The safety of dental amalgam fillings*, 1996; [http://www.hc-sc.gc.ca/dhp-mpps/md-im/applic-demande/pubs/dent\\_amalgam-eng.php#a11](http://www.hc-sc.gc.ca/dhp-mpps/md-im/applic-demande/pubs/dent_amalgam-eng.php#a11); Haley B. *A study on the release of mercury from dental amalgams...*, May, 2007, [http://iaomt.org/articles/category\\_view.asp?intReleaseID=278&month=7&year=2007&catid=36](http://iaomt.org/articles/category_view.asp?intReleaseID=278&month=7&year=2007&catid=36)), following a careful protocol (International Academy of Oral Medicine and Toxicology. *Safe removal of amalgam fillings*, <http://www.iaomt.org/articles/files/files288/Safe%20Removal%20of%20Amalgam%20Fillings.pdf>).
- Some medical specialists are trained in the appropriate application of a careful protocol for chelation of retained heavy metals (Genuis SJ. *Elimination of persistent toxicants from the human body*, *Hum Exp Toxicol OnlineFirst*, April 16, 2010, doi:10.1177/0960327110368417).
- Increased excretion of some persistent compounds via sweat has been reported using a combination of exercise and sauna while maintaining optimal metabolism and elimination (Rea WJ, Pan Y, Johnson AR, Ross GH, Suyama H, Fenyves EJ. *Reduction of chemical sensitivity by means of heat depuration, physical therapy and nutritional supplementation in a controlled environment*, *Journal of Nutritional and Environmental Medicine*, 1996; 7:141-8; Dahlgren J, Cecchini M, Takhar H, Paepke O. *Persistent organic pollutants in 9/11 world trade center rescue workers: reduction following detoxification*, *Chemosphere*, 2007; 69:1320-5; Genuis SJ. *Elimination of persistent toxicants from the human body*, *Hum Exp Toxicol OnlineFirst*, April 16, 2010, doi: 10.1177/0960327110368417).
- Very recently, clearance of persistent, bioaccumulated perfluorinated compounds via stool has been reported using a bile acid sequestrant cholestyramine, and, although further trials are needed, thus far the method appears to be safe and effective (Genuis SJ, Birkholz D, Ralitsch M, Thibault N. *Human detoxification of perfluorinated compounds*, *Public Health* 2010;124:367-75; Genuis SJ. *Human detoxification of perfluorinated compounds*, *Syllabus*, 45<sup>th</sup> Annual Scientific Assembly, American Academy of Environmental Medicine, 21 October, 2010, La Jolla, CA).

#### ***Symptomatic Treatment and Desensitization***

- As noted previously, there is a strong overlap of allergies with ES-MCS. Symptomatic treatment with antihistamines, decongestants or analgesics may be tried, usually starting at one quarter to one half the usual dose to assess tolerance. However, medications are often poorly tolerated, and standard dose desensitization with escalation may exacerbate allergy symptoms. Individually formulated desensitization with only needed antigens included in the formula, at the level of sensitivity to that antigen for that patient, with gentle or no

escalation, has repeatedly been reported to be helpful for those with ES-MCS at American Council of Continuing Medical Education-accredited conferences of the American Academy of Environmental Medicine ([www.aaemonline.org](http://www.aaemonline.org)).

#### **Oxygen**

- Baseline and post-chemical challenge brain perfusion decreases have been noted in MCS patients vs controls on single photon emission computed tomography (SPECT) brain scans (Orriols R, Costa R, Cuberas G, Jacas C, Castell J, Sunyer J. Brain dysfunction in multiple chemical sensitivity, *Journal of the Neurological Sciences*, 2009; 287:72-8). This may be why oxygen helps to relieve acute reactions (Rea WJ. *Chemical sensitivity, Volume 4, CRC Lewis Publishers, 1997:2554-63*). Empirically, Rea has also noted that severely ill chemically sensitive patients sometimes respond well to daily oxygen inhaled for two hours over an average of eighteen days. A hypothesized mechanism is that oxygen supplementation enables a microcirculation switch to allow better blood flow, more extraction of oxygen to the tissues and normalization of pH. (von Ardenne M. *Oxygen multistep therapy: Physiological and Technical Foundations. Trans. Kirby P, Kruger W. New York: Georg Thieme Verlag Stuttgart, 1990: 1-73*).

