# PUTTING THE CHEMICALS BACK IN "MULTIPLE CHEMICAL SENSITIVITY"

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**Ontario Environmental Health Advocates Address**

***Syndrome de sensibilité chimique multiple, une approche intégrative pour identifier les mécanismes physiopathologiques/ Multiple chemical sensitivity syndrome, an integrative approach to identifying the pathophysiological mechanisms***

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# CHEMICALS OR ANXIETY: WHAT CAUSES MULTIPLE CHEMICAL SENSITIVITY?

*The quote below was borrowed from Masri, S., Miller, C. S., Palmer, R. F., and Ashford, N., (2021), "Toxicant-induced loss of tolerance for chemicals, foods, and drugs: assessing patterns of exposure behind a global phenomenon," Environmental Sciences Europe.*

> The sharp growth in reports of TILT ["toxic-induced loss of tolerance," a synonym for MCS], appears to coincide with the post-WWII expansion of the petrochemical industry and widespread growth in the production of petrochemicals such as organophosphate pesticides, solvents, dyes, and fragrances. U.S. production of the so-called "synthetic organics," which had been less than 1 billion pounds per year, soared to over 460 billion pounds per year by 1994 (of note, while the term "synthetic" can be interpreted differently, its use in this paper is in reference to compounds whose chemical structures do not appear in nature). The same pattern can be seen for pesticide use in U.S. agriculture, which grew from 200 million pounds of active ingredient in 1960 to over 600 million pounds by 1980. Assuming that exposure to synthetic pesticides and other chemicals is a function of their production and use in everyday society, it is reasonable to assume that these trends have led to increased human exposure over time. Importantly, given their absence prior to modern history, such chemicals can be considered evolutionarily novel and may present particular challenges as [they] relate to the body's ability to process them through detoxification or elimination pathways. Furthermore, while the human toxicity of pesticides is widely recognized, regulations to safeguard the public are likely insufficient given their focus on the toxicity of individual chemical ingredients . . . as opposed to complex mixtures of multiple chemicals, the latter being more reflective of commercial chemical products and other environmental exposures.

*The quote below was borrowed and translated from The Institut National de Santé Publique du Québec, (2021), Syndrome de sensibilité chimique multiple, une approche intégrative pour identifier les mécanismes physiopathologiques, p. 811.*

> The authors of this report conclude that MCS . . . is due to fear conditioning accompanied by chronic anxiety resulting from the constant desire to avoid exposure to odours that cause these people to develop or exacerbate symptoms because they consider this exposure to be threatening to their health.

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## PREFACE: WHY THIS COMMENTARY CAME TO BE WRITTEN AND ABOUT ITS SIGNATORIES

The year 2021 was, for the most part, a good year in multiple chemical sensitivity (MCS) studies. Several major research articles that we substantially draw on in the commentary you are about to read were published. An extensive literature review from Alberta Health was released. In a field so terribly underfunded, these important additions were very welcome.

However, the INSPQ report, *Syndrome de sensibilité chimique multiple, une approche intégrative pour identifier les mécanismes physiopathologiques,* came to our attention in the fall of 2021, and although we looked forward to reading and learning from it, as soon as we began, the alarm bells went off. For we saw that it had taken an approach and arrived at conclusions highly divergent from the other new pieces, and that, it soon became clear, were both wrong and dangerous. The Québec Environmental Health Association (ASEQ-EHAQ), similarly concerned about the INSPQ report's conclusions, asked their Minister of Health and Social Services to remove the report from the institute's website and update it. The ASEQ-EHAQ letter of appeal, which we support, is included as an Appendix to our commentary.

Our fears were deepened when, in early 2022, a member of our community, "Sophia" (a pseudonym) ended her unbearable MCS-induced pain and hardship with MAiD (medical assistance in dying). After years of desperately seeking a safe place to live where, on a limited budget, she could be free of the fumes of her neighbours' cleaning products and cigarette smoke, her suffering became unbearable and she chose to end her life. Some of us knew her and had worked directly with her, so her death was particularly difficult. Despite the advocacy of doctors and disability professionals, every level of government refused her help. Except for six units created long ago in Ottawa, no dedicated safe housing units have ever been built, finding a an affordable safe unit is extremely difficult and there are no programs to assist people like her to find safer places elsewhere. We have learned since that a number of others facing a similarly dire situation have also applied for MAiD.

Our fear is that if the conclusions about the nature and mechanisms of MCS in the INSPQ report attain acceptance by any government or medical association, they will have extremely deleterious consequences. Because these conclusions are wrong, authorities will treat Sophia's physical suffering as a mental illness, deny appropriate medical care, leave disability needs unmet and thereby doom many more people to the same fate. Out of this profound concern, we decided that the erroneous and dangerous conclusions of the INSPQ report had to be disputed and refuted substantively and piece by piece. Thus, this critique and counterargument was born.

Though we find the report conclusions frightening, we used the opportunity that its critique presents to showcase some of the exciting work and top-tier researchers in MCS studies, environmental studies and myalgic encephalomyelitis (ME) studies, not included in the INSPQ report. This is work that policy makers, health providers, those working in the disability field, and many others really need to know about. It will help to explain what MCS really is, and, to a

certain extent, also ME (myalgic encephalomyelitis/chronic fatigue syndrome). This knowledge is critical in assisting these groups to understand and to help modernize health care in general to address complex, environmentally-linked diseases and to develop healthier public policy on chemical use – a modernization that is very badly overdue.

The patient perspective is essential for any illness, and its incorporation has become common practice. It is needed in any process that seeks to identify any or all of the nature, mechanisms and definitions of MCS, and it is also essential to the creation of clinical programs and sites, disability needs, population health and prevention strategies and research priorities. But it is entirely missing from the INSPQ report. It is a perspective we have used to frame our critique, and included it in key junctures within it.

We are an Ontario-based, ad hoc group of advocates for the recognition and inclusion of the medical conditions ES/MCS, ME/CFS and FM, with which about one million Ontarians live and struggle. These are often devastating and disabling conditions, but have little to zero care and support from our provincial health and social services systems, with ES/MCS the most excluded of the conditions. Our group includes environmental health consultants and educators, writers, health and social policy planners, participants in national research efforts (ME), senior health system administrators, health system change experts, human and disability rights advocates, educators, patient organization leaders, a lawyer and caregivers. Some of us live with one or more of the conditions, some of us do not. More details about us can be found in Appendix 1 "Information about the Signatories."

We have worked along with the Ontario Ministry of Health in leading roles since 2010 – some even earlier than that – towards bringing into existence a centre of excellence in environmental health with dedicated affiliated local clinics and a specially trained cohort of family physicians across the province. In other words, we have worked for a system of care for our groups, and for the kind of policy change that is needed to turn the recognition of these as disabilities into meaningful rights in real life. Foundational to the work has been the understanding that the three conditions are biophysical medical conditions with neurological and other body system effects not, as the INSPQ report concludes, mental illnesses, psychological or psychiatric in nature.

The Ontario project, involving extensive research and planning, has had three major phases and has produced a number of important documents (linked below), to which we refer in our commentary. The implementation phase, COVID delayed, is still to come; however, we have been assured that it is an active file within the Ministry.

Our commentary is based both on the best of what we know of research to May 2022, and the knowledge we have gathered from and about our communities as advocates. We learn every day about lived experience, including experiences with physicians and the health care system. So, with this perspective, our critique of, and counterargument to the INSPQ report provides:

1. An explanation for how the science reviewed and approved in the report does not describe, explain or accord with the real-life experience of people living with MCS. The research that we cite, much of it more recent, does accord with that experience, and corrects an incomplete and erroneous picture painted by the INSPQ report.

2. Important dimensions of the experience of those living with MCS, which the report is entirely lacking. We evaluated the conclusions of the INSPQ report in the light of the patient experience and found the conclusions neither credible nor well-supported. We have identified some of the relevant literature and given a voice to the missing patients in a number of ways throughout.

3. Key lessons from the clinical experience, also missing from the report, and which are also absolutely necessary to validate its conclusions. We introduce a body of clinical work, evolving in state-of-the-art settings of environmental and functional medicine outside of our public health care system, especially but not only in the United States, for decades.

4. A set of recommendations for moving forward at both federal and provincial levels. Informed by the 10-year process in Ontario as well as our work in this counterargument, these recommendations hold many useful features for other governments, federal, provincial and territorial.

We hope that this contribution can go some distance to providing what is needed to correcting deficiencies and errors of the INSPQ report and averting their potential negative consequences.

Varda Burstyn, Maureen MacQuarrie, Bev Agar, Ted Ball, Mike Ford, John Doherty, Izzat Jiwani, Denise Magi, Scott Simpson and Adrianna Tetley

Toronto, June 27, 2022

The documents from the first phase of the Ontario study can be found at http://recognitioninclusionandequity.org/resources/ .

The second major study process produced two reports: The Interim Report - Time for Leadership: Recognizing and Improving Care for those with ME/CFS, FM and ES/MCS and the final report, Care Now: An Action Plan to Improve Health for People with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), Fibromyalgia (FM) and Environmental Sensitivities/Multiple Chemical Sensitivity (ES/MCS).

The document from the third phase, “Laying the Groundwork” is not yet a public document, but in process at Ontario’s Ministry of Health

# EXECUTIVE SUMMARY

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## PUTTING THE CHEMICALS BACK IN "MULTIPLE CHEMICAL SENSITIVITY"

## HIGHLIGHTS

- We disagree with the fundamental premises and main conclusions of the INSPQ literature review*, Syndrome de sensibilité chimique multiple, une approche intégrative pour identifier les mécanismes physiopathologiques*: that multiple chemical sensitivity (MCS) is not linked to the toxicity of chemicals, but is a neurotic reaction to "odours;" anxiety and inappropriate fear are its causes, and MCS constitutes a somatoform illness – in other words, that MCS is a psychogenic condition and chemicals "at normal concentrations" are "harmless".
- Although there is much more to be discovered regarding the pathophysiological mechanisms of MCS, based on our experience and on research, it is chemicals (not odours) that are involved in onset and in maintaining the condition. Further, even when they do not trigger MCS reactions, these chemicals are not "harmless" on a population health basis.
- The INSPQ report did not take into account contrary research on mechanisms, nor does it hold up against the important new research recently published, both which suggest the contrary conclusion: that MCS is a biophysical-toxicological syndrome and disease process, very much linked to chemicals.
- There is also a body of clinical experience, and a literature on patient experience that were not considered, but that support the biophysical-toxicological paradigm.
- Our analysis leads us to the conclusion that the INSPQ authors have wrongly reduced a very complex illness with multiple causes and symptoms to a singular unproven mechanism, thereby making it impossible to develop correct analytical accounts and the right practical steps for treatment and accurate assessment of MCS as a disability.
- When anxiety is experienced as a result of an MCS reaction, it is one among many in a basket of neurological symptoms, also accompanied by other body symptoms; it is the effect of an exposure, not the cause of reactivity, and it disappears when the reaction subsides.
- Further, in most cases, as the qualitative patient literature shows, fear about and concern with encountering inciting substances is legitimate, the circumstance of living with the condition and the medical injunction to avoid these, so is an extrinsic and appropriate response, again an effect not a cause, and not neurotic.
- We disagree with the report's conclusion that a range of conditions, including ME, what the report calls 'chronic fatigue syndrome,' and fibromyalgia have chronic anxiety in common and that this chronic anxiety is causative.
- There is sufficient research, clinical and patient experience to move ahead on a system of care for people with MCS based on a biophysical approach. It must be sought out and utilized, not be hidden away. We include recommendations for how to create this system of care, including a centre of excellence, dedicated affiliated local clinics and a specially trained cohort of family physicians, and recommendations for a federal safe housing program in our Part 10.

## OVERVIEW

We have written this commentary – *Putting the Chemicals back in Multiple Chemical Sensitivity* – because we completely disagree with the central conclusions of the INSPQ report. This disagreement arises out of our own expertise and deep concern for the implications of the report's conclusions for recognition, physician and public education, clinical programs, disability policies, and broader public health policies. We are keen to share the important work, including very new work that confirms these concerns and provides alternative directions for the future.

The INSPQ report was massive in length – 823 pages – and ambition, and its authors stated that their objective was "to identify the pathophysiological mechanisms that underlie MCS [for multiple chemical sensitivity] using an approach that considers all the research conducted on the hypotheses put forward to date." (INSPQ, Summary, Objective, p. 3. This and a few other key quotations from the INSPQ report have, for ease of reference, been collected in a box at the end of this executive summary. The INSPQ authors believe that they have found this mechanism – only one mechanism; that it is not a reaction to chemicals, rather a biological cascade that takes place in the brain due to fear conditioning accompanied by chronic anxiety. They are so confident that have settled all outstanding questions, that they propose a new name for MCS.

Further, these authors dismiss the role of chemicals in MCS and give them a free pass. They write, "there is no evidence to support the hypothesis of a relationship between MCS and the toxicity of chemicals at their usual concentrations in the environment. People with MCS, therefore, are not hypersensitive to chemical substances. … (Summary, Conclusion, p. 3)

Finally, they claim that the anxiety-causation thesis also applies to chronic fatigue syndrome, post-traumatic stress disorder, electromagnetic hypersensitivity, fibromyalgia, chronic anxiety, depression, somatization disorder, phobias, and panic disorder. They write "Chronic anxiety is an element common to all the syndromes studied and its main feature is the *anticipation of danger,* i.e., feeling a persistent, excessive, and inappropriate concern about one's day-to-day activities. (Summary, Results, p. 3)

In this commentary we dispute and refute all three major conclusions.

To us, the reactivity or intolerance of MCS is a complex reaction involving many more body systems and possibly several neurological and immunological mechanisms, in which encounters with particular chemicals, even at very low concentrations, do indeed cause onset, and perpetuate chronicity. This document, element by relevant element, shows why and how this is the case.

We have been able to cite very recent work from MCS studies and environmental health studies against which the INSPQ report must be measured, and against which it does not stand up. By contrast, this work, in addition to older but neglected research, does provide an alternative way

to understand MCS and chart a course toward action. We have also offered insights from both the patient and the clinical perspectives.

This "alternative way" we have summarized in a description of MCS that counters that of the INSPQ's. This description, based on multiple sources, as explained in detail in the main text in Part 2.3 is:

MCS is a multi-system, recurrent, environmental syndrome and disease process that flares in response to different exposures (i.e., pesticides, solvents, toxic metals, fragrances, cleaning products, cigarette smoke, certain foods, drugs/medicine, mold and other vehicles of exposure) at concentrations that do not provoke such symptoms in other people. It is characterized by neurological, immunological, cutaneous, allergic, gastrointestinal, rheumatological, cardiological and endocrinological signs and symptoms. MCS is a widespread condition and the majority of those who live with it (approximately 70 percent) are women, though a significant minority are men.

Onset, which may happen slowly over time or rapidly, begins on exposure to a particular chemical or mixture of chemicals (including bio and well as synthetic toxicants) that commonly affect the immune system and/or nervous system, such that MCS appears to be primarily a neuroimmune disease process. This chemical exposure interacts with one (or both) of these systems in a way that renders individuals intolerant to subsequent exposures, which are then experienced as triggering or flaring events. After the initial onset, some new triggering events may result in "crashes" - additional worsening to qualitatively greater degrees of severity that are not easily reversible without intervention.

Affected individuals no longer tolerate everyday exposures to a wide range of structurally diverse substances at levels that never bothered them previously, including ingestants, inhalants, implants, and skin contactants. Many previously tolerated foods and drugs may trigger symptoms. At times, onset is not observed or reported immediately, and the phenomenon of "masking" can obscure MCS and delay diagnosis.

MCS ranges in severity. Early, milder stages are often erroneously perceived to be allergies, require adjustments and avoidance, but go undiagnosed. Moderate to severe MCS involves greater intensity and duration of symptoms. Severe MCS brings intense reactions, great physical suffering and can be life-threatening for some people when exposed to some chemicals. Major efforts to avoid triggers are required, making life in the ambient air of chemically-laden everyday environments unsustainable. This is how MCS disables those affected. When co-morbidities are present – often the case – overall health is further compromised, and additional barriers are encountered.

MCS is usually responsive to appropriate measures and treatments, but becomes worse without these.

The elements in this description helped us select the issues and evidence we take up, part by part, in our extended critique.

The INSPQ report has very little to say about the clinical implications of their conclusions, except to say that MCS is a "real health issue" that should be addressed in dedicated programs. But all MCS definitions have embedded within them a clinical agenda and implications for disability rights, public health policy and research priorities. The errors of the report's conclusions are, in our view, so grave that the report's implications for these fields would be dangerous to patients, potentially violate both medical and disability rights, go in the opposite direction of what is needed for regulation of common chemicals on a population health basis, and suggest a research program that would miss the many marks that must be hit in basic, epidemiological and clinical dimensions. In our conclusion (Part 10) especially, we offer a set of recommendations for what is needed going forward, to ensure that these issues are explicitly identified and addressed.

The ground that we cover to reach our conclusions is divided into ten parts:

- Contextualizing the INSPQ report on Multiple Chemical Sensitivity
- Missing pieces in basic research and epidemiology
- Deficiencies in epidemiological, clinical and socio-political analysis
- Chemicals and MCS
- Lessons from the clinical experience
- Women and MCS
- Understanding chronic stress, anxiety and MCS
- Socially determined stress in chronic MCS exacerbates illness
- Myalgic encephalomyelitis (ME) and long COVID: What can we learn?
- Recommendations for moving forward

## PART BY PART SUMMARIES

### Part 1: Contextualizing the INSPQ report on Multiple Chemical Sensitivity

With 1.1 million Canadians, or 3.5 percent of the population, diagnosed with MCS, an often severe and disabling condition, and after emerging as a distinct clinical entity as early as the 1950s, MCS remains excluded from Canadian health care. This poses a medical crisis for those who live with it and what should be a moral and medical crisis for our health care systems. MCS has been a contested illness, with two diverging schools of thought, or paradigms, on its causes and mechanisms: the biophysical-toxicological school, in which patients and MCS clinicians have long located themselves since the 1960s; and the psychological school, of which the INSPQ is the latest iteration, with founding documents from the 1990s.

This divergence, and the historical, now obsolete attachment, of many medical associations to the psychological school has served as a pretext for provincial health ministries to do nothing about MCS. But by 2010, when numbers approached one million, and new efforts were made by

advocacy groups and individuals, three provincial processes were initiated. Ontario's has been the most extensive by far, with three major phases of study and planning, and an implementation report, delayed by COVID, awaiting the attention of a new health minister. The signatories of this document have all been participants and leaders in this process. All the phases of Ontario's process have been based on the biophysical-toxicological paradigm of MCS.

In 2013, Québec commissioned a literature review as a first step to policy development. Alberta's review of the state of the science was commissioned a year or so later in response to recommendations from the Alberta Energy Regulator regarding health concerns of residents in the Peace River area. Both reviews took place over many years, but were released within a month of each other-- May 2021 (Alberta Health) and June 2021 (Québec National Institute of Public Health). The reviews diverged in methodology and conclusion, both reviewed in Part 1.3 of our main text. Alberta's report found the greatest weight of evidence for olfactory dysfunction, neurologic sensitization and neuroinflammation on exposure to chemicals and the psychological line of research of low utility, noting it was impossible to determine whether the affective symptoms reported were causes of MCS, or, in fact and more likely, the effects of MCS. The INSPQ report concluded there was no link between MCS symptoms and chemicals, and anxiety explains MCS.

Last in Part 1 we explain why, despite the long way to go in arriving at definitive answers regarding pathophysiology (true for many diseases and medical conditions), the current state of knowledge, detailed in its main features in Part 5, is fully sufficient for health ministries to proceed with creating clinical programs, making disability rights meaningful and advancing work on improved indoor air quality and regulation of common chemicals.

## Part 2: Missing pieces in basic research and epidemiology

In order to deepen understanding of the differences in the science called on by the two broad schools of thought in MCS studies – the psychogenic and the biophysical-toxicogenic – Part 2 begins with a more detailed history of the ideas and the authors in the respective schools. This clarifies how the INSPQ report is the latest iteration of the former, and why we consider ourselves squarely located in the latter. Then, to illuminate why we have selected key pieces of scientific research that dispute the INSPQ conclusions and, in other chapters, why we draw on scholarship in the wider field of environmental health studies, we provide our working description of MCS. In it, we take care to specify what from the patient experience is clear about MCS – especially that is a staged disease process, divisible at least into onset and chronicity. This understanding, key to many research and clinical accounts, is absent from the INSPQ report, and so, conveniently, is the role of chemicals in triggering onset, a strategic and important omission.

We then proceed to provide our first discussion of the omitted or neglected toxicologically-informed research on potential MCS mechanisms that disputes the INSPQ conclusions. We begin by describing a "unifying theory" based in environmental factors that links all the disorders the INSPQ report ascribes to anxiety: the "cell danger response" theory of physician and researcher Robert Naviaux (Naviaux 2018), a theory that describes the adverse health effects of

documented body burdens of common chemicals that disrupt mitochondrial function. Though we endorse no individual theories – we are advocates, not physicians or scientists – we do advance work that is much more plausible, is harmonious with the science that we consider enlightening, and grounded in environmental health studies than the INSPQ report. From this basis, we then discuss two very important lines of research on different sensitization mechanisms that have been, respectively, neglected and omitted in the report. These provide toxicologically-linked explanations for sensitization: the TRPV1 and TRPA1 receptors – a neurological discussion; and mast cell activation syndrome (MCAS), an immunological discussion. We want in particular to discredit the INSPQ proposition at that "low" or "normal" or "usual" concentrations "odours" (i.e. chemicals) cannot enter the brain or set off the biological triggers responsible for the symptoms of MCS. This is a very important, foundational idea for the INSPQ report that we begin to contest and refute here, and return to specifically in Part 4.

We also review several other fields in MCS studies that, thanks to low funding (a function of the politicization of MCS), have yet to be fully explored, but are very promising with respect to the identification of biological markers – unlikely to be present if MCS were an anxiety disorder. These include the study of what biophysical findings are common to other hypersensitivity illnesses; to the presence and role of specific genetic polymorphisms and epigenetic changes, and the information that the application of metabolomics (the study of metabolites) may yield in terms of specific MCS markers. The research in these fields has not emerged anxiety as a factor in any way.

Finally, we introduce the critical concept of biological individuality (and return to it at various junctures), which is central to understanding MCS both as a whole, in addressing individual patients and in rejecting the idea that anxiety is responsible for MCS in all patients all of the time. Again, this is missing from the INSPQ report.

## Part 3: Deficiencies in epidemiological, clinical and socio-political analysis

The problems in the INSPQ report are not only that it is missing science to describe neurological and immunological mechanisms for sensitization, and promising biomarkers. There are a number of other important deficiencies in the overall analysis that must also be factored in. To begin with, epidemiologically, the report's outdated statistics understate the prevalence of MCS and the rapidity with which numbers are increasing, tending to trivialize the urgency of understanding causes and developing serious, health and societal responses. Further, the preponderance of women (70+ percent) is barely noted, but must be accounted for by any categorical assertion of mechanism. We return to this in Part 6.

Another omission of great importance is the clinical knowledge that has been amassed by environmental health physicians in diagnosing MCS, and whether or not that experience confirms or contradicts the INSPQ conclusions. This is an astounding omission. Perhaps it is explained by the politicization of MCS. We provide a framework and historical account to this, including the early attacks on the "reality" of MCS, and the competence of the medical practitioners who care for MCS patients. This attack was led –we document this – by the

chemical industry, which explicitly declared MCS to be a threat to it, beginning in the late 1980s-early 1990s. It was also supported by a number of doctors and scientists whose work became well known thereafter. This politicization has skewed MCS research and impacted clinical publication. Likewise, we find the complete absence of the patient experience from the INSPQ report surprising, very troubling and undermining of its credibility, a discussion we begin in this Part.

Finally, there is no discussion, not even a mention, of MCS in children, or of what factors in childhood can increase risk for MCS in later stages of life. Just as with the missing "onset" discussion, this severs chronic MCS from the real life of individuals prior to and during onset. It also makes MCS children invisible. Finally, it obscures the urgent necessity of reducing the presence of both industrial and consumer chemicals in children's lives – an issue we do discuss, and return to again.

By way of conclusion, for Part 2 and 3, we underline that a definitional process that omits all these critical items cannot be considered comprehensive, and nor can its conclusions be considered well-substantiated, let alone final. We then move on to look more closely at the dismissed role of chemicals in MCS.

## Part 4: Chemicals and MCS

We begin the discussion of the links between chemicals and MCS – a link that is dismissed by the INSPQ report – by explaining why it is a fundamental error, to define MCS in relation to "odours" and not to chemicals. In addition to respiration, MCS reactions take place through ingestion, eyes and skin contact and even through internal tissue contact (e.g. via surgical implants) – pathways that have nothing to do with odours, but everything to do with chemicals, and are not accounted for by the INSPQ report. In discussing MCS links to chemicals, we are particularly interested in neurological impacts, but there are other pathways to sensitization as well, including immunological ones. Accordingly, we begin with a discussion of the many toxic chemicals that comprise today's synthetic fragrances, a topic that has been studied academically, but is not well-understood by the general public or medicine, even though many of these chemicals are implicated in a host of other chronic and serious diseases, and are neurotoxic. We then present important recent findings on what we might term "non-fragrant" chemicals, such as pesticides, printer inks, traffic emissions, building materials that equally trigger MCS and equally are implicated in multiple disease processes, including cancer, and also neurotoxic. We discuss the extent of toxics-related disease on a global basis, and link MCS to this trend.

With these factors in mind, we then extend the discussion of the neurological and immunological mechanism research on TRP channels and mast cell activation we started in Part 2.5. In doing so we deepen our presentation of the science and how it shows the links between chemicals, sensitization and MCS. We proceed to a discussion of the impact of many common chemicals on neurological/mental functions, the role of chemicals in MCS onset, and report on a 2021 empirical study demonstrating the MCS-chemical link.

## Part 5: Lessons from the clinical experience

The search for one mechanism is MCS is very likely misguided because there are many pathways to sensitization, a fact that has emerged from the clinical experience. That clinical experience is missing from the INSPQ report, and we briefly review and document some of its most important findings.

Very importantly, having a body burden of heavy metals and/or toxic chemicals such as pesticides, all measurable by standard tests, affects the central nervous system and can lead to sensitization and make de-sensitization difficult or even impossible, though modalities of treatment exist that can be helpful. Very importantly, toxic chemicals such as pesticides can also damage gastrointestinal health in several ways and particularly affect the health of the gut, which has a direct relationship with the brain and affective states, which we document. Brain injuries are likewise risk factors for sensitization when chemicals become involved. Fundamentally important from the clinical experience has been the role of serious but chronic and often, due to our inadequate testing, sub-clinical bacterial, viral, fungal and parasitical infections that affect the nervous system in a number of ways, including through the production of biotoxins. In the last decade or so, clinicians have found when Lyme disease is present, sensitization persists. Mold and mycotoxin illness, a common problem, also acts as a sensitizer and a retardant on recovery. In addition, many patients present with immunological deficiencies related to other immune functions, e.g. immunoglobulins.

The overarching point of this catalogue is to underline the specific paths to sensitization, the existence of clinical practice that concerns itself with them, and to demonstrate that the idea of one anxiety-driven mechanism is not plausible where the all-important clinical experience is concerned.

## Part 6: Women and MCS

Women comprise more than 70 per cent of MCS sufferers, internationally, a long and well-established fact. Any account of MCS that does not grapple with this must by definition by incomplete at best, erroneous at worst.

The INSPQ report attributes this preponderance to women's greater propensity to anxiety, and makes no effort to determine whether there are important links between women's biology, their chemical exposures relative to men, and their mental health. We do. First, we introduce a number of toxicological factors linked to women's greater share of MCS. We explain how women's special biological makeup puts them at greater risk than men during chemical exposure – a fact proven in the proportionally greater severity of Gulf War illness among women veterans than men. We also delineate the factors in women's social role – in women's workplaces and at home – that expose them to unregulated chemicals, at "normal" but truly unhealthy concentrations. We look at the tragic fact that the chemicals in many beauty products are also toxic, and have added to women's load.

Also, importantly but never addressed by the INSPQ report, is women's much greater medicalization than men, and the massive doses they receive, particularly of gut disturbing antibiotics as compared with men, and how this undermines neurological health. We also discuss the gender bias against women in medicine, lending their reports of illness less credibility than men's to physicians who have been shown to much more frequently ascribe symptoms of emotional and mental disturbances than with men.

Finally in this section, we introduce the findings of a very important new field of study, the synergistic effects of chemical exposures, socio-economic stressors and trauma with respect to maternal health – a field that does not counter pose these factors and create a false choice between them, but shows their respective as well as highly negative synergistic effects. This emerging field should have a great deal to offer MCS studies in the future. We conclude that there is overwhelming evidence for adverse impacts of chemicals on women's mental and neurological health, all of which undercut the simple and simplistic "anxiety causation" theory.

## Part 7: Understanding chronic stress, anxiety and MCS

In the INSPQ report chronic stress leading to, or along with chronic anxiety is seen to cause the "biological cascade" that causes MCS symptoms. The relationship of stress to anxiety and of these to symptoms is formulated differently at different times, so we begin Part 7 by attempting to clarify the key terms of this central tenet, and then set about addressing them.

We introduce the distinction between fear and anxiety – an issue we return to at length later in Part 7. We use the example of the life and death need for chemically-safe housing to demonstrate that people with MCS have fears of real dangers, rather than an anxiety disorder related to vague and unjustified concerns, but underline that these fears do not cause MCS, rather stem from it. Then, moving to a more theoretical formulation, we address the conceptual error, central to the INSPQ report, of counter posing "biopsychosocial" factors to "toxicological" ones.

We unpack this problem by introducing the types of chronic stress – personal, social (as in determinants of health), physical and toxicological, and their relation to individual and population health and how they figure in MCS. We discuss the now accepted understanding that personal and psychosocial stress underpin all forms of disease and in so doing draw on the work of Selye, the ACE project and the multi-decade Whitehall study. Next, we extend this understanding to MCS with the thesis that personal or psychosocial stress, without the involvement of other factors, does not create MCS. Our analysis shows that physical and toxicological stressors are the additional factors that are needed to tip people into MCS.

To illustrate this proposition with respect to onset, we turn to the lessons of Gulf War Illness (GWI). We first point out that GWI is not PTSD, as the INSPQ report erroneously states. We note that GWI need not include PTSD and even when it does, it is much more than that, including chemical intolerance. Drawing on the work of many distinguished researchers, we then analyze the presence and role of chemicals in Gulf War 1, now acknowledged to be the key factors in the

development of GWI. We also add a discussion of the illness-exacerbating role of high stress – combat stress – augmenting the vulnerability of soldiers to the chemical insults, in aid of understanding both the leading role of chemicals, and the synergistic effects of chemical and non-chemical stressors.

## Part 8: Socially determined stress in chronic MCS exacerbates illness

We start with a short discussion of the causative role of chemicals versus anxiety in illness to take us from group exposures during onset, to individual life with MCS. The example we use to illustrate this causative role is the development of chemical intolerance in a subset of female breast implant recipients. Then, we move on to looking at the role of all stress factors – personal, socio-economic, physical and toxicological – in the life of post-onset MCS patients, as documented in a major, qualitative needs-identification study conducted in Ontario for the Ministry of Health from 2011 to 2013. We use the framework of the WHO social determinants of health because deficits in these are well known to have adverse health impacts, so we queried these for participants. The study showed that, for every determinant, the overall burden of stress skyrockets during the chronic phase of MCS, and becomes an exacerbating factor in illness, undermining recovery.

We break our discussion of the study results into four main clusters: the determinants of disability, employment, income security, housing, food, clothing and transportation; the determinants of social environments, support networks and healthy child development; the determinants of discrimination, genetics, personal care practices and coping skills; and finally, but massively important, the determinants of access to health services of a decent quality. The study revealed almost unbelievable deficits in all these determinants as a result of the stigmatization of MCS by the medical profession and, in lock step, by society as a whole; by the inescapability of triggering chemicals and enormous difficulties in practicing avoidance; and by the complete vacuum in care and support for people who live with MCS.

The key takeaways of this section are a) it is the unbearable weight of real existential dangers that causes fear and vigilance in MCS, not an anxiety disorder, per the INSPQ report and b) stress reduction for people with MCS can be easily achieved with the right program of health and social supports – a social and moral decision within easy reach for our governments if they so choose.

Our final section discusses the psychological and neuro-plasticity derived therapeutic modalities relative to MCS. Given the anxiety-causation theory of the INSQP report, it would be logical that these would be the modalities that would be privileged and implemented for MCS patients. We review the dismal record of classical talk therapy, and CBT (cognitive behavioural therapy) in resolving MCS, and note the better success, at least anecdotally, in *some* people, of approaches that seek to "retrain the brain." We also note how these do not work for others, for whom biophysical interventions work better. We conclude that psychoneurological modalities, as well as support counselling, should be offered in clinical settings, but cannot replace the biophysical-toxicological clinical program discussed in Part 5 and again in the conclusion.

## Part 9: Myalgic encephalomyelitis (ME) and long COVID: What can we learn?

In Part 9, we take on the erroneous claim that chronic anxiety is what is common to, and causes MCS and a long list of other conditions, chronic fatigue syndrome and fibromyalgia among them. We express grave concern that the INSPQ report authors buttress their conclusions on such a faulty basis, for us one of the most fundamental errors in the report's conclusions.

In order to make our point we specifically look at the case of ME (myalgic encephalomyelitis, also known as ME/CFS and formerly as chronic fatigue syndrome). We show that research into ME is ongoing and active, with important projects supported by national research efforts, for example, in the US, through the National Institutes of Health, and in Canada, through the Canadian Institutes of Health Research. The research, growing in scope and depth as more funding is brought online, is showing ME to be a complex and multi-system biomedical disease. And more and more, there is an understanding that one single mechanism is unlikely to explain all pathophysiological processes for all people and that subgrouping is needed—not everyone with the condition is the same.

Treatment guidelines deal with ME as a biomedical disease, including those recently released from the UK prepared by the National Institute for Care and Excellence (NICE). ME is marked by many symptoms, with post-exertional malaise being the most characteristic. Anxiety, not amongst the disease's diagnostic criteria, can be present in some cases, but it is not causative, and recommendations for its treatment are similar to those that are given for any medical condition. There are cautions against the use of cognitive behaviour therapy (CBT) and graduated exercise therapy (GET), and in one example, best practices from the US Clinicians Coalition, these treatments are highlighted as an out-dated standard of care.

We also discuss long COVID, which is a newly recognized and yet-to-be understood condition that follows infection by the virus causing COVID-19. Like ME MCS and FM, its symptoms are multi-system; indeed, many people with long COVID are qualifying for a ME diagnosis. We note that there is an underlying tendency when pathophysiologic mechanisms are not known to assume the condition in question is psychogenic. We caution against this happening with long COVID.

## Part 10: Recommendations for moving forward

Our conclusion is devoted to practical conclusions and recommendations, to help advance the discussion from literature reviews to practical steps in establishing – recognizing, including and creating access for – MCS in health care and disability rights, and in population health and research. We agree with the INSPQ that MCS qualifies it as a "real health issue," that "centres of expertise specializing in MCS" should be created, and that MCS should continue to be tracked and researched. But what definition of MCS will guide the clinical programs and facility creation in these proposed dedicated centres of expertise, and what research will be funded and prioritized?

In terms of medical care, working from clear needs identified by patients, physicians and health ministry officials, we recommend a process to establish a case definition and clinical guidelines that could work across the country, including in identifying the appropriate roster of effective diagnostic and treatment services. It makes no sense to have multiple, diverging versions, so we recommend that Health Canada fund a process to bring this about. We urge that for this, expert clinicians practicing state-of-the art environmental medicine with established clinical track records from Canada and internationally, along with the handful of knowledgeable clinicians in Canada who work within the public system, be recruited, and that expert patient advocates be fully integrated into this process. We emphasize the need for safe air quality – and all that makes it possible – must be indicated for MCS clinical sites, as a fundamental medical need.

With respect to disability rights, we urge that recognition, policy, education and enforcement of MCS accommodation as a disability be enacted to maximize accessibility and maximize equity. We explain the main issues and measures in this respect, including accessibility and equity in inclusion in the many social assistance entitlements and programs now available to other disabled Canadians, including medical device and pharma care subsidies.

MCS-safe housing is both a medical necessity and disability need, so we strongly support the call of the *Association de la santé environnementale du Québec* (ASEQ/EHAQ) for a national MCS housing program, as well as for safe medical facilities and safe schools. We detail the components of what such a program ought to include.

As well, the federal government can and ought to fund research through the Canadian Institutes of Health Research, create at least two research chairs at major medical schools and jump-start funding to help provincial/territorial governments to create appropriate services along the continuum of care and integrated into our health care systems.
Provincial/territorial governments need not wait for federal action and can move forward on many fronts on their own. This will mean new diagnostic and treatment services, new ways of practicing medicine and new funding mechanisms. The experience of clinically responsive patients to such specialized treatment shows that it makes more fiscal sense to provide appropriate and effective care than to continue with high costs for current, but often useless, physician utilization.

We do have the knowledge and we do have the financial resources to deal with MCS, and if we do, everyone wins: people with MCS and their families, the modernized health care system and governments that truly spend less for good care than more for bad.

*Multiple Chemical Sensitivity Syndrome, an integrative approach to identifying the pathophysiological mechanisms*

## EXCERPTS FROM THE INSPQ REPORT'S KEY MESSAGES AND SUMMARY
## English language version

The objective of this [INSPQ] report is to identify the pathophysiological mechanisms that underlie MCS using an approach that considers all the research conducted on the hypotheses put forward to date. (Summary, Objective, p. 3)

Considering the chronic polysymptomatic nature of MCS and other related syndromes (chronic fatigue syndrome, post-traumatic stress disorder, electromagnetic hypersensitivity, fibromyalgia, chronic anxiety, depression, somatization disorder, phobias, and panic disorder), the authors of this report hypothesize that recent research on MCS, as well as on other related health conditions, may help to explain the origin of the observed symptoms. (Summary, Objective, p. 3)

Over the past two decades, advances in neuroscience, in particular in psychoneuroimmunology, and the availability of new techniques for measuring biological parameters and performing functional brain imaging have shed light on the pathophysiological mechanisms underlying MCS. **These scientific advances confirm that the psychological, biological, and social aspects of this syndrome are inextricably linked.** (Key Messages, p. 1, Emphasis added)

Studies have found the following changes in all the syndromes and pathologies studied: a disruption of the hypothalamic-pituitary-adrenal axis, an increase in inflammatory cytokines, a disruption in oxidative homeostasis, a chronic decrease in neuromodulator levels (serotonin, dopamine, norepinephrine). In addition, using brain imaging, alterations in brain function and structure were observed that affect the limbic system circuits (emotions, memory, learning) and the prefrontal cortex (attention, reasoning, strategic thinking, judgment). (Summary, Results, p. 3)

Collectively, these changes help to explain all the acute symptoms (those observed at the time of exposure to odours) and chronic symptoms reported by people with MCS. As a consequence of these alterations, MCS-affected individuals **develop neuronal sensitization.** This makes them more vulnerable **to subsequent episodes of stress triggered by the perception of odours,** which they consider a threat to their health. (Summary, Results, p. 3, Emphasis added)

**Chronic anxiety is an element common to all the syndromes studied and its main feature is the *anticipation of danger,* i.e., feeling a persistent, excessive, and inappropriate concern about one's day-to-day activities.** A number of factors may be involved, e.g., an individual's temperament, personal history, and psychosocial makeup. The severity of the syndrome

depends on its duration and the comorbidity that MCS patients frequently experience, i.e. chronic fatigue syndrome, electromagnetic hypersensitivity, fibromyalgia, and depression, etc. (Summary, Results, p. 3, Emphasis added)

Affected individuals perceive odours as a threat to their health. When they detect odours they experience acute stress symptoms that manifest as ailments that they attribute to chemical products associated with those odours. (Key Messages, p. 2)

What is more, olfactory studies have demonstrated that there is no absorption of odorous substances at the low ambient concentrations to which people with MCS are exposed. These individuals have a normal capacity for detecting odours, while exhibiting reduced, rather than increased, activation in the brain regions that process these signals. This reduced activation points to the suppression of activity in olfactory pathway structures by regions within the neocortex. If, indeed, people with MCS are hypersensitive to odours, one would expect to see increased, not decreased, brain activity when compared with control subjects. (Summary, Results, p. 3)

The authors of this report conclude that, based on the available data, there is no evidence to support the hypothesis of a relationship between MCS and the toxicity of chemicals at their usual concentrations in the environment. People with MCS, therefore, are not hypersensitive to chemical substances. Nonetheless, the chronic biological disturbances observed, the severity of the symptoms experienced, the impact on the social and professional lives of affected individuals, and the high prevalence of MCS in the population qualify it as a real health issue. (Summary, Conclusion, p. 3)

## EXCERPT FROM ELSEWHERE IN THE INSPQ REPORT

[Translated] The authors of this report conclude that MCS . . . is due to fear conditioning accompanied by chronic anxiety resulting from the constant desire to avoid exposure to odours that cause these people to develop or exacerbate symptoms because they consider this exposure to be threatening to their health. (p. 811)

# PART 1: CONTEXUALIZING THE INSPQ REPORT ON MULTIPLE CHEMICAL SENSITIVITY

# PART 1: CONTEXTUALIZING THE INSPQ REPORT ON MULTIPLE CHEMICAL SENSITIVITY

## 1.1 PRELIMINARY THOUGHTS IN SETTING THE CONTEXT

This document presents our counter argument to the central findings and conclusions of the Institut National de Santé Publique du Québec's June 2021 report *Syndrome de sensibilité chimique multiple, une approche intégrative pour identifier les mécanismes physiopathologiques*.[1] At the same time, it is also a vehicle that allows us to present many exciting new research efforts that are not contained in the INSPQ report despite its 824 pages and which, based on our experience, provides a more accurate account of multiple chemical sensitivity (MCS). We also include a wealth of knowledge from the clinical experience, which, we hope, truly advances the larger discussion to the next level, that of care provision, where both those who live with MCS and those who will be involved in creating new care capacity need it to be. All of this we present in a positive and constructive spirit, intent on moving the field forward.