#### **Randomized Controlled Trials of Therapies**

- While randomized controlled trials (RCTs) are extremely useful for deciding on the efficacy of a specific treatment such as a medication in comparison with other treatments or placebo, treatments such as desensitization for those with ES-MCS and severe allergies are individualized with respect to antigens, doses and timing, and so are not amenable to group RCTs. Two systematic reviews by the Succinct and Timely Evaluated Evidence Reviews (STEER) group in 2001 and 2003 noted this limitation. STEER was mounted to assist funding decisions in the National Health Service in the United Kingdom.
- In group RCTs, there must be strict subject inclusion and exclusion criteria to reduce the ‘noise’ of other variables in assessing treatment outcomes. The population of potential ES-MCS subjects is extremely heterogeneous, and so, even if sufficient subjects could be found to meet eligibility criteria, the results would be unlikely to be generalizable to individual patients presenting to their physicians. Outcomes may be heterogeneous and difficult or impossible to quantify.
- We are familiar with the method of critically appraising scientific papers called Grading of Recommendations, Assessment, Development and Evaluation (GRADE) method (Guyatt GH et al, *GRADE: an emerging consensus on rating quality of evidence and strength of recommendations, BMJ 2008; 336: 924-926*) as two of us, along with other members of the Environmental Health Committee of the Ontario College of Family Physicians, met with Dr. Gordon Guyatt last year about the possibilities of implementing the method in literature reviews in environmental health. As already discussed, environmental health is an extremely complex area to study.
- Single subject (N-of-1) longitudinal treatment trials with extreme limitation of extraneous exposures in an environmental control unit have been suggested (Spencer TR, Schur PM. *The challenge of multiple chemical sensitivity, Journal of Environmental health, June 2008; 70(10):24-7*), and were successful in relieving symptoms, but with the disadvantage of extreme cost (Ross GH. *History and clinical presentation of the chemically sensitive patient. Toxicol. Ind. Health. 1992; 8, 21-28*).

- In theory, N-of-1 randomized controlled, double blind crossover trials of therapies, although cumbersome, might provide a level of evidence similar to group RCTs and have been tried with a university-based referral service doing N-of-1 trials at the requests of community and academic physicians (Guyatt GH, Keller JL, Jaeschke R, Rosenbloom D, Adachi JD, Newhouse MT. The n-of-1 randomized controlled trial: clinical usefulness, our three-year experience, *Annals of Internal Medicine*, February 15, 1990; 112(4):293-99). However, their utility was questioned (Tsapas A, Matthews DR. Using N-of-1 trials in evidence-based clinical practice, *JAMA*, March 11, 2009; 301(10), and Montori and Guyatt replied that the method worked best in individuals with a stable condition seeking symptom relief, and that the effect of the intervention should be short-lived (Montori VM, Guyatt GH. Reply, *JAMA*, March 11, 2009; 301(10)). Unfortunately, this method may not be applicable to individuals with ES-MCS, given that their condition is chronic and very unstable depending on their daily exposures, and improvement would need to be evaluated over a longer period.

### ✚ *Self-management Strategies*

- In addition to reduction of exposure to triggering or toxic agents, individuals with MCS, as with other chronic illnesses, try many therapies to relieve symptoms and to improve quality of life. In the Gibson et al survey, a very wide range of therapies had been tried by a variable number of subjects for variable lengths of time. The therapies tried were perhaps attempts to address various determinants of health, for example nutritional/dietary interventions, physical therapies, medical interventions (e.g. oxygen therapy), psychosocial support therapies, and contemplative therapies. For example, our team has found, as did Gibson et al, that prayer, meditation and other contemplative methods, chosen according to each patient's needs and preferences, are frequently somewhat helpful, often in combination with other therapies listed. They are hypothesized to both dampen the overstimulation of the sympathetic nervous system related to the body's repeated recognition and response to symptom-initiating exposures in MCS, and to assist with coping (Gibson PR, Elms AN-M, Ruding LA. Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity, *Environmental Health Perspectives*, September 2003; 111(12):1498-1504).
- In attempting to enhance the doctor-patient relationship and to encourage self management, we at the Environmental Health Clinic (EHC) in Ontario have sometimes used a slightly whimsical metaphor, asking patients what they think might be needed in their particular situation to "plant a health garden", so that we could enjoy watching their health slowly grow. Tongue in cheek, we have noted that weeding, seeding and feeding is usually needed to grow a garden, and have asked what unnecessary aggravators they might 'weed' out of their lives, ask them to work with us on the individual components of planting SEEDS of health, and then 'feed' whatever helps. SEEDS is an acronym for Sleep, Exercise (and pacing), Environment, Diet (nutrition), and Support, and provides a framework for self-management that patients seem to find easy to follow. The application of this framework is described in a requested article based on a presentation to physicians at "Saturday at the University" at the University of Toronto (Marshall LM, Bested AC, Bray RI. Tools to treat Multiple Chemical Sensitivities, Chronic Fatigue Syndrome and Fibromyalgia, *Canadian Journal of CME*, University of Toronto Edition, January, 2004: 56-65).
- An EHC physician is the primary author of a book with many self-management ideas (Bested AC, Logan AC, Howe R. Hope and help for chronic fatigue syndrome and fibromyalgia, 2<sup>nd</sup> Edition, 2008, Cumberland House, Nashville, Tennessee).

- The EHC nurse provides a set of printed resources as well as individualized verbal and written information and web links as appropriate to each patient, and is available to answer questions by telephone. Under her tutelage, University of Toronto nursing students research the literature and develop easily understood posters and pamphlets.
- Das-Munshi et al suggested that “A multifactorial model incorporating behavioural, physiological and sociological approaches may be useful”, but focused on psychological, behavioural and conditioning factors and only suggested treatment in these areas, sometimes in combination with antidepressants ([Das-Munshi J, Rubin GJ, Wessely S. Multiple chemical sensitivities: review, Current Opinion in Otolaryngology & Head and Neck Surgery, 2007; 15:277](#)). The evidence of effectiveness cited by the authors, two psychologists and a psychiatrist, seemed to be largely based on single case reports or small case series. The authors also did not mention that antidepressants were found more likely to harm than help in the Gibson et al survey ([Gibson PR, Elms AN-M, Ruding LA. Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity, Environmental Health Perspectives, September 2003; 111\(12\):1502](#)).
- The experience of the EHC team and other clinicians in Ontario and the U.S. has been in agreement with Gibson et al’s finding that individuals with MCS often tolerate medications poorly. If prescribed, they commonly require much lower doses than usual, possibly because their capacity to metabolize drugs is compromised. Thus pharmaceuticals in MCS not only may not suppress symptoms, but also may exacerbate them. If symptoms are relieved, the underlying etiology may be obscured. Also, following avoidance of triggering agents, the symptoms in various body systems, including the central nervous system (e.g. emotional and cognitive symptoms), may improve significantly without need for medication.
- In response to a clinic needs assessment, EHC offered group classes to inform EHC patients about indoor air quality, nutrition, exercise and pacing, and the adverse impact of negative thinking on progress.
- In addition, from 1999-2005 (until resources ran out), a psychologist and an EHC physician ran an annual 10-week group psycho-educational program for EHC patients for 2 hours weekly, along with a 1 year follow-up group session for consolidation and evaluation, and a parallel individual counselling program. The program was conducted in a fragrance free environment, stretching and moving around as needed were encouraged, and a “smorgasbord” of strategies was used to meet needs while recognizing fluctuating neurocognitive deficits. The strategies included use of film clips to bridge sensation, affect and cognition, meditative inductions for grounding, relaxation, and symptom relief, education about the General Adaptation Syndrome ([Selye H. The Stress of life, New York: McGraw-Hill, 1956](#)), dealing with stressful situations, creating boundaries, and strengthening the ego, as well as locating new life purpose. Qualitative evaluations one year after completion of each group program repeatedly revealed surprisingly strong and unique uptakes and applications of various features of the program.
- Telemedicine, recently being piloted in the EHC, offers a tantalizing opportunity to serve more Ontarians with complex, chronic conditions with individual clinical consultations

and group programs close to home, as well as with educational programs for patients and health professionals.