The ground-breaking material found in the following pages comes both from MCS studies as such, and from relevant and related fields in environmental and women's health. Some of the articles and papers were published between the INSPQ report release date of June 2021 and May 2022; a larger number were published either after research collection had been completed for the report or because the authors were not aware of, or did not choose to address certain efforts, though we think they should have done.

This paper, then, offers researchers, clinicians, policy makers in health services, people working in public and environmental health, women's health and disability rights studies and organizations, as well as other scholars, patients and families the up-to-date knowledge and analysis they need in order to truly understand MCS – at least, to the state-of- the-science as it now stands. It also provides the information they need to evaluate the validity of the INSPQ conclusions, and to understand the debates surrounding the key questions of causation and mechanisms to which the report addresses itself. We think great strides have been made recently, and we welcome the occasion to make this research better known, as well as to explain in depth why we take issue with the INSQP report.

The INSPQ report authors state that "the objective of this report is to identify the pathophysiological mechanisms that underlie MCS (for multiple chemical sensitivity) using an approach that considers all the research conducted on the hypotheses put forward to date." (Summary, Objective p. 3) Notwithstanding this ambition and scope, we think the report fails in making the case for its main conclusions, namely:

[1] The whole INSPQ report comprises four documents written in French: a full version, a synthesis, key messages, and summary and appendices. Only the key messages and summary were translated into English as "*Multiple chemical sensitivity syndrome, an integrative approach to identifying the pathophysiological mechanisms*." Throughout our response, we will refer to the documents collectively as "the INSPQ report" and will, where possible, use the officially translated wording of the English version.

a) that MCS is not linked to chemicals "at usual concentrations" (Key Messages, p. 2; Summary, Conclusions, p. 3)

b) that MCS is a somatoform condition caused and perpetuated by chronic stress and anxiety. (Key Messages, p. 2; Summary, Results, p. 3)

The gaps, deficiencies, omissions and errors of the report, as well as the new material since publication show that it cannot be considered comprehensive. And the missing or neglected research we present in substance calls these conclusions into question. As we show, the report's findings and conclusions do not accord with the bodies of knowledge of expert clinicians or of patients, knowledge that has found no place in the report. Beyond this, the way that the report declares "everyday" chemicals at so-called "usual" or "normal" concentrations to be "harmless" – to borrow the report's language – flies in the face of the core findings of the environmental health movement and the corresponding fields of study that have developed in the past half century with respect to adverse health effects on population health more generally, as well as with respect to MCS.

For all these reasons, it must be said from the outset that as a basis for any policy or action, this report has the potential to do grave harm to people with MCS, and to set the MCS, environmental health, women's health and disability fields back a long, long way.

## 1.2 MCS: WIDESPREAD YET EXCLUDED FROM CANADIAN HEALTH CARE

As a first step, we want to locate the INSPQ report within the larger picture of the way MCS has been dealt with by health ministries and health systems in Canada. The INSPQ report was not written in a vacuum, and its implications will not unfold in one, either.

Let us begin with the stark reality of current prevalence.

In 2020, the Canadian Community Health Survey showed that about 1.1 million Canadians, 3.5 percent of Canada's population, had been diagnosed with MCS, or multiple chemical sensitivity, (of whom 72 percent were women) – a finding consistent, if somewhat low, relative to the UK, Sweden, Australia, USA, where an average of 7.4% have been found to be medically diagnosed. What we call MCS today – and a host of other names, as well - emerged as a distinct clinical entity as far back as the 1950s, when it was rare. Today, it is extremely widespread, with both absolute numbers and percentage of population growing every year. Part 3.2 below discusses prevalence issues in detail.

We do not track severity in Canada, but we do know that for many of those diagnosed, MCS is severe, creating devastating physical symptoms and effectively isolating those who live with it from family, employment, social and community life. MCS means having serious, multi-system symptoms when encountering many "everyday" chemicals – from pesticides to solvents to printer ink to synthetic fragrances in everything from laundry products to baby wipes. Having

MCS makes living in our chemically-saturated environments impossible without serious health consequences, and in severe cases, life-threatening ones.

This is why MCS has been recognized as a disability federally (since 2007 – Canadian Human Rights Commission; Sears, 2007; Wilkie & Baker, 2007) and in a number of provinces, although the de jure rights this is meant to confer are never available de facto without a fight, and even then, rarely. And that is because MCS is not recognized by our public health care system or by the major medical associations, whose physician members are both the gatekeepers and tone-setters for all government services and for public perception.

Indeed, despite the relentless increase in MCS over the last half century, aside from a partial service clinic near Halifax (Fall River), and a tiny, diagnosis-only clinic in Toronto (Women's College Hospital), both founded in the mid-1990s, no medical care is provided for these 1.1 million people for what is usually their most pressing and difficult medical condition. Since we do not teach MCS in our medical schools when those with MCS seek care for other conditions, it is provided in ways that do not account for, or may even worsen, their chemical intolerance. As well, for those with moderate to severe MCS, the nature of the condition and disease process is such that attending physician's offices exposes them to chemicals that can greatly worsen their symptoms, to the point that many avoid seeking even the most basic care for even very serious conditions. The situation is worse for those spending time in hospitals, even if their time is short.

People with MCS are, as a result, effectively excluded from Medicare and live without the universal right to health care that Canada promises its citizens. The de facto delegitimization of MCS has translated into deep stigmatization, complete disregard for urgent medical needs, massive barriers in exercising disability rights and entitlements, complete absence of public health measures to support those with MCS or to prevent new cases, and, shockingly, no research funding at all.

Despite decades of attempts, more or less protracted, by different groups and individuals, persistent, conscious refusal to create and incorporate care and appropriate social supports and disability rights by our governments has prevailed. This is the result of a number of factors, some explored in our document (especially but not only in Part 3.4). What is crucial here is to note that governments have not been transparent about all their motivations, instead citing solely the confusion and disagreement among physicians. Physician organizations, in turn, historically took a position that MCS was not a "real" condition or disease, or at best, was an expression of a psychological disturbance that distorted patient perception, not a biophysical disease triggered by synthetic or biological toxicants, either in onset or chronicity.

The causative role of common chemical toxicants in onset and their ongoing role as triggers in chronic MCS, by contrast, has been insisted on by MCS patients, by a very few knowledgeable clinicians within the public system and by specialized environmental health physicians, internationally as well as in Canada, for more than 50 years.

Accordingly, two schools of thought have developed in MCS studies. We address these in greater detail in at several junctures (Part 2.2, Part 7.3), but for now, let us summarize these and their import. What can be termed the "biophysical-toxicogenic school" was the first to emerge in the mid 20th century among newly ill patients and a few pioneering clinicians who sought to understand the phenomenon they were witnessing. Since then, this school of thought has posited that MCS is a type of toxic injury to the immune and central nervous systems most importantly, created by an overwhelming exposure for a given individual to a chemical or chemicals, over a short or long period, that results in an intolerance to many chemicals, even those apparently unrelated. The challenge of finding biomarkers and explaining mechanisms in a new disease process, some in this school have pointed out, has to do with novel disorders due to novel conditions.

Today, research over decades employing ever-newer modes of investigation – for example, brain imaging, exposomics (toxicant body burden measurements), immunological discoveries, including at the cellular level and with respect to the effects of long-term infections, genetic studies and metabolomics have produced an increasingly robust, authoritative and promising body of knowledge in MCS studies. It has validated the importance of the central nervous and immune systems, a very important issue we discuss at length at several points in this commentary. At the same time, cutaneous, allergic, gastrointestinal, rheumatological, endocrinological and cardiological signs and symptoms have also been identified. This makes MCS, in the view of the biophysical-toxicogenic school, a complex, multi-system syndrome and disease process, generally accompanied by a number of co-morbidities, with an onset period and a period of chronicity that can be life-long if appropriate interventions are not made.

The other school of thought, which we call the "psychogenic school," surged in the early 1990s, coinciding with the moment that the chemical industry went on the attack to delegitimize MCS (then called EI, for environmental illness), labelling it as an emotional disturbance, not a "real" and "physical" disease (detailed discussion of this history is provided in Part 3.4). These germinal words are taken from an industry briefing paper in 1990.

> Environmental illness patients generally lead troubled lives and have genuine problems in coping with family, work and life-style pressures. They often eagerly accept environmental illness as the explanation for their condition." (Environmental Illness Briefing Paper, 1990,Executive summary, paragraph 5).

Throughout the 1990s, a select number of health providers picked up this torch and carried it. Three of their leading voices, publishing multiple articles on their own and with colleagues through the decade, were Herman Staudenmayer, PhD, a psychologist and Ronald E Gots MD PhD and Toronto allergist-immunologist Arthur Leznoff MD. Works from these are referenced in the INSPQ report, Staudenmayer's most frequently. With other colleagues they wrote multiple articles advancing the conviction that in MCS,

> biological and physiological sequelae stemming from early, chronic trauma have been identified which could explain many of the multisystem complaints. The incidence of

> childhood abuse reported by EI/MCS patients is strikingly high, and it is recollection of trauma that many EI/MCS patients avoid by displacing the psychologic and physiologic adult sequelae onto the physical environment. (Staudenmayer, 1996, Abstract)

In these articles, the notion of mass contagion of MCS as a psychological mechanism for acquiring the belief that chemicals are harmful was also introduced, presumably to account for group poisonings that resulted in a subset of people with MCS (e.g. Gulf War 1 veterans). The epitome of articulation of this school came in 2003 in a pair of articles claiming there was no proof for the toxicogenic hypothesis according to the Bradford Hill criteria,[2] and defining MCS as form of cognitively mediated panic disorder and somatoform illness (Staudenmayer et al. 2003a, 2003b) with no "neurobiologically plausible mechanism" to explain it otherwise.

Since then, in contrast to the negligible funding for studies looking at a bio-toxicological basis, there have been many well-funded studies seeking to show that it is not chemicals but the subjective experience, generally of expectation and fear of harm, on the part of the chemically intolerant that is responsible for their symptoms, not any chemical substance or, more usually for this school, any "odour." Often the term "odours" is substituted for "chemicals" in such studies. And, these studies conclude that it is this subjective belief experience (thought to arise from disturbed mental health) that results in distressing symptoms, in other words, in somatization. In this account, chemicals are rendered harmless and blameless and play no role in causing or perpetuating illness. MCS is thus a mental illness, not a physical one, and the two are counter posed. No explanations for why some people develop this form of mental illness nor why psychology or psychiatry have failed to help the vast majority of MCS patients have generally been offered.

MCS patients, individually and through advocacy groups, have long rejected this view, which does not correspond to their experience. They have held that their experience is much better expressed in the ways the biophysical-toxicogenic school explains the action of chemicals and MCS reactivity in MCS, as we discuss at a number of junctures below.

This matter of the nature of causation and the mechanisms of MCS – biophysical-toxicogenic or psychogenic? – has then, become the fundamental issue to address in seeking to create effective, appropriate care for those with MCS. Certainly, it goes directly to what kind of clinical programs are needed and what kind of facilities are required to deliver them. But it is also central to the matter of whether safe housing is a medical need, to what disability rights should be granted, to what kind of public health policies for support and prevention are indicated, and for how much funding is needed for what types of research.

This is why the INSPQ report, located by dint of its method and conclusions firmly inside the psychogenic school, devotes more than 800 pages to the matter; and why we, located firmly inside the biophysical-toxicogenic school, consider it vital to dispute these conclusions. It is why

[2] Bradford Hill criteria for causation: Strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment and analogy

we have pointed out key omissions and distortions of research showing bio-toxicogenic mechanisms in that report. And it is why we have provided an alternative account of MCS, and offered a set of recommendations that flow from our understanding of MCS and of the vacuum of care and support for those living with MCS today.

## 1.3 THREE PROVINCIAL PROCESSES SINCE 2010 ON MCS

Within this divided field, it is important to note that for a very long time, despite rising numbers, health ministries were not even interested in considering MCS, and refused periodic initiatives to draw attention to new research and seek their attention and action. Then, in the early 2010s, with prevalence continuing to grow, increasing awareness by the public and patient's groups and, in some cases, with these groups united with health providers (both physicians and administrators), health planning experts and social policy experts, three processes were launched to address MCS in three different provinces.

### 1.3.1 Ontario: An extensive process of study, planning and design for new care capacity

The process in Ontario, the most extensive to date has had three stages, funded by its Ministry of Health, beginning in 2012. These were geared to providing the ministry with all the necessary inputs to create a system of care within the pubic health care system, meant to include ES/MCS, as well as ME/CFS (myalgic encephalomyelitis/chronic fatigue syndrome) and FM (fibromyalgia).

- Phase one: A major research and planning project was conducted between 2011 and 2013. It resulted in a number of important research and design documents for a centre of excellence, affiliated regional clinics and the training of a layer of primary care providers across the province. The package of research and planning documents produced included *Chronic, Complex Conditions: Academic and Clinical Perspectives* (Molot, 2013), comprising a literature scan, descriptions and definitions, and a proposed approach to the clinical framework of best and promising practices in a research framework for new clinical programs. This report explained and affirmed the biophysical-toxicogenic view, and built from there. Another major research report, *Recognition, Inclusion and Equity: Perspectives of Ontarians with ES/MCS, ME/CFS and FM,* (Burstyn & MEAO, 2013) included the findings of a major, qualitative, patient needs-identification study for medical care and other health and disability needs – as relevant today as when it was completed – and detailed recommendations for policy and practical action. This too, rooted firmly in patient reporting, expressed the biophysical-toxicogenic view. *Recognition, Inclusion and Equity: Solutions for of Ontarians with ES/MCS, ME/CFS and FM – The Business Case Proposal* (Steering Committee of the OCEEH Business Case Project, 2013) was the sequenced, budgeted, costed plan that was developed from these two research documents. Its programs, professionals, dedicated housing personnel,

special safe-building specifications, education, training and public awareness programs were all built on the basic tenets of the biophysical-toxicogenic understanding of MCS.[3]

- Phase two: In 2016, the Ontario Task Force on Environmental Health was established, and it deliberated until late 2018. The task force too built on the positions of the clinical approach of the previous phase (biophysical-toxicogenic approach). It validated the essential design of a centre of excellence, clinics and training for physicians, and produced additional research reports on historical funding and support for the three conditions and on needed early first steps in *Time for Leadership*, its 2017 interim report. In *Care Now*, its 2018 final report, it made a number of recommendations, some reiterations for rapid action on older recommendations – the 3-tiered system, updating OHIP codes, government initiated major awareness campaigns, creating safe care in medical and long term care facilities; and some new recommendations, shared practice tools and the creation of a community of practice. (Care Now, 2018) Additional research was included on several relevant fronts as well.

- Phase Three: An implementation plan, *Laying the Groundwork*, was written during 2020 but COVID has interfered with moving forward and the report still remains an internal document. We look forward to seeing these next steps enacted by Ontario's new government, incoming June 2022.

A strong basis for the biophysical-toxicogenic framework for MCS upon which the Ontario process has been proceeding was provided by two central documents.

First from 2010, *Environmental Sensitivities-Multiple Chemical Sensitivities Status Report 2010, Advances in Knowledge and Current Service Gaps* (Marshall et al., 2010). It was written by Drs. Lynn Marshall, Alison Bested, John Molot, Kathleen Kerr and Riina Bray, all of the Environmental Health Clinic (EHC) at Women's College Hospital in Toronto. The doctors set out to report on the scientific evidence available, to that time, underpinning the assessment and management of ES-MCS (environmental sensitivities-multiple chemical sensitivities) (Marshall, 2010). While the report focused on evidence it was also practical, incorporating as appropriate clinical viewpoints and input from the patient perspective.

The second document is the already mentioned *Chronic, Complex Conditions: Academic and Clinical Perspectives* (Molot, 2013). It is "[a] broad-based scoping, but non-systematic, review of

[3] Find *Chronic, Complex Conditions: Academic and Clinical Perspectives* [Molot 2013], *Recognition, Inclusion and Equity: The time is now: Perspectives of Ontarians living with ES/MCS, ME/CFS and FM*, and *Recognition, inclusion and equity: Solutions for people living in Ontario with ES/MCS, ME/CFS and FM – The Business Case Proposal*, and more research documents for this phase of study **for** an Ontario Centre of Excellence in Environmental Health (2011-2013) at http://recognitioninclusionandequity.org/. [The 2010 ES-MCS Status Report, which we will soon be discussing, can be found as Appendix B to Molot, 2013]. Find the interim and final reports of the Ontario Task Force on Environmental Health (2016-2018) at https://www.health.gov.on.ca/en/public/programs/environmentalhealth/

the scientific literature related to environmental associations with chronic complex health conditions." It focussed on three conditions: myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), fibromyalgia (FM) and ES/MCS. It primarily looked at peer-reviewed literature, "supplemented on occasion by credible reports by government agencies, professional associations and environmental/patient support organizations." (Executive Summary, Introduction)

In Ontario, the 2010 Status Report plus the 2013 Academic and Clinical Perspectives, along with extensive research on the patient experience provided a clear foundation for the planning and design of a multi-component, three-tiered system of care, under consideration for implementation at this time.

### 1.3.2 Québec and Alberta: divergent literature reviews

In both Québec and Alberta in the early 2010s, demands for action resulted in promises by their respective health ministries to undertake substantive literature reviews. The expectation was that these governments would take their cues for further policy development and practical action from these reviews.

In Québec, the Ministry of Health and Social Services commissioned INSPQ to produce a report in response to individual requests as well as requests made by the Environmental Health Association of Québec/ L'Association pour la santé environnementale du Québec for government assistance to create a safe-housing complex for people living with MCS, as well as for the provision of appropriate health care.

Alberta Health commissioned its review as part of its response to recommendations from the Alberta Energy Regulator stemming from an inquiry into citizen concerns about a cluster of health problems, including MCS, linked to ambient gases in the Peace River area in the early 2010s. Both reports could be expected to be consequential in new policy setting, once completed. In 2021, two major literature reviews (not planning documents for new programs) on the subject of the nature and mechanisms of MCS were finally released.

Alberta Health made available *Multiple Chemical Sensitivity: Literature Review and State of the Science* in May, 2021. The review was commissioned from Intrinsik, a consultancy with expertise in toxicological and environmental health fields. This 250-page document was a serious effort to examine MCS-related research[4] since 2000, using a "weight of evidence" approach, reviewing both the standard and grey literature.

One month later, Québec's National Institute for Public Health (INSPQ) released a long-awaited report entitled *Syndrome de sensibilité chimique multiple, une approche intégrative pour identifier les mécanismes physiopathologiques* (in English, *Multiple Chemical Sensitivity*

[4] In addition to "multiple chemical sensitivity," search terms used in the peer-reviewed literature included "idiopathic environmental intolerance" and "toxicant induced loss of tolerance." (p. 12)

*Syndrome, an integrative approach for identifying the pathophysiological mechanisms,* (henceforth 'the INSPQ report,' June 2021). It was a document of more than 800 pages that included a lengthy review of literature on MCS since the 1950s and an excursion far afield into neuroscience, notably neurochemistry and neurocircuitry.

The two reports arrived at very different assessments of MCS causation and mechanisms, diverging both methodologically and substantively from one another, with Québec's INSPQ report diverging as well from the paradigm adopted by the Ontario process .

## Methodologically:

For the Alberta-commissioned authors, any conclusion on the nature and mechanisms of MCS, based on a literature review only, especially one with so little clinical literature and patient experience, must still be tentative and partial given the scarcity of research literature overall, which, in their view, has resulted in serious gaps in knowledge, even on promising lines of research. As well, they found important problems with the consistency of research approaches, which, they explained, makes comparisons and conclusions difficult. As a result, though the report did not question the validity or reality of MCS, the Alberta authors ranked the overall weight of evidence for MCS as a whole as only moderate, in the sense that the literature overall was modestly good for only two out of seven lines of research – the olfactory dysfunction, and neurologic sensitization and neurogenic inflammation lines of research – but not for the others. The authors specified lack of funding as the major cause of this problem and called for much more of it, specifying what types would be important. (Excerpts from their specific discussion of limitations, uncertainties and data gaps can be found in Appendix 2 in this document.)

The INSPQ report, by contrast emphasized the comprehensiveness of its literature review and concluded, by implication, that this had been more than sufficient to permit the authors to solve categorically the matter of MCS mechanisms and settle the great questions of MCS studies. However, as our extended discussion in Parts 2 and 3 shows, the review was not comprehensive as claimed. It omitted, or described but failed to engage, or distorted key pieces of analysis and research that in themselves dispute the INSPQ conclusion on mechanisms, by their absence, giving the lie to the reports claim to comprehensiveness.

## Substantively:

Among seven lines of research identified by the Alberta authors, the report concluded that "olfactory dysfunction, neurologic sensitization and neurogenic inflammation showed the highest utility and consistency," a finding they substantiated in detail. The report also hypothesized that these factors may have a three-way synergistic interaction and/or impact that needs further investigation. They concluded the psychological line of evidence was of low value, poor consistency and poor methodology. These conclusions place the Alberta report within the biophysical-toxicogenic school.

By contrast, the INSPQ report, while it examined these lines of investigation to a certain degree (its omissions or lack of engagement with key research is very important, and we detail it below), rejected these findings as useful. This report eventually centred on the neurochemistry and neurocircuitry of anxiety and fear, to which it attributed all meaningful causality in MCS.
For this report, chronic anxiety "helps explain" MCS, in which, thanks to that anxiety, "harmless odours" (note: not chemicals) present in the environment at "low concentrations" are wrongfully perceived by individuals to be dangerous. It is this subjective feeling of danger that sets off a cascade of biological consequences that produce distressing MCS symptoms. The INSPQ report went further to "rebut the hypothesis that there is a relationship between MCS and the toxicity of chemicals present at normal concentrations." (Key Messages, p. 2) Thus, for them, MCS is a somatoform illness and chemicals at these concentrations are blameless.

So certain are the INSPQ report's authors that they have explained the cause and mechanisms of MCS that they even suggest a new name for the condition: CSMCS (central sensitivity to multiple chemical substances.) (translated[5], p. 811) Their two central conclusions – anxiety causes MCS; there is no link to chemicals – place them squarely in the psychogenic school of thought, in opposition to both the Ontario and Alberta approaches as well as to numerous and distinguished researchers, clinicians and patient and other lay experts across the country and the world.

With respect to the divergence between the Alberta Health and INSPQ reports, we think Alberta trends in the right direction, although we also think that the paucity of literature relative to important and promising lines of research (immunology, exposomics, metabolomics, genetics and epigenetics, all discussed below), the direct result of lack of funding and perhaps also of lack of access to more current publications, means that the WOE approach did not capture all that is important in MCS studies.

Whereas, to the contrary, we think the INSPQ report trends strongly in the wrong direction. We do not agree that its review of literature was complete, despite its length. And we think its conclusions obscure critical clinical issues by reducing a complex disease process – complex in causation and symptomatology – to one psychoneurological mechanism. This type of reductionism can only have harmful consequences if it is not corrected.

Further, the INSPQ report's conclusion about the "harmlessness" of chemicals (which it reframes as "odours') at low concentrations flies in the face of the core findings of the environmental health movement and the corresponding fields of study that have developed since the 1990s and now inform – or should inform – our understanding of the adverse impacts of common "everyday" chemicals, even at the molecular level.

As the literature we reference throughout this commentary and especially in Part 4 demonstrates, many chemicals at concentrations normally found in indoor or outdoor environments, what the INSPQ report calls "normal" or "low" concentrations, are in fact, quite dangerous to human health in a great number of ways that are heavily implicated in many

[5] Sensibilité central aux substances chimiques multiples (SCSCM)

environmentally-linked diseases and disorders. One of the diseases that toxic everyday chemicals, as well as occupational and industrial chemicals, can lead to is MCS. By severing the link between chemicals and MCS, the INSPQ report also contributes to obscuring the broad adverse effects of these common chemicals on all human populations, a real step backwards in population health.

As well, across countries, we find a very striking phenomenon: about 70 per cent of MCS sufferers are women – a very concerning issue that cries out for explanation as well as prevention. The INSQP report did not engage with this issue at all. We have taken it up in some detail in Part 6. But by dismissing everyday exposures to common chemicals as "harmless", the INSPQ report also radically obscures the particular dangers of common toxicants to women in general, and to their fetuses and infants – meaning, as has been addressed in these studies, to the future of our species – as well as side-stepping a critical issue in MCS understanding.

## 1.4 CURRENT STATE OF KNOWLEDGE *IS* SUFFICIENT TO PROCEED ON CLINICAL FRONT

To conclude this introduction, we want to make clear that while we know much more remains to be understood about MCS, we also think that existing research and clinical experience with MCS more broadly – not captured in the Alberta or Quebec reviews – is sufficient to arrive at important conclusions about MCS causes, characteristics and treatment, and to create clinical sites and programs, disability protections and healthy public policy. However, as we argue at appropriate junctures below, the development of these essential measures can only be achieved by seeking out additional literature, both that neglected by the INSPQ report or new since its publication, and other forms of aggregated knowledge, above all the clinical experience of advanced practice environmental medicine physicians where this knowledge has been gathered (discussed in 3.3 and Part 10), and drawing as well on the knowledge of the few clinicians who have long been working with patients with MCS within the public system, as well as expert patients.

This is, finally, the critical, real-world point for people living with MCS, for health providers who treat it and try to prevent it, or want the means by which to do so, for colleges of physicians and surgeons who need to face the real challenges of the 21st century by adopting new medical approaches, and for government officials who can enable the creation of policies, programs, and services at all levels. Although the INSPQ report does not advance explicit clinical guidelines and recommendations, a clinical agenda is embedded in its conclusions and seems consistent with the few clinical suggestions made during a presentation about the report to members of the Réseau d'échanges sur les enjeux en santé environnementale on November 23, 2021 (Coté, 2021). In our view, these implicit clinical directions would be just as erroneous and just as dangerous, as the report's conclusions.

We identify some of the key lessons of clinical practice in environmental medicine and MCS specifically in Parts 3.3, Part 5 and in Part 10, our conclusion. But before we arrive at those, many issues need addressing to lay the groundwork for that discussion. Part 2 lists and discusses issues in basic and epidemiological research missing from the INSPQ report, while Part 3 further

elaborates on deficiencies with respect to prevalence, politicization, patient input and childhood issues. These are then further elaborated in Parts 4, 5 and 6. We begin with these gaps and deficiencies, because these missing pieces not only weaken the INSPQ report, many are so important that they invalidate the report's key conclusions.

# PART 2: MISSING PIECES IN BASIC RESEARCH AND EPIDEMIOLOGY

## PART 2: MISSING PIECES IN BASIC RESEARCH AND EPIDEMIOLGY

### 2.1 INTRODUCTION

The claim of the INSPQ report to have solved all questions surrounding MCS mechanisms is based largely on

> [Translation]: . . . recent research carried out thanks to the dazzling advances in the fields of neuroscience since the end of the 1990s and especially after 2000. This research has allowed, among other things, the discovery, in immunology and neurology, of previously unknown biological markers and to measure them at the molecular, cellular and structural levels and even to visualize them using innovative imaging techniques. These markers made it possible to study dysfunctions in the structures of the nervous system in relation to several health problems mentioned earlier in this document and to compare these observations with those noted in groups of MCS subjects. Moreover, the new imaging techniques make it possible to measure the activity of brain structures in real time and thus explore the dysfunction of the structures of the limbic system involved in the functioning of the olfactory system and in neuronal plasticity. These new approaches have also been used to study the role and function of structures involved in the sense of smell and in the response to stress and chronic anxiety.[6] (INSPQ Synthèse, p 7)

We agree that advances in neuroscience have been remarkable and enlightening. But **we emphatically do not agree that all of these, as well as all relevant advances in several other fields, were addressed and incorporated in the INSPQ analysis or reflected in its conclusions. Indeed, thanks to the report's lack of engagement, omission, and minimizing of key areas of research that conflict with or contradict its conclusions, we find the INSPQ report to be significantly incomplete despite its length. We find that, as a result, it has not provided a full and accurate account of the causation and mechanisms of MCS, as it claims to do, and its conclusions are not supported or credible.**

To set the context for these missing pieces, we need to return briefly to a more detailed discussion of the different paradigms or schools of thought in MCS studies.

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[6] Original French from Synthèse page 7 of the INSPQ report: "**. . .** ils se sont basés sur les recherches récentes réalisées grâce aux avancées fulgurantes dans les domaines des neurosciences depuis la fin des années 1990 et surtout après 2000. Ces recherches ont permis, entre autres choses, de découvrir, en immunologie et en neurologie, des marqueurs biologiques inconnus jusque-là et de les mesurer aux niveaux moléculaire, cellulaire et structurel et même de les visualiser au moyen de techniques d'imagerie novatrices. Ces marqueurs ont rendu possible l'étude des dysfonctions dans les structures du système nerveux en relation avec plusieurs problèmes de santé mentionnés plus tôt dans le présent document et la comparaison de ces observations avec celles notées chez les groupes de sujets SCM. De plus, les nouvelles techniques d'imagerie permettent de mesurer l'activité des structures du cerveau en temps réel et, ainsi, d'explorer le dysfonctionnement des structures du système limbique impliquées dans le fonctionnement du système olfactif et dans la plasticité neuronale. Ces nouvelles approches ont été utilisées également pour étudier le rôle et le fonctionnement des structures impliquées dans le sens de l'odorat et dans la réponse au stress et à l'anxiété chronique. »

## 2.2 TWO BROAD SCHOOLS OF THOUGHT IN MCS STUDIES

In Part 1, we provided a very brief discussion of the two schools of thought – some prefer the term two paradigms – in MCS studies, in order to provide context for the current state of knowledge, debate and lack of care capacity despite the high prevalence of this serious condition. Here, we want to extend that important discussion.

The 2021 Alberta MCS report states that that in relation to the research on the phenomenon of chemical sensitivity or intolerance, the most significant roadblock to progress is

> the lack of clear case definition and diagnostic criteria for which there is consensus among international experts and organizations.
>
> This deficiency affects everything from the development of a concise clinical profile, the consistent diagnosis of patients within and between centres, the design of research studies, to effective health-care management. (p. 76)

This deficiency is reflected in a confounding multiplicity of names for the complex phenomenon of chemical intolerance, arising from a variety of analytic approaches. But it would be unhelpful not to explain that these multiple names, reflecting different analytic emphases, are clustered within the two broad approaches that can be called the psychogenic and the biophysical-toxicogenic schools of thought on MCS. The differences of emphasis and analysis *within* each school have been, so to speak, fraternal. The differences *between* the two schools, on the other hand, have to date marked a fundamental cleavage that the conclusions of the INSPQ report have not, alas, succeeded in bridging or repairing.

### 2.2.1 The psychogenic school of thought and the INSPQ report

The favoured term for the school of thought that proposes MCS as a psychological disorder has been "idiopathic environmental intolerance" or IEI. This term has traditionally been used to communicate that little of decisive importance is understood about the condition and that, much extant research notwithstanding, MCS is not a biophysical disorder or disease process linked to toxicological factors. Rather, those in this school explain MCS as psychological disorder based in a subjective experience of expectation or fear of "odours" that those with MCS *believe* are harmful chemicals, but are in fact "harmless" (INSPQ, p. 11, translated). The core articulations of this school can be found in Staudenmayer et al.'s pair of articles from 2003, "Idiopathic environmental intolerance: Part 1: A causation analysis applying Bradford Hill's criteria to the toxicogenic theory"[7] and "Idiopathic environmental intolerance: Part 2: A causation analysis applying Bradford Hill's criteria to the toxicogenic theory." The final words of the abstract from their Part 1 sum up the rejection of a role for chemicals

[7] Bradford Hill criteria again: strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, analogy

> The results of this analysis indicate that the toxicogenic theory fails all of these criteria. There is no convincing evidence to support the fundamental postulate that IEI has a toxic aetiology; the hypothesised biological processes and mechanisms are implausible.

The final words of the abstract from the Staudenmayer et al. Part 2 article sum up the central idea that MCS is a subjective belief experience based in fear and a somatoform disorder:

> We conclude that IEI is a belief characterised by an overvalued idea of toxic attribution of symptoms and disability, fulfilling criteria for a somatoform disorder and a functional somatic syndrome. A neurobiological diathesis similar to anxiety, specifically panic disorder, is a neurobiologically plausible mechanism to explain triggered reactions to ambient doses of environmental agents, real or perceived. In addition, there is a cognitively mediated fear response mechanism characterised by vigilance for perceived exposures and bodily sensations that are subsequently amplified in the process of learned sensitivity.

The argumentation for how such a panic disorder develops is to be found in the earlier work of Staudenmayer and colleagues, and centres around childhood trauma and abuse. This hypothesis met with protest and criticism by MCS patients and environmental physicians alike, and we take up the subject in detail in our Part 7.

However, while leaving aside this highly controversial claim at least in so many words, the INSPQ report still falls squarely into the psychogenic school and seems a direct descendent of Staudenmayer et al.'s conceptual framework. According to its authors,

a) "MCS is a chronic disorder characterized by multiple recurrent non-specific symptoms triggered or exacerbated by exposure to odours present in the environment at low concentrations – concentrations tolerated by most people. People who are most severely affected suffer from a chronic impairment that prevents them from functioning normally in their social and professional lives." (Key Messages, page 1).

b) The previously mysterious ("idiopathic") mechanism of MCS, was, as Staudenmayer and others claimed, the missing "neurobiologically plausible mechanism". Now this has been identified by the INSPQ authors as "chronic anxiety [whose] main feature is the *anticipation of danger*." (Summary, Results, p. 3) Chronic anxiety, triggered by "odours," sets off a biological cascade responsible for MCS symptoms, involving

> a disruption of the hypothalamic-pituitary-adrenal axis, an increase in inflammatory cytokines, a disruption in oxidative homeostasis, a chronic decrease in neuromodulator levels (serotonin, dopamine, norepinephrine). In addition, using brain imaging, alterations in brain function and structure were observed that affect the limbic system circuits (emotions, memory, learning) and the prefrontal cerebral cortex (attention, reasoning, strategic thinking, judgment). (Summary, Results, p. 3)

c) On this basis, as noted above, the report "rebut[s] the hypothesis that there is a relationship between MCS and the toxicity of chemicals present at normal concentrations." [8] (Key Messages, p. 2)

In this explanation chemicals do not enter the brain and affect the limbic system – the system seen as responsible for the biological cascade – in ways capable of causing these effects, a point we take up in detail below at a number of points. Crucially, the INSPQ authors arrived at a major conclusion.

> [C]onsidering the mechanisms explained in the preceding chapters and all the results presented … it must be concluded that these mechanisms support a biopsychosocial model for multiple chemical sensitivity syndrome and not a toxicogenic model related to the toxicity of chemicals (p. 646, translated, emphasis added).[9]

To be clear: the psychogenesis account *counter poses* biopsychosocial factors to toxicological factors, and rejects toxicological factors as important agents in the MCS complex.

Hence, for the INSPQ authors, with anxiety in the lead, the syndrome is psychological but no longer mysterious or idiopathic, and therefore requires a new name. The authors propose, as we have previously noted, "central sensitivity to multiple chemical substances."(p. 811, translated). From the patient perspective, IEI has never fit their experience, and now "central sensitivity to multiple chemical substances" will likely suffer the same fate.

### 2.2.2 The biophysical-toxicogenic school of thought and the INSPQ report

The second school of thought – the biophysical-toxicogenic school – considers MCS to be a biophysical condition conceived as a syndrome and a complex, multi-system biophysical disease process linked to toxicological impacts of synthetic or biochemical origin (xenobiotics) in onset and in chronicity. We place ourselves squarely within this school.

In recent years, there has been an international trend to call MCS simply "CI" or "CS" for "chemical intolerance" or "chemical sensitivity." Nevertheless, it is worth identifying a number of the names that have evolved within this school, each embodying an analytical preference about mechanisms, symptoms, phases, and so forth. Canada's federal government and Ontario have used the terms "ES" (environmental sensitivities) or "ES/MCS." However, it has also been variously called, in addition to ES and MCS, toxic encephalopathy, environmental illness,

[8] Normal, low, usual, are all terms used at various times in the INSPQ report to describe the concentrations of chemicals present in the environment.

[9] Donc, considérant les mécanismes expliqués dans les chapitres précédents et l'ensemble des résultats présentés dans le présent chapitre, il faut conclure que ces mécanismes soutiennent un modèle biopsychosocial pour le syndrome de sensibilité chimique multiple et non un modèle toxicogénique en lien avec la toxicité des produits chimiques. p. 646.

twentieth century disease, and, since the 1990s by some important researchers whose work has been adopted more broadly, toxicant-induced loss of tolerance, or TILT.

The term "TILT" was originated by Claudia Miller, MD, of the University of Texas Health Sciences Center at San Antonio in the mid 1990s, and more recently, it has been taken up by a new program there: the Hoffman TILT Program. Miller is one of the most important researchers in environmental health and chemical intolerance, and we call on her work and that of her team in many places in this commentary. She works with colleagues at the University of Texas Health Sciences Center at San Antonio, the Massachusetts Institute of Technology, University of California, Irvine and AIM Center for Personalized Medicine. These include environmental health scientist Shahir Masri, biostatistician/epidemiologist Raymond F. Palmer, esteemed professor of technology and policy Nicholas Ashford and two well-known mast cell researchers and clinicians Tania Dempsey and Lawrence B. Afrin. Miller and colleagues consider TILT to be a disease category rather than a syndrome, condition, or disorder.

Under the name EI, for environmental illness, William J. Rae, MD, originally a thoracic surgeon (more than 150 research papers related to the topics of thoracic and cardiovascular surgery) and the founder and 40-year director of the leading MCS clinic in North America, the Environmental Health Centre-Dallas, has a body of work spanning decades, many articles, seven medical textbooks and a book on the effects of the home environment on health.

Japan has been the locus for a lot of research on MCS, most of it in the biophysical-toxicogenic stream. Italy has become a site for MCS research in etiology, mechanisms, clinical guidelines and genetics, with recent articles by teams of mostly physicians that will be cited in this commentary, including in Parts 2.2 and 2.3, below. An important team of French-Belgian researchers located in Paris and Brussels, led by oncologist Dominique Belpomme (Belpomme, 2015) also consider MCS and EHS (electrohypersensitivity), very similar in their neurological manifestations, to be neurodegenerative diseases in their latter (severe) stages.

In Canada, Stephen Genuis, MD, of the University of Alberta at Edmonton medical school, has presented multiple articles on the pathophysiology of MCS and the errors of the pathopsychological view (e.g., Genuis, 2013) focussing on publications targeted to Canadian physicians. Clinician John Molot and colleagues (Molot et al., 2021) have recently published an article documenting the similarities between neurodegenerative disease and MCS. We will be referring to this article and to Dr. Molot's other work below.

For now, we note that the terms ES, MCS, TILT, EI, CI and CS have all been used more or less interchangeably, and will appear as such when quoted in this document. For our commentary will use the simple term "MCS" because of its familiarity and closeness to historical usage in Canada and the United States. In Part 3.3, we have cited a modest patient literature that affirms the second school of thought, and will refer throughout this document to the major qualitative study we conducted between 2011-2013 (Burstyn &MEAO, 2013). All these sources express that for patients, the right approach lies within the biophysical-toxicogenic school.

This school of thought has presented, year by year and according to the fresh evidence provided by ever more sophisticated diagnostic methods, increasingly clear propositions for causation and ongoing mechanisms within a very complex disease with many contributing factors and, usually, co-morbidities.

As well, this school holds the potential for the worthy project, in the near future, of correctly bridging the psychogenesis/toxicogenisis gap. Historically, it has always held that while a toxicological element is needed for MCS, it is the "total load" of stressors – physical, emotional, socio-economic and toxicological – for each individual that informs both onset and chronicity. As a result, the approach of this school is in complete harmony with recent, very compelling scholarship that is demonstrating, especially though not only in the field of maternal and child health, the powerful *synergies* between toxic chemical exposures (e.g. pesticides, petrochemical emissions) individual level stressors (e.g. family, spousal relationships) and socio-economic stressors (e.g. poverty, job insecurity, poor nutrition, unhealthy neighbourhoods, expressions of racism and so forth.)

This new field is articulated succinctly and referenced extensively in the work of Emily Barrett, Department of Biostatistics and Epidemiology, Environmental and Occupational Health Sciences Institute at Rutgers School of Public Health, and Amy Padula, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco, San Francisco, CA. In their 2019 article, on which we will call several times in the coming pages, they provide many examples where such synergies have been studied. They write

> Not surprisingly, exposures to synthetic chemicals and non-chemical stressors often go hand in hand, with exposure to non-chemical stressors often driving increased chemical exposure (4). For example, a 2018 review of the literature on endocrine disrupting chemicals (EDC) and metabolic disease observed that exposures to synthetic chemicals including polychlorinated biphenyls, phenols, and phthalates were consistently higher among low income individuals and racial minorities compared to higher income, white participants (22). As a result, the associated economic burden of EDC-related disease is estimated to be disproportionately high among African-American and Mexican-Americans, and plausibly among other disadvantaged populations as well (23). … One study examined residential proximity to unconventional gas development as a source of exposure to both chemical (e.g., air pollution and water contamination) and non-chemical stressors (e.g., noise, light pollution, noxious odors and psychosocial stressors), observing associations with preterm birth and fetal death (24).… Similarly, individuals with low food security are more likely to consume canned and processed foods, resulting in higher levels of Bisphenol A (BPA) and phthalate metabolites (25, 26). (Barrett & Padula, 2019, Exposure assessment and co-occurrence, Joint exposure to synthetic chemical and non-chemical stressors, paragraph 1)

Analyzing multiple studies that used objective measures such as blood and urine markers, stress inventories, measures of IQ and reproductive health in children and other indicators, they show both the extensive, specific, adverse effects of chemical exposures and what can now be seen as

an *amplification* of those effects by individual-level and social stressors. Here is how the synergistic relationship between chemical and non-chemical stressors is being conceived.

> Mechanistically, chemical and non-chemical stressors may act upon the same biological systems (Figure 1). For example, maternal exposures to psychosocial stress and endocrine disrupting chemicals (such as PBDEs and PFASs) have each individually been linked to altered cytokine profiles (8, 30, 31). Similarly, phthalates and psychosocial stressors may both act upon oxidative stress pathways (32, 33). Even when mechanisms are unknown or disparate, chemical and non-chemical stressors may influence the same outcomes. For example, prenatal exposures to psychosocial stress and pesticides have each individually been linked to adverse neurodevelopmental outcomes, though the hypothesized mechanisms may differ (34, 35). For these reasons, it is increasingly clear that chemical and non-chemical stressors need to be considered together. … exposures to stressors may potentiate or exacerbate the impact of chemical exposures on health outcomes. (Barrett & Padula, 2019, Exposure assessment and co-occurrence, Joint exposure to synthetic chemical and non-chemical stressors, paragraph 3; emphasis added)

These findings and premises are entirely harmonious with those of the biophysical-toxicogenic school, which has always emphasized the total effects of multiple causes while maintaining the necessity of understanding the distinct roles of toxicants. But they are entirely at odds with one of the most central conclusions of the INSPQ report, cited above, that counter poses toxicological to psychosocial factors which it affirms as causative and excludes toxicology completely, resulting in simplistic, reductionist and erroneous conclusions.

## 2.3 OUR WORKING DESCRIPTION OF MCS

The understanding of MCS is in evolution, and changing names reflect this. This is a good reason for us, as an ad hoc group of advocates, not to formally adopt one definition above the others. However, in order to stake out the key issues and communicate the patient perspective in this document, we need a working description that conveys our understanding and experience of MCS. Among the different but fraternal definitions, both consensus and individual, in the biophysical-toxicogenic school of thought, some are decades old, others more recent and elaborative of earlier efforts. While we are not advancing a definition as such, our description seeks to include elements from several of these fraternal definitions that resonate with our patient perspective and embody criteria evolved since the last consensus definition for MCS was developed (Lacour et al., 2005). So, in addition to resting on older iterations, and to adding important elements from the patient perspective, *our description also draws on, and extensively borrows some wording from two new efforts by important teams of researchers in Italy and in the United States, recorded in Damiani et al. (2021) and Masri et al. (2021).* We have opted for comprehensiveness rather than brevity, for MCS is a very complex entity and requires complexity in its description. Here is ours:

MCS is a multi-system, recurrent, environmental disorder that flares in response to different exposures (i.e., pesticides, solvents, toxic metals, fragrances, cleaning products, cigarette smoke, certain foods, drugs/medicine, mold and other vehicles of exposure) at concentrations that do not provoke such symptoms in other people. MCS is characterized by neurological, immunological, cutaneous, allergic, gastrointestinal, rheumatological, cardiological and endocrinological signs and symptoms. MCS is a widespread condition and the majority of people who live with it (approximately 70 percent) are women, though a significant minority are men.

Onset, which may happen slowly over time or rapidly, begins on exposure to a particular chemical or mixture of chemicals (including bio and well as synthetic toxicants) that commonly affect the immune system and/or nervous system, such that MCS appears to be primarily a neuroimmune disease process. This chemical exposure interacts with one (or both) of these systems in a way that renders individuals intolerant to subsequent exposures, which are then experienced as triggering or flaring events. After the initial onset, some new triggering events may result in “crashes” - additional worsening to qualitatively greater degrees of severity that are not easily reversible without intervention.

Affected individuals no longer tolerate everyday exposures to a wide range of structurally diverse substances at levels that never bothered them previously, including ingestants, inhalants, implants, and skin contactants. Many previously tolerated foods and drugs may trigger symptoms. At times, onset is not observed or reported immediately, and the phenomenon of "masking" can obscure MCS and delay diagnosis.

MCS ranges in severity. Early, milder stages are often erroneously perceived to be allergies, require adjustments and avoidance, but go undiagnosed. Moderate to severe MCS involves greater intensity and duration of symptoms. Severe MCS brings intense reactions, great physical suffering and can be life-threatening for some people when exposed to some chemicals. Major efforts to avoid triggers are required, making life in the ambient air of chemically-laden everyday environments unsustainable. This is how MCS disables those affected. When co-morbidities are present – often the case – overall health is further compromised, and additional barriers are encountered.

MCS is usually responsive to appropriate measures and treatments, and becomes worse without these.

There are several points that we wish to introduce at this stage, to be taken up at greater length below.

First, it is important, from our perspective, to clearly identify onset, sometimes called “initiation” or “sensitization,” because one of the INSPQ report’s greatest omissions is a discussion of this phenomenon. The patient experience indicates the importance of onset as a distinct experience,

and critical to the chronicity that follows it (Burstyn & MEAO, 2013). Indeed, the chronic nature of MCS cannot be understood without understanding what takes place in onset.

Second, MCS reactions are not only to inhaled odours but can involve several other forms of encounter of chemicals, especially ingestion and skin contact. This is critically important because the INSPQ report, like many other accounts within the psychogenic school, discuss MCS as a reaction to odours, not chemicals, and odours are not involved in skin contact or ingestion. This is taken up in detail in Part 4.4.

Third, there has been a long search for the one biological mechanism or marker that explains MCS. As noted, the INSPQ report has declared that it has found that mechanism and it is anxiety, triggering the amygdala and causing it to create the described cascade of biological consequences that produce MCS symptoms. But this reductionist conclusion is erroneous, and it may well be that MCS will never be reducible to only one mechanism, even one that is more accurate in terms of pinpointing the action of neurological and immune cells than the INSPQ'S proposed mechanism. There may be cross-component, cross-system, cross-cell interactions. There may be a number of factors associated with specific co-morbidities (see Part 5) in given individuals (see "biological individuality," Part 2.7) that may always have to be taken into consideration person by person as they affect sensitization mechanisms in different ways, creating a number of possible roads to sensitization. As Miller et al. (2021) explain while outlining some of the challenges with chemical sensitivity,

> many patients attribute onset of their illness and intolerances to a well-defined exposure event [7, 8]…. Different family members or co-workers who become ill frequently exhibit different manifestations, confounding physicians and investigators [6]. Individuals affected by a *particular* infectious agent or toxicant often share recognizable constellations of symptoms. This is not the case for CI [chemically intolerant] patients, which has hampered efforts to establish a consensus case definition for CI. It also suggests a mechanism for CI which is distinct from other infectious/toxicant exposures. . . .
>
> The origins of these intolerances variously have been attributed to classical toxicity, allergy, and psychological factors [10,11,12]. Up to now, an understandable biological mechanism for them has remained elusive. (Introduction, Chemical intolerance)

At this juncture, we want to highlight that, from the biophysical-toxicogenic school of thought, there are several other contenders (not necessarily competing) for the role of such a mechanism or mechanisms that the INSPQ report either did not include or did not substantively engage with. These include TRP (transient receptor potential) channels and the role of mast cell activation, which we will take up below and which speak much better to the MCS experience. As well, there is an important theory about toxics and underlying chronic disease that is relevant to this discussion, and promising research in genetics, epigenetics and metabolomics. Also, there is much to be learned about mechanisms by identifying subgroupings, both within MCS, and other

types of sensitivity diseases. We explain these in greater detail in Part 2.5.5. But first a few more words on onset in MCS.

## 2.4 CHEMICALLY-TRIGGERED ONSET IS ABSENT FROM THE INSPQ REPORT

Based on our experiences, on what we have heard from others, and in concert with many researchers and clinicians, we believe that MCS cannot be understood without a clear conceptualization of both onset and resulting chronicity, as what happens in the former affects what happens in the latter and each stage has its own features. Additionally, from a clinical standpoint, the importance of being able to identify and either prevent or intervene soon after onset to repair the damage done cannot be overstated, so understanding it is critical.

As noted, the INSPQ report simply does not address onset, where chemical exposure has its first dramatic effects and where chemical concentrations are often higher for an individual than their usual "normal" or, indeed, what would be normal for any human being – consider the chemical exposures in Gulf War 1, (Masri et al., 2021) which resulted in the onset of chemical intolerance in tens if not hundreds of thousands of healthy young people. But exposures to chemicals at "normal" but "weak" or "healthy" concentrations is also a feature of many low-income neighbourhoods, especially though close to petrochemical production, manufacturing and high traffic zones. We will also return to the high concentrations of chemicals in many unregulated workplaces for women (Part 6).

Not addressing the conditions of onset makes it much easier for the report to dismiss the role of chemicals in MCS, likewise indeed to reduce chemicals to "odours" that are inhaled rather than to chemicals, with or without odours, that are encountered and experienced with or without respiration. This is a huge gap in terms of the report's explanatory power and validity, apparently justified by the *false* claim that most individuals cannot recall if chemicals were involved in initiation. We address these problems further in Part 4 when we look at the impacts of chemicals on those who develop MCS and on population health more broadly

For now, let us note that Masri et al.'s (2021) TILT paper shows that chemicals, and even very specific chemicals, are indeed the agents of onset for those who are susceptible. Here, Masri and colleagues reported on an ambitious and wide-ranging study of eight chemically exposed groups across time, types of exposure, and geographic dispersion. Many more studies of the scope and detail of the longitudinal and cohort study reported, a study that was undoubtedly costly to research and record, are needed in MCS literature, but lack of funding make them very difficult to conduct.

In this study, Masri and colleagues were able to review the exposure and health experiences of eight groups of people: workers at the US Environmental Protection Agency (EPA) headquarters during renovations, Gulf War veterans, casino workers exposed to pesticides, a group of workers exposed to aircraft oil fumes, people directly involved in the World Trade Center tragedy, people with surgical implants, people who live in moldy environments, and tunnel workers exposed to solvents.

Patterns common to these events emerged, including that TILT/(MCS) does involve onset clearly provoked by specific chemical exposure, which then leads to chronicity/triggering/flaring that continues after the initiation event or process, brief or prolonged, is over. The authors found,

> "For the cases, (*n*=4) in which both the number of people exposed and the number who developed TILT-like symptoms was reported, the proportion of those who developed TILT-like symptoms ranged from 0.4% (EPA Building Renovation) to 44% (moldy home case), with an average of 25%. This average decreased to 20% when excluding the moldy home case where the sample size was low and individuals genetically similar (same family) " (Comparing case studies, paragraph 2)

Chemical intolerance, in these instances in any event, was not idiopathic; rather, its causes were clearly identifiable. Specifying the chemical culprits and developing a those-most-likely-to-harm list is another invaluable contribution of this study.

> Mixed volatile and semi-volatile organic compounds (VOCs and SVOCs), followed by pesticides and combustion products were most prevalent across TILT/[MCS] initiation events. As a broader category, synthetic organic chemicals and their combustion products were the primary exposures associated with chemical intolerance. Such chemicals included pesticides, peroxides, nerve agents, anti-nerve agent drugs, lubricants and additives, xylene, benzene, and acetone. (Abstract, Results)

Even more precisely,

> The mixed VOC/SVOC group of chemicals included such VOCs as benzene, acetone, toluene, and xylene as well as SVOCs including BFRs, PCBs, dioxin, phthalates, and triphenyl and tricresyl phosphates. Among this group of compounds, xylene was identified most frequently across exposure events, followed by both benzene and acetone. Pesticides included carbamates, organophasphates, and organochlorides ...(Results, Comparing case studies, paragraphs 4, 5)

Let us now look a little more closely at some important research, neglected by the INSPQ report, that does implicate toxicogenic factors in MCS, at both stages, and whose neglect or distortion seriously undermine the report's validity.

## 2.5 NEGLECTED OR OMITTED TOXICOLOGICALLY-INFORMED RESEARCH

### 2.5.1 Introducing the omitted or neglected literature

One challenge that readers of the INSPQ report face in grappling with its conclusions is a lack of clarity regarding the last date of the literature reviewed and its comprehensiveness across the board. We understand that the literature was first assembled in 2013, and different chapters seem to have different final review dates. In the report's methodology, the authors state that

they conducted their review on a thematic basis until July 2019. At the same time the authors also state that they conducted their review for the epidemiology chapter until December 2016. In the psychogenesis hypothesis chapter, they describe an entirely separate and focused review process undertaken in January 2018. In the chronic anxiety chapter, they yet again used a different methodology, pursuing a deep dive into post-1960 scientific literature on animal or human research on fear and pathological anxiety. These differences in literature collection and review make it very difficult for readers to achieve clarity on what has been included, engaged with or omitted, overall.

Regardless, it is obvious that new work released in 2021 and into 2022 was not included. Some of this work is very important (e.g., Damiani et al., 2021; Molot et al., 2021; Masri et al., 2021; Miller et al., 2021; Perales et al., 2022), and we draw on it in this document. It appears, though, that other literature from the previous two or three years might also have gone unreviewed (some omitted, some described but unengaged), making the currency of the INSPQ report problematic. While final review dates are always necessary, it is also true that the validity of any study must always be measured against new findings to see if it holds up. The INSPQ conclusions must be measured against the latest work as well as long-standing supporting research that it did not engage to begin with. If the conclusions of such measurement demonstrate flaws and errors, then the report's findings must be evaluated accordingly.

In Part 4, we extend our challenge to the INSPQ's rebuttal of "the hypothesis that there is no relationship between MCS and the toxicity of chemicals present at normal concentrations" (Key Messages, p 2) in several ways. Here we want to establish the basis for that challenge, particularly by reporting on several important hypotheses from research in environmental health and medical studies on biological mechanisms that do allow for multi-system reactivity due to brain absorption and reaction to trace amounts of many different chemicals, including at what the INSPQ authors might consider as "normal," and therefore "harmless" concentrations.

### 2.5.2 The cell danger response theory

One compelling theory about chronic illness, especially chronic, complex, environmentally linked illnesses, is known as the "cell danger response." It is a much more plausible "unifying theory" than anxiety for the list of conditions the INSPQ report named (chronic fatigue syndrome, post-traumatic stress disorder, electromagnetic hypersensitivity, fibromyalgia, chronic anxiety, depression, somatization disorder, phobias, and panic disorder) plus a number of other better understood diseases (that the theory also encompasses). The theory was elaborated by distinguished physician, autism researcher and University of California San Diego medical school professor Robert Naviaux, MD, PhD. Cell danger response theory (Naviaux 2018) suggests that ubiquitous toxic molecules at the cellular level disrupt the most basic functions of life and good health, including neurological health.

> The cell danger response (CDR) is a universal response to environmental threat or injury. Once triggered, healing cannot be completed until the choreographed stages of the CDR are returned to an updated state of readiness. Although the CDR is a cellular response, it

> has the power to change human thought and behavior, child development, physical fitness and resilience, fertility, and the susceptibility of entire populations to disease. Mitochondria regulate the CDR by monitoring and responding to the physical, chemical, and microbial conditions within and around the cell. In this way, mitochondria connect cellular health to environmental health. Over 7,000 chemicals are now made or imported to the US for industrial, agricultural, and personal care use in amounts ranging from 25,000 to over 1 million pounds each year, and plastic waste now exceeds 83 billion pounds/year. This chemical load creates a rising tide of manmade pollutants in the oceans, air, water, and food chain.
>
> Fewer than 5% of these chemicals have been tested for developmental toxicity. In the 1980s, 5–10% of children lived with a chronic illness. As of 2018, 40% of children, 50% of teens, 60% of adults under age 65, and 90% of adults over 65 live with a chronic illness. Several studies now report the presence of dozens to hundreds of manmade chemicals and pollutants in placenta, umbilical cord blood, and newborn blood spots.
>
> New methods in metabolomics and exposomics allow scientists to measure thousands of chemicals in blood, air, water, soil, and the food chain. Systematic measurements of environmental chemicals can now be correlated with annual and regional patterns of childhood illness. These data can be used to prepare a prioritized list of molecules for congressional action, ranked according to their impact on human health. (Abstract)

Naviaux has also concluded—as have many others—that a significant portion of the human population (around 25 percent) is even more poorly genetically-equipped than the rest to manage today's cellular toxic burdens and is particularly vulnerable to emerging disorders and diseases. For Naviaux, the sharp and expansive increase in chronic illness—including neurological illness and disorders comprising cognitive and affective health—is first and foremost a problem of massive new levels of toxic chemicals in the human environment. These chemicals impact physiology, including the central nervous system and are not a problem of psychology in the first instance, but of toxicology. And as far as MCS is concerned, evidence and experience align strongly with the clinical conviction that toxic injury and toxic body burden play a major role in chemical intolerance. There is also evidence that genetic factors related to detoxification often play a part.

### 2.5.3 TRPV1 and TRPA1 receptors: the neurological research neglected by the INSPQ report

The INSPQ report mentions and even describes some very important research on transient receptor potential (TRP) channels, in particular the TRPV1 receptor although it also mentions the TRPA1 receptor, but for some reason, does not take this further. Studies that have investigated these receptors provide evidence that volatile and semi-volatile chemicals, even at extremely low concentrations, do enter the brain via these channels, since this is one of the places where these receptors are found. They are also found in many other parts of the body, a feature well described in the INSPQ report Part 8.5.2 on vanilloid receptors:

> Topical application of capsaicin or chemical irritants such as xylene, mustard oil, or formaldehyde has been shown to stimulate C-fibers by binding to nociceptive receptors, identified today as being vanilloid receptors (named TRPV1 or VR1), and to induce the release of SP contained in these C fibers, a role of danger sensor for our tissues. Vanilloid receptors are present on the surface of peripheral sensory nerves (e.g. skin, lips, tongue, respiratory tract, digestive tract, bladder), also on the C fibers of the trigeminal nerve, as well as in the brain and spinal cord (Gavva et al., 2008a, 2008b). They are identified as a molecular target in the treatment of pain associated with inflammatory diseases and cancer. These receptors also play a pivotal role in the molecular regulation of body temperature in humans (Gavva et al., 2008a, 2008b) and the respiratory response to irritants (Geppetti et al., 2006; Adcock, 2008; Takemura et al., 2008). Indeed, in the respiratory tract, TRPV1 agonists cause coughing, bronchoconstriction, microvascular leakage (plasma extravasation), hyperreactivity and hypersecretion of the mucous membranes. Patients with asthma and chronic obstructive pulmonary disease are more susceptible to cough induction by vanilloid receptor agonists. Their activation may contribute to respiratory symptoms caused by exposure to acidic environments present in the airways during asthma exacerbation, gastroesophageal reflux-induced asthma, or in other conditions (Geppetti et al., 2006; Takemura et al., 2008; Adcock, 2008).[10] (p. 354; translated).

It is difficult to understand why, after having described these receptors and their functions, capacities, and multiple locations, the INSPQ report does not engage with the MCS literature that posits these as mechanisms of MCS. Certainly, the multiple locations of these receptors affirms our rejection of the definition of MCS as a disorder simply of odour, rather than one with many other potentially reactive sites that require no respiration and no odour.

In his response to the INSPQ report, environmental physician, associated with the University of Ottawa, John Molot (2021) writes that

[10] French original: "Récepteurs vanilloïdes -- Il a été démontré qu'une application locale de la capsaïcine ou d'irritants chimiques tels que le xylène, l'huile de moutarde ou le formaldéhyde avait la propriété de stimuler les fibres C en se liant à des récepteurs nociceptifs, identifiés aujourd'hui comme étant des récepteurs vanilloïdes (nommés TRPV1 ou VR1), et d'induire la libération de SP contenue dans ces fibres C. Ils sont considérés comme des transducteurs des stimuli thermiques et irritants (Gavva *et al.*, 2008a, 2008b) et jouent donc un rôle de capteur de danger pour nos tissus. Les récepteurs vanilloïdes sont présents à la surface des nerfs sensitifs périphériques (peau, lèvres, langue, voies respiratoires, tube digestif, vessie par exemple), également sur les fibres C du nerf trijumeau, ainsi que dans le cerveau et la moelle épinière (Gavva *et al.*, 2008a, 2008b). Ils sont identifiés comme étant une cible moléculaire dans le traitement de la douleur associée à des maladies inflammatoires et le cancer. Ces récepteurs jouent également un rôle pivot dans la régulation moléculaire de la température corporelle chez l'humain (Gavva *et al.*, 2008a, 2008b) et la réponse respiratoire aux substances irritantes (Geppetti *et al.*, 2006; Adcock, 2008; Takemura *et al.*, 2008). En effet, dans les voies respiratoires, les agonistes du TRPV1 provoquent de la toux, une bronchoconstriction, des fuites microvasculaires (extravasation plasmatique), de l'hyperréactivité et de l'hypersécrétion des muqueuses. Les patients atteints d'asthme et de bronchopneumopathie chronique obstructive sont plus sensibles à l'induction de toux par des agonistes des récepteurs vanilloïdes. Leur activation peut contribuer aux symptômes respiratoires causés par l'exposition aux milieux acides présents dans les voies aériennes pendant l'exacerbation de l'asthme, l'asthme induit par le reflux gastro-oesophagien ou dans d'autres conditions (Geppetti *et al.*, 2006; Takemura *et al.*, 2008; Adcock, 2008).

> [t]he position of the INSPQ that VOCs do not enter the brain is wrong. The absence of any significant literature review of the TRPV1 and TRPA1 receptors well-known to be stimulated and potentially sensitized by chemicals has contributed to biased conclusions. (p. 8).

In "Neurological susceptibility to environmental exposures: pathophysiological mechanisms in neurodegeneration and multiple chemical sensitivity," (2021) Molot along with co-authors Margaret Sears, Lynn Marshall and Riina Bray offer a substantive discussion of the role of these receptors. It is regrettable that this article, along with several others mentioned here, was not available to the INSPQ authors; however, a) literature on these receptors has been available for many years, and b) the validity of the INSPQ conclusion must be measured against what we know today, not what we knew some years ago.

Very significantly, in contrast to the INSPQ findings, and using weight of evidence for consistency and utility, the Alberta Health report found that "two areas of research emerged as having the most support: 1. Olfactory processing dysfunction and 2. Neurologic sensitization and neurogenic inflammation" (Executive Summary, p. viii). The report posited a relationship between these phenomena:

> These two areas were found to overlap with some of the most commonly reported symptoms in the literature in patients with diagnosed MCS. It is possible that the biological processes involved in MCS may involve olfactory processing, neurogenic sensitization and neurogenic inflammation, as these involve the nervous system and the reaction of the brain to stimuli (irritant and olfactory) and irritation effects on mucosal membranes of the eye and respiratory tract.

With respect to neurological sensitization and neurogenic inflammation, they further noted that,

> symptoms involving the upper and lower airways are commonly reported among MCS sufferers, and one potential biological mechanism is airway sensory hyperreactivity attributable to neurogenic inflammation. Neurogenic inflammation is not isolated to the respiratory tract, as studies investigating dermal exposures and neurogenic inflammation were also identified. (p. 44; emphasis added)

The Alberta report authors go on to provide the following "Background information for neurologic sensitization and neurogenic inflammation":

> Both the upper and lower airways contain sensory neurons from the parasympathetic and sympathetic nervous systems (CoA, 2010). In the upper airways, the olfactory and trigeminal nerves mediate the detection of chemicals (Claeson and Andersson, 2017). Many of these nerves express ion channel proteins belonging to the transient receptor potential (TRP) superfamily that can act as sensors to various stimuli, including the presence of chemicals, temperature changes, oxidation, and pH variation. When TRP channels are activated, they depolarize cells and produce an action potential and sensory

> nerve activation that can trigger several responses. In mammals, six sub-families of TRP have been identified that have a common amino acid sequence, with one group being the TRP vanilloid (TRPV) family. The TRPV1 ion channel (which is discussed in some of the studies presented within this section) is activated by high temperatures and a range of both endogenous and exogenous chemicals, including the hot-pepper derivative capsaicin. Other TRP channels that have been reported to be involved in the perception of inhaled irritants include TRPA1 and acid sensing ion channel receptor 3 (ASIC3) (Omar et al., 2017). Acrolein is a stimulant of TRPA1 in airways (Claeson and Andersson, 2017). TRPV1, TRPA1 and ASICS3 are all known to be upregulated by hypoxia and respiratory viruses (Omar et al., 2017). . .
>
> TRPV1 has been found to be expressed in certain ganglia neurons, and in neurons within the dorsal root and trigeminal ganglia, as well as in non-neuronal cells. Stimulation of the trigeminal nerve can result in the sensations of irritation and pain, while stimulation of the olfactory nerve results in the detection of odours. (p. 46; emphasis added)

Of note, we searched for but did not find mention of the above-referenced Claeson and Andersson article in the INSPQ report. Also of note, hypoxia, an up-regulator of TRPV1, TRPA1 and ASICS3, has long been identified as an important characteristic of MCS. See among others, Belpomme et al.'s 2015 paper, "Reliable disease biomarkers characterizing and identifying electrohypersensitivity and multiple chemical sensitivity as two etiopathogenic aspects of a unique pathological disorder."

For the Alberta reviewers, TRP-related factors are central to the lines of research they found most useful and consistent, but consideration of their role seems to have dropped out of the INSPQ report. It seems clear to us that much more work and research were needed before the categorical conclusions reached in the INSPQ report regarding the impact of chemicals on the brain could have been be justified.

### 2.5.4 Mast cells and mast cell activation syndrome (MCAS): an important immunological issue missing from the INSPQ report

We also want to draw your attention to another new theory of MCS mechanism, a harmonious theory to Naviaux's. Researchers at the University of Texas Health Science Center at San Antonio, along with colleagues at the Massachusetts Institute of Technology, and the AIM Center for Personalized Medicine, in their article "Mast cell activation may explain many cases of chemical intolerance," have recently advanced the theory that mast cell activation syndrome (MCAS) and mediator release may be the underlying mechanism for chemical intolerance.

In reading the quote that follows, recall that TILT and MCS are basically synonymous terms and CI stands for chemical intolerance. In the abstract to their study Miller et al. (2021) write:

> We present data suggesting that xenobiotic activation of mast cells may underlie CI/TILT[/MCS]. The strikingly similar symptom and intolerance patterns for MCAS and TILT

> suggest that xenobiotics disrupt mast cells, leading to either or both of these challenging conditions. . . . More than half (59%) of the MCAS group met criteria for CI. A logistic regression model illustrates that as the likelihood of patients having MCAS increase[s], their likelihood of having CI/TILT similarly increase[s], to a near-perfect correspondence at the high ends of the [Quick Environmental Exposure and Sensitivity Inventory] and clinical MCAS scores. Symptom and intolerance patterns were nearly identical for the CI and MCAS groups. . . . Increasing our understanding of the connection between TILT and [mast cell]s has the potential to expose a new link between environmental exposures and illness, offering new opportunities for improving individual and public health. (Abstract)

Mast cell study has only recently been taken up within MCS studies (for about 10 years), but has been a promising avenue for understanding a variety of conditions, including Gulf War Illness, breast implant illness, MCS, and possibly even long COVID (Lee, S., Dec. 2, 2021). These are all conditions we discuss in this report. At least as far as MCS and other frequent co-morbidities are concerned, the field of mast cell studies might have been in its infancy when the INSPQ authors began their literature review in 2013, but it was already a feature of consideration and treatment by environmental physicians by 2018, when Neil Nathan published his important clinical contribution, the book *Toxic: Heal Your Body from Mold Toxicity, Lyme Disease, Multiple Chemical Sensitivities and Chronic Environmental Illness*, a compendium of environmentally-linked disorders and diseases with relevant diagnostics and treatments in widespread clinical use among environmental physicians. (See Nathan's Chapter 5, pp. 99-114, for a discussion of MCAS). It is regrettable that the INSPQ investigators did not include this in their review.

Miller et al.'s 2021 article has taken the consideration of MCAS in MCS to a compelling new level. The article begins by commenting on why it has taken so long for chemical intolerance research to focus on mast cells (MCs), suggesting that a number of factors have resulted in a likely underestimation of mast cell's pivotal role in disease.

> (1) [S]ince the discovery of IgE,[11] allergy's principal focus has been on the humoral, as opposed to the cellular, immune system; (2) MCs' typically tiny numbers and their sparse distribution in most tissues have contributed to their anonymity; and (3) MCs are minimally present in the blood, and even where they are present, it has been a challenge to identify and isolate them. (Introduction, Mast cells, paragraph 1).

However, as the authors point out, the massive increases in concentrations of pollutants, especially but not only, of indoor air pollutants[12] seems to have provoked a release of mast cell inflammatory mediators in a significant number of people. The authors point out that MCs have an evolutionary path half a billion years old, but that the emergence of the chemical industry is relatively recent, and the massive influx of synthetic organic chemicals into our personal

[11] "Immunoglobulin E (IgE) are antibodies produced by the immune system. If you have an allergy, your immune system overreacts to an allergen by producing antibodies called Immunoglobulin E (IgE). These antibodies travel to cells that release chemicals, causing an allergic reaction." American Academy of Asthma, Allergy and Immunology. https://www.aaaai.org/Tools-for-the-Public/Allergy,-Asthma-Immunology-Glossary/Immunoglobulin-E-(IgE)-Defined

[12] A phenomenon that shows why the idea of "normal" concentrations is misguided.

environments really began in earnest only in the post-World War II era, accelerating since that war. They note:

> This has resulted in the accumulation of every sort of indoor air pollutant to levels higher than ever before (e.g., volatile, and semi-volatile organic chemicals outgassing from new construction and remodeling materials, pesticides, mold, disinfectants, and cleaning agents) [6,7]. Only now are we learning that our contemporary exposures may be provoking [mast cells] to release their inflammatory mediators, resulting in a condition often referred to as "mast cell activation syndrome" (MCAS) [29]. (Introduction, Mast cells, paragraph 6).

These releases of inflammatory mediators are an important part of what mast cells are meant to do under conditions of threat:

> These sentinel cells guard the perimeters of our skin and other organs, warding off invaders and protecting our internal milieu. They serve as first responders to most bodily invasions and insults. Mast cells originate in the bone marrow and migrate to the interface between our tissues and the external environment [14, 15]. They are highly evolved, critical components of the cellular immune system [15], supporting both innate and adaptive immunity. Largely lying in wait, these warriors spring into action if they perceive a major threat, releasing a vast array of mediators all at once. (Miller et al., 2021, Introduction, Mast cells, paragraph 2).

The authors point out that mast cells have long been known for their ability to cause anaphylaxis in response to "bee stings, peanuts, and other allergens in previously sensitized individuals. [Mast cells'] release of histamine into the surrounding tissues and bloodstream leads to immediately recognizable hives, hypotension, syncope, respiratory arrest, and even death [25, 26]." (Introduction, Mast cells, paragraph 4)

What is newly found is their ability to react to "low molecular weight chemicals like formaldehyde and volatile organic compounds [21, 27]." (Introduction, Mast cells, paragraph 4) This has raised them into candidate position for MCS mechanisms. Mast cells have been shown to have an "enormous repertoire of cell-surface receptors [that] can identify an extraordinary array of signals and effect precise responses [15, 17, 21]." (Introduction, Mast cells, paragraph 4) How these responses play out is truly remarkable, and relevant to MCS.

> Even while [a mast cell] is launching its preformed armaments, it signals other cells to join the battle. Meanwhile, behind the frontline, [mast cells] are reloading their weapons and stockpiling new munitions [22, 23, 25, 26]. Thus, our so-called "primitive" immune system is, in fact, quite sophisticated. It was many decades following the discovery of IgE and its relationship to anaphylaxis and classical allergies (such as pollen, animal dander, and dust mites) that we learned of [mast cells] capacity to respond to a vast range of stimuli—revealing new, alternative pathways for their activation and degranulation, even

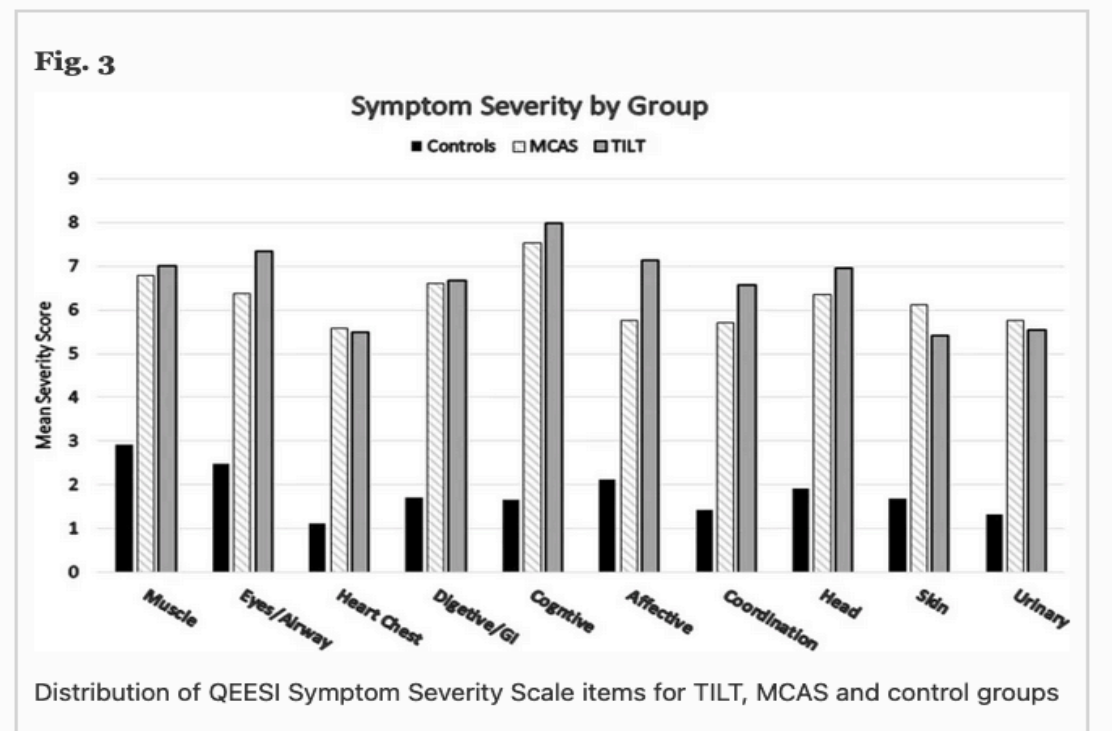
> in the absence of "classic" binding of antigen with immunoglobulins. (Introduction, Mast cells, paragraph 4)

In detailing the characteristics of mast cells, the article speaks to one of the most perplexing and challenging aspects of chemical intolerance: the rapidity –often, instantaneity – of its flares, during which some of its symptoms are provoked. This is an issue that has demanded explanation and led some "to speculate that the mechanism underlying [chemical intolerance] must be neurological." (Introduction, Mast cells, paragraph 5) It has also led others to speculate that the underlying mechanism must be psychological. However, as Miller et al. explain, mast cells "can explosively release, or gradually leak, their mediators. In fact, there is no cellular element of the immune system that reacts faster than mast cells." They explain that lymphocytes take hours to activate and neutrophils require minutes, "but [mast cells] can respond to a trigger in sub-second time [16, 17, 28]." (Introduction, Mast cells, paragraph 5) [emphasis added].

Mast cells can equally, the authors explain, be responsible for very severe and prolonged reactions, two features of MCS chronicity that have also challenged investigators. In this explanation, note the close relationship between mast cells and neurons, lending validation to the theory that MCS is a condition that is both neurological and immunological.

> As immunologic "first responders" activated [mast cells] can initiate, amplify, and prolong wide-ranging neuroimmune responses [50]. Several investigators have pointed to neurogenic inflammation as a mechanism for CI [chemical intolerance][10, 51-53]. Rather than being the mechanism for CI, neuroinflammation may be the consequence of [mast cell activation] and mediator release initiated by xenobiotic/chemical exposures. [Mast cells] affect neural function via their released mediators, which bind with specific neuronal receptors [18, 54]. Also, [mast cells] physically abut neurons in many tissues. Wherever such dyads are present, there is constant mediator "cross-talk" between the two cell types. Thus, [mast cell activation] can provoke nearby neurons, inducing their associated symptoms; similarly, neurons can provoke nearby [mast cells], inducing their associated symptoms. (MCAS, TILT, and the nervous system, paragraph 2) [emphasis added].

Miller et al. look at lines of evidence that support the MCAS/TILT [MCS] hypothesis. Much of their paper is devoted to a detailed description of the methods and findings that compared MCAS in three groups: one with healthy controls, another with diagnosed MCS, and a third with diagnosed MCAS. An example of one of these comparisons is presented below. This is symptom severity by group and body system.