### **Primary Prevention:**

Dr. Herbert Needleman, Professor of Psychiatry and Pediatrics at the University of Pittsburgh suggested “We are conducting a vast toxicological experiment in which our children and our children’s children are the experimental subjects” (Quoted by Dr. Philip Landrigan, Mount Sinai School of Medicine, keynote address to Children’s Environmental Health II: A Global Forum for Action, Washington, DC, September, 2001, CPCHE Primer, August 2005:5). Protective policies have been successfully implemented in the face of some remaining scientific uncertainties in the case of tobacco smoke and pesticides. Reduction of exhaust fumes from vehicle idling, decreased exposure to smoke in public places, and the banning of the use of pesticides for cosmetic purposes have reduced exposure to these harmful substances for the entire population, and have been particularly helpful for the chemically sensitive.

### **✚ Health Promotion and Partnerships**

- Although we at the Environmental Health Clinic work at the individual clinical level through comprehensive assessments and development of individualized treatment plans, we also work, often as volunteers, towards preventing or minimizing environment-associated illnesses at the population level through collaboration with universities, associations, and coalitions of like-minded, multi-sector organizations in research, education and promotion of policy changes. There has been growing public awareness of the impacts of various environmental exposures on health, aided in part by increased media attention and the explosion of information available on the internet. Since internet information is not always trustworthy, more and more patients are asking their most trusted health advisors, their physicians and other healthcare professionals, what actions they should be taking to protect themselves and their families (Hesse BW, Nelson DE, Kreps GL, Croyle RT, Arora NK, Rimer BK, Viswanath K. Trust and sources of health information, Archives of Internal Medicine, December 12/26 2005; 165:2618-24). This may be particularly so if patients have noticed associations between their symptoms and exposures to environmental substances or locations, or if their symptoms are ongoing and unexplained.
- We think the physicians of tomorrow will need to be very conversant with the latest credible environmental health information. We teach/train a small number of medical and environmental studies students, nurses, residents and graduate physicians in collaboration with the Departments of Family and Community Medicine and Continuing Education and Professional Development at the University of Toronto. As long as clinic resources would permit, we also maintained a series of six annual accredited rounds and a one-year academic Environmental Health Fellowship Program. We also lecture to medical students at the University of Ottawa, University of Western Ontario, Northern Ontario School of Medicine, and to Master of Public Health students at Lakehead University.
- The Environmental Health Clinic Staff Physicians, Nurse Educator, and Community Outreach Coordinator have served on international, national, provincial and local committees and panels to try to influence precautionary, protective policy development- for example, on an international Expert Medical Consensus Panel on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome selected by Health Canada; on Health Canada Committees and in Workshops on Children’s Environmental Health and Impacts of the Environment on Older Adults; on the Canada Mortgage and Housing

Corporation’s Task Force on Material Emissions; on the Ontario Ministry of the Environment’s Toxics Reduction Scientific Expert Panel; on the Ontario Accessible Built Environment Standards Development Committee; and on the Occupational and Environmental Working Group of the Toronto Cancer Prevention Coalition.

- We have also participated in many reviews of scientific studies, synthesis of the evidence, and translation into papers, reports, primers, brochures, websites, case studies, teaching modules, and presentations for a variety of target groups locally, provincially, nationally, and internationally, in partnership with many different organizations.
- Some of our productive partnerships in environmental health promotion are listed in **Table 6** with websites for more information, and brief descriptions of projects we have, or are collaborating on with the listed organizations.

**Table 6:**

**Examples of Environmental Health Promotion via Partnerships**

**Staff Physicians, Nurse Educator, and Community Outreach Coordinator of the provincial Environmental Health Clinic, Ontario, at Women’s College Hospital**

<p><b>Canadian Coalition for Green Health Care</b> (<a href="http://www.greenhealthcare.ca">www.greenhealthcare.ca</a>)- on an Ontario Trillium Foundation (OTF)-funded project on toxics reduction in health care facilities, fragrance free program/policy development, local food use in hospitals, + active problem solving via listserv.</p>
<p><b>Canadian Environmental Law Association</b> (<a href="http://www.cela.ca">www.cela.ca</a>) and the <b>Environmental Health Institute of Canada</b> (<a href="http://www.ehicanada.ca">www.ehicanada.ca</a>)- on an Ontario Law Foundation-funded project “Making the Links” between pollution, chronic health effects and poverty in six Ontario communities, selected for high prevalence of these and interest in addressing them.</p>
<p><b>Canadians for a Safe Learning Environment</b> (<a href="http://www.casle.ca">www.casle.ca</a>)- on “Guidelines to Accommodate Students and Staff with Environmental Sensitivities”</p>
<p><b>Canadian Institute of Child Health</b> (<a href="http://www.cich.ca">www.cich.ca</a>)- on Physician Master Training Program to train physicians to adapt World Health Organization modules on Children’s Health and the Environment to their communities and to present them in day-long workshops. Five workshops were presented across Ontario in 2009, funded by the Ontario Ministry of the Environment.</p>
<p><b>Canadian Institutes of Health Research</b>-funded “Toxic metals in Canadians and their environments- Exposures, health effects and physical and public health management standards: A scoping review”- Co-principal investigators Drs. Margaret Sears and Riina Bray; acknowledged consultants Drs. John Molot and Lynn Marshall.</p>
<p><b>Canadian Partnership for Children’s Health and the Environment</b> (CPCHE) <a href="http://www.healthyenvironmentforkids.ca">www.healthyenvironmentforkids.ca</a>- 12 health, public health, environmental, and child care partner organizations that have worked together on multiple projects since 2001- e.g. collection of training materials and resources, fact sheets and flyers posted on website in English and French including <a href="#">Child Health and Environment: A Primer</a>, and the CPCHE brochure <a href="#">Playing it Safe: Childproofing for Environmental Health</a>, 2005; <a href="#">Playing It Safe: Service Providers Strategies to Reduce Environmental Risks to Preconception, Prenatal and Child Health</a>, 2006; <a href="#">National Policy Consultation</a> in 2007; <a href="#">First Steps in Lifelong Health: A Vision and Strategy for Children’s Environmental Health in Canada</a>, 2008; a multi-year “Engage, Enable and Empower (E3)” project, funded by the Public Health Agency of Canada (PHAC) to create local community champions, completed in 2009; <a href="#">Advancing Environmental Health in Child Care Settings: A Checklist for Child Care Practitioners and Public Health</a></p>