Source: Miller et al., 2021, Discussion

We will have occasion to return to this paper, but to conclude this section, here are its key findings:

> Mast cell activation and mediator release appear capable of explaining the increasingly frequent observations by physicians and their patients of chronic multi-system symptoms and new-onset chemical, food and drug intolerances following exposure to a wide variety of xenobiotics.
>
> Our logistic regression model demonstrated that as the likelihood of patients having MCAS increases, their likelihood of having CI/TILT/[MCS] similarly increases, to a near-perfect correspondence at the high ends of these scales. Association is, of course, not proof of causation. Nevertheless, the strikingly similar symptom and intolerance patterns for the MCAS and TILT populations suggest that xenobiotics can disrupt mast cells, resulting in either or both of these challenging conditions. . . . (Conclusion, paragraph 1, spacing added)

### 2.5.5 Findings common to other hypersensitivity illnesses may advance MCS research and point to subgroups

Some investigators suggest pursuing yet other fruitful directions, seeking to find ways to create subgroupings of MCS patients according to their signs and symptoms, to better account for the differences in the most impactful symptoms among MCS sufferers and point to treatment paths. In this regard, the work of Laurie Dennison Busby (2017), which builds on findings from senior

clinician and researcher William J. Rae, is beginning to advance a template—at least in part—for how some of these subgroups might help move research forward. Busby writes that

> multiple chemical sensitivity and other hypersensitivity illnesses share signs and symptoms, similar triggers, a female predominance, and some test results: defects in tight junctions, increased neuropeptides after provocation, XME polymorphisms, and probably TRPV1 activation. One way to expedite MCS research in the future is to focus on other applicable research findings from well-known hypersensitivity illnesses. Based on the findings in those other illnesses, it is likely there are subgroups of patients with MCS. (2017, Conclusion)

The hypersensitivity illnesses that Busby writes about in her 2017 work include, among others, asthma, chronic urticaria (CU), chronic fatigue syndrome, migraine and rhinitis. This work suggests that there is a great deal yet to be discovered in seeking both unifying and subgrouping features and mechanisms within MCS and across to other illnesses, and that both types of research are needed. The INSPQ report has concentrated on only one area of commonality when it suggests "chronic anxiety" as the unifier for the whole range of disparate conditions it puts into its 'basket'. Busby points to many more areas of commonality with other, what she terms hypersensitivity illnesses, including TRPV1 and TRPA1 mechanisms we have just discussed. As Busby writes in her Abstract,

> Asthma was among the illnesses once thought to be psychological. In order for doctors and researchers to reach similar conclusions about multiple chemical sensitivity, they have had to overlook a great deal of valuable evidence including the signs and symptoms of patients as well as the commonalities this illness shares with other now well-recognized hypersensitivity illnesses.

While officially adopting any of the approaches discussed in this section is beyond the scope of this commentary, we still want to draw them to your attention as compelling alternatives to the INSPQ report's chronic anxiety causation thesis. At the very least, they should provide strong evidence that these discussions are still evolving and that the psychogenic view of the chronic, complex conditions espoused by the INSPQ report has no consensus or even support in the environmental health field.

## 2.6 GENETICS, EPIGENETICS AND METABOLOMICS: NEGLECTED OR UNDER-DISCUSSED YET PROMISING AVENUES OF RESEARCH

The search for reliable biological markers to identify MCS has uncovered additional avenues of research, among which genetics and metabolomics have shown great promise. Unfortunately, one of these, genetics, while dealt with in the INSPQ report (Chapter 4) was essentially discarded. These avenues await funding commensurate with their promise (and with the prevalence of MCS in general) and they await in-depth research to demonstrate their applicability and utility, either across all those with MCS or to determine important subgroupings. Incomplete as current research is, it is very suggestive, and clearly points toward

biophysiological factors in the genesis and nature of MCS, and away from psychogenesis, so the two approaches deserve mention here. The burgeoning field of epigenetics was also dealt with only in passing in the INSPQ report.

We suggest that it is very premature to dismiss the role of genetic and epigenetic factors in MCS and their relationship with environmental factors. Other complex diseases where pathogenesis is still being uncovered bear this out, with idiopathic pulmonary fibrosis being an excellent example. As the name implies, there is no clearly defined cause of idiopathic pulmonary fibrosis. However, over the past decade, scientists have begun to unravel the complexities of the disease process. While efforts are underway to discover all its pathogenesis, it is now commonly understood that both genetic and epigenetic factors (e.g., exposures) are involved. (Lai, R. May 16, 2022). Another example is sarcoidosis. When it was first identified in 1879 it was thought to be a dermatological condition, although it is now known to be a multi-system disorder often with respiratory involvement. In 1984 it was called a "continuing riddle" and that riddle is still being investigated (Young et al, 1984; Spagnolo, 2015). Again, while many questions about pathogenesis remain unanswered, genetics are now understood to play an important role, and the link to the environment and environmental agents is being explored. (Spagnolo, 2015; Moller et al. 2017).

Beginning in the early 2000s, benefiting from the work on the sequencing of the human genome from the 1980s and 1990s, researchers began to investigate whether people with MCS showed particular genetic patterns, and if so, what did the patterns reveal? Certainly, if there are meaningful patterns, this information can shed light on susceptibility, be helpful in prevention and aid in diagnosis, pointing to particular substances that are likely to present particular difficulties for those who develop MCS.

The INSPQ report did mention and discuss the pioneering work done by a group of researchers funded by the Ontario government looking at genetic pathways and detoxification (McKeown-Eyssen et al., 2004). Their work, although promising, itself called for replication and more study. Various other research teams, as the INSPQ report noted and described, have done some genetic research, but their findings were mostly dismissed by the INSPQ authors on the basis of the Bradford Hill criteria for causation. Yet these criteria (strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, analogy) have not at all been adequately tested, due, as usual, to underfunding and the small number of independent researchers. With so much to be discovered and with such great potential utility, at this stage of knowledge the role of genetics needs to be further investigated and refined, not dismissed.

Molot explained the hypothesized intriguing link between genetically-determined inferior enzyme systems for detoxification and the phenomenon of sensitization, and once again we find the TRPV1 receptors:

> Sensitization of the nervous system to chemicals and subsequent increased sensitivity has been demonstrated in animal models and there is evidence that ES/MCS patients are genetically predisposed to have inferior enzyme systems for detoxification. Because they

> are less capable of efficiently detoxifying, oxidative stress occurs, which can sensitize TRPV1 receptors. These receptors are widespread and are found in the brain, eye, bladder lining, mast cells, stomach lining, intestines, larynx and bronchial tubes. They are capsaicin (hot pepper) sensitive. Capsaicin sensitivity has been documented in ES/MCS. (Molot, 2013. p 53)

Genetic research has subsequently covered greater ground with certain sub-groups of specific genes and particular types of reactions. In a 2013 study of 324 male Japanese workers, for example (cited in the INSPQ report), chronicled in "Evaluation of genetic polymorphisms in patients with multiple chemical sensitivity," Xiaoyi Cui and a team of Japanese researchers investigated a number of genes which encode enzymes affecting the metabolic activation of a large number of xenobiotic compounds, including those for superoxide dismutase (SOD) 2. The authors found,

> Significant case-control distributed differences were observed in SOD2 polymorphisms and allele frequency distribution in high chemical sensitive subjects. We observed that high chemical sensitive individuals diagnosed by using Japanese criteria as MCS patients were more significantly associated with SOD2 polymorphisms. (Cui et al., 2013, Abstract, Results (part), Conclusions)

Of course, this is not the end of the story. Research is ongoing with several papers,

> providing evidence for a correlation between MCS and chemical defense system alterations, occurring in the presence of gene polymorphisms of detoxification phase 1 [CYPs] and phase II enzymes [GST, NAT, and UGT, amongst other), as well as antioxidant enzymes SOD2 and GPX [5, 9-17]. (Cannata et al, 2021, Discussion, paragraph 1)

Several of these papers are not included in the INSPQ analysis, including the one referenced above by Cannata and colleagues which, while calling for larger studies, found evidence supporting Cui's findings in some MCS patients.

Also, in 2021, Masri et al. wrote about further refinements in research on the genes that code for cytochrome P450 enzymes:

> [P]olymorphisms in the genes that code for various cytochrome P450 (CYP) enzymes have been shown, for instance, to produce different metabolic phenotypes and in turn play a role in such variation. For example, individuals whose CYP2D6 phenotype renders them poor metabolizers of debrisoquin are at risk of various adverse drug reactions, whereas extensive metabolizers are at greater risk of lung cancer, perhaps due to the production of carcinogenic metabolites. (TILT-related dose and exposure levels, paragraph 1)

Research for genetic markers for poor detoxification is not just confined to MCS studies. As Molot noted (2013)

> People who are genetically poor detoxifiers are also more susceptible to the cardiovascular and respiratory effects of air pollution.[136, 137] In particular, having such an abnormality has been shown to have an adverse impact on the effects of pollution exposure by modifying heart rate variability,[138, 139] lengthening of the QT interval on electrocardiograms,[140] contributing to the risk of endothelial inflammation caused by traffic particles,[141] and increasing homocysteine levels,[142] all of which are risk factors for heart disease. Having an abnormal genotype for detoxification can adversely affect lung function, including increasing the risk of ozone-induced asthma[143, 144, 145] and wheezing.[146] (Molot, 2013, p. 20)

In another example, which also demonstrates the importance of what can be found when research takes place, we want to highlight a recent 2021 study from investigators in Finland of reactions to damp and moldy buildings among subjects identified with IEI, idiopathic environmental intolerance, and those with asthma. This study revealed clear, consistent biophysical characteristics among the IEI subjects, and not among controls.

> We found a distinct molecular pathological profile in nasal and blood immune cells of IEI subjects, including several differentially expressed genes that were also identified in AAD [dampness-and-mold-related asthma] samples, suggesting IEI-type mechanisms." (Suojalehto et al., 2021, Abstract).

Not only does this study point to genetic linkages, but it strongly suggests that IEI (MCS), at least in a subset of individuals, is less "idiopathic" than this terminology would suggest.

Epigenetics has only recently begun to be explored for its connection to environmental chemicals, including heavy metals, and mechanisms of action are still not completely understood (Baccarelli & Bollati, 2009). What is known is that epigenetics is involved in adverse health effects of pollutants, diesel exhaust, for instance and its impacts should be considered when looking at interactions between environmental exposures and biological systems (Jiang et al.'s 2014; Pinel et al., 2018).

An even more recent arrival on the biomarker scene is a new field called "metabolomics." In their 2016 article, "Application of Metabolomics to Multiple Chemical Sensitivity Research" T. Katoh and a team of Japanese scientists reported their findings in a small but suggestive study (available only in Japanese, alas.) The abstract of their paper, in English, explains:

> Metabolomics comprises the methods and techniques that are used to determine the small-level molecules in biofluids and tissues. The metabolomic profile-the metabolome-has multiple applications in many biological sciences, including the development of new diagnostic tools for medicine.
>
> We performed metabolomics to detect the difference between 9 patients with MCS and 9 controls. We identified 183 substances whose levels were beyond the normal detection limit. The most prominent differences included significant increases in the levels of both

> hexanoic acid and pelargonic acid, and also a significant decrease in the level of acetylcarnitine in patients with MCS. In conclusion, using metabolomics analysis, we uncovered a hitherto unrecognized alteration in the levels of metabolites in MCS. These changes may have important biological implications and may have a significant potential for use as biomarkers.

Metabolomics is being researched with respect to a number of chronic, complex conditions, including ME/CFS ("chronic fatigue syndrome") and FM, and preliminary results have been promising. In the search for disease biomarkers – a virtual holy grail to some in medicine – this field has immense promise. What it does not have, like the work in MCS genetics and epigenetics, is commensurate funding to take the promising preliminary work and test it on the scale all three conditions need and deserve.

## 2.7 BIOLOGICAL INDIVIDUALITY AND BODY BURDEN OF TOXIC CHEMICALS

Because we do not keep track of the chemicals that we encounter either in our daily lives or, for the most part, in our work and institutional lives, physicians, epidemiologists, and biostatisticians have discovered that critical information is very difficult to obtain in environmental and chemical exposure health studies, and that the original situations are virtually impossible to duplicate under experimental conditions. Exposure histories are marked by individual, occupational, and geographical factors, including the ways in which these involve multiple chemicals at multiple concentrations at multiple times. Because all these factors intersect with age, sex, socio-economic status, health status, and genetics, the usual blinded study (single or double) methods cannot be applied with any accuracy. Other methods must be developed and relied on, such as taking large numbers of histories, tracking disease clusters, and tracking clinical populations and their outcomes over long periods. The Masri et al. (2021) study is so important because it provides us with a major effort to track these complex factors in eight important and diverse groups.

As we have seen (in our Part 2.4) the Masri et al. (2021) study documented macro (group) exposures in eight situations (e.g., employees in the EPA headquarters building exposed to renovations, a group of tunnel workers exposed to solvents, casino workers exposed to pesticides, women exposed to silicone breast implants) and drew important lessons from the patterns they found. At the level of individuals, whether a part of a group or alone, there is a principle that must also be honoured in MCS investigation – that of biological individuality. This is missing from the INSPQ analysis and is an additional methodological deficiency in the report.

The following description from 2012 of onset of severe MCS symptoms in an occupational setting in an early-middle aged woman with the initials A. R. illustrates the complexities involved in the impacts of multiple chemicals at the micro (individual) level. Note that the chemicals that Masri et al. reported most likely to initiate MCS were present in her situation.

> I worked in a building for four years in a loft office over a chlorine pool with a glass atrium dome, no ventilation at all; our office had plate glass windows. They had high school kids

> putting chemicals in the pool, and on many occasions, we had to evacuate the building because of the toxic fumes. The building was also being turned from a hotel into vacation condos, so everything was gutted, including drywall, and redone. So, for four years we not only breathed maximum strength chlorine, but drywall dust, epoxy paint, carpet glue, bug spray, solvents etc. Everyone that worked there was sick all the time and we all, about 14 people, complained daily that we needed clean air to breath, but no one cared. (V. Burstyn, consultative correspondence, Sept 24, 2009)

A. R. reported that this situation persisted for four years. She and her colleagues put her complaints in writing, but nothing was done to correct the situation, and instead, she and another colleague were finally fired for complaining. However, the methodological point—how to isolate and tease apart the way that multiple exposures affect biologically unique individuals—was illustrated at that time. A. R. was one of half a dozen people who became very ill but with different symptoms.

> One person had a heart attack and quit because he couldn't take it anymore. One has hepatitis, one tumours cropping up all over his body, one chronic pain all over her body, one breast cancer, one chronic heartburn and headaches, one skin rashes that won't go away. I have all the classic symptoms of MCS including chronic fatigue, pain everywhere, sense of smell and taste seem broken, flu-like symptoms all the time, vision problems, memory problems etc. I am all messed up and don't feel like I can work because I am too tired and I get sick when I go in some buildings or stores and I never know when it will happen and sometimes my throat closes and I can't breathe or swallow and it's terrifying. (V. Burstyn, consultative correspondence, Sept 24, 2009)

(A short digression, but two questions pose themselves here: Is it credible that A. R.'s symptoms were attributable to chronic anxiety only, while those of her colleagues were attributable to physical and chemical injury only? How does the idea of chemicals at so-called normal concentrations – a concept fundamental to the INSPQ report – work in this context?)

The following quote from Masri et al. (2021) adds validation to the understanding of biological individuality interacting with a toxicant. This understanding, long held by environmental doctors, has appeared until recently to escape or confound much of medicine as practiced by most physicians day to day.

> As it relates to the toxicity of various compounds, it has long been understood by toxicologists that the "dose makes the poison." A more nuanced approach to toxicology, however, is to say that the "dose plus host makes the poison." This latter concept highlights the important role that person-to-person biological variation plays in determining the toxicity of a given xenobiotic to a particular individual. (TILT-related dose and exposure levels, paragraph 1)

Because of the complexity of MCS, specifically in the factors that inform etiology—including a history of exposures to multiple chemicals, a specific body burden of chemicals, previous and

current infections, state of immune system, lower-level symptoms prior to initiation, and injuries, particularly to the central nervous system, and how these are implicated in both onset and chronicity of MCS, all taken up in Part 5—each person is indeed a unique case. As founder and 40-year director of the Environmental Health Centre-Dallas, the late William J. Rea (2016) observed in his list of eight principles to be used in defining and treating chemical and electromagnetic fields sensitivity, "Biochemical individuality occurs where each individual has his own specific individual reaction and threshold for triggering chemical sensitivity (42), (44), some of which can be fended off while others cause chemical sensitivity." (Principle 3)

This individuality, which is also dynamic on a day-to-day and certainly on an environment-to-environment basis, presents researchers with a novel set of challenges that must be met but were not met in the majority of studies reviewed in the INSPQ report, including studies on neurobiological and neurochemical mechanisms related to stress, fear, and anxiety.

(Certainly, one issue that numerous investigating teams (including those at the Hoffman TILT program) are pursuing, to understand better both individual dimensions and the broader nature of MCS, is the role genetic factors play in biological individuality and MCS.)

Linked to biochemical individuality is the concept, again missing in the INSPQ report, of the "total load of exposure," which is partly included in the term "exposome," and to significant extent embodied, literally, in the body burden of chemicals. The exposome is the history of all chemical exposures in an individual's life and how those exposures affect health (DeBord et al., 2016, Karlsson et al., 2021[13]). It is a very useful concept, but due to biochemical individuality, is not identical to the notion of body burden—rather, the chemicals that have been bioaccumulated in any given body will differ from individual to individual to a meaningful extent.

People who develop MCS – a strong and atypical intolerance to particular properties of certain chemicals – like others, but often more so, carry with them what known as a "body burden" of toxic substances. In Part 5, we discuss at greater length how the chemicals in such a body burden can, for some people, contribute to chemical sensitization. This factor, linked to Naviaux's cell danger response theory on the one hand, and to damage done specifically to neurological and immunological systems on the other, is very important. At this point we simply want to introduce it to the discussion and to our narrative. Barrett & Padula, in writing about maternal health discuss ways of measuring this burden, and what results this type of testing has found in US and European women. As they state

> The gold standard for assessing human exposure to synthetic chemicals is by collecting biospecimens such as urine or blood and then measuring concentrations of chemicals of interest and/or their metabolites. Using this approach, biomonitoring studies in the U.S. and Europe have demonstrated that the average pregnant woman has measurable levels of dozens of identifiable synthetic chemicals and their metabolites in her body (9, 10).

[13] Karlsson et al.'s 2021 article, "The human exposome and health in the Anthropocene," also has helpful discussions of epigenetics and other 'omics,' and about the environmental health movement.

> These include organophosphate and organochlorine pesticides, polybrominated diphenyl ethers, perfluoroalkyl substances, phthalates, and phenols, among others. Most of these analytes (or their metabolites) are detectable in >90% of women sampled suggesting that exposure is nearly ubiquitous. (Barrett & Padula, 2019, Exposure assessment and co-occurrence, Synthetic chemicals)

The key points here are that everyone is carrying a body burden of toxic chemicals – a most unwelcome development for population health globally. However, for MCS, that body burden – its relative complexity, its weight, where in the body it is sequestered, whether it is possible to rid the body of it, how genetic factors affect the individual's ability to metabolize it – all these factors play an important role in biological individuality. But they are not addressed in the INSPQ analysis.

In terms of reactivity or triggering, an exposure from volatile or semi-volatile organic compound molecules may seem insignificant to those with a low body burden but may trigger an alarm response in those with a high body burden. Indeed, Rae's first principle deals with the issue of the total body pollutant load, obtained from the environment in air, food and water and notes that "when the body's pollutant load stays too high, it can trigger or exacerbate chemical sensitivity (41)." (Rea, 2016, Principle 1)

The studies reviewed in the INSPQ report did not successfully take into account and/or control for the above factors. Therefore, among other analytical consequences, this means a lack of comprehension of the appearance of certain impacts on the brain during reactions, anxiety being one such impact. We will return to this in a later section, but here is Rea (2016) again:

> Bipolarity of the response [reaction], where there is a stimulating phase and a depressive phase from the same exposure . . . often can confuse the clinician as to the cause of the original disease (13). Often, the clinician misinterprets this problem to be a psychosomatic disease without any proof. (Principle 5)

We further take issue when, in studies such as those relied on by the INSPQ report, chronic anxiety is not measured alongside other equally or more common neurological symptoms as part of a package of such symptoms, including cognitive, speech, and motor impairments and depression in participating individuals. This separation and elevation of anxiety gives a false impression about the unique presence and/or action of it relative to other neurological impacts, especially given biological individuality.

# PART 3: DEFICIENCIES IN EPIDEMIOLOGICAL, CLINICAL AND SOCIO-POLITICAL ANALYSIS

# PART 3: DEFICIENCIES IN EPIDEMIOLOGICAL, CLINICAL AND SOCIO-POLITICAL ANALYSIS

## 3.1 INTRODUCTION

In Part 2, we listed and discussed important research effectively missing from the INSPQ report. We said that these missing pieces were so substantial that they effectively invalidated the INSPQ's claim to comprehensiveness of review of critical issues, and therefore, its conclusions. In Part 3, we list and discuss a number of other issues that seriously undermine the power and credibility of the report.

We begin with the massively important matter of prevalence

## 3.2 OUT-DATED STATISTICS UNDERSTATE THE PREVALENCE OF MCS

The INSPQ report's presentation of MCS prevalence seriously understates how widespread MCS and related conditions have become. The English Key Messages and Summary devotes few words to this extremely significant issue, stating that "[v]arious epidemiological studies have found different levels of prevalence of MCS in the general population, ranging from 0.5% to 3% for cases diagnosed by a doctor. This figure can be as high as 32% when self-diagnosed cases are included" (Key Messages, p. 1). This terse account, based on the epidemiological reviews in the report (which, apparently, extends to 2016), misleads and significantly understates prevalence of medically diagnosed MCS in Canada and comparator countries.

The number (and percentage) of people with MCS has increased substantially since the INSPQ report research began, both absolutely and as a percentage of the population. Indeed, the fact that MCS is increasing in this way is one of the most important things about it.

So, by contrast to the figures in the INSPQ report, in 2020, Statistics Canada's Canadian Community Health Survey (CCHS) found that, as we have previously noted, 1.1 million Canadians had been diagnosed with MCS, equivalent to 3.5 percent of Canada's population. Of these people—and consistent with findings in other countries—72 percent were women. Of these, more than 50 percent were over the age of 45. (Canadian figures available at https://aseq-ehaq.ca/en/environmental-sensitivities/statistics/.)

The 2020 figures were up from 2016, when people with MCS made up 3.1 percent of the population, reflecting an upward trend since 2005, the year the CCHS started tracking MCS. In other words, MCS is on the rise, and it is very widespread in this country. For context, consider that the number of Canadians with MS is about 90,000, and those living with HIV-AIDS is about 70,000.

These findings are low compared to international figures from what might be considered comparator countries. Anne Steinemann PhD, has done extensive and respected work that is relevant today. Steinemann, some of whose older work the INSPQ report did cite, is a long-time,

world-renowned researcher on MCS and the toxic properties of consumer chemicals. She is a professor of civil engineering and heads a major program at the University of Melbourne. She surveyed MCS numbers across the United Kingdom, United States, Australia, and Sweden between 2016 and 2018 (2018a, 2018b, 2019a, 2019b). Working with these findings, she looked at co-prevalence of MCS with asthma and autism as well as with fragrance sensitivity (2019c). Her findings, as stated in the abstract to her 2019c study, present an epidemiological picture that is more serious than that presented by the few words in the INSPQ report:

> [A]cross the four countries, 19.9% of the population report chemical sensitivity, 7.4 percent report medically diagnosed MCS, 21.2 percent report either or both, and 32.2 percent report fragrance sensitivity. In addition, 26.0 percent of the population report asthma/asthma-like conditions, of which 42.6 percent report chemical sensitivity and 57.8 percent fragrance sensitivity. Also, 4.5% of the population report autism/ASDs, of which 60.6% report chemical sensitivity and 75.8% fragrance sensitivity. Among individuals with chemical sensitivity, 55.4% also report asthma/asthma-like conditions, 13.5% autism/ASDs, and 82.0% fragrance sensitivity. Although the prevalence of chemical sensitivity across the countries is statistically different, its co-prevalences with other conditions are statistically similar.
>
> Results also found that, for 44.1% of individuals with chemical sensitivity, the severity of health effects from fragranced products can be potentially disabling. Further, 28.6% of those with chemical sensitivity have lost workdays or a job, in the past year, due to exposure to fragranced products in the workplace. Results indicate that chemical sensitivity is widespread across the four countries, affecting over 61 million people, that vulnerable individuals such as those with asthma and autism are especially affected, and that fragranced consumer products can contribute to the adverse health, economic, and societal effects. (emphases and paragraph spacing added)

In the United States, where many more doctors know about and diagnose MCS than in Canada,[14] Steinemann found prevalence of medically diagnosed MCS at 12.8 percent.

[14]The number of physicians in Canada who specialize in the comprehensive assessment and treatment of MCS is, to our knowledge, less than five, though a larger number of integrative/functional physicians also take on MCS patients. In the United States, there are many more environmental and integrative/functional medicine physicians. An idea of their numbers can be had by visiting their associations, which provide education to physicians as well as information. These include the American Academy of Environmental Medicine (https://www.aaemonline.org/) and this list of affiliated physicians (https://www.aaemonline.org/find-a-practitioner/#alabama) as well as the International Society for Environmentally Acquired Illness (https://iseai.org/), the Institute for Functional Medicine ( https://www.ifm.), International Lyme and Associated Diseases Society (https://www.ilads.org/), Forum for Integrated Medicine (https://forumforintegrativemedicine.org/), the Academy of Integrative Health and Medicine (https://forumforintegrativemedicine.org/), and the American College for the Advancement of Medicine (https://www.acam.org/). In addition, integrative/functional/environmental medicine is taught in over 75 medical schools in the United States, including top-tier institutions such as Stanford, Yale, Johns Hopkins, Harvard Medical School, the Mayo Clinic, Duke University Medical Center, Children's Memorial Hospital, and the University of California-San Francisco Osher Center for Integrative Medicine. Visit the Academic Consortium for Integrative Medicine and Health (https://imconsortium.org/).

Figures from other researchers in Japan and Korea also show high levels in the general population, while Germany's were lower, at least in 2005. As the Alberta MCS report (2021) states:

> Depending on the criteria that were used to evaluate patients, Azuma et al. determined that prevalence estimates range from 4.4% to 24.1% in the Japanese population. In the general German adult population, Hausteiner et al. (2005) determined that the prevalence of self-reported MCS and physician-diagnosed MCS was 9% and 0.5%, respectively. Within the Korean adult population, Jeong et al. (2014) determined that the prevalence was 16.4%. (p. 27)

Of note here, since the INSPQ report dismissed allergenic factors even though clinicians and other researchers include them as common co-factors, is that "when participants [in the aforementioned Jeong et al., 2014] were grouped as allergic or non-allergic participants, the allergic participants had higher estimated prevalence of MCS (19.5% vs 11.3%)" (p. 27).

Other than Germany, Canada's figures are lower than any of these other countries. This may accurately reflect Canadian prevalence, but we need to consider that because Canadian doctors are not trained to recognize MCS, particularly in its early stages, MCS is underreported here.

Underestimating prevalence and related co-morbidities diminishes not only the number of those who live with MCS and related problems but also the urgency of addressing the causes of their conditions, developing clinical programs to assist them, addressing their needs and rights as disabled persons and developing healthy public policy for prevention and support.

Further, since a substantial majority—and this is a large figure, about 815,000 in Canada as of 2020—are also women, understating prevalence helps to obscure the extent of a very serious health problem confronting a great many women today. A specific discussion regarding women and MCS can be found in Part 6 of this report.

## 3.3 MCS CLINICAL KNOWLEDGE IS MISSING FROM INSPQ REPORT YET INDISPENSABLE

Literature developed by clinicians willing to work within the dangerous environment we will describe in the next Part dealing with politicization is especially important in assessing what physicians and patients find effective for diagnostic and treatment purposes. This knowledge should bear back on and validate or invalidate understandings of mechanisms. Here are some examples that should be sought out:

- The publications of W. J. Rea are an important reservoir of such knowledge, based in his 40-year experience as the director of the Environmental Health Centre-Dallas. By 2016, this leading clinic had treated over 30,000 patients. We have his 2016 publication in our reference list.

- The work of Stephen J. Genuis, an Edmonton physician and professor of medical studies, who has written about chemical sensitivity extensively, both analytically and clinically. (Genuis 2012, 2013, 2014; Sears & Genuis 2012; Genuis & Tymchak, 2014)[15]. In a similar vein to Naviaux, he sees **"**epidemics of multimorbidity with sensitivity" in the context of environmental toxicants, and wants to address the frustration of physicians in dealing with patients presenting in this way. He and co-author Marko Tymchak write:

> It has been said that "chronic disease is the great epidemic of our time (56)." Most patients with chronic illness now present with multimorbidity, and many of these individuals experience associated sensitivities. Multimorbidity with sensitivities generally results in much frustration for both physicians and patients, as no cause is usually found and [the] results of routine laboratory testing are unremarkable (57, 58). Psychiatric attribution is commonplace; outcomes are generally poor; and associated healthcare costs are enormous.
>
> Over the past four decades, a plethora of potentially adverse anthropogenic agents have been inadvertently unleashed into the environment for reasons of convenience, beauty, financial gain, safety, and other perceived needs within our culture (17). Increasing evidence indicates that some of these agents, as well as certain biotoxins and toxic elements, might bioaccumulate within the human organism and, after surpassing a certain accrued threshold, disrupted physiology ensues (19, 21, 22, 48). Many adverse effects of toxicant accrual have been recognized, one of which is TILT [toxicant-induced loss of tolerance, another name for MCS] (37, 59), a pathognomonic feature of SRI [sensitivity related illness] and the disordered pathway to a clinical presentation of MWS [multimorbidity with sensitivity] (22).
>
> … Many primary care practitioners and specialists are not yet familiar with this common mechanism of illness or the required interventions to address this affliction. The protocol of removing triggers, optimizing biochemistry, removing future sources of exposure, and eliminating the stockpile of existing toxicants can be successfully employed to ameliorate the health status of countless patients with previously inexplicable multimorbidity. (Genuis & Tymchak, 2014, Conclusion)

- The article by Damiani et al. (2021), reviewing MCS literature and setting out clinical approaches has recently made a very important contribution. We will have more to say about this article and referenced it in our description of MCS.

[15] Other publications by Genuis on environmental health and on MCS available at https://www.stephengenuis.com/research

- The extremely important 2018 book by Nathan, "*Toxic: Heal Your Body from Mold Toxicity, Lyme Disease, Multiple Chemical Sensitivities and Chronic Environmental Illness*" which is (despite its subtitle) a manual or text book for physicians more than for patients. It sets out in great detail the characteristics, diagnostic procedures, and treatment methods that can be used, and are in common use among environmental physicians' practices, to deal with MCS and common co-morbidities. Previously cited in the discussion in Part 2.5.4, we will return to it at various junctures.

- In France and Belgium, the articles and website of the Research and Treatment European Group,[16] led by oncologist Dominique Belpomme. One article by Belpomme et al. (2015), was cited and discussed in the INSPQ report, but there is much more that is very valuable, both on chemical and electromagnetic hypersensitivity.

- Finally, there is a rich trove of clinical experience to be found in the conference papers and, particularly in the educational offerings of the American Academy of Environmental Medicine.[17] This is a body of work that represents decades of experience in diagnosis and treatment by dedicated professionals, and should be prioritized for further investigation.

- Likewise, another rich source of clinical experience and insight can be found at the International Society for Environmentally Acquired Illness. [18]

With the exception of one article (2015) by Belpomme et al., this work is entirely missing from the INSPQ report. We devote Part 5 and portions of Part 10, Recommendations for Moving Forward, to discussing key lessons from the clinical experience.

For the moment, we want to note that what unites the work of all these clinicians is the understanding is that while exposure to chemicals (and electromagnetic fields, though we have not specifically included this topic In this discussion) certainly does impact the limbic system – the privileged system in the INSPQ report – this is only one region of several in the brain, not to speak of many other systems in the body affected during an MCS flare. We emphasize again: chemical intolerance produces a package of multiple neurological symptoms, among which chronic anxiety can be one effect, but this work does not see chronic anxiety as causative. We will continue to address this larger point from several angles in this commentary.

As well, and importantly, in relation to the studies the INSPQ report reviewed, we share the Alberta report's caution that with respect to MCS studies that specifically address so-called

[16] Find at www.ehs-mcs.org and www.ehs-mcs.org/en
[17] Find at https://www.aaemonline.org/category/position-papers/); association's educational offerings (https://www.aaemonline.org/video-education/).
[18] International Society for Environmentally Acquired Illness, find at https://iseai.org/education/

psychological factors such as anxiety and depression, untangling the cause and the effect is crucial but has not been effectively achieved:

> It is difficult to understand from the overall weight of evidence for psychological outcomes, whether the observed symptoms and disorders in MCS populations make individuals more susceptible to developing MCS, or that several side effects associated with MCS (once established) are psychological and may lead to the development of psychological or psychiatric conditions. (p. 58)

## 3.4 HOW POLITICIZATION HAS SKEWED MCS RESEARCH AND IMPACTED CLINICIAL PUBLICATION

Relative to its widespread prevalence, and even to the less-than-adequate research available on, for example, ME ("chronic fatigue syndrome" in the INSPQ terminology) and FM, there is strikingly little research on MCS. This is the result of extraordinary underfunding. Indeed, the infusion of funds to the UT San Antonio Health Sciences program,[19] which helped researchers establish the Hoffman TILT Program, enabled the extensive work that produced the articles on group poisonings (Masri et al. 2021) and mast cell activation syndrome (Miller et al, 2021) we have been citing from.

The Ontario Ministry of Health Task Force on Environmental Health's 2017 report contained, as Appendix 4, an evidence brief/white paper. The white paper discussed findings regarding the size of the evidence base for the three conditions of ES/MCS, ME/CFS and FM from a June 2017 search on the U.S. National Library of Medicine's PubMed system.[20] [It] uncovered approximately 7,453 references specific for ME/CFS, 9,846 references specific for FM, but only 320 specific references for ES/MCS." (paragraph 6) The paper went on to speculate that

> [t]he aforementioned imbalance in research is likely related to the history and balance in associated research funding, which appears to have been sustained, albeit modest (in comparison to other chronic diseases) for ME/CFS and FM, but virtually non-existent for ES/MCS. For example, a recent search of the NIH Reporter database of grants funded in 2007, 2012, and currently by the U.S. National Institutes of Health revealed for ME/CFS: 34 in 2007, 37 in 2012 and 48 current; for FM: 58 in 2007, 54 in 2012, and 53 currently; and for ES/MCS, 0 in all years. (Hu et al., 2017, paragraph 7, emphases added)

MCS has effectively been shunned by key public and university funders of health research on this continent and, to date, this state of affairs continues. It arises directly out of the extremely contested nature of MCS, which has resulted in its politicization,[21] a phenomenon briefly mentioned but not engaged in the INSPQ report. Certainly, there was no attempt by the report to come to grips with the heavy presence, in MCS studies and litigation, of the aggressive commercial interests of the chemical industry in a decades long attempt to undermine the

[19] The Marilyn Brachman Hoffman Foundation, a non-profit corporation, was established in 2013 to support education, outreach, and research on TILT. Decisions on funding are made by a four-member board of directors.
[20] https//www.ncbi.nlm.nih.gov/pubmed
[21] "La question est devenue très politisée" (p. 620).

legitimacy of MCS on multiple levels– these actions being fundamental, if largely opaque, sources of organized hostility.

Such organized hostility is well-known among environmental health scholars and activists with respect to other contested diseases linked to chemical exposures – popular films such as Dark Waters (2019), Erin Brokovitch (2000) and A Civil Action (1998)[22] dramatized the extraordinary lengths specific corporate actors in the chemical industry have gone to suppress the validity of claims of serious, indeed, disabling and lethal health effects. But while corporate efforts worked to sever causation from disease outcomes in these cases, they did not actually challenge the validity of the diseases themselves. This is what the chemical industry has done with MCS, which seems to have merited a particularly vicious and long-standing effort.

The core ideas around which the attack has been conducted are both definitional and political. Below are quotations from the Chemical Manufacturer's Association briefing paper (1990). We have added the headings and groupings for clarity only.

> Definitional: A psychological genesis in emotional disturbance
>
> Environmental illness patients generally lead troubled lives and have genuine problems in coping with family, work and life-style pressures. They often eagerly accept environmental illness as the explanation for their condition. (Executive summary, paragraph 5).
>
> Political: Why MCS ("Environmental Illness") is a threat and what to do about it
>
> The impact [of recognizing chemical sensitivity], however, would not be restricted to the chemical industry. Commonly used chemicals are found everywhere, in the home, the workplace, outdoors, shopping malls and even hospitals. Potentially affected industries include the textiles, clothing, lawn care products, household cleaners, dry cleaners, paints and solvents, perfumes, hair treatment products, plastics, paper and many other consumer goods industries. ("Environmental illness" Impacts, paragraph 9)
>
> Forming Coalition: Because it has the potential to impact many segments of society, many groups have an interest in placing environmental illness in its proper perspective Among them: medical associations; manufacturers and applicators of agricultural and pesticide products; personnel, labor relations, etc.; food dealers; restaurants; insurance companies; self-insurers; soap and detergent manufacturers; chambers of commerce; lawn care services; homebuilders; aerospace industry; retailers; and automobile manufacturers. (Forming Coalition, paragraph 1)

[22] De La Garza, A. (November 25, 2019). Dark Waters Tells the True Story of the Lawyer who took DuPont to Court and Won. But Rob Bilott's Fight is Far from Over. https://time.com/5737451/dark-waters-true-story-rob-bilott/ : Marc Dorian, Tim Gorin, Haley Yamada and Allie Yang( June 10, 2021) .Erin Brockovich: the real story of the town three decades later https://abcnews.go.com/US/erin-brockovich-real-story-town-decades/story?id=78180219 ; https://www.tcm.com/tcmdb/title/336331/a-civil-action#synopsis.

Definitional and political: mobilize physician's organizations to delegitimize MCS ["EI"]

> Because environmental illness is a health issue, the only people who can legitimize it are physicians, and they have not. Should environmental illness arise as an issue, a coalition with the state medical association is absolutely necessary. (Forming Coalition, paragraph 2)

Readers can find the entire "briefing paper" as Appendix 4a, and evaluate the nature of the founding ideas for themselves. Also provided in Appendix 4b is a more detailed discussion of the measures taken by the chemical industry subsequent to that paper, by New Mexico physician Ann McCampbell (2001).

Since the time of this infamous paper, studies attempting to prove that MCS is psychogenic have been richly funded, and constant legal challenges to claims for compensation and benefits have resulted from the playbook set out in the paper, which also labels environmental physicians as quacks doing harm to their patients. For more on these efforts, also see emergency medicine and Gulf War physician William Meggs (2016), history of the war on MCS. From the article's abstract his conclusion about why this must stop:

> As the field of environmental medicine emerged, commercial interests, including the corporate food industry, chemical industry, pharmaceutical industry, and workers' compensation insurance companies, were threatened. The same techniques used to suppress scientific discoveries that smoking cigarettes causes cancer and heart disease, burning fossil fuels deranges the biosphere, and using leaded gasoline damages children's brains were used to suppress that dietary and environmental exposures could cause disease. As a number of diseases ranging from obesity and diabetes to depression increase at devastating rates, a return to the principles of environmental medicine becomes imperative. (Meggs, 2016)

The extreme politicization of MCS that resulted from the industry campaign, including its impacts on medical associations, public and private insurers and governmental neglect, has been expressed in stigmatization of patients as mentally disturbed and their doctors as quacks, by contestation of legal battles for recognition and compensation, by funding scientists to "disprove" links between the illness and chemicals and by a proactive campaign to influence American state and Canadian provincial medical organizations and governments. From the 1990s to the 2010s, many environmental physicians were faced with harassment and even loss of licence as a result of such influence. As late as 2010 (we do not know the current situation which may have improved), Australian health professionals faced similar attitudes. Medical anthropologist Tarryn Phillips' 2010 publication, "I never wanted to be a quack!", is a chilling explication of the severity of penalties for professionals who swam against the current with respect to MCS in that country.