<p><a href="#">Inspectors</a>, funded by the Ontario Trillium Foundation and Health Canada, 2010.</p> <p><b>CPCHE and Ontario Chronic Disease Prevention Alliance</b> (<a href="http://www.ocdpa.on.ca">www.ocdpa.on.ca</a>)- together on an Ontario Trillium Foundation (OTF)-funded project studying early life exposures and the risk of chronic disease- held day-long evidence/policy workshop on bisphenol A in May, 2010.</p>
<p><b>Canadian Transportation Agency</b>-on a commissioned report “Air travel and chemical sensitivities”, co-authors Drs. John Molot, Lynn Marshall and Margaret Sears.</p>
<p><b>Centre for Equality Rights in Accommodation</b> (<a href="http://www.equalityrights.org/cera">www.equalityrights.org/cera</a>)- on an OTF-funded “Creating Healthy Housing” project to address the needs of the chemically sensitive.</p>
<p><b>Community Care Access Centres Ontario</b>- on interactive presentations and resources to improve accessible home care for those with MCS.</p>
<p><b>Environmental Health Association of Nova Scotia</b> (<a href="http://www.environmentalhealth.ca">www.environmentalhealth.ca</a>)- e-mail contact and use of guide to less toxic cleaning, laundry, and personal care products, <a href="http://www.lessstoxicguide.ca">www.lessstoxicguide.ca</a>.</p>
<p><b>Environmental Health Association of Ontario</b> (<a href="http://www.ehaontario.ca">www.ehaontario.ca</a>) provides representative consumer advisors to the Ontario Environmental Health Clinic on an ongoing basis.</p>
<p><b>Environmental Health Association of Quebec</b> (<a href="http://www.aseq-ehaq.ca">www.aseq-ehaq.ca</a>)- on simultaneously translated workshops on Children’s Health and the Environment and Complex Chronic Conditions ME/CFS, FM and MCS at Annual Scientific Assembly, November 2009, which had an Environmental Health theme.</p>
<p><b>Environmental Health Institute of Canada</b> (<a href="http://www.ehicanada.ca">www.ehicanada.ca</a>)- on the “Making the Links” project with the Canadian Environmental Law Association, the Ontario Trillium Foundation grant on toxics reduction in health care with the Canadian Coalition for Green Health Care, and on the Environmental Health Day to be held in November, 2010.</p>
<p><b>Healthy Indoors Partnership</b> (<a href="http://www.healthyindoorspartnership.ca">www.healthyindoorspartnership.ca</a>)- on development of multi-stakeholder consensus brochures on “Products and Services with Low Chemical Emissions”.</p>
<p><b>Myalgic Encephalomyelitis Association of Ontario (MEAO)</b> <a href="http://www.meao.ca">www.meao.ca</a>- provides ongoing consumer advisory service to the Ontario Environmental Health Clinic; worked with <b>National ME/FM Action Network</b> <a href="http://www.mefmaction.net">www.mefmaction.net</a>, and <b>Environmental Health Association Ontario (EHAO)</b> <a href="http://www.ehaontario.ca">www.ehaontario.ca</a> - on International ME/FM/MCS Day, May 12, 2010.</p>
<p><b>National ME/FM Action Network</b> <a href="http://www.mefmaction.net">www.mefmaction.net</a>- on extracting needed data from the public use microdata files of the Canadian Community Health Survey, Statistics Canada.</p>
<p><b>Nurses’ Environmental Reference Group</b>, now part of the <b>Canadian Nurses’ Association</b>- a teleconference and listserv started by the Environmental Health Clinic nurse after publication of an article in Canadian Nurse (Fraser G. Environmental Health and Nursing, Canadian Nurse, 16 January, 2004). <a href="http://www.cna-aiic.ca/CNA/issues/environment/default_e.aspx">http://www.cna-aiic.ca/CNA/issues/environment/default_e.aspx</a></p>
<p><b>Ontario College of Family Physicians</b> <a href="http://www.ocfp.on.ca">www.ocfp.on.ca</a> → <b>Environmental Health Committee</b>- on many projects e.g. on Children’s Environmental Health, Complex Chronic Conditions, Heavy Metals, Outdoor and Indoor Air quality, Uranium Mining, Urban Sprawl etc. Affiliated with Environmental Health Committees of the <b>College of Family Physicians of Canada</b> and the <b>World Organization of Family Doctors, WONCA</b>.</p>
<p><b>Toronto Cancer Prevention Coalition</b> <a href="http://www.toronto.ca/health/resources/tepc">www.toronto.ca/health/resources/tepc</a> - on a GTA Cancer Prevention and Screening Network-funded pilot project to increase awareness of environmental links to breast cancer, and spearheaded the establishment of an Environmental Disclosure and Reporting Bylaw in Toronto: the first “community right to know” bylaw in Canada.</p>
<p><b>Toronto Public Health and South Riverdale Community Health Centre</b>- on updated resource</p>

for prenatal educators, Hidden Exposures: Informing pregnant women and families about harmful environmental exposures <a href="http://www.toronto.ca/health/hphe/pdf/hidden_exposures.pdf">http://www.toronto.ca/health/hphe/pdf/hidden_exposures.pdf</a> .
<b>University of Toronto Medical students’ ‘Determinants of Community Health 2’</b> - on course projects annually- e.g. in 2009-2010 a student interviewed patients and hospital staff for ideas on updating “Environmental Health in Hospitals: Environment-sensitive Care” guidelines, that are posted as a patient/physician resource on <a href="http://www.mcscanadian.org/hospital.html">www.mcscanadian.org/hospital.html</a> .
<b>U.S. Environmental Protection Agency</b> -funded study of heat depuration/nutrition treatment in chronically ill, chemically sensitive 9/11 rescue workers is underway- co-investigator Dr. Kathleen Kerr, Environmental Health Clinic physician.
<b>Women’s College Hospital Green Team</b> - energy conservation, recycling, and toxics reduction, e.g. mercury in medical devices, safer cleaning products, fragrance free program/policy.
<b>Women’s Health Matters</b> <a href="http://www.womenshealthmatters.ca">www.womenshealthmatters.ca</a> - <b>Environmental Health Centre</b> - information and answers to questions from the public.