In 2012, a number of participants in our qualitative needs-identification study (Burstyn & MEAO, 2013) spoke about how this problem affected not only them but their own physicians, either in terms of being afraid to take on MCS themselves, or in terms of disrespecting those who did. One participant, reporting on the experience of friend with MCS who lived in a small Ontario town and was trying to get disability status, said

> The doctors at the local clinics don't believe in MCS. They say … that the Environmental Health clinic is encouraging mass hysteria with people, that she just needs to expose herself more and develop a tolerance for these chemicals again." LMS (p. 145)

At the time of writing of this report, we noted:

> When stigma extends from the perception of patients to their doctors, many harmful outcomes result. Most important is that the stigma becomes a powerful counter-incentive that has discouraged all but a handful of brave souls from taking on these conditions. That number has been shrinking in Ontario, even where it has grown in less restrictive jurisdictions - the United States for example, where need and a market system have combined. Neighbouring Michigan has more than 20 physicians who list care of these diseases [MCS, ME and FM] in the services they provide. Hence our current state … .'(p. 145)

In turn, the refusal of physicians' organizations to recognize MCS has long justified governments and private insurers in excluding care for MCS in clinical services and in payment programs, despite various study processes, at least in Ontario, dating back to 1985 calling for such care. Most provincial governments have done nothing to stop hostility to MCS or to bring it and its physicians into their systems. Two provinces – Ontario and Nova Scotia – took promising steps in the 1990s in establishing clinical services (Ontario, diagnostic only), but none since, so relative to need, the situation has greatly deteriorated in those provinces as well as all others.

To this day, there are no government departments with official carriage of MCS, despite its widespread prevalence. As CTV reportage (Favaro, 2022a) noted in its coverage of the choice MCSer "Sophia" made for medically assisted death in February 2022, after trying desperately for two years to get help to obtain a safe place to live, "the underlying problem is that there is no government agency that is assigned to help people with environmental sensitivities get housing free from chemicals" – or any other help, we can add. As of this writing at least one other woman in Ontario has obtained agreement to MAiD for the same reasons as Sophia, (Favaro, 2022b)[23] and others have already applied.

[23] Although we are able to add as a postscript that people have since stepped in to assist by finding housing. Favaro, A. (May 28, 2022) (Favaro, 2022c) https://www.ctvnews.ca/ctv-news-channel/woman-with-disabilities-approved-for-medically-assisted-death-relocated-thanks-to-inspiring-support-1.5921893

This poisoned environment has directly and massively undermined funding sources and investigators willing to take MCS on. As the previously cited White paper for the Ontario Ministry of Health Task Force on Environmental Health (2017) noted with admirable understatement,

> the task force is . . . aware of anecdotal reports of scientists avoiding research on these conditions [ME/CFS, FM, and ES/MCS] due to perceived stigmas associated with being a researcher in this area. The task force is also aware of the reluctance of many clinicians and researchers to handle patients and/or conduct research in this area because of the controversies and litigation that are often associated with these conditions in relation to disability, suspicions of malingering and/or secondary gain, requests for accommodations, etc. The issues of stigma, controversy, and litigation are particularly acute with respect to ES/MCS, which regularly involves questions regarding environmental or occupational causation. (Hu et al., 2017, paragraph 9; emphasis added)

The major cleavage in MCS studies – into the psychogenic and toxicogenic schools – is a product of this deep politicization. The attack on the reality and legitimacy of MCS as a biomedical clinical entity since at least 1990 by the chemical industry, and the alliances this industry has actively sought with physicians' associations, governments and insurers cannot simply be ignored, for these remain factors at work behind closed doors in the lobbying of governments and very likely influential physicians and/or their associations to this day.

Yet the consequences of MCS's politicization by non-medical interests are not addressed in any way in the INSPQ report, even as they have profoundly affected, directly and indirectly, the body of research and resulting literature and the biases in medicine and society that have subsequently developed in their wake. Unless these factors are named, they cannot be countermanded. It is essential for the health of all Canadians that commercial interests do not trump medical and population health interests, and that the public interest is reflected going forward in the creation and integration of MCS services, programs and research into our health institutions.

## 3.5 THE PATIENT EXPERIENCE IS ENTIRELY ABSENT FROM THE INSPQ REPORT

We are profoundly struck by the complete absence of the voices of people who live with MCS. Best practice in recent years has clearly been to include patients in research generally; and to include that qualitative research in reviews. Even if scant, there is important and well-known experiential literature that gives MCSers a voice, especially the work of James Madison University professor Pamela Reed Gibson and that of registered nurse and medical anthropologist Juliene Lipson, department of community health systems in the School of Nursing at the University of California, San Francisco.

In the grey literature there is also the previously mentioned qualitative needs identification study of Ontarians living with MCS (as well as those with ME and FM) (Burstyn, V., Phillips, A. PhD., McKweon, P. & Halapy, E., MSc., Parts 3 and 4 of Burstyn & MEAO, 2013). Illustrative extracts

appear in Appendix 3, and the stresses of post-onset life with MCS, derived from that study, are discussed in detail in Part 8 of this document.

This qualitative study was conducted as an in-depth needs identification process in Ontario (2013), as a research document that identified life experience and unmet needs in spheres based on the World Health Organization's social determinants of health (experience of health and post-onset illness, economic consequences, physical environment, family and social relationships, cultural discrimination, negative and positive experiences with doctors and the health care system, patient recommendations). It included special analysis of women's, children's, stigmatization issues; in-depth exploration of model of care and delivery; in-depth discussion of issues in barrier removal across government and the public sector.

A needs identification study specified by Ontario's Ministry of Health and Long Term Care, was completed over two years, and, as mentioned, was used to inform the design of the proposed Centre of Excellence in Environmental Health, affiliated clinics and training for primary care providers.[24] A study of physician knowledge and attitudes followed three years later, commissioned by the Ontario Ministry of Health and Long-Term Care for the Task Force on Environmental Health, which validated the conclusions drawn from the patient experience with the doctors and the health care system. (Ipsos Public Affairs, 2018)

For the moment, we draw your attention to the following sources for patient experience – and there very well may be more:

- Sacristán J.A. et al. (2016) "Patient involvement in clinical research: why, when, and how."

- Gibson, P.R. (1993). Environmental Illness/Multiple Chemical Sensitivities: Invisible Disabilities in Women with Disabilities: Found Voices.

- Gibson, P. R. (1997). Multiple Chemical Sensitivity, Culture and Delegitimization: A Feminist Analysis.

- Gibson, P. R. (2007). *Multiple Chemical Sensitivity: A Survival Guide*. Earthrive . 2006

- Gibson, P.R. & Lindberg A. (2007) Work accommodation for people with multiple chemical sensitivity.

- Gibson, P. R., et al. (2011). Isolation and lack of access in multiple chemical sensitivity: A qualitative study.

- Lipson, J. (2004). Multiple chemical sensitivities: stigma and social experiences.

[24] Delayed by the pandemic, this process is still on the agenda.

- Lipson, J & Doiron, N. (2006). Environmental Issues and Work: Women with Multiple Chemical Sensitivities.

Especially in the field of MCS, where the patient experience so frequently and strongly contradicts certain conclusions drawn by researchers advancing the idea that MCS is a psychological disorder, it is essential to listen, and listen carefully to and consider the people who live with and experience the condition in a very difficult world. Their absence is one of the great weaknesses of this review.

## 3.6 CHILDREN AND CHILDHOOD ARE MISSING FROM THE INSPQ REPORT

A major emphasis of the environmental health field has been the impact of many different kinds of toxicants on children—from fence-line exposures in industrial-adjacent residential zones, to pesticides in agricultural settings, to everyday consumer products such as phthalates, flame retardants, and synthetic fragrances in middle-class homes and heavy traffic emission along major thoroughfares. There is has long been a consensus across the board that children are much more vulnerable than adults to these insults (Hu, 2002, Burstyn & Fenton, 2006, Landrigan, 2007, among many, many others).

Not surprisingly, then, it is also clear from the very broad literature, including, for example, a huge and very frightening longitudinal report on children in 20 US jurisdictions published in 2017 by the US National Institutes of Health, that children's health has been deteriorating greatly in the chemical age. This deterioration shows up during childhood, and has major consequences for health and overall well-being and success in later life. (NIEHS/EPA, 2017; Cooper et al., 2011.)

It is clear from this and many other studies that children in lower income-higher chemical areas are handicapped chemically-physically, as well as socio-economically, and this leads to an intensification and perpetuation of socio-stratification that is rarely discussed outside environmental health studies. Note the following point too: the chemicals such children (and their parents) are exposed to in such settings may be "normal" for those settings – but they are clearly neither "weak" nor "harmless" in their impacts on health.

It is a great pity that the politicized lack of recognition of MCS has meant that this condition is not generally tracked in the types of studies just cited, for it would doubtless appear as one adverse health outcome, add to the grimness of the picture, and demonstrate the correlation of MCS to chemical impacts. But there is very little literature on the subject of MCS and children specifically, which makes it all the more important to engage with what does exist.

For example, with respect to the question of whether maternal MCS affects children's health adversely – one which indirectly poses a question about the potentially more harmful role of toxic body burden in such mothers than in others – Lynne P. Heilbrun, of the University of Texas Health Science Center at San Antonio and the Department of Pediatrics, Children's Hospital of San Antonio/Baylor College of Medicine, with colleagues found that "chemically intolerant mothers were three times more likely to report having a child with autism and 2.3 times more

likely to report a child with ADHD" (Abstract, Results), and they were also more likely to have more chemically sensitive children (Heilbrun et al. 2015) This is a very significant and concerning finding, not plausibly explained by a maternal anxiety disorder.

In 2018, Professor Kenichi Azuma, of the Department of Environmental Medicine and Behavioral Science, Kindai University Faculty of Medicine (Japan), and colleagues found

> The current chemical intolerance of the mother was significantly associated with allergic rhinitis (OR, 2.32; 95% CI, 1.19–4.53), bronchial asthma (OR, 3.66; 95% CI, 2.00–6.69), and chronic bronchitis (OR, 3.69; 95% CI, 1.04–13.03) in her 3-year-old child.
>
> Conclusions:
> The results suggest that inherent physical constitution and childhood housing environment are associated with a risk of acquiring chemical intolerance. Children of mothers with chemical intolerance have a possible risk of respiratory hypersensitivity or inflammation. Further investigation is recommended to determine the inherent physical constitution and background environmental factors associated with the risk of acquiring chemical intolerance. The impact of having mothers with chemical intolerance on the health of children also requires further study. (Azuma et al. 2018)

In a PubMed search, we were able to find only one publication on MCS in a child, by Alan Woolf, of Children's Hospital Boston. In the 2000 article, "A 4-year-old girl with manifestations of multiple chemical sensitivities," Woolf presents a case from the Pediatric Environmental Health Subspecialty Unit at Boston's Children's Hospital. The case was of

> a preschool child who had suffered from milk allergy and poor weight gain as an infant, and then later developed asthma, allergic symptoms, sinusitis, headaches, fatigue, and rashes precipitated by an expanding variety of chemicals, foods, and allergens. [Woolf reviews] definitions, mechanisms, diagnostic strategies, and management, and discus[es]s some uniquely pediatric features of MCS as illustrated by this case. (Abstract)

But again, lack of funding and institutional support has thoroughly undermined an area that cries out for further research, both on MCS in children, and on factors in childhood and youth that predispose or prefigure adult initiation. Surely, it is not possible to wholly understand MCS as a clinical entity without this information, just as it is not possible to diagnose, treat and help children with MCS without such knowledge. We do know that MCS is present in children, and histories of some adult MCS patients can show both exposures and reactions that date back very early in life, including infancy.

Notably, in the books written by paediatrician Doris Rapp (1992, 2004) about chemically sensitive children, and in more recent studies, scarce as they are, chronic anxiety has not appeared as an etiological issue; rather, exposure to substances such as chemicals and molds has been highlighted (Azuma et al., 2021, Masri et al. 2021, Suojalehto et al., 2021). It is difficult to understand how an anxiety disorder would be responsible for these findings. By contrast, with

the understanding of how mothers bioaccumulate endocrine-disrupting and neurotoxic pollutants and transfer these via cord blood and breast milk to fetuses, it is not difficult to imagine that the excessive body burden of chemically sensitive mothers can affect the development of their children's neurological and immunological health. It is also not difficult to understand how toxicants in indoor and outdoor childhood environments could initiate MCS in susceptible children, as it does with adults.

## 3.7 CONCLUDING REMARKS FOR PARTS 2 AND 3

Some maps are better than others in capturing the features of the territory they represent. To do the job well, they must include all the features of that territory, in detail, accurately and proportionately placed. A body of research literature can be thought of as a map to the territory of the lived experience of its subject matter: the experience of those who live with a disease, and the experience of their clinicians and researchers. To be a sufficient map, it must accurately represent that experience. The literature on MCS is very far from a complete map. A literature review is, in a real sense, a map of the map, or a meta-map, so it must be even more refined. Its accuracy depends on not only on the quality of the literature that describes the territory but also on what parts were selected and how they were analyzed in the review. To the extent that the peer-reviewed literature on MCS does not contain extensive clinical studies and studies of lived experience, and to the extent that the INSPQ literature review is missing both those studies and all the other important research that we have discussed in detail, it cannot be considered an adequate meta-map. Its conclusions cannot be accepted as a sufficient or correct guide to get us through the real territory. Certainly, they cannot justify its declaration that it has identified one sole mechanism – a psychological mechanism at that – to explain MCS and dismiss all other explanations.

We will now proceed to a more detailed examination of the role of chemicals as such in MCS and health in general, a role rebutted and dismissed by the INSPQ report.

# PART 4: CHEMICALS AND MCS

# PART 4: CHEMICALS AND MCS

## 4.1 INTRODUCTION

As we have explained, we take issue with both central conclusions of the INSPQ report, namely that chronic anxiety causes MCS; and that chemicals play no causative role in MCS. We note that the anxiety causation theory – expressed variously in different parts of the report – is *predicated* on rejecting a link between MCS and chemicals "at normal concentrations," which the INSPQ report reframes as "odours." These it classifies as "harmless signals" because they are "not absorbed at low ambient concentrations."[25]

In Part 4, therefore, we wish to address the critical matter of chemicals at greater length and in several relevant ways.

## 4.2 A FUNDAMENTAL DEFINITIONAL ERROR: CHEMICALS NOT ODOURS

Throughout the INSPQ report, MCS is described as a syndrome in which "affected individuals perceive odours as a threat to their health" (e.g., Key Messages, p. 2). While in some places there is more detail about what might constitute an odour, this message is consistent throughout, including in the all-important key messages and summary sections (available in both English and French), which will be the main reference point for a great many readers:

To re-iterate the claims of the INSPQ report:

> Multiple chemical sensitivity syndrome (MCS) is a chronic disorder characterized by multiple recurrent non-specific symptoms triggered or exacerbated by exposure to odours present in the environment at low concentrations—concentrations tolerated by most people.
>
> Affected individuals perceive odours as a threat to their health. When they detect odours, they experience acute stress symptoms that manifest as ailments that they attribute to the chemical products associated with these odours.
>
> What is more, olfactory studies have demonstrated that there is no absorption of odorous substances at the low ambient concentrations to which people with MCS are exposed. (Summary pp 1,2)

These messages are also there in other parts of the report, including this one:

[25] All words in quotes appear in the Key Messages and Summary except for "harmless signals," which appears on p. 11 and has been translated from "Dans les situations de stress chronique, les sujets atteints de SCM interprètent les signaux inoffensifs de l'environnement ou du corps comme des dangers, et cela perturbe leur capacité d'adaption."

> In chronic stressful situations, people with MCS interpret harmless signals from the environment or the body as dangers, and this interferes with their ability to cope" (p. 11, translated (see footnote 25, previous page)).

For the INSPQ report, it is the acute anxiety arising out of chronic stress that creates a baseless anticipatory fear of "odours," which in turn provokes the cascade of neuro-biological effects – meaning symptoms -- seen in MCS and previously cited in Part 2.2.1. For clarity, we repeat what this cascade effects:

> A disruption of the hypothalamic-pituitary-adrenal axis, an increase inflammatory cytokines, a disruption in oxidative homeostasis, a chronic decrease in neuromodulator levels (serotonin, dopamine, norepinephrine). In addition, using brain imaging, alterations in brain function and structure were observed that affect the limbic system circuits (emotions, memory, learning) and the prefrontal cerebral cortex (attention, reasoning, strategic thinking, judgment). (Summary, Results, p. 3)

That the volatile and semi-volatile chemicals comprising ambient "odours" can be toxic or play a causative part in this process as a result of their toxicity is, in their view, entirely wrong:

> Based on these new insights, the authors of this report rebut the hypothesis that there is an association between MCS and the toxicity of chemicals present at normal concentrations. (Key Messages, p. 2).

There are a number of problems to unpack in these statements.

In the Part 2.3, we offered a preferred working description of MCS that was synthesized from a number of sources, including from two teams who published important papers in 2021. This description is worth restating to contrast with the INSPQ definitions and to clarify our approach, especially regarding the role of chemicals.

> MCS is a multi-system, recurrent, environmental disorder that flares in response to different exposures (i.e., pesticides, solvents, toxic metals, fragrances, cleaning products, cigarette smoke, certain foods, drugs/medicine, mold and other vehicles of exposure) at concentrations that do not provoke such symptoms in other people. MCS is characterized by neurological, immunological, cutaneous, allergic, gastrointestinal, rheumatological, cardiological and endocrinological signs and symptoms. MCS is widespread condition and the majority who live with it (approximately 70 percent) are women, although a significant minority are men.
>
> Onset, which may happen slowly over time or rapidly, begins on exposure to a particular chemical or mixture of chemicals (including bio and well as synthetic toxicants) that commonly affect the immune system and/or nervous system, such that MCS appears to be primarily a neuroimmune disease process. This chemical exposure interacts with one (or both) of these systems in a way that renders individuals intolerant to subsequent

exposures which are then experienced as triggering or flaring events. After the initial onset, some new triggering events may result in “crashes” - additional worsening to qualitatively greater degrees of severity that are not easily reversible without intervention.

Affected individuals no longer tolerate everyday exposures to a wide range of structurally diverse substances at levels that never bothered them previously, including ingestants, inhalants, implants, and skin contactants. Many previously tolerated foods and drugs may trigger symptoms. At times, onset is not observed or reported immediately, and the phenomenon of "masking" can obscure MCS and delay diagnosis.

MCS ranges in severity. Early, milder stages are often erroneously perceived to be allergies, require adjustments and avoidance, but go undiagnosed. Moderate to severe MCS involves greater intensity and duration of symptoms. Severe MCS brings intense reactions, great physical suffering and can be life-threatening for some people when exposed to some chemicals. Major efforts to avoid triggers are required, making life in the ambient air of chemically-ladden everyday environments unsustainable. This is how MCS disables those affected. When co-morbidities are present – often the case – overall health is further compromised, and additional barriers are encountered.

MCS is usually responsive to appropriate measures and treatments, but becomes worse without these.

In this definition,

- Chemical intolerance is first a reaction to xenobiotics in the environment, not a feeling of anxiety within the individual;
- Chemically intolerant people are hypersensitized to chemicals that can be, but are not necessarily odorous;
- Triggering takes place at levels that do not trouble the general population, and that did not bother the individual before onset—but this does not mean the triggering substances are “harmless”; and
- Symptoms within body systems are sufficiently specific and documented that they can be named: “cutaneous, allergic, gastrointestinal, rheumatological, endocrinological, cardiological and neurological” (from Damiani et al., 2021, Abstract). For Miller et al. (2021), the symptom list is overlapping with that of mast cell activation syndrome and includes “muscles, eyes and airways, heart and chest, digestive/GI, cognitive, affective, coordination, head, skin and urinary” (See Figure 3, reproduced in this report in Part 2.5.4). This specificity implicitly disagrees with the idea of non-specific symptoms and certainly with the idea that one uber-symptom—an affective symptom in only one part of the brain, namely chronic anxiety—is responsible for all the others.

Naming MCS as an *environmental* disorder and naming some of the types of chemicals that commonly act as incitants or triggers for both onset and chronicity in the descriptions affirms the

link between MCS symptoms and chemicals. Masri et al. (2021) and Miller at al. (2021) have now provided longer and more precise lists of chemicals most likely to initiate chemical intolerance in a given subset of people upon group exposure, and continue to play triggering roles in chronicity (See Part 2.4), worth repeating:

> Mixed volatile and semi-volatile organic compounds (VOCs and SVOCs), followed by pesticides and combustion products were most prevalent across TILT/[MCS] initiation events. As a broader category, synthetic organic chemicals and their combustion products were the primary exposures associated with chemical intolerance. Such chemicals included pesticides, peroxides, nerve agents, anti-nerve agent drugs, lubricants and additives, xylene, benzene, and acetone. (Masri et al., 2021, Abstract, Results)

> The mixed VOC/SVOC group of chemicals included such VOCs as benzene, acetone, toluene, and xylene as well as SVOCs including BFRs, PCBs, dioxin, phthalates, and triphenyl and tricresyl phosphates. Among this group of compounds, xylene was identified most frequently across exposure events, followed by both benzene and acetone. Pesticides included carbamates, organophasphates, and organochlorides (Masri et al., Results, Comparing case studies, paragraphs 4, 5)

At this juncture, we want to stress how important it is in describing MCS to use the word "chemicals" instead of "odours." All odours are made up of chemicals, a fact that needs to be transparent, not obscured, in the language used. But not all chemicals have odours, an issue we will return to in Part 4.4. Some of the worst reactions people report, be it during onset or thereafter, occur when a person has no idea that chemical residues are present, precisely because either at, or not long after, application and initial dispersal of concentrated volatile and semi-volatile organic compounds, there are no odours to perceive (Burstyn & MEAO, 2013). The absence of odours frequently results in people inadvertently coming into contact with specific chemicals, which in turn leads to adverse health events. Moreover, as the symptom lists show, reactions can take place via ingestion and dermal contact, not only via the olfactory or respiratory systems.

Since chemically intolerant people do react to chemicals even when in the absence of odour, the "odour -> chronic anxiety -> anticipation of danger -> false attribution to chemicals -> symptom flare" sequence the report posits cannot be the sole or even the main cause of those symptoms.

## 4.3 FRAGRANCES ARE CHEMICALS WITH ADVERSE HEALTH EFFECTS

Synthetic fragrances are famously troublesome for the chemically intolerant, so it is worth analyzing why this is so. As noted, all odours are made up of chemicals. Many fragrance chemicals are made of a number of chemicals that are indeed toxic, even at trace amounts, with adverse health effects on humans even when individuals do not have an MCS-type intolerance reaction. As we will see, fragrances adversely affect a great many people.

Steinemann (2020) writes that a

"fragrance" is a scent and, despite its singular name, it is a formulation of dozens of chemicals, such as volatile organic compounds (VOCs). Nearly 4000 ingredients have been documented for use in the composition of a fragrance (IFRA 2020b). A fragrance is generally intended to "provide an aroma, to mask an odor, or both" (Steinemann, 2019a).

A "fragranced consumer product" (or "fragranced product" for brevity) is a product that "contains an added fragrance or that is largely comprised of fragrance"(Steinemann, 2016). Fragranced products cover hundreds of everyday items, such as air fresheners, deodorizers, cleaning supplies, laundry detergents, fabric softeners, essential oils, candles, soaps, personal care products, colognes, and hand sanitizers.

Among these thousands of chemicals in these hundreds of everyday products we find chemicals such as acetone, ethyl acetate, benzaldehyde, formaldehyde, methylene chloride, and phthalates, all neurotoxic and identified as chemicals likely to initiate MCS in a predictable subgroup of people (Pinkas et al., 2017; Masri et al. 2021).

These chemicals have a host of other health-harming properties as well, even, in the terminology of the INSPQ report, at "normal concentrations." In recent times, these fragrances have come to penetrate virtually all social spaces. Research shows that even if most people do not have an instantaneous full-blown MCS reaction to common fragrance chemicals, a great many do feel other immediate adverse effects. The American Lung Association's web-page, Cleaning Supplies and Household Chemicals, is one of hundreds of such alerts by medical and environmental organizations on the dangers of common fragranced products, presumably "at normal concentrations."

AMERICAN LUNG ASSOCATION ON FRAGRANCED CLEANING PRODUCTS

Many cleaning supplies or household products can irritate the eyes or throat, or cause headaches and other health problems, including cancer. Some products release dangerous chemicals, including volatile organic compounds (VOCs). Other harmful ingredients include ammonia and bleach. Even natural fragrances such as citrus can react to produce dangerous pollutants indoors.

VOCs and other chemicals released when using cleaning supplies contribute to chronic respiratory problems, allergic reactions and headaches. Studies are underway to assess how these chemicals affect people who have asthma and other respiratory illnesses.[1] However, past studies link exposure to chemicals from cleaning supplies to occupational asthma and other respiratory illnesses.[2,3]

Cleaning supplies and household products containing VOCs and other toxic substances can include, but are not limited to:

- Aerosol spray products, including health, beauty and cleaning products;
- Air fresheners;
- Chlorine bleach*;
- Detergent and dishwashing liquid;
- Dry cleaning chemicals;
- Rug and upholstery cleaners;
- Furniture and floor polish; and
- Oven cleaners.[1,2]

***Never mix bleach or any bleach-containing product with any cleaner containing ammonia.** The gases created from this combination can lead to chronic breathing problems and even death.[2] Recent research has found that even natural fragrances in cleaning products, particularly in air fresheners, may react with high levels of ozone from indoor sources (for example, from some air cleaning devices)or from outdoor air to form formaldehyde, a known human carcinogen, and dangerous fine particles indoors.[5,6] Ozone is a harmful, but invisible, gas that worsens asthma and other lung diseases. Particles are also common air pollutants that can worsen asthma and other lung diseases and risk heart attacks and stroke. Both ozone and particles can be life-threatening.

https://www.lung.org/clean-air/at-home/indoor-air-pollutants/cleaning-supplies-household-chem (accessed May 23, 2022)

Recall that in her article on co-prevalences with MCS, Steinemann (2019c) found that across the UK, Sweden, the US and Australia, 19.9% of the population reported chemical sensitivity 7.4% report medically diagnosed MCS, 21.2% report either or both, and 32.2 % report fragrance sensitivity. Moreover, in the twenty-six percent of the population reporting asthma or asthma-like conditions, 42.6% report chemical sensitivity and 57.8% report fragrance sensitivity. Also, note that in the 4.5% of the population reporting autism or autism spectrum disorder, 60.6% report chemical sensitivity and 75.8% fragrance sensitivity. We are speaking of very large numbers of people experiencing adverse effects from synthetic fragrances.

Steinemann's study further noted that of those with MCS, 28.6% lost workdays or a job in the year prior to the study, as a result of exposure (Abstract).

Perhaps it is worth asking whether the fragrance sensitivity of all these people is an expression of a danger-anticipating anxiety disorder? We think, to the contrary, it is triggered by the physically disrupting effects of these toxic synthetic chemicals, now found in every type of social space.

For a more in-depth hypothesized connection between perfumes and autism, please see Bagasra et al., 2013.

## 4.4 NON-ODOROUS CHEMICALS EQUALLY INCITE CHEMICAL INTOLERANCE AND OTHER ADVERSE HEALTH EFFECTS

Just as important for MCS and for many other serious illnesses and disorders are the chemicals that have no particular odour at normal or usual concentrations. These chemicals release quantities of volatile and semi-volatile organic compounds that initiate and continue to trigger MCS flares and also silently contribute to other adverse health effects in broader populations. The red flag raised by the emergence of MCS decades ago, when it was called "environmental Illness" and so agitated the chemical industry has been more than justified. Today, there is a very extensive, authoritative literature on many aspects of the adverse harms of "everyday chemicals," and many academic and non-profit organizations dealing with these issues have been established.

Here we would like to cite only one important and relatively recent publication out of many thousands of articles and books reporting on studies in this broad field, for this is a study that looked at newly identified adverse effects from a multiplicity of these chemicals, rather than only one. In 2018, atmospheric scientist Brian C. McDonald and 20 international associates came together under the auspices of the US National Oceanographic and Atmospheric Administration Earth System Research Laboratory in Boulder, Colorado and authored "Volatile Chemical Products Emerging as Largest Petrochemical Source of Urban Organic Emissions," published in the prestigious journal *Science*. They presented compelling evidence of a new, mammoth-sized problem, reporting that as far as smog sources are concerned, "transportation emissions in the United States and Europe have declined rapidly," but these have been rapidly replaced by "

> the use of volatile chemical products (VCPs)—including pesticides, coatings, printing inks, adhesives, cleaning agents, and personal care products, [which] now constitute half of fossil fuel [volatile organic compound] emissions in industrialized cities" (both quotes from the Abstract).

McDonald et al. noted their astonishment and dismay at this finding – that 50 percent of ozone-destroying and global warming chemicals in the air of cities now come from consumer product sources. And we note that these are the same chemicals that have been shown in many air pollution studies to harm our neurological, vascular, cardiological, endocrinological, immunological, hepatic, renal, gastrointestinal, and reproductive health. These are the same chemicals that are associated with MCS onset and chronicity, and to which, even absent "odours," MCS sufferers have rapid and sometimes long-lasting reactions, which are very often severe reactions. The chemical soup of smog is a major problem for people with MCS. (Again, recall the overlapping chemicals in synthetic fragrances, in smog and in the list that Masri et al. (2021) compiled.)

In opposition to the INSPQ report, our conclusions are:

- "Normal" or "usual" concentrations (imprecise terms) of chemicals today do not cause chemical intolerance reactions in all people, but, as stated, they are not "harmless" by any means; and
- To people who have MCS, trace amounts—or more—of these chemicals can often signal real, not imagined danger.

In fact, the burden of toxicological-related illness has become unsustainable for human society. A 2017 article by Philippe Grandjean, Harvard environmental epidemiologist, and Martine Bellanger, professor of health economics at l'École des Grands Études en Santé Publique, estimated the worldwide extent and costs of disease linked to chemical exposures.

> Our economic estimates based on available exposure information and dose-response data on environmental risk factors need to be seen in conjunction with other assessments of the total cost for these environmental risk factors, as our estimate overlaps only slightly with the previously estimated environmental DALY [Disability-adjusted life years] costs and crude calculations relying on attributable risks for environmental risk factors. The three approaches complement one another and suggest that environmental chemical exposures contribute costs that may exceed 10% of the global domestic product and that current [disability-adjusted life years] calculations substantially underestimate the economic costs associated with preventable environmental risk factors. By including toxicological and epidemiological information and data on exposure distributions, more representative results can be obtained from utilizing health economic analyses of the adverse effects associated with environmental chemicals. (Abstract; emphasis added)

One of the most serious developments over the last 30 years is that MCS (due to the way the psychogenic school has repeatedly classified it as a mental or somatoform disorder and the parallel way in which the research of the biophysical-toxicogenic school has remained little known) has been separated from diseases whose link to toxicological factors has been better known. As a result, MCS has been under-addressed by the broader environmental health movement as well as the women's health movement when, in fact, it is an environmental health issue par excellence.

Our main point, however, is that toxicological factors—including the role played by everyday chemicals at normal concentrations—do play a massive role in disease worldwide, and MCS is part of that trend, not separate from it. The chemicals that have been responsible for the burden of disease more broadly cannot be written out of the initiation and continuing symptomatology of MCS. For this, the concepts of toxic body burden and total load, introduced in Part 2.7 and taken up in Part 5.2, are critical. But first, we return to other issues we introduced in Part 2.

## 4.5 NEUROLOGICAL AND MAST CELL FINDINGS ON CHEMICALS AND MCS

In Part 2 we specified which critical pieces of research and clinical findings are omitted, or mentioned but not engaged, in the INSPQ report, and we provided a preliminary discussion of

them. In this section, in the context of a deeper discussion of the role of chemicals in MCS, we now extend our analysis of two of these areas of investigation in particular: the neurobiology of MCS and the hypothesized role of mast cell activation.

### 4.5.1 Neurological function and low-concentration chemicals

To begin this section, we would briefly like to draw attention to the unacceptable treatment of brain imaging studies in the INSPQ report, for this problem is tied closely to the neglect of the TRP channels which many MCS researchers believe to be very important in MCS mechanisms, as we discussed in Part 2.5.3. We refer once again to Molot (2021, pp. 6-7), who, using more recent studies (e.g., Azuma et al., 2019) to support his submission, disputes the presentation and conclusions the INSPQ report draws from the studies it cites. Given how important these are, especially those that measure the activity in the brain on exposure to given substances, this is another example that both contradicts and shakes confidence in the INSPQ report.

Moving on to the substance of the disagreement on the role of chemicals and how this can be understood in neurobiological terms, we want now to build on our initial discussion, calling upon Molot's elucidation of the factors that link the neurology of MCS to chemical exposures, including from chemicals emanating from everyday products, and how these exposures affect the brain as well as other organs and tissues.

Molot (2021) notes that the "most common route of exposure is through inhalation. Because most VOCs are lipophilic (oil soluble) they are easily absorbed from the lungs"(p. 2) – though for clarity, we need to add, other routes are also possible. Whatever the route, "VOCs are transported by the arterial blood to tissues throughout the body."(p. 2) "Lipophilic VOCs can quickly accumulate in the brain and can affect function." (p. 3) [emphasis added]. In keeping with what we know of biological individuality, Molot goes on to say, their "impact may be significantly affected by variables, like age, sex, genetics, physiological condition, or lifestyle." (p. 3)

The role of oxidative stress and its relationship to extrinsic agents is considered by many to play a very important part in adverse effects of pollution more widely (e.g. Mudway et al. 2020). Molot highlights the important role of oxidative stress, in MCS as well as other diseases:

> Given the compositional complexity of the cocktail of pollutant gases and particles we breathe from both ambient and indoor sources, there is scientific consensus that oxidative stress is an integrative biological pathway that bridges the causal gap between cause (the initial molecular trigger) and effect (adverse health outcome).- What this means is that oxidative stress helps to explain how pollution exposures, which eventually result in damage to cells, contribute to the development of environmentally linked diseases, including MCS . . . (Molot, 2021, p. 3)

Molot points out that, as discussed in Part 2.5.3, "TRP receptors were barely acknowledged and inadequately considered,"(p. 4) yet, "TRPV1 and TRPA1 sensitization has been consistently and

repeatedly demonstrated in MCS." (p. 6) He covers a lot of territory in the following quote in which he explains that while the INSPQ report reviews

> hypotheses regarding altered neural plasticity, mechanisms that lead to disturbances that affect the state of individuals and cause mood disorders, mediators of change and the hippocampus, [the report] fails to engage the literature demonstrating the role of pollution exposure, oxidative stress, systemic inflammation and the TRPV1 and TRPA1 receptors in synaptic plasticity and brain excitability. The [INSPQ] authors did not mention that these receptors exist in the structures involved in neural plasticity. They also did not review the association of TRPV1 receptors with fear, anxiety or stress. These are the same receptors that have been shown to be sensitized in MCS. . . .(p. 6)

As we have previously mentioned, Molot concludes that "[t]he position of the INSPQ that VOCs do not enter the brain is wrong," (p. 8) and that "absence of any significant literature review on TRPV1 and TRPA1 receptors has contributed to biased conclusions." (p. 8)

As a reminder, the 2021 Alberta MCS report did include and describe literature on the TRP channels and the role of these receptors in the research they ranked as most consistent and must useful on MCS (see our Part 2.5.3). This is an additional affirmation that the neglect of this topic in the INSPQ report is highly consequential.

Another recent article (Molot et al. 2021), also previously cited, takes a deeper dive into these matters. "Neurological susceptibility to environmental exposures" provides a more detailed explanation of the way that pollutants impact brain health in both neurodegeneration and MCS, again raising issues that were omitted or analyzed outside of a chemical causation framework in the INSPQ report. The abstract reads in part:

> Significant long-term airborne exposures can contribute to oxidative stress, systemic inflammation, transient receptor subfamily vanilloid 1 (TRPV1) and subfamily ankyrin 1 (TRPA1) upregulation and sensitization, with impacts on olfactory and trigeminal nerve function, and eventual loss of brain mass. The potential for neurologic dysfunction, including decreased cognition, chronic pain and central sensitization related to airborne contaminants, can be magnified by genetic polymorphisms that result in less effective detoxification. Onset of neurodegenerative disorders is subtle, with early loss of brain mass and loss of sense of smell. Onset of MCS may be gradual following long-term low dose airborne exposures, or acute following a recognizable exposure. Upregulation of chemosensitive TRPV1 and TRPA1 polymodal receptors has been observed in patients with neurodegeneration, and chemically sensitive individuals with asthma, migraine and MCS. In people with chemical sensitivity, these receptors are also sensitized.

The highly significant import of the above analysis for this debate is that low concentrations of chemicals certainly do enter the brain, and can bring about MCS-typical symptoms. They can cause anxiety, among a host of other neurological effects, though anxiety is not singled out as exceptional in occurrence or effect. As well, Molot and colleagues show that these MCS-relevant

findings are of a larger body of research on adverse effects of common pollutants, in contrast to the conclusion that MCS science belongs in the field of anxiety and fear studies, per the INSPQ report.

### 4.5.2 Mast cell activation and chemical sensitization

Here, again with the purpose of deepening our understanding of the role of chemicals in MCS, we want to extend our discussion, begun in Part 2.5.4 of the role of mast cell activation syndrome (MCAS) with Miller et al.'s (2021) hypothesis that mast cell activation may be an important underlying mechanism for chemical intolerance.

MCAS is not an alternative diagnosis to MCS (or, in Miller's terminology, TILT) but an overlapping or accompanying one in any given individual. It is illuminating to see the way that Nathan (2018, previously cited), a long-time clinician who works with very serious cases of chronic, environmentally-linked illnesses, describes MCAS symptoms (pp. 99-114).

- intense anxiety and depression;
- severe pain that can localize to joints, muscles, tendons, and bones;
- unusual neurological symptoms, like numbness and tingling in different parts of the body, paralysis, and pseudoseizures;
- headaches;
- ringing in the ears (tinnitus);
- sensitivity to a wide variety of stimuli, such as light, touch, sound, smell, food, chemicals, and electromagnetic fields;
- sore throat;
- swollen lymph glands;
- indigestion, including diarrhea, constipation, bloating, gas, distension, and heartburn;
- chronic, debilitating fatigue;
- insomnia;
- cognitive difficulties, including brain fog and decreased memory and concentration;
- pelvic pain;
- interstitial cystitis;
- shortness of breath;
- air hunger [need for and difficulty in obtaining sufficient air];
- skin rashes; and
- difficulties with equilibrium and balance.

Of this disturbingly long list of symptoms, Nathan writes:

> The most obvious response to someone who presents with such a broad array of symptoms is to think, "No one could have all these symptoms, they must be in your head." It should not come as surprise that the vast majority of these unfortunate individuals are treated as if this litany is psychosomatic and dismissed with a prescription for an anti-depressant or ant-anxiety drug and a clear message: "I can't help you. You

> need a good psychiatrist." . . . [Untreated,] years pass. The patients do not get much better, in fact they often get worse. . .. . . I want to emphasize that mast cell activation is a real, physiological process [that is] frightening, chaotic, random and very hard to deal with. (Nathan, 2018 p. 103)

What lies behind this difficult reality?

Recall from our earlier discussion of mast cells and the findings of Miller et al. (2021) that many mast cell mediators have "potent but short-lived effects. They are released locally in sensitized tissues and are exquisitely thermolabile, posing major challenges for measurement." Mast cell mediators

> produce multi-system inflammation at minimum, and not uncommonly allergic-like phenomena, and sometimes aberrancies in growth and development (typically benign) in virtually any tissue. (MCAS, TILT, and the nervous system, paragraph 1)

Recall too that activated mast cells are "immunologic 'first responders'", that can "initiate, amplify, and prolong wide-ranging neuroimmune [50] responses."(MCAS, TILT, and the nervous system, paragraph 2)

Very significantly, the Miller et al. article provides insight into how MCS can be both a neurological and immunological disease process at the same time. This quote is worth repeating from our discussion on mast cells in Part 2.5.4.

> Several investigators have pointed to neurogenic inflammation as a mechanism for [chemical intolerance] [10, 51-53]. Rather than being the mechanism for [chemical intolerance], neuroinflammation may be the consequence of [mast cell activation] and mediator release initiated by xenobiotic/chemical exposures. MCs affect neural function via their released mediators which bind with specific neuronal receptors [18. 54]. Also, [mast cells] physically abut neurons in many tissues. Wherever such dyads are present, there is constant mediator "cross-talk" between the two cell types. Thus, MCA can provoke nearby neurons, inducing their associated symptoms; similarly, neurons can provoke nearby [mast cells], inducing their associated symptoms. . . . (MCAS, TILT and the nervous system, paragraph 2)

The article then focuses in on how specific chemical classes – in the below case, organophosphate chemicals – impact neurology, including specific regions of the brain to which the INSPQ report attributes a central role in anxiety, and how such chemicals can produce the "package of neurological effects" to which we have several times referred.

> Both MCAS and TILT/[MCS] have prominent neurological features. For example, organophosphate pesticides, which bind irreversibly to cholinergic receptors in the parasympathetic nervous system, appear to be among the most severe and permanently damaging TILT/[MXS] initiators. Correspondingly, organophosphates have been shown to

> trigger degranulation in human and animal [mast cells]. The parasympathetic nervous system also modulates [mast cell] activity via a cholinergic pathway [64]. [Mast cells] play pivotal roles in regulating cerebral blood flow[65], directly affecting brain function. Notably, both MCAS and TILT patients commonly report cognitive difficulties which may be the result of reduced cerebral blood flow due to chemical exposures, such as vehicle exhaust or pesticides [66]. Brain [mast cells] lie close to cerebral blood vessels, nerves, and the meninges, and inhabit the area postrema, choroid plexus, thalamus, hypothalamus, and limbic system, thus affecting memory, mood, and concentration. [Mast cells] can migrate between nerve tissue and lymphatics and appear to contribute to neuroinflammation in many disorders [67-69]. (MCAS, TILT and the nervous system, paragraph 4)

MCAS can very clearly account for all the neurological symptoms in MCS, and this includes affective or mood impacts. In MCAS – again, take note – it is the encounter with chemicals, even at very low concentrations, that sets off the mast cell reaction, not anxiety, even if anxiety is included in the inventory of MCAS effects.

Moreover, as Miller et al. explain, there is a strong explanatory feature of mast cells that accounts for the worsening effect of stress—a major causal factor according to the INSPQ report and others—in chemical intolerance.

> Notably, during stress, corticotropin-releasing factor is secreted by the hypothalamus, and, together with neurotensin, triggers [mast cells] to release inflammatory and neurotoxic mediators, thereby disrupting the blood-brain barrier leading to neuroinflammation.[70] Referring to ADHD, Song et al. [55] cite increasing evidence that [mast cells] are involved in brain inflammation and neuropsychiatric disorders. Selective release of inflammatory mediators by [mast cells], interacting with glial cells and neurons, may activate the hypothalamic–pituitary–adrenal axis and disrupt blood-brain barrier integrity. (MCAS, TILT and the nervous system, paragraph 6)

We will return to the important question of stress in Parts 7 and 8.

Meanwhile, it is time to begin looking at the implications of these analytic findings for clinical practice. With respect to MCAS, understanding its causes can help to understand what measures may improve it, which is what really counts for sick individuals and their physicians.

Nathan's explanation of MCS, entirely within a clinical framework, now draws in the critical matter of chronic and undetected infections, a matter we will soon take up:

> Mast cell activation is often triggered by mold toxicity and/or infections like bartonella and Lyme disease, as well as a wide variety of viral infections. Many patients have a genetic disposition to mast cell activation, but whether or not it ever manifests in their lifetime depends to a large extent on their exposures and how well their immune systems function. . . . It is not rare. While we have only recently begun to understand it, it is

> estimated that mast cell activation may be present to some extent in up to 10 percent of the population. I would estimate that 50 percent of my ultrasensitive patients have a mast cell activation component. (Nathan 2018, p. 103)

Nathan and other complex, environmental disease physicians use laboratory tests to identify the physical and toxicological stressors that have activated the mast cells, as well as tests for MCAS as such, and then treat what they find through appropriate modalities.

Miller et al. (2021) write that while "trigger identification and avoidance, rather than medications, are . . . the first steps for managing MCAS" nevertheless, "medications or desensitization procedures benefit many MCAS patients [31]". (Assessing and treating TILT/CI) Along with environmental medicine as a whole, the Miller team addresses food sensitivities as very important in treatment.

> Both TILT[/MCS] and MCAS patients report adverse reactions to foods. Most of these adverse food reactions are *food intolerances,* as opposed to immunoglobulin-mediated *food allergies,* e.g., to peanuts, discoverable through skin or blood testing. The gold standard for identifying food intolerances involves the rigorous elimination of suspect foods for 4 to 7 days, followed by judicious reintroduction of single foods, one at a time, under close medical and dietary supervision. We recommend assistance from dieticians who understand food intolerances, food addiction, and elimination diets. Note that foods themselves may be triggers, but food additives and chemical residues on foods also are frequent triggers. Many CI patients opt for organic foods where available and affordable. (Dietary interventions, emphases in original)

In addition, Miller et al. offer pharmaceutical suggestions:

> After trigger identification and avoidance strategies are implemented, potential medical interventions for CI may include many of those used to treat MCAS, including agents that prevent MC degranulation like cromolyn and/or reduce tissue inflammation caused by MC mediators, such as H1 and H2 antihistamines administered *simultaneously* [31, 32, 76, 77]. Patients who respond adversely to excipients in commercially available medications may require compounded formulations. Interestingly, low-dose benzodiazepines help some MCAS patients due to the presence of benzodiazepine receptors on not only neurons, but also MCs [78, 79]. Pharmacotherapy for TILT/CI is by no means simple and requires minimizing exposures to chemicals known to precipitate adverse reactions and monitoring for inadvertent introduction of known triggers into the patient's regimen, such as when a different formulation is provided as a refill. These same challenges exist for MCAS patients. (Medical interventions, emphasis in original)

We will return to mast cells in Part 5, devoted entirely to lessons from the clinical experience.

## 4.6 COMMON CHEMICALS IMPACT ON NEUROLOGICAL/"MENTAL" HEALTH

We want to pause the MCS specific discussion here for a moment and broaden out what is known about the effects of common chemicals such as heavy metals, pesticides, PCBs, vinyl chloride, phthalates, PBA and more in terms of their impact on mental health, or perhaps better put on neurological health. For the central tenet of the INSPQ report is that at "normal concentrations" – clearly, an increasingly vexed and imprecise formulation – these and other chemicals are harmless and can't affect the brain sufficiently to account for MCS signs and symptoms. But this is not true.

In addition to the mechanisms we have just discussed, we want to offer for consideration the 2008 16-page fact sheet by the Collaborative on Health and the Environment's Learning and Disabilities Initiative "Mental Health and Environmental Exposures."[26] The authors open by writing:

> This fact sheet discusses the connections between environmental exposures to physical and chemical agents and mental health symptoms and conditions. While many of us recognize that environmental exposures to toxic substances can lead to disease, disability and other medical conditions, the connections to psychiatric conditions are not as well-known. However, there is a substantial amount of scientific evidence that certain exposures can lead to both temporary and long-term psychiatric symptoms and illnesses.

In this fact sheet, [there is] a summary of what is known about the connections between these substances and mental health symptoms, the most common sources of exposure, and ways that you might reduce or prevent these exposures.

What is particularly useful about the format of the fact sheet is that it provides a number of charts that list the neurological/"psychiatric" symptoms on one side, and the sources of exposure for the given chemical on the other, showing both the breadth of the symptomatology and the ubiquity of exposure sources. In this way, it provides invaluable information on heavy metals (lead, mercury, aluminum, arsenic, manganese, thalium and tin), pesticides of several kinds, solvents, toxic gases, PBBs and PCBs, and other chemicals and compounds, including alcohol and recreational drugs, tobacco, boron, carbon dioxide, vinyl chloride, endocrine disruptors, food additives and ionizing radiation – all substances that have been identified (as we shall see even more clearly in Part 5) as problematic in MCS.

What emerges from this aggregation of information is the clear and profound neurotoxicity of these chemicals as we encounter them in the environment, in many different ways. What also emerges is that the neurological symptoms – affective, cognitive, neuro-motor and more – that environmental physicians have ascribed to MCS are all to be found in these lists, and that the

[26] The Collaborative on Health and the Environment (CHE) is an international partnership, founded in 2002 at Commonweal, committed to strengthening the scientific and public dialogue on environmental factors linked to chronic disease and disability. https://www.commonweal.org/program/che/

psychiatric symptoms ascribed by the INSPQ report, including anxiety, somatization and personality change/disorder above all, are also to be found. This strongly suggests that the hypothesis that within MCS's neurological symptoms, linked to chemical exposure, include, anxiety it should not be privileged as causal within the larger basket of neurological reactions. This is a much more accurate account than the INSPQ report's, and the view of the psychogenic school more generally, that anxiety and psychological disorders are the generative problems in MCS, not chemicals.

Take for example, this chart for mercury. When environmental physicians test for mercury, often using a DMPS chelation challenge and 24-hour urine collection method, they frequently find abnormally high levels of mercury in MCS patients, and mercury has certainly been shown to be neurotoxic. Note with mercury the symptom of anhedonia is listed, not a symptom discussed in MCS clinical findings, but identified by the INSPQ.

**Mercury**

| Symptoms | Sources of Exposure |
|---|---|
| abusive language<br>academic decline<br>anhedonia<br>anxiety/nervousness<br>apathy<br>crying<br>depression<br>excessive embarrassment<br>excitability<br>explosive speech<br>fatigue<br>hallucinations<br>inability to take orders<br>insomnia<br>irritability<br>loss of libido<br>memory loss<br>mood lability<br>nightmares<br>paranoia<br>personality change<br>phobic avoidance<br>poor attention<br>poor concentration<br>shyness<br>social withdrawal<br>suicidal/homicidal<br>timidity<br>violence | fish or shellfish contaminated with methylmercury, especially shark, swordfish, king mackerel, tuna, sea bass, Gulf Coast oysters and others<br>vapors in air from spills, incinerators or industries that burn mercury-containing fuels, including coal<br>dental work and medical treatments<br>some substances used in folk or religious rituals<br>release of mercury from dental work and medical treatments<br>latex paint made before 1990<br>**Occupational exposures:**<br>contaminated workplace air or skin contact during use in dental services, health services, chemical and other industries that use mercury |

Taken from: Fact Sheet "Mental Health and Environmental Exposures" *Collaborative on Health and the Environment*, Learning Disabilities Initiative (2008)

Now, consider the chart for pesticides encountered in agricultural and horticultural work, and almost universally in the food most of us eat. Note here the appearance of "personality change", also featured in the INSPQ account.

**Pesticides and Symptoms**

**CH Insecticides**
academic decline
agitation
anxiety
confusion
depression
fatigue
hallucinations
insomnia
irritability
loss of libido
memory loss
mood lability
nervousness
nightmares
personality change
poor appetite
somatic complaints

**Methyl Bromide (Fumigant)**
anxiety
apathy
confusion
decreased libido
delusions
depression
euphoria
hallucinations
homicidal/suicidal ideation
hypersomnia
impotence
insomnia
irritability
mania
melancholia
neurosis
paranoia
poor concentration
violence

**OP Insecticides**
academic decline
anxiety
apathy
change in libido
confusion
depression
dissociation
excessive dreaming
fatigue
giddiness
hallucinations
hyperactivity
insomnia
irritability
memory loss
mood lability
nightmares
paranoia
poor appetite
poor concentration
restlessness
somatic complaints
suicidal ideation

**Carbamates**
confusion
irritability
memory loss
mood lability

Taken from: Fact Sheet "Mental Health and Environmental Exposures"
*Collaborative on Health and the Environment*, Learning Disabilities Initiative (2008)

These charts – only two of 19 in total – speak volumes in themselves. We hope they convey something of the magnitude of the impacts the chemical age has inadvertently, but nevertheless extensively had on our brain health lives, including in producing disorders that psychiatry and the INSPQ report commonly consider psychogenic. MCS is part of that impact. Readers who can search out this resource and who can take the time to read through all these lists, will gain an even greater understanding of this overarching issue, so relevant to our understanding of MCS specifically.

## 4.7 THE ROLE OF CHEMICALS IN ONSET

Now we wish to turn briefly to the problems in the INSPQ-report with respect to toxicological issues in onset.

Let us begin with the INSPQ report's assertion that the vast majority of MCS subjects cannot associate MCS onset with any given chemical exposure (p. 289[27]). This claim undermines the association of MCS with chemicals, but we do not accept its veracity. As Molot (2021) observed in his short-form critique of the INSPQ report,

> According to the INSPQ report, the proportion of subjects able to specifically identify a chemical exposure episode as a trigger for their MCS is rarely higher than 30%. It is not clear where this statistic was obtained, and it is not consistent with clinical experience.
>
> Many published papers report the onset of MCS following recognized or well-defined chemical exposures including indoor air contaminants caused by new construction or renovation of a home or office (63.2%), exposure to various solvents and cleaners (54%), indoor air contaminants (45%), followed by exposure to pesticides or agricultural chemicals (27.4%), and exposure to chemicals at work or engaged in hobbies (26.3%). (p. 5)

This accords with our qualitative research, with historical experience including in Canada, (for example, at the Nova Scotia Camp Hill hospital 1987-1993, that turned into a group poisoning event [Jones, 1992]), and with ongoing reports from our community: the great majority of MCS sufferers are able to identify the triggering chemical exposures that were involved in onset (initiation) or in deterioration from one stage to another. In the study we conducted (Burstyn & MEAO, 2013), participants reported on sharp, intense exposures or on longer processes at onset, but all could remember chemical involvement:

> It all happened as a result of exposure to incorrectly mixed adhesive chemical to repair a windshield in my vehicle. I started getting symptoms within about 15 minutes of being in my vehicle. Things started to go weird and life . . . went to hell in a hand basket. . . . It wasn't until I saw Dr. B. that she diagnosed the FM and chemical sensitivity and the toxic brain injury. Sandra (MCS, FM, Appendix 3)

> It's been about half my life that I have had chemical sensitivities, multiple chemical sensitivities. . . . I think what happened was when I was young, I had a major inner ear infection. Then I went to the hospital; I had surgery; I had tubes put in and I had them taken out. Then I started having the asthma attacks in the fall. Then when I was in my early 20s—I was in nursing school actually—that's where it started. I started to have

[27] Toutefois, dans les études épidémiologiques de type descriptif, la proportion des sujets capables de précisément identifier un épisode d'exposition chimique comme facteur ayant déclenché leur SCM est rarement supérieure à 30% (voir chapitre 3 "Épidémiologie de la SCM").

> reactions to chemicals and perfumes and things around—the cleaners and stuff. I couldn't even continue in the class. I had moved to Montreal, and there I found out that it could be this multiple chemical sensitivities. Petra (MCS, Appendix 3)

Further, Masri et al. (2021)'s already discussed sweeping study in patterns in initiation of chemical intolerance among eight groups of people experiencing exposures to a variety of chemicals, in different circumstances, clearly demonstrates key links between certain types of chemical exposures and the development of MCS among a subset of those exposed. It is worth repeating the groups reported: people working at the EPA headquarters during renovations, Gulf War veterans, casino workers exposed to pesticides, workers exposed to aircraft oil fumes, people directly involved in the World Trade Center tragedy, women with surgical implants, people who live in moldy environments, and tunnel workers exposed to solvents.

However, the key point must inevitably be that whether individuals can remember the chemical(s) involved in onset or not, in group events there is an objective pattern not dependent on individual recollection. In individual cases, there are many objective tests to determine what chemicals have been encountered – if only an individual can access these tests, not possible today through our health care systems.

Also worth noting in a discussion of patient awareness of triggering chemicals is that onset and transition to a chronic state can be very traumatic. Whether over a period of time or suddenly, and sometimes with extreme severity, people find themselves sick in all the environments in which they had previously lived, worked, studied and played. In the process of figuring out what has happened to them if they cannot remember one agent, they note what specifically triggers their new symptoms, which, they discover, are specific chemicals, at trace levels or more. They also note that without those triggers, they can function normally. Once that learning has taken place it becomes a matter of logic and prudence, not neurosis, to avoid exposure to such substances.

Those lucky enough to consult with physicians who understand MCS and the consequences of exposure in it have this learning reinforced when told that avoidance of their chemical incitants is a critical part of stopping their decline and stabilizing.[28] That the emotion of fear, possibly involuntary but not illogical, of such substances comes into play in anticipation of similar exposures in any number of the daily settings that people with MCS must navigate is a reasonable reaction to a dangerous and threatening situation. We return to this issue in Parts 7 and 8.

The INSPQ report's interpretation of the data on initiation, the lack of attention given to onset and the role of chemicals in it are yet more problems that undermine confidence in the report's conclusions.

[28] See our earlier comments, in Part 3, about the difficulty of practising in this area of medicine.

## 4.8 CHEMICALS AND REACTIVITY DEMONSTRATED IN A 2021 EMPIRICAL STUDY

Finally, to these technical neurological and immunological discussions, we want to offer a simple, empirical and recent study by Perales et al. (2022) "Does improving indoor air quality lessen symptoms associated with chemical intolerance." These authors report on an experiment to determine whether identifying and then removing volatile organic compound–producing products, such as cleaners and fragranced personal care items, would improve symptoms of chemical sensitivity.

A primary care practice allowed the research team to screen patients for chemical intolerance using the Brief Environmental Exposure and Sensitivity Inventory (BREESI), followed by the Quick Environmental Exposure and Sensitivity Inventory questionnaires (QEESI).[29] People identified as intolerant typically reported "symptoms such as headaches, fatigue, 'brain fog,' and gastrointestinal problems—common primary care complaints"(Abstract, Aims)

The researchers stated that "substantial evidence suggests that improving IAQ (indoor air quality) may be helpful in reducing symptoms associated with CI [chemical intolerance]" (Abstract, Background). This motivated their offer of an environmental house call to first perform an independent volatile organic compound inventory of indoor air, and then to remove any products thought to contribute to unhealthy levels. They found clear results: some people with chemical intolerance improved, but others did not. Perales et al. found that

> the improvements were based upon decreased airborne [volatile organic compounds] associated with reduced use of cleaning chemicals, personal care products, and fragrances, and reduction in the index patients' symptoms. Symptom improvement generally was not reported among those whose homes showed no [volatile organic compounds] improvement" (Abstract, Findings).

The authors explained that when initially interviewed, the participants had not considered their homes to be problematic. They were surprised by the results.

It is worth noting that the experiment validated the use of the chemical sensitivity screening tools by primary care providers, and the importance of putting indoor air issues into doctor's normal differential diagnosis process. According to one of the study's conclusions,

[29] The Quick Environmental Exposure and Sensitivity Inventory, as noted in the Perales et al. study, is a validated, self-administrable questionnaire that helps differentiate chemically intolerant individuals from the general population. It has been long used in MCS and other chemical intolerance studies and is referred to in the INSPQ report. The Brief Environmental Exposure and Sensitivity Inventory is a more recent tool developed for screening purposes. The three-question survey asks about adverse reactions to chemical inhalants, foods/food additives, and drugs/medications. Its use for screening purposes and has been validated in a couple of previous studies.

> indoor air problems simply are not part of most doctors' differential diagnoses, despite relatively high prevalence rates of [chemical intolerance] in primary care clinics. Our three-question screening questionnaire—the BREESI—can help physicians identify which patients should complete the QESSI. After identifying patients with [chemical intolerance], the practitioner can help by counseling them regarding their home exposures to [volatile organic compounds]. The future of clinical medicine could include environmental house calls as standard of practice for susceptible patients. (Abstract, Conclusion)

For us, the takeaways from the Perales study are as follows. First, chemical intolerance, even if not yet full-blown or early-stage MCS, can be identified objectively, and it can be improved by reducing the burden of volatile organic compounds in the indoor residential air environment. In this experiment, the sources of such compounds were removed, and improvement followed. Physicians can easily incorporate assessment tools into their practice, and can prescribe proactive VOC reduction.

We now put forward the key question relative to the INSPQ conclusions: Given the improvement in reactivity, did the team also remove anticipatory fear and chronic anxiety? They would have had to do so in order for their results to align with the INSPQ report's conclusions. And if they did not remove fear and anxiety, then the simplest explanation for participants' improvement is the right one: the responsible chemicals were taken away and the symptoms improved.

# PART 5: LESSONS FROM THE CLINICAL EXPERIENCE

# PART 5: LESSONS FROM THE CLINICAL EXPERIENCE

## 5.1 KEY CLINICAL ISSUES NEGLECTED OR OMITTED IN THE INSPQ REPORT

The issues raised so far by this commentary seriously undermine confidence in the INSPQ report's conclusions, affirming a number of possible, plausible and not necessarily exclusive neurobiological mechanisms, and broadening out to examine the adverse health effects – and especially the neurotoxic effects, since this is the most contested matter – of common chemicals, even at normal concentrations. But as we have pointed out before, the MCS picture is often complex and additional factors that overlap and/or feed into those just discussed must also be part of the picture when understanding the causes and mechanisms – and hence, the all-important treatment for MCS.

There is no way around the following challenge: The answers needed to understand and care for MCS today cannot be found only in the peer-reviewed journals or grey literature, because the clinical experience and the experience of patients is so scantily represented there. In the steadily growing body of practice embodied in the curricula of a number of medical associations, including the previously referenced American Academy for Environmental Medicine and the International Society for Environmentally Acquired Illness, a set of parameters that clinicians investigate as part of the process of diagnosing people with chemical sensitivities and treating them if the results indicate abnormalities has evolved.[30] This must be brought into the present discussion. It appears to have found no place in the INSPQ report.

What this body of practice has found and this is reflected in its educational offerings is that MCS is truly a complex illness and that all the elements of a patient's biological individuality must be identified through hard evidence via clinical testing, after which appropriate interventions must be undertaken. It is this complexity, the paradigm shift in how to clinically address this complexity and the connection to chemical stressors that the INSPQ report has dismissed, opting instead for a reductionist and, therefore, erroneous explanatory account.

As part of this broader account, consider this description translated [31] from the INSPQ report:

> People who suffer from MCS usually have normal medical and biochemical evaluations (aspects covered in the previous chapters), there are therefore no screening

[30] A good compendium of these can be found in Nathan, 2018.

[31] Original French language text: Les personnes qui souffrent de SCM on généralement des evaluations médicales et biochimiques normales (aspects traits dans les chapitres precedents), il n'y a donc pas d'examens de dépistage sur lesquels compter pour poser un diagnostic (Labarge et McCaffrey, 2000). De plus, les symptoms manifestés, les facteurs de risqué, les comorbidities et les prognostics sont similaires et sont communs á de nombreux troubles mal defines comme la fatigue chronique, la fibromyalgia, le syndrome des bâtiments malsains et le syndrome de la guerre du Golfe (Bell, Baldwin, et Schwartz, 1998; Buchwald et Garrity, 1994; Clauw, 2001; Fiedler, Kipen, Deluca, Kelly-McNeil, et Natelsom, 1994; Ford, 1997). Sur le plan clinique, il s'agit donc d'un diagnositic d'exclusion (diagnostic posé après un investigation clinique servant à exclure toute autre affection pouvant expliquer les symptoms) qui est basé uniquement sur l'histoire du sujet. pp. 628, 629.

> examinations to rely on for a diagnosis (Labarge & McCaffrey, 2000). In addition, the symptoms manifested, the risk factors, co-morbidities and prognoses are similar and are common to many ill-defined disorders such as chronic fatigue, fibromyalgia, sick building syndrome and Gulf War syndrome (Bell, Baldwin, & Schwartz, 1998; Buchwald and Garrity, 1994; Clauw, 2001; Fiedler, Kipen, Deluca, Kelly-McNeil, and Natelson, 1994; Ford, 1997). Clinically, this is therefore a diagnosis of exclusion (diagnosis made after a clinical investigation to rule out any other conditions that may explain the symptoms) that is based solely on the story of the subject. (Chapter 10, Psychogenic Hypothesis, Case Definition, pp. 628, 629)

This is another example of the distorted presentation of key information about MCS, and manages in one stroke to pull a curtain over the invaluable acquisitions of the clinical experience. It is true that there is no one biological marker so far found that can say, "this patient has MCS," and that, given what we do test for in our physician's offices today, individuals may show "normal medical and biochemical evaluations." However, as we have repeated, it may be that we will always need to look for multiple signs to actually paint an accurate picture of each biologically unique individual, and so to altogether omit the methods that are in use every day in the offices of environmental physicians to identify these signs is thoroughly misleading and irresponsible.

We have already discussed, for example, the role of genetic polymorphism testing as one of those methods – to be further investigated, true, but already in frequent use in practice to help identify substances (chemicals and medications, especially) with which a person may have particular problems, and to show what detoxication and other metabolic issues need support. We also have the findings of Dominque Belpomme et al. (2015) on 521 patients with EHS, 52 with MCS, and 154 with both EHS and MCS. They found that

> Our data strongly suggest that EHS and MCS can be objectively characterized and routinely diagnosed by commercially available simple tests. Both disorders appear to involve inflammation-related hyper-histaminemia, oxidative stress, autoimmune response, capsulothalamic hypoperfusion and BBB opening, and a deficit in melatonin metabolic availability. (Abstract)

All these disorders, all making sense of multiple symptoms, can be tested for with conventional methods, which Belpomme lists. But it happens that these tests are never performed, and never thought to be performed, in Canadian physician's offices. If you don't test for an issue, you will not find it. This does not mean it is not there.

So, at this point, we want to present some of the best known of the factors environmental medicine has identified and included in a check list of issues repeatedly found, some or all, to be involved (for the vast majority of patients) in their development of chemical intolerance. Out of a larger field, we have selected to discuss:

- heavy metal and toxic chemical body burden

- how gastrointestinal/gut health is affected by chemicals
- the role of brain and nerve injuries in chemical sensitization
- chronic bacterial, viral, fungal and parasitical infections and sensitization
- mold and mycotoxin illness
- numerous immunological factors

Again, the majority of the tests being used to measure these issues, all of them scientific, are either unknown to our physicians and/or more advanced than those we employ and/or unpaid by our public systems, so never called upon.

Finally, the most important of all, this also gives the lie to this statement: "Clinically, this is therefore a diagnosis of exclusion (diagnosis made after a clinical investigation to rule out any other conditions that may explain the symptoms) that is based solely on the story of the subject." To imply that the screening questionnaires and detailed medical and exposomics histories taken by physicians are simply the (implied: unreliable) "story of the subject" is another tactic of trivialization, of both patient and physician. We urgently need to move beyond this approach and grasp the valuable tools already available to us to help people and doctors as they deal with MCS.

## 5.2 HEAVY METAL AND TOXIC CHEMICAL BODY BURDEN

We have previously noted that the body burden of toxicants has been identified by environmental physicians as critical to the health status of their patients. To begin by restating the obvious, though: if physicians do not test for toxicant load they will not find it. In this matter, as in others in the clinical experience, dismissing the existence of body burden without doing the most accurate testing invalidates a claim that this is not an important or even present issue. And of course, not testing is harmful to patients, because absent or erroneous results will lead to failure to treat appropriately.

And so, to the main point here: when individuals carry a high body burden (e.g., heavy metals, pesticides, phthalates, biotoxins), they are at greater risk for all kinds of illness, including MCS; and once they become sensitized, if their bodies cannot hold any more toxicants and still maintain health and homeostasis, even trace amounts can set off the toxicity alarm. It is worth repeating Rea's (2016) dictum from his list of principles:

> Total body pollutant load (sum total of pollutants in the body) . . . when the body's pollutant load stays too high, it can trigger or exacerbate chemical sensitivity. (Principle 1)

The body burden of heavy metals and chemicals is measured through, as appropriate, urine and blood tests, and/or biopsies (again, usually via more accurate and different tests than we offer in our publicly funded primary care system).

The understanding of the adverse effects of heavy metals extends, of course, far beyond MCS. For example, the great Herbert Needleman, a psychiatrist turned crusader on the neurotoxic impacts of lead, in work beginning in the 1970s, showed that this metal harms brain health as well as other organs and tissues once ingested (Anson. W., 2017), causing behaviours previously thought psychogenic. Since then, a whole body of study has developed to address other metals, including mercury, cadmium, arsenic, aluminum and manganese, culprits often testing positive among MCS patients as well.

Equally, we have come to understand that a burden of toxic chemicals—for example, fluoride, chlorpyrifos, DDET/DDE, tetrachlorethylene, polybrominated diethyl esters, toluene, ethanol and polychlorinated biphenyls (PCBs), to name only some—bioaccumulate in many people and harm many aspects of health, including brain health (Dick, 2006). Chlorpyrifos, for example, has recently been found to disrupt acetylcholine metabolism across the blood-brain barrier, a barrier found to be damaged in many people with MCS and heavily implicated in MCAS (Miller et al., 2021; Belpomme et. al, 2015).

Therefore, determining the presence of persistent toxicants must be part of the clinical program for MCS. The chronic anxiety that plays such a central role in the INSPQ report causation theory can be created or greatly exacerbated by such a body burden, quite independently of "personal temperament" and "psychosocial history" (INSPQ terms) as we explain in Part 7 and by our reference from the Collaborative in Health and Environment, (2008).

It is worth restating the while anyone can suffer from the adverse effects of a toxic body burden, mothers with such a burden involuntarily transmit it via cord blood and breast milk to their infants, who must start out life already handicapped in a variety of possible ways as a result (Perera et al., 2005; Mitro et al., 2015; Rauh et al., 2012). MCS mothers, as we have seen, have higher rates of children with autism and ADD (Heilbrun et al., 2015), as well as chemical sensitivity.

It is not always possible to rid the body of sufficient toxins to effect resolution of MCS and other symptoms, but often improvements can be achieved. For decades environmental health physicians have been developing approaches that seek to reduce this body burden sufficiently to effect improvement, whether in MCS in adults or, for example, in children and youth who are struggling with second generation toxicity and its effects. These modalities range from infrared sauna depuration to IV and oral chelation (Rae, 2016) and to supplementation with nutrients that help the body both expel and repair damaged tissue.

## 5.3 HOW GASTROINTESTINAL/GUT HEALTH IS AFFECTED BY CHEMICALS

Accumulated heavy metals, pesticides, micro-plastics, and some pharmaceuticals (especially antibiotics) are among the chemicals that affect digestive health and create gut bacterial

dysbiosis, which then interferes with many functions.[32] These disturbances have been described in many places, but recently, in "The Impact of Environmental Chemicals on the Gut Microbiome," published in *Toxicological sciences."* Chiu, K et al. (2020) write:

> Herein we summarize the current knowledge on major classes of environmental chemicals (bisphenols, phthalates, persistent organic pollutants, heavy metals, and pesticides) and their impact on the gut microbiome, which includes alterations in microbial composition, gene expression, function, and health effects in the host. We then discuss health-related implications of gut microbial changes, which include changes in metabolism, immunity, and neurological function." (Abstract)

All the "health-related implications of gut microbial changes" that Chiu notes are involved in MCS.

Further, when dysbiosis affects the permeability of the gut, accumulated chemical load can also affect the integrity of the blood-brain barrier and other aspects of brain health, including the production of serotonin. As Tang et al. (2020) note

> Based on our description and summarization of the effects of the gut microbiota and its metabolites on the nervous, endocrine, and immune systems and related signaling pathways and the resulting destruction of the [blood-brain barrier], we suggest that regulating and supplementing the intestinal microbiota as well as targeting immune cells and inflammatory mediators are required to protect the [blood-brain barrier]" (Abstract)

As Belpomme et.al. (2015) have pointed out and the previous citation mentions, a damaged blood-brain barrier is an important marker of chemical hypersensitization.

Therefore, addressing both toxic body burdens and gut dysbiosis is very important in improving brain health so as to reduce many neurological symptoms, including anxiety and chemical sensitivity.

Indeed, functional, nutritional, and biological psychiatry – a discipline in which the apparently "emotional" is addressed by seeking out "physical" causes – today looks increasingly to interventions in gut health that directly impact the brain for the better. For example, the highly proactive approach of transplantation of a healthy gut biome (fecal transplant) into a person with mental health problems has been shown to help many patients. In a meta-study of 21 studies of this procedure, Chinna Meyyappan et al. (2020) note that

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[32] For impact of heavy metals on baby neurological health, see Houlihan, 2019. What's in my baby's food: "Summary: The four heavy metals we found in baby food have a unique significance: All are developmental neurotoxins. They can harm a baby's developing brain and nervous system, both *in utero* and after birth … All four metals are linked to IQ loss from exposures early in life. The scientific evidence spans decades and continues to build. . . These metals are so prevalent in foods eaten by babies and toddlers that every child could be exposed daily to all three of the most common heavy metals detected in food—lead, arsenic, and cadmium" (p.6).

> all studies found a decrease in depressive and anxiety-like symptoms and behaviours resulting from the transplantation of healthy microbiota. The inverse was also found, with the transmission of depressive and anxiety-like symptoms and behaviours resulting from the transplantation of microbiota from psychiatrically ill donors to healthy recipients. (Abstract, Results)

Dealing with gut health directly at the clinical level often means addressing toxic burdens and food sensitivities as well as inflammation and nutritional deficiencies, then aggressively supporting detoxification, probiotic replacement, healing diet and avoidance of gut-harming substances, such as toxic chemicals. This is an important example of the way in which symptoms that appear psychogenic and brain-situated can be treated with a physical intervention in another organ system entirely.

## 5.4 THE ROLE OF BRAIN AND NERVE INJURIES IN CHEMICAL SENSITIZATION

Other types of injury can also contribute to central nervous system sensitization and exacerbate chemical sensitivity. According to Rea (2016):

> The law of nerve injury: when the injury heals, it results in hypersensitivity to subsequent incitants i.e. scar sensitivities. The clinician often is confused about the origin of the problem. (Principle 7)
>
> Subtle or large head injury: results in memory loss; usually, short-term memory loss or episodes of confusion and imbalance may occur. Like the bacterial or viral disease, these injuries can predispose a subject to chemical sensitivity when another exposure occurs later in life. (Principle 8)

Rea further reports that with

> Butler and Didriksen at the University of North Texas [he] developed psychological profiles [of Environmental Health Clinic Dallas patients] objectively showing brain injury, not psychological conditions. Over the years, approximately 2000–3000 profiles were done; approximately 2000 showed brain injury, not psychological conditions. (Rea, 2016, psychological scan)

A brain that has been physically injured is a brain that is more prone to other disorders, including to chemical sensitization, as well as to cognitive, coordination and affective symptoms. Combine the injury with chemical exposure via body burden and/or new exposure, and an injured brain does not have the resilience of an uninjured brain. Therefore, many environmental physicians, as well as functional psychiatrists, try to determine brain health status.

This is an area that cries out for further investigation, not only for diagnosis, but to determine the most effective clinical approach. In relatively new neuropsychological approaches to MCS (and other chronic illnesses) called “limbic” or “amygdala retraining,” (discussed in more detail in

Part 8.9) success is considered to be the result of the building of new, healthy neuronal pathways that can substitute for those that are damaged and sensitized. But this approach, as we point out below, does not work for everyone. It may well be that certain types of brain injury – as well as other clinical issues such as ongoing infections – interfere with that process, in which case it would not be helpful to prescribe it, while other modalities would be sought.

## 5.5 CHRONIC BACTERIAL, VIRAL, FUNGAL AND PARASITICAL INFECTIONS

The role of acute, but especially chronic bacterial, viral, fungal and parasitical infections has been considered extremely important as a contributor to MCS sensitization, but is not taken up at all in the INSPQ report, or in the scores of trials cited by the report that test for odour reactivity and consistently posit a psychological etiology. Using both common and more precise tests than are available through our public health care systems, clinicians have found such infections in a significant proportion of patients. Rea (2016) writes that "diseases like polio or other bacteriological or virus problems can predispose to chemical sensitivity with a subsequent lighter exposure of the chemicals or mycotoxins years later" (Principle 7).

Nathan (2018) offers a detailed discussion of the most common infections found to accompany and play a part in initiating MCS (likely by producing biotoxins but possibly also via other mechanisms) as well as perpetuating it, and lists the advanced testing procedure and treatment protocols to deal with them. He explains that patients who are slow or fail to respond to the usual approaches to MCS (e.g. chemical avoidance, dietary modification and nutritional supplementation) in his practice almost always show signs of such infections. He addresses Lyme, babesia, and bartonella at length, as they have been shown to exacerbate and retard improvement from chemical sensitivities, and they are greatly underdiagnosed and undertreated. As well, mycoplasma and chlamydia have often been found. He includes viruses such Epstein-Barr, cytomegalovirus, and members of the human herpes virus in the list of usual suspects. Even parasitic infections of the nasal passages have been directly implicated, though this is a new finding that requires more investigation (Nathan, 2018). All these must be part of the issues queried during diagnosis. For if our physicians do not look for these multiple types of infections, they will not find them and will not be able to address their ongoing role in sensitization.

Nathan's book demonstrates the scope and sophistication that both diagnostic testing and treatment modalities have attained for these MCS (among other chronic environmental illnesses). It enumerates the ways in which these can be deployed to address infective agents and the damage they cause. Once again, the recurring point: It is not fear and anxiety, but biotoxicity and immune stress that cause the apparently affective symptoms of MCS.

## 5.6 MOLD AND MYCOTOXIN ILLNESS

Mold and mycotoxin illness are very rarely known to the vast majority of physicians as causative of chemical sensitivity and so almost never tested for, but they have emerged as important common disorders that often form part of a complex picture or even the main factor of

causation and retardation of recovery (Hyvönen et al., 2021). Nathan's book (2018, pp. 41-82) has an informative section on this problem, which has increasingly been found to be involved in many intractable MCS cases, and in MCAS as well.

Treatment requires the achievement of a mold-free residential environment; a very demanding requirement frequently entailing either expensive remediation and rebuilding or a new residence that is free from toxicants (found in building materials such as those made with volatile organic compounds). Additionally, depending on severity, specific pharmaceutical and nutraceutical substances that address specific molds and mycotoxins in the body need to be taken over a prolonged period of time, ranging from many months to a couple years.

Functional psychiatrists in the United States—at the Amen Clinics, for example—now routinely query and test for mold and mycotoxins and treat when appropriate, as applicable treatment has been shown to be of major importance in attenuating anxiety, depression, and chemical sensitivities in a significant number of patients (Filledi, 2021). In this regard also, this approach acknowledges that it is not fear but biotoxicity that causes the apparently affective symptoms. Nathan (2018) wrote, and note once again, the way these toxins affect the amygdala

> Ritchie Shoemaker MD . . . has published a paper clearly showing that mold toxins (and Lyme toxins, in a different way) specifically affect the area of the brain in which emotions are processed, called the amygdala. Changes in the structure of the amygdala, measured on a special MRI called the NeuroQuant, can be reversed with the proper treatment of mold toxicity with a concomitant improvement in all the symptoms of mold toxicity. What this means, in simple English, is that the symptoms of mold toxicity, even those that appear to be psychological in nature, are physical and treatable. (Nathan, 2018 p. 273)

To paraphrase and hammer the lesson home: mold toxicity causes affective symptoms that clear up when that toxicity is eliminated; affective symptoms do not cause mold toxicity.

## 5.7 NUMEROUS IMMUNOLOGICAL FACTORS ARE CRITICAL

The state of a patient's immune system has long been shown to be an important factor for clinicians, and the new field of mast cell studies reinforces this emphasis. As intake histories and symptoms indicate, however, *all* relevant components of the immune system should be tested alongside chronic infections. If there are immunologic deficiencies or syndromes, then the therapies that address those components are needed. If mast cell activation is found, treatments are available to help with this problem. If testing for chronic infections shows one or more of these issues present, the right anti-microbial drugs (antibiotics, antifungals, antivirals, and anti-parasitic drugs) along with appropriate nutraceuticals, especially for those who are intolerant of certain medications, are indicated. Other immunological interventions may also be called for, if, for example, there is a finding of hypoglobulanemia (primary or secondary) – another problem for which our primary care physicians do not adequately test. Immunoglobulin therapy is a well-established treatment for immunodeficiency disorders (Albin, S. & Cunningham-Rundles, C.,

2014). In many cases, this treatment has multi-system impacts, greatly reducing chronic infections and chemical sensitivity, increasing energy and reducing affective and cognitive symptoms. For patients with this issue, immunoglobulin therapy at appropriate intervals can rapidly achieve what years of treatment aimed at anxiety reduction never will. But at this time, MCS patients cannot access this treatment without the prescription of hospital-based immunologists, who understand nothing about MCS.

In fact, immunoglobulin replacement therapy[33] is increasingly used for mental health, meaning for people showing affective symptoms originally thought to be of psychogenic but instead found to be caused by infective agents. In 2013, Susannah Cahalan wrote about this in *Scientific American*.

If anxiety based in personal temperament is considered the sole or primary cause of MCS, these other critical physical issues are likely to remain unsought, undetected, unaddressed and unimproved. Sole reliance on blanket psychotherapeutic approaches cannot but fail many patients in whom causes for chemical intolerance are to be found in in biophysical disorders, not psychological factors.

## 5.8 PSYCHOTHERAPY AND MEDICATION FOR AFFECTIVE SYMPTOMS

We take up this issue in more detail in Parts 7 and 8, in our extended discussion of stress and anxiety. What needs to be noted here is that environmental and functional physicians are closely focussed on the mind-body relationship. If issues of anxiety and depression, or other apparently affective symptoms are present, they will seek to identify the issue and their causes. For many with MCS, the flares themselves will involve such feelings, and this should be part of the overall treatment. However, physicians will ask patients about their stress levels, and will consider issues of personal trauma and social stress as factors in their overall health picture. They understand that these factors can play an important role in undermining health in all conditions, not just in MCS, and that helping to alleviate these stressors, if possible, can greatly support improvement.

If these issues emerge as important, in addition to the medical interventions discussed above to restore health to physical functions with affective consequences, practitioners also suggest appropriate psychoneurological supports, including talk therapy, psychotropic medication (where tolerated), mindfulness approaches, and amygdala-retraining methods that seek to build new, healthy neuronal circuits in the brain. These, along with a method known as Heart Math, are all described in Nathan's (2018) book. We take these approaches up again in Part 8.9.

The critical issue to bring this part of our discussion to a close, however, is that as important as these approaches can be, they must be understood and prescribed as part of a larger program needed when chemical, infective, mycotoxic, immunological, hormonal, gastro-intestinal and

[33] "Intravenous immunoglobulin (IVIG) is … used to manage various immunodeficiency states and a plethora of other conditions, including autoimmune, infectious, and inflammatory states." Arumughan V.B., & Rayi A. (2021, Dec 12). https://www.ncbi.nlm.nih.gov/books/NBK554446/

even genetics issues have been identified. They are not a substitute for appropriate biomedical-toxicological elements of that program. A comprehensive, integrative approach that does not counterpose the mind and emotions to the body but assesses and treats all affected aspects of an MCS individual to bring the mind and body into harmony again is the key to improvement.

# PART 6: WOMEN AND MCS

# PART 6: WOMEN AND MCS

## 6.1 TOXICOLOGICAL FACTORS LINKED TO WOMEN'S GREATER SHARE OF MCS

The preponderance of women over men (70 percent plus) in MCS, internationally, is a phenomenon that begs for explanation so as to craft prevention and treatment strategies; further what it says about MCS needs to be understood in the search for mechanisms. This preponderance is clearly an expression of widespread sex (biological) and gender (social role) related issues within today's chemical and socio-cultural realities. Yet this issue – major but largely unexplained and unresearched – finds very little discussion in the INSPQ report, other than a mention in chapter on epidemiology and the following translated paragraph[34] from the chapter devoted to the psychogenic hypothesis, typical in that the report ties this phenomenon to women's greater incidence of anxiety disorders.

> As seen in the chapter on epidemiology, women are overrepresented in groups of MCS - OR cases ranging from 1.63 to 3.0 (Hojo, Ishikawa, Kumano, Miyata, and Sakabe, 2008; Kreutzer, Neutra and Lashuay, 1999). This is consistent with other published disease data on mental health issues in the Canadian population (Canada, 2015). These data indicate that women report certain anxiety disorders more often than men. There are also differences in types of personality disorders, for example, antisocial personality disorder is more common in men, whereas borderline, dependent and histrionic personality disorders are more common in women. These disorders and personality traits are also more common in MCS cases (Witthöft, Rist and Bailer, 2008). In addition, women were hospitalized more frequently than men in each age group, mainly for anxiety disorders (Canada, 2015). These differences in prevalence could be due to real differences between the sexes. It could also be due to the fact that women consult health professionals more readily and are also more likely to obtain health services than men. Similarly, classification bias among health professionals could explain this gap between men and women (Canada, 2015). (INSPQ report, Chapter 10, Predisposing Factors, p. 634)

[34]Original French language text: Comme vu dans le chapitre sur l'épidémiologie, les femmes sont surreprésentées dans les groups de cas SCM – OR variant de 1,63 à 3,0 (Hojo, Ishikawa, Kumano, Miyata, et Sakabe 2008; Kreutzer, Neutra et Lashuay, 1999). Cela est coherent avec d'autres données publiées sur les maladies mentales dans la population canadienne (Canada, 2015). Ces données indiquent ques les femmes signalent certains troubles anxieux plus souvent que les hommes. Il existe ausi des differences dans les types de troubles de la personalité, par example, le trouble de la personnalité anitsociale est plus courant chez les hommes, alors ques les troubles de la personnalité limite, dépendante et histrionique sont aussi plus frequents chez les cas SCM (Witthöft, Rist et Bailer, 2008). De plus, les femmes ont été hospitalisées plus fréquemment que les hommes dans chaque groupe d'âge, principalement pour des troubles anxieux (Canada, 2015). Ces differences de prevalence pourrraient être attribuables à de véritables differences entre les sexes. Cela pourrait aussi être attributable au fait que les femmes consultant plus facilement des professionnels de la santé et obtiennent aussi plus aisément des services de santé que les hommes. De meme, des biais de classement chez les professionnels de la santé pourraient expliquer ce écart entre les hommes et les femmes (Canada, 2015).

The INSPQ report, then, correlates the preponderance of women in MCS with their relatively poorer mental health and greater incidence of "borderline, dependent and histrionic personality disorders", a highly troubling finding in and of itself.

Even if women's greater propensity to anxiety disorders were alone responsible for their greater MCS numbers – and it is not – this would demand some attempt to address why anxiety, and particularly the kind of anxiety that spawns an often disabling "somatoform disorder," in which women erroneously ascribe their anxiety to chemicals appears to be rising year by year in their ranks. But attempting such an account would entail an analytic effort to assess the impact of the stressors that women encounter in modern life, including impacts of toxic body burdens and ongoing exposures to chemicals on mental as well as physical health, a task studiously avoided by the INSPQ report.

Fortunately, Emily Barrett of the Department of Biostatistics and Epidemiology at the Environmental and Occupational Health Sciences Institute of the Rutgers School of Public Health, and Amy M. Padula, of the Department of Obstetrics, Gynecology and Reproductive Sciences at the University of California San Francisco, have undertaken just such an enterprise. In their 2019 "Joint Impact of Synthetic Chemical and Non-chemical Stressors on Children's Health," as we have already noted (in our Part 2.7) they write of women's (maternal) body burden:

> The gold standard for assessing human exposure to synthetic chemicals is by collecting biospecimens such as urine or blood and then measuring concentrations of chemicals of interest and/or their metabolites. Using this approach, biomonitoring studies in the U.S. and Europe have demonstrated that the average pregnant woman has measurable levels of dozens of identifiable synthetic chemicals and their metabolites in her body (9, 10). These include organophosphate and organochlorine pesticides, polybrominated diphenyl ethers, perfluoroalkyl substances, phthalates, and phenols, among others. Most of these analytes (or their metabolites) are detectable in >90% of women sampled suggesting that exposure is nearly ubiquitous. (Exposure assessment and co-occurrence, Synthetic Chemicals, paragraph 1).

It is important to underline here that the chemicals named by Barrett & Padula have already been shown, in the cited charts from the fact sheet of the Collaborative on Health and the Environment (2008) as well as by many researchers in the field of environmental health, to have serious and wide-ranging neurological effects that are generally classified, especially by unaware physicians, as "psychiatric." There is no iron wall between physical and mental health, and especially not for women who have a high body burden and exposure rate.

How did women accumulate these toxic chemicals capable of disrupting neurological (affective as well as cognitive), immunological, metabolic and other aspects of health? This is a story of a chemical society meeting the female body and the social roles it performs, within a stratified socio-economic context.

## 6.2 WOMEN'S BIOLOGY A RISK FACTOR DURING CHEMICAL EXPOSURE

Both male and female bodies are disrupted and their health adversely impacted by toxic chemicals and their bioaccumulation but it appears, not to the same extent. As we have already pointed out, Naviaux (2020) suggested in his cell danger response theory that the accumulation of toxicants disrupts the mitochondria and underlies all types of chronic disease, including affecting mental health. That said, it is thought that male and female bodies have different properties and react to different toxicants in ways that are related to their differing biology (Caporossi & Papaleo, 2015; Vahter et al., 2007). Evidently, the female body accumulates more of certain chemicals that impact women in sex-specific ways (Jackson et al., 2017; Caporossi & Papaleo, 2015). Immunity and neurology seem to be two of those ways.

In his research report for the Ontario Centre of Excellence business case project, Molot (2013) summarized a number of key features of women's biology that would affect the likelihood of their developing environmentally-linked illness, including MCS.

> There are sex differences in how the limbic system responds. Functional brain scans reveal that, when challenged, men and women activate different limbic structures following the same provocative stimuli. There are sensory differences which are related to limbic system function. Women have a higher prevalence of several pain-related conditions … . On average, women are more responsive to painful stimuli, and women also tend to have a heightened inflammatory response compared to men.
>
> Statistics gleaned from the National Health and Nutrition Environmental Survey (NHANES) in the US suggest that environmental pollution exposures affect women more than men. Women biologically handle chemicals differently compared to men. The enzyme systems for detoxification are more active than men. Normal kidney clearance of chemicals is lower in females compared to males. Also, women retain more inhaled volatile organic compounds than men. This is likely because women have a higher percentage of body fat which affects the distribution of chemicals that are not easily eradicated.
>
> In summary, the prevalence of environmentally linked illnesses, as seen particularly well in ES/MCS, are more common in women because they are more responsive to their environment via both the limbic and immune systems, have a greater body burden of chemical exposures and less efficient detoxification systems compared to men. (pp. 41, 42; emphasis added)

The greatest on-the-ground proof of women's greater susceptibility to chemical toxicity is that more women per capita than men developed Gulf War Illness, at greater severity than men (Sullivan et al., 2020). The chemical exposures were so great during that war that tens of thousands of men also succumbed. (We will have more to say about the legacy of that war in Part 7.5).

Having a significant body burden of chemicals is a risk factor for MCS. So, likely, would be the differences in limbic function and pain tolerance observed. To what extent some people are genetically endowed with stronger or weaker detoxification abilities is under investigation at this time, but the existing research suggests that this may be an aggravating factor in body burden accumulation. In any case, since it is often the total load of toxicants that provokes a "crash" in MCS (a sudden initiation, or dramatic deterioration to a stage of greater severity), this can mean that the final exposure of a given chemical or chemicals may not appear to be a major incident if measured on its own in a given moment, but it becomes significant when seen as the final contributor to a large body burden, which women often carry.

These biological factors contribute to the large number of women who develop MCS more frequently than men, but they are not the end of the story.

## 6.3 WOMEN'S SOCIAL ROLES CREATE ONGOING CHEMICAL EXPOSURE

### 6.3.1 Women at work

Women's social roles and the types of workplaces large numbers typically inhabit also contribute to greater chemical exposure and, therefore, greater risk of developing MCS and a host of other chemically related diseases, including breast cancer. There is a whole literature on the adverse health effects of the chemicals women encounter in their home and work lives, showing that working class women are more likely to suffer these workplace effects. Here are some examples: Workplaces such as retail outlets, nail salons, automotive plastics factories, and even offices, where women in clerical positions are more often closely co-located with printers and photocopiers, tend to be unregulated, poorly ventilated and have no or low unionization and no or low occupational health features compared to workplaces by where men are more often co-located (Ford, 2014; Nguyen et al., 2022; Brophy et al., 2012; Guo et al., 2020). Women's work as professional cleaners falls into this category as well. Rosales et al. showed that a 15-minute exposure to a common fragranced commercial cleaning agent (monoterpenes that smell like citrus or pine) was equivalent to a volatile organic compound exposure produced by 28,000 automotive vehicles (Rosales et al. 2022). Carissa Wong wrote a piece for *New Scientist* in February 2022, 'Cleaning products cause indoor pollution levels similar to a busy road' discussing this study.

The concentrations of chemicals in all the above-named workplaces are, presumably, considered "normal" or "usual" (to use terms from the INSPQ report), but are they "weak" and "harmless"? Compared to fresh air, these concentrations can be so great that, as we have pointed out from the first page of this critique, a whole environmental health movement and a major subset of it—the women's environmental health movement—have grown to address the multiple and synergistic disease-causing effects of these chemicals.[35] Calls to have such chemicals disclosed, regulated, and, in many cases, banned reflect these concerns. To dismiss the toxicity of such

[35] See, among others, Women's Voices for the Earth. https://www.womensvoices.org/about/why-a-womens-organization/

chemicals or imply with descriptions such as “normal,” “weak,” or “at low concentrations” that they would have no power to injure and continually harm an injured body contributes to a widespread illusion that these chemicals are safe and that people—women, in these cases—do not need protection from them. The dismissal also feeds – in the INSPQ report, creates – the impression that hypersensitization must be an emotional rather than a biological outcome.

### 6.3.2 Women’s work at home

We can extend the same elements of analysis to women’s ongoing performance of the bulk of indoor housekeeping which exposes them to many petrochemically derived synthetic fragrances. Even the American Lung Association (as we saw in Part 4.3) warns about the harmful effects of many household cleaning agents, a category that includes bleaches, rug- and dry-cleaning chemicals, fragranced laundry products, furniture and floor polish, and oven cleaners. These are acknowledged toxicants, and they are hazardous to health even at normal concentrations (Piazza & Urbanetz, 2019; American Lung Association). That such chemicals at everyday concentrations could trigger MCS reactivity in some women with an already high body-burden of chemical and biotoxins makes perfect sense.

### 6.3.3 Women and beauty enhancement

Finally, in terms of social roles, women’s acculturated tendency to modify their appearance for the sake of beauty has meant far greater exposure to toxic chemicals in hair dyes, makeup, shampoos and soaps, creams, deodorants, and other grooming products that are unregulated but clearly identified by many researchers (Zota & Shamasunder, 2017).

Women’s greater body burden of persistent toxicants from multiple sources is, in fact, a very serious public health issue that calls out for public policy to minimize it. This is because certain types of bioaccumulated toxins can, as previously mentioned, not only harm women but also fetuses, increasing adverse outcomes in infant health that follow children throughout the life course (Di Renzo et al., 2015). Focusing on MCS, let us mention once again the 2015 study by Heilbrun et al. (2015), which found that “chemically intolerant mothers were 3 times more likely to report having a child with autism or 2.3 times more likely to report a child with ADHD, as well as more chemically sensitive children” (Abstract). Again, we note that chronic anxiety is not a credible explanation for this phenomenon.

## 6.4 SEX-GENDER BIAS IN MEDICINE CONTRIBUTES TO INVISIBILITY OF TOXICS-RELATED DISORDERS

The literature on sexism in medicine is decades old. It is very well established that female bodies have not been researched, as a rule, independently of men’s or even alongside them in countless research and clinical efforts. The result is that when women’s symptoms do not fit with those considered universal (but are really male-derived), many doctors tend to doubt or disbelieve women, and ascribe their “complaint’ to psychological reasons. This has been shown in Canada as well as elsewhere for decades. This means that at the same time as women have a greater

burden of disease with MCS than men, they have considerably less credibility with their physicians.

Samulowitz et al. (2018) demonstrated that the long-standing tendency to ascribe bravery to men who complain of pain but melodrama or neurosis to women is still very much alive in health care. Therefore, when a physician with sex-gender bias—unconscious, of course—meets a female patient with MCS, a disorder the doctor generally believes to be a disowned emotional problem to begin with, the patient is very likely to have a negative experience produced by this double whammy.

In our qualitative patient study (Burstyn & MEAO, 2013, pp. 59-166), every woman participant spoke explicitly about how sexist bias had been evident and damaging in her experiences with MCS and physicians. Indeed, so extensive and even traumatizing was the reporting on this theme that a whole chapter had to be devoted to reporting the findings.

The expression of sex-gender bias with respect to what physicians perceive as non-specific, functional, and somatoform syndromes (NFS)[36] is to be found in the fact that such diagnoses are made much more often for women than for men. This phenomenon has received some study. In "Physicians' gender bias in the diagnostic assessment of medically unexplained symptoms and its effect on patient-physician relations," Claréus & Renstrom report:

> Nonspecific, functional, and somatoform (NFS) syndromes is an umbrella term for various diagnoses with medically unexplained symptoms. These syndromes are more prevalent among women than among men, and associated with negative preconceptions that can impede rehabilitation. In two studies, we quantitatively assess how patients' gender affects the diagnostic assessment of NFS syndromes, as well as the healthcare experiences of individuals diagnosed with NFS syndromes. In the first study, our vignette-based experiment showed that Swedish general practitioners (N = 90) were gender biased in their diagnostic assessment of NFS syndromes, such that a female patient with back pain was more likely to be assigned an NFS syndrome compared to an otherwise identical male patient. In the second study, a large community sample of Swedish individuals with medically explained (n = 432) and unexplained pain (n = 521) evaluated their treating physician's relational conduct. Even after accounting for a variety of sociodemographic variables and other pain characteristics, women with at least one NFS syndrome perceived their physician's relational conduct as significantly poorer than other women as well as men with and without NFS syndromes. When women's pain is more likely than men's to be assessed as NFS, their rehabilitation could be prolonged as pertinent alternative diagnoses and treatments are omitted and their negative healthcare experiences lower their volition to partake and persevere in treatment. (Claréus & Renstrom, 2019, Abstract).

[36] Nonspecific, functional, and somatoform syndromes (NFS) is not a terminology to which we ascribe, but for some it covers a whole range of conditions among which are MCS, ME and FM.

Part of the gender bias is the attitude of sexism and women's inferior credibility resulting in a much greater willingness on the part of physicians to ascribe the NFS label to women – "up to 10 times more frequently in women," according to Barsky et al. (2001). The additional complicating factor, however, is the lack of understanding of many of these so-called NFS conditions as biophysical illness, such as MCS, ME and FM. The conditions are in many cases still medically invisible, and women, who suffer more from them, suffer from that the bias that results from that invisibility as well.

Finally, and with respect to medical practice, women are much more affected by direct toxicological (iatrogenic) harms due to their overmedication (Morgan et al., 2016). Women's use of antibiotics (even setting aside UTIs) over the course of their lives is much greater than men's. For example, in the UK in 2018,

> female patients received 67% more prescriptions than male patients, and 43% more when excluding antibiotics used to treat urinary tract infection (UTI). These gaps were more pronounced in adult women (99% more prescriptions than men; 69% more when excluding UTI) than in children (9%; 0%) or the elderly (67%; 38%). (Smith et al, 2018, Abstract)

Antibiotics are known for serious disruption of the gut microbiome, which is associated, as we have seen, with brain health and mood modulation, affecting anxiety levels, contributing to a toxic body burden and to a chemically stressed nervous system (Smith et al., 2018), all risk factors for chemical intolerance. A new study from Harvard underlines a link between antibiotic use and cognitive (neurological) decline in women (Mehta et al., 2022).

Women are also prescribed more psychotropic drugs than men, even though women seem to suffer more unwanted side effects, as noted by Jacobson (2014).

Environmental physicians look for pharmaceutical problems when they investigate chemical issues, and intolerance of specific pharmaceuticals is part of the genetic polymorphism profile when genetic status is measured.

## 6.5 ADVERSE SYNERGIES OF CHEMICAL AND NON-CHEMICAL EXPOSURES IN WOMEN

Again, we cannot emphasize enough how critical it is to understand all the environmental and toxicological impacts on women in accounting for the etiology and growing incidence of MCS, its ongoing symptomatology, and the preponderance of female sufferers. The INSPQ report does not do this. Instead, it asks us to believe that year by year and decade by decade, more and more women, especially middle-aged women, have such serious personal stress levels that, in the prime of life, they have developed a strange type of chronic anxiety disorder of which they are unaware but which causes them suffering and disability. For the INSPQ report, as previously noted, the mechanism is an unconscious "anticipation of danger" that causes them to falsely attribute devastating, disabling, and isolating physical symptoms to odours, an anticipation of

danger which then triggers a neuroinflammatory cascade of biological events that damage the brain and body – a somatoform condition of psychological origin.

At the same time the report asks us to believe that the greater preponderance of women with MCS, and, indeed, their greater incidence of anxiety disorders, has nothing to do with the almost incalculable spread of everyday chemicals that are known to be harmful, including endocrine-disrupting and neurotoxic chemicals with which we did not co-evolve as a species. This is completely implausible.

What research is showing today is that there is a synergistic effect between toxicological exposure and psycho-socio-economic stressors – a central point we address in more detail in Part 7. But we need to pursue it a little here, to account for women's experiences with toxicologically-related ill health. Unsurprisingly, the people most heavily affected by chemical exposures, and certainly by the combination of chemical plus non-chemical stressors are women and children. As we have seen in today's world, chemical exposures are ubiquitous, and put virtually everyone at some degree of risk. However, the most extensive and inescapable exposures face women (and children) at the lower end of the socio-economic scale – the women who must live and bear and raise their children near oil refineries or manufacturing centres or high-volume traffic routes, or work in nail salons or plastics factories or even shopping malls, for example. Barrett & Padula (2019) write:

> Not surprisingly, exposures to synthetic chemicals and non-chemical stressors often go hand in hand, with exposure to non-chemical stressors often driving increased chemical exposure (4). For example, a 2018 review of the literature on endocrine disrupting chemicals (EDC) and metabolic disease observed that exposures to synthetic chemicals including polychlorinated biphenyls, phenols, and phthalates were consistently higher among low income individuals and racial minorities compared to higher income, white participants (22). (Barrett & Padula, 2019, Exposure assessment and co-occurrence, Joint exposure to synthetic chemical and non-chemical stressors, paragraph 1)

Note the chemicals in the referenced study on endocrine disrupting chemicals and metabolic disease, "polychlorinated biphenyls, phenols, and phthalates," are included in the adverse mental health charts cited above. Here is Barrett & Padula's more detailed discussion of the ways in which socio-economic stressors are found side by side and interact with the chemical stressors for these women, and, crucially, the biological consequences of this:

> Exposure to non-chemical stressors is similarly widespread and can occur at multiple levels. Macro-level, social-structural stressors such as racism, sexism and other forms of discrimination pervade daily life in the form of overt bias as well as micro-aggressions (11). Co-occurrence of these stressors is common (e.g. racism and sexism) and social-structural disadvantage may be further compounded by exposure to neighborhood and community-level stressors such as physical disorder, safety concerns, and poverty (12, 13). Demographic data (e.g. race, ethnicity, immigrant status, income, sexual orientation) is often used as a proxy for social-structural stress, but it can also be subjectively

> evaluated through questionnaires regarding experiences of discrimination (14). Similarly, neighborhood-level stressors may be quantified through objective geospatial measures (e.g. census tract level poverty) as well as subjective measures of neighborhood quality (e.g. cohesion, safety, violence) (15, 16). Importantly (from a public health perspective), chronic exposure to societal and neighborhood level stressors can become biologically embedded, resulting in long-lasting or permanent changes in physiology (sometimes called "weathering") that may be measurable in altered neuroendocrine activity and metabolic function or increased inflammation (17, 18). … (Barrett & Padula 2019, Exposure assessment and co-occurrence, Non-chemical stressors, paragraph 1, emphasis added)

Personal traumatic history too has an important place in the adverse health synergies with chemical exposures. On a social scale, it too is frequently worse when keyed to socioeconomic status.

> Individual level psychological stressors examined in studies of air pollution have included income, education, health insurance type, perceived stress, discrimination and stressful life events (36 - 40). For example, maternal stress, as measured by the crisis in family systems (CRISYS) questionnaire assessing negative life events in 11 domains, has been demonstrated to modify the effects of particulate matter and risk of wheeze (41). A more recent study examined air pollution and maternal lifetime traumatic stressors in relation to mitochondrial DNA copy number (a measure of mitochondrial response and dysfunction) in cord blood and placental tissue at birth, and found that the combination of air pollution and lifetime trauma was associated with a higher number of mDNA copies, indicating greater mitochondrial dysfunction, among mothers carrying boys (42). (Barrett & Padula, 2019, Air pollution-stress interaction example as a model, paragraph 2)

The INSPQ report basically ignores both toxicological exposures among women, and fails to adequately discuss how socioeconomic stressors function as enabling influences for ill-health among them. Certainly, it does not describe how these can become "biologically embedded," and greatly exacerbate the effects of chemical exposure in ways that create disorders seen in MCS, such as altered neuroendocrine activity, metabolic function, increased inflammation and mitochondrial dysfunction (recall Naviaux's thesis). As well, there is almost no discussion of trauma in the INSPQ report, except as one possible predisposing factor in an entirely psychogenic account of MCS.

The report thus asks us to set aside the world-historic changes in the spread of chemicals in the human environment and to believe that the increase in MCS, especially among women, is due, one more time, to their predisposition to anxiety.

Note that the report also asks us to believe that there is a similar trend among people, mostly women, who have ME, FM, and electro-hypersensitivity conditions, among others.

Given all the factors we have enumerated, this account leaves an enormous a hole in the INSPQ's account of MCS mechanisms. Without environmental health research and toxicological issues factored into the whole picture, this account is simply not credible and would be a very bad basis for any type of policy or action going forward.

## 6.6 CONCLUDING REMARKS FOR PARTS 4, 5 AND 6

The critical issue in clinical programs, disability accommodation, and population health measures – the issues that matter most to people who must live with MCS – are what factors are contributing to MCS, and what measures can most effectively address their consequences, preventively if possible (reducing chemical use and exposures everywhere, ensuring a safe domicile), and with appropriate, effective health care measures and disability accommodation once MCS has set in.

With respect to the INSPQ report, neglecting key research that shows links between chemical exposures and MCS (e.g., onset triggers, TRPV receptors, mast cell research), as well as not integrating the findings of toxicological epidemiology in general, dismissing the effects of environmental toxicants and body burdens on mental health, neglecting gut health and nutritional deficiencies, ignoring other important immunological deficiencies and the presence of chronic infections, and, finally, neglecting to show the heavy impact of everyday toxicants and medications on women—all biophysical-toxicological problems with impacts on the brain that contribute to hypersensitization—means that the INSPQ report's conclusions are extremely deficient and, ultimately, wrong.

# PART 7: UNDERSTANDING CHRONIC STRESS, ANXIETY AND MCS

# PART 7: UNDERSTANDING CHRONIC STRESS, ANXIETY AND MCS

## 7.1 CLARIFYING THE INSPQ CONCLUSIONS AND KEY TERMS

Once again: The INSPQ report comes to two main conclusions, which are identical with the two key tenets of the psychogenic school.

> a) "The authors of this report rebut the hypothesis that there is a relationship between MCS and the toxicity of chemicals present at normal concentrations." (Key Messages, p. 2.) So, in their view, MCS is not linked to, and is not caused by chemicals.

We have disputed and refuted this erroneous thesis at length in Parts 2, 3, 4, 5, and 6.

> b) "Chronic anxiety helps explain all of the symptoms of SCM syndrome. The same alterations and dysfunctions are found and measured there." (Key Messages, p. 2.)

In other words -- predicated on the first conclusion (i.e., the condition has nothing to do with the toxicity of chemicals), chronic anxiety, caused by chronic stress, causes the somatization involved in MCS, so anxiety "explains" MCS.

We now wish to speak more directly to this second erroneous thesis at the core of the psychogenic school as well as of the INSPQ report.

The INSPQ report presents us with a number of different formulations regarding the stress-anxiety- symptomatology relationship. We leave it to the reader to determine exactly what this is from these statements:

- "In chronic stressful situations, people with MCS interpret harmless signals from the environment or the body as dangers, and this interferes with their ability to cope" (translated, p. 11)."[37] Here, stress leads to misperception of "harmless signals" as chemical dangers, and to loss of coping capacity.

- "Affected individuals perceive odours as a threat to their health. When they detect odours, they experience acute stress that manifests as ailments that they attribute to the chemical products associated with these odours." (Key Messages, p. 2) Here, people with MCS perceive odours (presumably "harmless signals") as dangerous, which causes them acute stress, which they mistakenly believe comes from chemicals, and this causes symptoms ("ailments").

[37] Original French language text - Dans les situations de stress chronique, les sujets atteints de SCM interprètent les signaux inoffensifs de l'environnement ou du corps comme des dangers, et cela perturbe leur capacité d'adaptation" (p. 11).

- "During chronic stress, inflammation can persist and become detrimental to physical and mental health" (translated p. 790).[38] The inflammation caused by chronic stress – presumably augmented by misinterpretation of "harmless signals" – causes physical and mental damage that, in a vicious circle, then creates more stress.

Whatever inconsistencies or variations there are in these statements, chronic stress is framed as the major culprit behind the anticipatory anxiety that causes people to somatise symptoms. Indeed, both in the INSPQ report and going back all the way to the 1990 Chemical Manufacturer's Association briefing paper, it is the purported inability of people with MCS to cope with life's stressors plus their denial of this inability that leads them to develop MCS. Recall the words of the Chemical Manufacturer's Environmental Illness briefing paper:

> Environmental illness patients generally lead troubled lives and have genuine problems in coping with family, work and life-style pressures. They often eagerly accept environmental illness as the explanation for their condition. (CMA 1990 Executive Summary, paragraph 5)

(Recall too the language of Staudenmayer et al.'s articles (2003a, 2003b), of which the INSPQ report seems a direct descendant.)[39] Cited approvingly at several junctures in the INSPQ report, the fingerprints of Staudenmayer's work can also be found in Chapter 10 (10.6.8, p. 644) of the INSPQ report's presentation of the idea of an "illness belief system," here described as

> [translated[40]] The belief that the disease and its presumed causes exist may be the starting point for the symptoms experienced. This process can be perpetuated and reinforced by contextual information (activists, support groups, environmentalists and the media). In addition, the media such as television reports, newspaper articles and internet sources could play a role in the etiology of MCS by inducing negative expectations or catastrophic thoughts in vulnerable people. … Some also suggest that

[38] "En situation de stress chronique, l'inflammation peut se maintenir et devenir préjudiciable à la santé physique et mentale."p. 790.

[39] Staudenmayer (2003b): "We conclude that IEI [idiopathic environmental intolerance] is a belief characterised by an overvalued idea of toxic attribution of symptoms and disability, fulfilling criteria for a somatoform disorder and a functional somatic syndrome. A neurobiological diathesis similar to anxiety, specifically panic disorder, is a neurobiologically plausible mechanism to explain triggered reactions to ambient doses of environmental agents, real or perceived. In addition, there is a cognitively mediated fear response mechanism characterised by vigilance for perceived exposures and bodily sensations that are subsequently amplified in the process of learned sensitivity." (Abstract)

[40] La croyance que la maladie et ses causes présumés existent peut être le point de départ des symptômes ressentis. Ce processus peut être perpétué et renforcé par des informations contextuelles (activistes, groupes de soutien, médicins écologists et médias). En outre, les médias comme les reportages télévisés, les articles de journaux et les sources Internet pourraient jouer un rôle dan l'étologie de la SCM en induisant des attientes négatives ou des pensées catastrophiques chez les personnes vulnérables … Certains suggèrent également que les symptômes sont amplifiés par un système de "croyances" iatrogénique établi par ceux qui dispensent le traitement (Black et *al*., 1993; Staudenmayer, 1996)

> symptoms are amplified by an iatrogenic "belief" system established by those who provide the treatment (Black et al., 1993; Staudenmayer, 1996).

We may presume that the factors thought to contribute to this "illness belief system" would also be considered social stressors for susceptible individuals.

Chronic stress is a heavily freighted issue in this whole account. In what follows, we therefore want to address it in some detail.

We also want to speak to the purported role of chronic anxiety. For the INSPQ authors, stress/and or "harmless signals"[41] lead to chronic anxiety in the subset of people who develop MCS. This anxiety is understood as a combination of a Pavlovian, limbic response and some involvement from the reasoning regions of the brain that causes people to falsely, alarmingly (patients "catastrophize"[42]), and uncontrollably misattribute danger to odour signals, provoking a cascade of adverse biological events resulting in MCS symptoms. Many other conditions are also considered to have the same "alterations and dysfunctions" explained by chronic anxiety (Key Messages, p 2), a point we take up in Part 9. Once again, for clarity, according to the report, and as previously cited, these ailment-producing adverse biological events are:

> a disruption of the hypothalamic-pituitary-adrenal axis, an increase in inflammatory cytokines, a disruption in oxidative homeostasis, a chronic decrease in neuromodulator levels (serotonin, dopamine, norepinephrine). In addition, using brain imaging, alterations in brain function and structure were observed that affect the limbic system circuits (emotions, memory, learning) and the prefrontal cerebral cortex (attention, reasoning, strategic thinking, judgment). (Summary, Results, p. 3)

And the main precipitating factor for this cascade is "the anticipation of danger."

> Chronic anxiety is an element common to all of the syndromes studied, and its main feature is *the anticipation of danger* i.e., feeling a persistent, excessive and inappropriate concern about one's day-to-day activities. (Summary, Results, p. 3)

What causes this anxiety? There is a stunning lack of discussion of this all-important factor in the INSPQ report. What we find is that it is presumably rooted in:

> a number of factors [that] may be involved, e.g., an individual's temperament, personal history and psychosocial makeup. (Summary, Results, p 3)

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[41] Examples: "..les sujets atteints de SCM interprètent les signaux inoffensifs de l'environnement ou du corps comme des dangers, et cela perturbe leur capacité d'adaptation" p.11; "Toutefois, la particularité avec la SCM est la nature des stimuli qui induisent un conditionnement de l'apprentissage de la peur à des stimuli odorants inoffensifs couramment rencontrés dans l'environnement dans ce cas-ci." p. 811

[42] As we have just seen, in translation, in speaking about the illness belief system : "En outré, les médias comme les reportages televises, les articles de journaux et les sources Internet pourraient jouer un rôle dans l'étiologie de la SCM en induisant des attentes négatives ou des pensées catastrophiques chez les personnes vulnérables." P.644.

Severity is seen not in relation to any physical or toxicological issues, or indeed specifically identified social stressors associated specifically with living with MCS. Rather,

> The severity of the syndrome depends on its duration and the comorbidity that MCS patients frequently experience, i.e., chronic fatigue syndrome, electromagnetic hypersensitivity, fibromyalgia and depression, etc. (Summary, Results, p. 3)

Before we begin our detailed consideration of the terms and features of this language, it bears repeating that MCS researchers and clinicians in the bio-physical-toxicogenic school of thought have long understood, and continue to reaffirm that MCS impacts the central nervous system, including the regions of the brain comprising the limbic system and the amygdala specifically (e.g., Rae, 2016, Belpomme et al. 2015, Molot et al., 2021, Miller et al 2021) as well areas of the brain involved in cognition, sometimes speech and coordination as well, and the autonomic nervous system. So, in this recognition among toxicogenic adherents, there is ample room for the biological events described above.

However, in the psychogenic paradigm, there appears to be no room for the physical and toxicological injuries or recurring sensitization factors (e.g. chronic infections, heavy body burden, immunological deficits) in onset and that continue to trigger flares in the absence of dedicated measures to address them.

Those in the biophysical-toxicological schools would likely point out, as we have done repeatedly, that MCS onset and ongoing chronic flares are characterized by a larger, consistent cluster of body-based and neurological symptoms, only one of which is anxiety. Other neurological symptoms include cognitive and speech impairment and deterioration of physical coordination, and, per Rea, a depressive phase that follows the initial reaction. These may also include a larger range of affective disruptions, variously described in the references cited just above and previously.

An even broader cluster of symptoms has been identified in mast cell activation syndrome (MCAS), proposed recently as a possible key mechanism of MCS/TILT (Miller et al., 2021).

> Cognitive and mood effects can include sudden rage (e.g., “road rage”); impulsive, violent, or abusive behaviors; addictive tendencies; mental confusion/fatigue; and/or a sense of depersonalization. [Mast cell] “twitchiness” renders these cells vulnerable to a host of unrelated exposures that never bothered the person before and do not bother most people. (MCAS, TILT, and the nervous system, paragraph 6)

Once again, chronic or otherwise, anxiety is not privileged as a determining factor in this account, either.

## 7.2 ANXIETY AND FEAR IN MCS AND THE EXAMPLE OF UNSAFE HOUSING

To place the discussion of MCS and anxiety in context, a few important realities must be kept in mind. First, anxiety is common in the population. US figures put it at approximately 20 percent in any given year[43], Statistics Canada's estimates over the course of the pandemic (released in September 2021) put it at 15 percent and CAMH put the figure for moderate to severe anxiety at over 25% in January 2022.[44] This appears to be a significant increase from Canadian figures from CCHS 2013 in response to the question "have you been diagnosed with a mood disorder?" which showed just over 10 percent. [45] So, it would not be unusual to find a proportional number of people with MCS who live with anxiety that may or may not be related to their MCS.

Second, having a chronic disease in general increases the prevalence of anxiety compared to the general population, with the directionality of causation an open question. Anxiety can predate the physical disease or it can follow it, although it seems most often it is the anxiety following the chronic disease. (DeJean et al. 2013)

Although MCS was not one of the diseases being examined in DeJean's 2013 study, this statement is worth bearing in mind:

> The estimated prevalence of anxiety and/or depression varies by the type and severity of chronic illness, and the setting and methodology for screening and diagnosis. However, rates are consistently higher across most chronic diseases compared to the general population, especially for people with stroke, cardiovascular disease, and diabetes." (Clinical Need and Target Population, Prevalence).

A 2017 study by researchers at the University of Manitoba speaks to the difficulty of teasing out the causality and/or interdependence of anxiety disorders and general medical conditions.

> The combination of anxiety disorders and general medical conditions creates significant challenges to accurate identification and treatment. Anxiety disorders may increase the likelihood of a variety of general medical conditions, and general medical conditions may worsen or increase the risk of anxiety. When combined with anxiety disorders, most general medical conditions incur greater morbidity and, in some cases, higher rates of mortality. (Aquin et al., Conclusion)

So, with anxiety (as with trauma and stress), we would expect to find similar numbers of people with it among those with MCS as in the general population, and, indeed, higher in keeping with a

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[43] https://www.nimh.nih.gov/health/statistics/any-anxiety-disorder

[44] Statistics Canada figures released September 27, 2021 https://www150.statcan.gc.ca/n1/daily-quotidien/210927/dq210927a-eng.htm ; CAMH figures released January 25, 2022 https://www.camh.ca/en/camh-news-and-stories/anxiety-depression-loneliness-among-canadians-spikes-to-highest-levels

[45] https://www.canada.ca/en/public-health/services/publications/diseases-conditions/mood-anxiety-disorders-canada.html

higher incidence among those with a chronic illness. These broader considerations therefore suggest that the data we do have from an analysis of CCHS figures by Margaret Parlor (2009)[46] showing mood disorders among those with MCS at about 15 percent, are in the above ranges, so on a par with the chronic diseases that were studied by DeJean.

These findings with respect to anxiety and general medical conditions are a useful backdrop to the discussion about anxiety and MCS as such. But such a discussion requires that we highlight two MCS-specific issues.

The first of these, as we have explained at length at various previous junctures, is that a feeling of anxiety in people with MCS can be one neurological symptom others provoked by chemical exposure that also disappears when the effects of the exposure subside. This means it is not a stand-alone anxiety disorder, free-floating and independent. Logically, if the exposures are constant, which happens when individuals are not able to live a largely toxicant-free life, then the chemical anxiety can become constant too, with consequences we explore below in Part 8. Again, the anxiety does not cause MCS, it follows it.

The second point can be made by introducing a central theme that will also be supported at greater length in Part 7: the matter of the difference between fear and an anxiety disorder, which is how the INSPQ report classifies MCS. This can most easily be illustrated by addressing the matter of safe or unsafe housing, which is also, as we shall see, both the first medical need of those living with MCS and the one most difficult to achieve and keep.

There is an important distinction to be made between fear and anxiety. Fear is an emotional reaction to a specific, real danger, while anxiety is an excessive and unfocused fear that may be triggered by a variety of stimuli, external or subjective. While anxiety caused by stress may persist long after the trigger is removed (or even arise with no trigger at all), constituting an anxiety disorder, fear arises in anticipation of a real threat. If that threat is constant then the fear can become longstanding as well. If the danger is removed, the fear subsides, though traumatization can occur.

With this distinction in mind, many persons with MCS experience “fear” – rather than “anxiety” – and they experience it all the time as a result of real extrinsic factors in their physical and social environment, not as a result of subjective feelings due to personal history and a resulting malfunction of neurochemistry or neurocircuitry. So, for example, if an individual finds it impossible to escape the sickness caused by constant chemical exposures because she lacks safe air quality at home, at work, in health facilities, at school and in places where she must shop to obtain the necessities of life, concern and indeed fear about how to negotiate these spaces and still avoid suffering and ill-health can be experienced alongside the physical suffering of the exposures.

[46] This analysis is contained as an Appendix to the previously cited Molot (2013). The table looks at CFS, FM and MCS as well as other chronic conditions.

This lack of safety is all too common, it is extremely serious, and the most serious part of it is what happens to those with MCS who cannot find or afford to create a safe place to live, a safe haven, in other words, needed for recovery from the unavoidable exposures in all other social spaces.

In March 2022, an Ontario MCS patient received medical assistance in dying (MAiD).[47] She sought and obtained it because after years of attempting, even with the assistance of four physicians and other advocates, she had been unable to find (afford, be granted through social housing) a residence that was free from the cigarette smoke and the cleaning chemicals of other tenants in her multiple-unit building that made her feeling unbearably sick. (Favaro, 2022a). Shelters were extremely toxic because of her MCS, and she could not go to friends whose homes were also not safe for her. To emphasize the lessons from this: as "Sophia"(a pseudonym) made clear, and as those who knew her well reported, it was the unbearable physical suffering of MCS and the complete exhaustion resulting from the struggle to find a safe harbour, not anxiety, that led her to choose to end her life. However, the double jeopardy described by Barrett & Padula (Abstract, 2019) of chemical exposures plus poverty and total rejection for assistance by her society would doubtless have increased Sophia's ill-health, and certainly contributed to the physical, emotional and spiritual fatigue that informed her choice.

Here are the words of a nurse from our 2013 study (Burstyn & MEAO) who became disabled with ME and MCS, speaking about her experience with housing. She explains the stakes and the consequences, not only of the denial of assistance, but of knowing that this "kept her in relapse" when basic help would have stopped that:

> That was a terrible journey. … It progressively became worse as I deteriorated. … [T]he City of Toronto Housing, when they got letters from my doctor saying I needed to be transferred, and even to the point where the doctor said I was concerned even about my life, that I could I die in … the available housing ... they said the only thing they could do was put me on the waiting list which is ten years, that I couldn't get special consideration for transfer. … I was ... being kept in relapse because I couldn't get to a place where I could be stable. So that was psychologically really awful, being in relapse and knowing that you don't have to be. ... It's been very sad. Almost every avenue where I've needed support or help, the initial and continued response was no response that helped me get a foot up. MaryLou (Appendix 3)

In late April of 2022, another CTV feature introduced "Denise" (also a pseudonym), who had also failed to find safe housing and had also been granted permission for MAiD, for which she had asked for an accelerated timetable (Favaro, 2022b). Her search for help through 10 different organizations met a dead end while her search for MAiD proved "surprisingly easy." (Favaro, May 28, 2022b)

[47] We briefly touched upon this situation in Part 3.4, when discussing how politicization has impacted the field of MCS.

Both “Sophia’s” and “Denise’s” stories were told in damning articles in the British and European press, stories that expressed horror and outrage at Canada’s willingness to deal with remediable suffering of the disabled by assisted death. (Very little outrage was expressed in Canada, the CBC remained completely silent). Only then did Marie-Claude Landry, Chief Commissioner of the Canadian Human Rights Commission, release a statement in which she said that MAiD should not be used as a solution to “systemic poverty” and “discrimination” (Canadian Human Rights Commission, May 10, 2022). Her entire statement made not one mention of MCS, an egregious omission, once again rendering MCS – so, therefore, the kind of solutions needed to avoid such MCS deaths as opposed to the generality of “systemic poverty” – invisible.

However, all this coverage sparked a GoFundMe campaign for “Denise.” Spontaneously, she was sent $65,000 from donors who wanted to assist her to find safe housing and live. This allowed her to find a temporary safe shelter without the cigarette smoke, cleaning products and air freshener fumes that had caused her to want to end her life, and her health improved dramatically in very short order. She is hoping to be able to find a permanent safe home, which would allow her to cancel plans for end of life rather than just pause them. “The ‘irremediable suffering’ that qualified her for a medically assisted death was fixable, said Dr. Riina Bray, the medical director of the Environmental Health Clinic at Women's College Hospital in Toronto, and one of Denise's physicians” (Favaro, 2022c).

There can be no more dire a sign of the pain of MCS than preferring death to living in a home full of chemicals, no clearer sign of the nature of MCS than the immediate return to well being that removing those chemicals can effect, and no clearer a measure of the utter indifference of our public authorities to this condition than refusing both individual and advocacy groups support to find or create safe housing. Canadian authorities were willing to help both women die, but not to obtain a safe domicile for them.

“Sophia’s” and “Denise’s” stories are not unusual. At the time of writing we are acquainted with at least one more person who is considering taking the same path, and we have been told others are now applying. Indeed, the complete vacuum in care and assistance, the institutional indifference in every area of health and social services to the needs of those with MCS is what people constantly face. The fear and dread that many with MCS live with on a daily basis is not rooted in personality or a subjectively generated “feeling [of] persistent, excessive and inappropriate concern about one’s day-to-day activities,” (INSPQ, Summary, Results, p. 3) but is rooted in harsh and at time unbearable realities.

## 7.3 FRAMING OPPOSING PARADIGMS IN UNDERSTANDING STRESS AND ANXIETY

Without analyzing either of these reality-based “anxiety-due-to-chemical-exposure” and “fear-of-real-danger” experiences in people with MCS, the INSPQ authors nevertheless reach an important overarching conclusion at the end of their study, which we will take as our departure point for the rest of this part of our commentary.

> [C]onsidering the mechanisms explained in the preceding chapters and all the results presented in this chapter, it must be concluded that these mechanisms support a biopsychosocial model for multiple chemical sensitivity syndrome and not a toxicogenic model related to the toxicity of chemicals (p. 646, translated).[48]

The term "biopsychosocial" is not defined in the INSPQ report, a serious omission for a term that becomes definitional. We assume that the "bio" component of this model refers to the biological cascade triggered by the anxiety described in the report, and that "psycho" and "social" refer to "a number of factors [that] may be involved, e.g., an "individual's temperament, personal history and psychosocial makeup." But if what is meant by "psychosocial" is a combination of "individual temperament" along with the influence of the social determinants of health, which are very important and multi-faceted factors in a given individual's life, these factors receive no analysis within the INSPQ account, and no weight in assessing MCS onset, or in determining the severity and duration of the chronic illness.

As mentioned in our discussion of female predominance in MCS and the work of Barrett & Padula (2019), a new field that measures the synergistic impacts of chemical and non-chemical stressors is beginning to emerge, in which the traditional firewall between such factors in research is turning out to be an analytic construct that does not reflect reality. In reality all forms of stress combine and adversely impact the individual or groups involved, in a mutually reinforcing play of illness-producing effects. In this emerging account, toxicological factors are strongly validated as having distinct impacts, very negative impacts, which are not discarded in favour of psycho-socioeconomic stressors but rather considered together. We've provided this quote previously in Part 2.2 but it bears repeating.

> Mechanistically, chemical and non-chemical stressors may act upon the same biological systems (Figure 1). For example, maternal exposures to psychosocial stress and endocrine disrupting chemicals (such as PBDEs and PFASs) have each individually been linked to altered cytokine profiles (8, 30, 31). Similarly, phthalates and psychosocial stressors may both act upon oxidative stress pathways (32,33). Even when mechanisms are unknown or disparate, chemical and non-chemical stressors may influence the same outcomes. For example, prenatal exposures to psychosocial stress and pesticides have each individually been linked to adverse neurodevelopmental outcomes, though the hypothesized mechanisms may differ (34, 35). For these reasons, it is increasingly clear that chemical and non-chemical stressors need to be considered together. From a modelling standpoint, this co-exposure suggests a need to consider effect modification, whereby exposures to stressors may potentiate or exacerbate the impact of chemical exposures on health outcomes. (Barrett & Padula, 2019, Exposure assessment and co-

[48] Donc, considérant les mécanismes expliqués dans les chapitres précédents et l'ensemble des résultats presents dans le présent chapitre, il faut conclure que ces mécanismes soutiennent un modèle biopsychosocial pour le syndrome de sensibilité chimique multiple et non un modèle toxicogénique en lien avec la toxicité des produits chimiques. p. 646.

occurrence, Joint exposure to synthetic chemical and non-chemical stressors, paragraph 3)

So, while we do intend to scrutinize personal trauma and the stressors that can arise out of the social determinants of health below, and see them as factors in a dynamic matrix of illness-enabling influences, we want to assert here that neither of these alone can account for MCS. These stressors may be so strong as to shatter health in many people. But without a toxicological input, a toxicological stressor if you will, ill-health does not evolve into chemical intolerance. We emphasize that toxicological factors are inherent and determinative of MCS in onset and during the chronic illness that follows it, for these factors are what makes MCS the distinct clinical entity it is.

## 7.4 TYPES OF CHRONIC PSYCHOSOCIAL STRESS AND THEIR RELATION TO INDIVIDUAL AND POPULATION HEALTH

The INSPQ authors have gone to extraordinary lengths to explain the neurocircuitry and neurochemistry of fear and anxiety that result from chronic stress. Unfortunately, they have devoted little attention to defining and addressing the many different sources of stress people encounter throughout their lives—their "total stress"—and how these different stressors can affect many aspects of health, including chemical sensitivity.

Technically, there are many types of stressors, but colloquially and confusingly, "stress" is usually used to refer primarily to psychological issues and sometimes to social issues, meaning, presumably, those arising from what the report calls "temperament, personal history and psychosocial makeup" (Summary, Results, p. 3). Here we will identify a fuller complement of stressors, including personal, social, physical, and toxicological (which would properly be subsumed under physical, but we need to tease these apart). We will follow this discussion with a review of key lessons from the study of Gulf War Illness as an example of how toxicants meet stress in onset of MCS. Then in Part 8 we will use a discussion of MCS among breast implant receivers to transition from group illness to individuals. And finally also in Part 8 we will discuss in detail the stressors involved in the life of those with MCS chronicity, and see how they retard and undermine recovery.

### 7.4.1 Stress underpins all forms of disease but does not alone create MCS

We have known since Hans Selye's work, referenced in the INSPQ report in titles that go back to 1936 and 1954, that excessive (or chronic) stress, conceptualized very broadly as a change in the environment, underpins the nonspecific signs and symptoms of illness writ large. Selye theorized that overexposing the body to stress could lead to shock, alarm, and eventually exhaustion.

In his article, (cited in the INSPQ report) "Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators," Bruce S. McEwen (2008) explains that though stress begins in the brain, chronic stress does more:

> Stress begins in the brain and affects the brain, as well as the rest of the body. Acute stress responses promote adaptation and survival via responses of neural, cardiovascular, autonomic, immune and metabolic systems. Chronic stress can promote and exacerbate pathophysiology through the same systems that are dysregulated." (Abstract)

The INSPQ report states (and McEwen would agree), that "during chronic stress, inflammation can persist and become detrimental to physical and mental health,"(p. 11, translated). All these effects explain why "stress" and "chronic stress" in particular – with its numerous but well-identified effects – underpin and create multiple avenues for ill-health, weakening an individual over time, making persons susceptible to disease. However, this understanding does not predict all the types of diseases an individual may will develop, even if disorders of the cardiovascular, autonomic, immune and metabolic systems, as well as the brain itself, can be said to be among those likely to develop due to the direct impact of stress on them.

Critically, let us note that whatever role anxiety may play in their origin, we do not treat cardiological, immunological and metabolic disease as anxiety disorders, as the INSPQ has classified MCS. So, this general understanding of stress does not yet get us to MCS.

### 7.4.2 Emotional trauma does not alone create MCS

The INSPQ report neglects to provide an adequate explanation for the psychological reasons an individual may develop MCS, though these are presumably, if implicitly, subsumed under the INSPQ's notions of "individual's temperament, personal history and psychosocial makeup." But the study sits firmly in the conceptual lineage of the psychogenic school, who's founding idea (cited in Part 1.2), is that in MCS,

> biological and physiological sequelae stemming from early, chronic trauma have been identified which could explain many of the multisystem complaints. The incidence of childhood abuse reported by EI/MCS patients is strikingly high, and it is recollection of trauma that many EI/MCS patients avoid by displacing the psychologic and physiologic adult sequelae onto the physical environment. (Staudenmayer 1996, Abstract)

Indeed, childhood emotional traumas of various kinds are well-known sources of stress with long-lasting. The Adverse Childhood Experience (ACE) Study (Filetti et al., 1998)[49] conducted between 1995 and 1997, examined a sample of tens of thousands of people and demonstrated that individuals who as children experienced particular types of adverse experience (trauma) were strongly predisposed to biophysical sickness in adulthood—all types of sickness, depending on other specific factors in their genetic, biomedical and personal histories.

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[49] The ACE Study conducted collaborative research between [the Centers for Disease Control and Prevention and Kaiser Permanente] from 1995 to 1997. Over 17,000 patients participating in routine health screening volunteered to participate. Data continue to be analyzed. The study has revealed staggering proof of the health, social, and economic risks that result from childhood trauma. More information as well as access to the peer-reviewed publications resulting from The ACE Study: https://www.cdc.gov/violenceprevention/aces/resources.html

But childhood trauma is extremely widespread in the population and by no means does it produce MCS in most who carry it with them. In fact, we would expect to find it among adults with MCS, as we would in people with other diseases and disorders (Saunders & Adams, 2014).[50] ACE, like Selye's conception of stress, predicts a predisposition to disease, not the disease itself. Some missing factor must be present, not identified by this school.

We noted in Part 3.6 that there is no discussion of children or childhood in the INSPQ report. This means that there is no attempt to understand what impact toxicological stressors have on children as distinct inputs, and as inputs interacting with other stressors within familial and social lives – an interaction that worsens the effects of both types of stressors (Barrett & Padula, 2019). Whether affected children must cope with the consequences of downloaded maternal body burden (a legacy of chemical stress); ongoing environmental exposures such as pesticides in rural and community settings (e.g., recurring pesticide application; macro petrochemical by-products in fence-line communities adjacent to industrial production); micro petrochemical products in domestic settings, including fragranced products and multiple chemicals from household furnishings and building materials; or mold and mycotoxins, these toxicological stressors clearly affect their especially vulnerable immunological, reproductive, and neurological health. They must be factored in, and are notably missing from the research reviewed by the INSPQ, and from its analytical speculation.

Further, it is well known that stress from emotional trauma in youth and later adult years, such as grief and loss, or painful relationships, or housing and food insecurity, and difficulties with other social determinants, also adversely affects health and if unrelieved, can result in physical and mental exhaustion, both risk factors for specific types of disease.[51] Therefore, childhood and adult interpersonal emotional stress, possibly acting in a cumulative manner, is understood as a weakening factor enabling disease development.

This type of stress is still not sufficient, however, to explain MCS.

### 7.4.3 Socioeconomic stress does not alone create MCS

Another major longitudinal study that came to ascribe a fundamental disease-enabling function to stress is the Whitehall study of British civil servants, begun in 1967, with two major 10-year cohort studies, and now an ongoing study on aging.[52] The Whitehall Study, designed initially to elucidate health inequities by seeking possible reasons in the workplace, demonstrated the

[50] See also Data and Resource Center for Child and Adolescent Health, which estimates about 50 percent of US children have suffered one or more forms of trauma.
https://www.childhealthdata.org/browse/survey/results?q+2614&r=1

[51] For a discussion of the psychological and physiological effects of stress-related mental fatigue, see Gavelin et al., (2020).

[52] Visit the study website at https://www.ucl.ac.uk/epidemiology-health-care/ See also: https://sheffieldequality.files.wordpress.com/2012/11/the-whitehall-studies.pdf; https://www.ucl.ac.uk/epidemiology-health-care/research/epidemiology-and-public-health/research/whitehall-ii

extremely close relationships between multiple socio-economic stressors and poor health. (While the study initially investigated workplace stress, it eventually turned to community, family, and physical stressors as well.) Indeed, the study was part of the broader research that led to the now commonly accepted understanding of the critical role the "social determinants" play in health.

The World Health Organization (WHO)[53] has listed the social determinants of health and we will come back to these in our discussion of the immense stress loads brought on by living with MCS. For the moment, however, let us use these to fill out what we need to understand as potential sources of stress in the social sphere, for where there are deficits in these, stress follows:

- employment and working conditions;
- income security;
- housing;
- food security;
- physical/healthy environments;
- social environments and social support networks (family and social inclusion/exclusion, friendships, community involvement and social status);
- gendered issues
- systemic racism, and ethnic discrimination;
- healthy child development;
- access to quality health services;
- biology and genetics;
- personal care practices and coping skills;
- disability (having it; societal recognition through accommodation, law, custom);
- education; and
- culture.

Returning to the Whitehall study, the researchers discovered an important factor that contributed to good or ill health, and that needed specific elucidation. It discovered that hard work and high responsibility – previously thought "stressful" on those who shouldered them – did not turn out to be disease-enabling stressors. The study found that when responsibility and hard work came with high authority, when the organization provided supportive colleagues and functions, and when effort and responsibility were rewarded financially and in high status, health tended to be very good.

Rather, health suffered among people who experienced heavy workload and responsibility, but with low authority, unsupportive managers and colleagues, imbalances between their work and its financial and status rewards, and job insecurity. People working under these conditions were much more likely to become sick. And of course, those at the lower end of financial reward also

[53] World Health Organization. Social Determinants of Health. Website at https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1

lived with more stressed conditions at home, with poorer nutrition, less healthy physical environments, poorer education and so forth.

The key lesson—and there have been many additional ones from that study since—is that it is not the amount of work, but the ability or lack of it to control the major impacts in one's work life, this is critical, and this is largely keyed to socioeconomic status. Not having control over the demands of work or having a low "span of control," is, literally, sickening.

Consider, as an example, cardiovascular disease, which is well-understood as affected by stress:

> Socioeconomic status (SES) refers to an individual's social position relative to other members of a society. Low SES is associated with large increases in cardiovascular disease (CVD) risk in men and women. … strong and consistent evidence shows that parental SES, childhood and early-life factors, and inequalities in health services also contribute to elevated CVD risk in people of low SES who live in high-income countries. In addition, place of residence can affect CVD risk…(Clark et al., 2009, Abstract)

So, stress is a major contributor to cardiovascular disease. But while we try to support patients in lowering or "managing" stress, we do not treat it as an anxiety disorder and withhold appropriate biomedical interventions for cardiological disorders. This is appropriate, and it is in keeping with the Whitehall authors' conclusions recommending that stress not be considered or treated as a mental illness, or as an individual responsibility that can be solved by individual action alone.

McEwen (2008), cited above, would agree, at least to this, as he states:

> From the standpoint of organization of society, the goal [of reducing chronic stress] should be to create incentives at home and in work situations and build community services and opportunities that encourage the development of the beneficial individual lifestyle practices. The Acheson Report (Acheson, 1998) from the United Kingdom in 1998 recognized that no public policy should be enacted without considering the implications for health of all citizens. Thus, basic education, housing, taxation, setting of a minimum wage, and addressing occupational health and safety and environmental pollution regulations are all likely to affect health via a myriad of mechanisms. At the same time, providing higher quality food and making it affordable and accessible in poor as well as affluent neighborhoods is necessary for people to eat better, providing they also learn what types of food to eat. Likewise, making neighborhood safer and more congenial and supportive (Sampson et al., 1997) can improve opportunities for positive social interactions and increased recreational physical activity. However, governmental policies are not the only way to reduce allostatic load. For example, businesses that encourage healthy lifestyle practices among their employees are likely to gain reduced health insurance costs and possibly a more loyal workforce (Aldana, 2001; Pelletier, 2001; Whitmer et al. 2003). (4. Interventions: conventional vs top down, paragraph 3)

The socially-dependent stressors McEwen enumerates map on to the list of the social determinants of health identified by the WHO. They are crucial in influencing good or poor health, but very often beyond the power of the most individuals to control. And, we will soon see, these social stressors skyrocket after the onset of MCS.

As for pre-onset life for those who develop MCS, given the high stress levels in society due to structural and ongoing inequities in these major social determinants, it is also to be expected that we would find high social stress levels along with lower socioeconomic status in many individuals prior to onset of MCS, *as with any disease.* But again, these added factors (with the exception of a healthy/unhealthy physical environment and possibly genetics) still do not explain why only some people's ill health is expressed in *chemical* sensitivity. Here again, in addition to social stressors, we need to factor in toxicological inputs for both stages of MCS.

Our needs-identification study (Burstyn & MEAO, 2013, pp. 59-166) was the core instrument used to assess patient health needs in Ontario in 2013. But it turned out to be a spectacular chronicle of the full range of stressors experienced in post-onset MCS. High on the list of stressors was life in the workplace. Participants spoke of the increasingly severe symptoms they experienced in work settings as their health deteriorated because management refused requests to control the substances that were making them sick, for example, printing chemicals, petrochemical fumes, building materials, mold and cleaning materials. So, lack of control of continued exposure to toxic chemicals produced MCS for them, not lack of control alone. Likewise, people living in industrial neighbourhoods, high-traffic zones, or multi-unit dwellings where cigarette smoke and fragranced cleaning and laundry products circulate through building ventilation systems must endure prolonged exposures but very frequently do not have the financial means to escape them. They are unable to effect a change in these ambient chemicals even if they know they need to. Such prolonged exposures too can lead to, and exacerbate, MCS.

### 7.4.4 Physical and toxicological stressors are needed to tip people into MCS

To arrive at a better understanding of the stressors – technically speaking – that do tip people into onset of chemical sensitivity and full MCS, we need to focus more closely on the physical—including toxicological—stressors they encounter. Let us review these here, because they are so important. It is not coincidental that this list overlaps with the issues addressed in Part 5 ("Lessons from the clinical experience"). While psycho-socio-economic stressors increase likelihood of disease in general, certain types of physical stressors can increase risk for MCS specifically, particularly if these include toxicological factors:

- Physical injury: Important injuries include brain and spinal cord injuries resulting in damage of brain and spinal health and consequent dysfunction, including sensitization, damage to other nerves, ongoing pain due to musculoskeletal injuries, arthritis and FM, and pain due to other chronic illnesses. Pain research shows that pain affects neurotransmitters that can trigger anxiety and depression, which lift when the pain is alleviated.

- Extreme heat, cold, exhaustion: Being consistently pushed past physical limits relating to heat, cold, and physical exhaustion is extremely stressful and can lead to various kinds of breakdown, both physical and mental. A growing literature on the physical effects of mental exhaustion shows that it can have severe physical effects (Gavelin et al., 2020).

- Infections, immune insufficiency, biotoxins: Acute or chronic viral, bacterial, fungal, and parasitic infections can affect the central nervous system as well as other parts of the body. They can cause cognitive and affective disturbances and need to be resolved before these disturbances disappear. Biotoxins produced by mold (mycotoxins) and by infections of various types can have similar effects. Many types of dysfunction can be provoked, including symptoms that are affective in appearance but not psychogenic in causation, and the duration of affective symptoms is also linked to the duration of the infection or exposure. A viral or bacterial infection of the nervous system can create depressive and anxious symptoms in significant numbers of people, symptoms that resolve when the infection is resolved. Toxic mold can have extremely damaging and multi-system effects that improve when the mold is removed and the body is cleared of mycotoxins (Hope, 2013, Nathan, 2018).[54]

- Hormonal imbalances and deficiencies: These can cause many physical problems and affect every function of the body, including cognition and mood. Restoration of thyroid and adrenal levels, for example, can much improve depression if they are low.

- Gastrointestinal insufficiency, gut health or dysbiosis, food allergies and nutritional deficiencies: All these stressors have been shown to have a major impact on overall health, energy, and brain functioning, including mood and cognition, and are usually co-morbid with MCS. Chronic vitamin deficiencies, including those caused by toxic overload and gastric insufficiency, play a part in sensitization. Many vitamins, but especially B vitamins, are needed for healthy affect. Vitamin D is essential for good immunity and, therefore, defense against infection. Nutritional deficiencies undermine detoxification and proper immune functioning.

- Chemical toxins of many kinds: As discussed at length, these can have major direct and indirect impacts on the brain and systems that affect it. They can cause many serious diseases, including cancers and lung, liver, and kidney disease, and they can adversely

[54] From Hope, 2013: "Physicians are increasingly being asked to diagnose and treat people made ill by exposure to water-damaged environments, mold, and mycotoxins. In addition to avoidance of further exposure to these environments and to items contaminated by these environments, a number of approaches have been used to help persons affected by exposure to restore their health. Illness results from a combination of factors present in water-damaged indoor environments including, mold spores and hyphal fragments, mycotoxins, bacteria, bacterial endotoxins, and cell wall components as well as other factors. Mechanisms of illness include inflammation, oxidative stress, toxicity, infection, allergy, and irritant effects of exposure. This paper reviews the scientific literature as it relates to commonly used treatments such as glutathione, antioxidants, antifungals, and sequestering agents such as Cholestyramine, charcoal, clay and chlorella, antioxidants, probiotics, and induced sweating" (Abstract).

affect the brain and its functions: cognition (executive function, language, writing, reasoning), neuromuscular coordination, and mood (causing depression, anxiety, and panic). With MCS sufferers, chemicals (as body burden, toxic injury events, and post-onset triggers) often provoke all these neurological symptoms, including what appear to be psychological symptoms in the central nervous system (crying, depression, anxiety), cognitive symptoms (difficulty thinking, speaking, and writing), and neuromuscular symptoms (pain, loss of coordination or mobility). When such symptoms are provoked, they resemble affective symptoms but are not psychogenic. When triggers are ubiquitous—this is the case if people with MCS continue to work and live in chemically saturated spaces—such symptoms may recur and persist for weeks at a time or simply be ongoing. Neuro-inflammation, produced by free radicals and oxidative stress as a result of toxicity, can provoke affective-like symptoms, as well as symptoms in many body systems.

- Pharmaceuticals: Certain types of medication, a subset of chemical toxins for some people among whom those with MCS feature prominently, need to be counted in the chemical category.

- Electromagnetic frequencies: These have been shown to provoke all the same symptoms as chemical toxins. While these are not addressed by the INSPQ or this commentary, they are real world stressors for many people, and will have to be factored into analysis and policy at some point.

In colloquial usage, physical and toxicological factors are rarely signified by the word "stress," but in their direct impact on the body and mind they provoke stress responses. A combination of these stressors alone can create mechanisms conducive to MCS. Miller et al.'s (2021) description of mast cells during stress, acting in ways that "may activate the hypothalamic–pituitary–adrenal axis and disrupt blood-brain barrier integrity" (Miller et al, 2021, MCAS, TILT, and the nervous system, paragraph 5) illuminates one of the ways that stress has physical consequences that enable neurological and immunological disease and chemical sensitization.

The Western paradigm of an impermeable division between the mind and the body has been dissolving under the weight of many types of research for many years. Now we know that cognitive and affective processes can be affected by many types of physical phenomena, and vice versa, in an interdependent and bi-directional manner. Stressors of many kinds interact in this complex matrix.

The key point for this debate, however, is that the mind body-relationship is a two-way street, and *directionality is critical when seeking to understand and treat any disease, including MCS.* When an injury is clearly physical—a break, a wound, an infection, a scar, a heart attack—certain psychoneurological modalities, such as psychotherapy, meditation, or limbic retraining, may be helpful in managing pain and reducing stress, which is often seen as a pre-condition to recovery. But, once again: we would never withhold direct medical care as the first line of treatment, be that a cast, surgery, stitches, or pharmaceuticals. This is how we must approach MCS, which

results in the first instance from toxicological and physical injuries, which, invariably interact with personal and social stressors.

## 7.5 GULF WAR ILLNESS HAS LESSONS FOR UNDERSTANDING MCS

### 7.5.1 Gulf War Illness is not PTSD

For the most part, we will leave to others specific comments related to the INSPQ report's conclusions vis-à-vis PTSD, anxiety, depression, and panic disorder as primary diagnoses. But we do want to discuss Gulf War Illness (GWI), and we want to begin by stating that PTSD is not the new name for Gulf War Illness, as the INSPQ report incorrectly indicates (p. 15; p. 218). [55] Not every person with Gulf War Illness has PTSD, but for those who do, the illness burden is magnified.[56] GWI comprises many more disorders than PTSD, including fatigue, pain, neurocognitive and neuromuscular dysfunctions, and chemical sensitivity. PTSD can be a co-morbid condition (Jeffrey et al., 2021). It is not the defining condition.

The illness is a syndrome that emerged from a short but exceptionally chemically laden war, the chemicals being an acknowledged feature in the syndrome's etiology. For a long time, institutional interests (above all, the United States government) did not want to recognize this, and instead tried to explain GWI as a psychological problem linked to a psychological susceptibility to stress.

But affected veterans, their medical champions and key administrators found this account completely lacking in evidence and credibility, and so a familiar cleavage in the field emerged, between psychogenic and toxicogenic schools. Eventually, the psychogenic school could not hold its own. Masri et al. (2021) write that

> numerous studies have shown that stress and psychological features are insufficient explanations. As noted by Golomb [18] (2008), post-traumatic stress disorder rates are not systematically higher among Gulf War veterans compared to soldiers deployed in other conflicts, yet the rates of chronic illness are substantially higher among soldiers deployed to the Gulf [18]. The Institute of Medicine noted that increased symptoms were also reported by veterans from other countries who participated in the Gulf War [19]. (Masri et al., 2021, Gulf War Illness, paragraph 1)

[55] Example: Original French language text (p. 15, 1.5.2) ,,, le syndrome de la guerre du Golfe – maintenant nommé syndrome de stress post-traumatique (SSPT ou PTSD en anglais) -- …

[56] A very recent study with the self-explanatory title, "The Impact of Post-Traumatic Stress on Quality of Life and Fatigue in Women with Gulf War Illness" illustrates this, as do the points in our previous section on the different biology of women vis-à-vis chemical exposure. Research into Gulf War Illness is very much alive including, recently, a major effort to define common data elements to enhance data quality and sharing in future research (Cohen et al, 2021).

In not considering Gulf War Illness, we think the INSPQ has closed the door on an extremely illuminating example of complex toxicological impacts interacting with clear and heavy physical, social and personal stressors.[57]

### 7.5.2 Toxic chemicals in Gulf War 1

In 1990, the United States went to war in the Persian Gulf (GW1) and concluded the war early in 1991. About 700,000 personnel served. Ninety-three percent of the soldiers deployed were male, the rest female. Fully 25 percent of the total, with women represented disproportionately, came back with a frightening legacy of health problems, which they soon began to report and continued to report over the ensuing decades—a legacy that from the beginning sounded astoundingly familiar to those who knew about MCS, ME, and FM.

Phil Brown, professor of sociology and environmental studies and founder of the Contested Illnesses Research Group at Rhode Island's Brown University, has been writing about environmental health since the mid-1980s, beginning with *No Safe Place: Toxic Waste, Leukemia and Community Action*. From the beginning he chronicled the struggle of Gulf War 1 veterans for recognition of their illnesses and for compensation. In a 2012 retrospective evaluation of this evolution, *A Narrowing Gulf of Difference? Disputes and Discoveries of Gulf War-Related Illnesses*, he and his colleagues commented on the symptoms that soldiers had reported in the early and mid-1990s:

> Symptoms of what has come to be called Gulf War-related illness include nausea, loss of concentration, blurred vision, fatigue, lack of muscle control and coordination, irritable bowels, headaches, respiratory problems, rashes, and other ailments that the affected individuals had not experienced prior to service in the Gulf. . . . Veterans' claims were supported by studies showing an excess of self-reported symptoms among deployed versus non-deployed troops, including chronic diarrhea, other gastrointestinal symptoms, memory loss, concentration difficulty, trouble finding words, fatigue, depression, PTSD, bronchitis, asthma, alcohol trouble, sexual discomfort, and anxiety. (pp. 79-80)
>
> Some symptom clusters resemble chronic fatigue syndrome, fibromyalgia or multiple chemical sensitivity, all of which are themselves poorly understood and subject to dispute. (p. 89)

Brown quoted James Binns, chair of the Research Advisory Committee struck by the American government to deal with the illness:

[57] Other major gulf exposure included combustion products from burn pits and oil well fires. One study determined that determined that Gulf War Illness was closely associated with taking pyridostigmine bromide tablets, being within one mile of an exploding scud missile, using pesticides on the skin, and being exposed to oil-well-fire smoke.

> This is a real condition, which affects at least one-fourth of the 700,000 veterans who served in the 1991 war. . . . It differs fundamentally from the trauma and stress related syndromes that had been described after other wars. (p. 103)

What was different about Gulf War Illness? Several types of synergistically interacting chemical exposures marked this war as different from others.

1. Ingestion of pyridostigmine bromide: Masri et al. (2021) write that

> an estimated 250,000 U.S. soldiers received pyridostigmine bromide (PB) pills as a pre-treatment drug to protect against possible nerve agent exposure. PB is a carbamate compound resembling [organophosphate] pesticides in its action on the central nervous system. Except for combat, PB in the U.S. was approved only for treatment of a chronic muscle disease known as myasthenia gravis, in which affected individuals have antibodies to their cholinergic receptors. PB had never been approved for individuals with normal nervous system function, much less chemically susceptible individuals. (Gulf War Illness, paragraph 3)

   This medication had been thought not to cross the blood-brain barrier. However, as was later learned, under stress conditions, it did breach that barrier and became a toxic agent in its own right.

2. Exposure to chemical warfare agents: Many combatants were exposed to such agents, originally in the hands of the Iraqi regime, via the vast, far-travelling plumes that were created when the chemicals were being destroyed by US forces. The makeup of these chemical weapons was known to the United States.

> When U.S. forces blew up an Iraqi weapons depot at Khamisiyah, 100,000 U.S. troops were exposed to the organophosphate (OP) nerve agents sarin and cyclosarin, which inhibit the enzyme acetylcholinesterase (AChE). Even minimal OP exposures can elicit acute symptoms, which may herald the onset of TILT[/MCS]. (Masri et al., 2021, Gulf War Illness, paragraph 2)

   A very recent detailed genetic study on GWI looking at the PON1 gene (one that has featured in MCS-related work as well), "Evaluation of a Gene–Environment Interaction of *PON1* and Low-Level Nerve Agent Exposure with Gulf War Illness: A Prevalence Case–Control Study Drawn from the U.S. Military Health Survey's National Population Sample," Robert W. Haley, a senior researcher at the division of epidemiology, Department of Internal Medicine, University of Texas Southwestern Medical Center in Dallas, and colleagues found "strong evidence for an etiologic role of low-level nerve agent in GWI" (Abstract, Discussion). This research, as well as background information on sarin was highlighted in a news release from UT Southwestern Medical Center on May 11, 2022, "UTSW genetic study confirms sarin nerve gas as cause of Gulf War Illness." Recall bias, which often plagues studies of this kind,

was minimized by questioning the veterans about chemical nerve gas alarms as well as by collecting blood and DNA samples.

These researchers do not rule out other causes of GWI in some instances, and we know from other studies that other toxicants were present in damaging concentrations. But the research does validate the hypothesis first advanced in the 1990s that genetic factors relating to abilities to metabolize chemical substances are very important in creating susceptibility to certain conditions, MCS included. As the news release about the study states, "Troops who had genes that help metabolize sarin were less likely to develop symptoms." Is it necessary to point out that not having certain genes is not an anxiety disorder?

3. Burning crude oil, pesticides and medical toxicants: This incredible cocktail included particulates from oil wells that burned for months. Furthermore, to reduce disease vectors, pesticides and insect repellants were used liberally and repeatedly at all camps (Masri et al., 2021, Gulf War Illness, paragraphs 2, 4). Both of these toxicants have been linked to MCS in other studies, and contributed to the toxic environment. A 2002 study by Wolfe et al. "Sixty percent of respondents met criteria for multi-symptom illness," and (among other factors) "ingestion of anti-nerve gas pills (pyridostigmine bromide), anthrax vaccination, tent heaters, exposure to oil fire smoke, and chemical odors were significantly related to multi-symptom illness in logistic regression analyses" (Wolfe et al., 2002, Abstract).

By 2000 and again by the early 2010s, a number of studies, including some that used new brain imaging technologies, showed that serious physical brain damage had been done and was still being found in vets, and it was responsible for the panoply of symptoms and loss of function involved in Gulf War Illness (Li et al., 2011; Rayhan et al., 2013; Innacchione et al., 2011).

Of those affected by the broad category of Gulf War Illness, a smaller but significant subset developed chemical sensitivity as part of their syndrome. In their study reviewing and revisiting the field of Gulf War Illness in 2021, Masri et al. (2021) note:

> The most striking symptoms reported by Gulf War veterans involved the central and peripheral cholinergic nervous systems (which require the neurotransmitter acetylcholinesterase) [16, 23-25]. Golomb [18] attributed excess illness in Gulf War veterans, in part, to exposure to acetylcholinesterase inhibitors, including [pyridostigmine bromide], pesticides, and nerve agents. Just after the Gulf War, one of the authors [CSM] served as environmental consultant to the VA Regional Referral Center in Houston, Texas, where she evaluated approximately 60 Gulf War Veterans with unexplained illness. In a 1995 paper, Miller and Mitzel [26] described 37 chemically intolerant individuals who developed TILT following OP pesticide extermination, and were first to point to organophosphates as probable initiators of Gulf War Illness. Miller subsequently coined the term "Toxicant-Induced Loss of Tolerance"[2] based in part on these observations. (Gulf War Illness, paragraph 5)

Given the extreme toxicity encountered by a significant number of military personnel in GW1, conditions were ripe to produce chemical sensitivity among at least some (a subset) of those who lived through this, due to hypothesized genetic factors and pre-existing chemical body burdens interacting with on-the-spot exposures.

### 7.5.3 Combat stress

Nothing happens in a vacuum, and the toxicological exposure of Gulf War 1 took place in the context of many other heavy stressors, notably those of battle. In addition to the usual complement of such stressors, in this war soldiers reported that the chemical alert sirens went off so often (daily or even more frequently), that they became terrifying. All personnel were required to suit up in chemical warfare gear for extended periods of time. According to United States Air Force Major David S. Fenton (retired),

> Soldiers regularly passed out when dressed in it, even in practice drills on US soil when there was no threat, simply from the hardships created by the masked helmets, full suit, gloves and boots. Severe claustrophobia was regularly reported by soldiers in the gear, in addition to ordinary difficulty with breathing, overheating and exhaustion" (V. Burstyn, personal communication, January 2012).

It stands to reason that the effect of the toxicological stressors of that war would have been amplified by the effects of multiple non-chemical stressors of combat and chemical threat, and would augment both short- and long -term physical illness. Applying the findings of Barrett & Padula (2019), GWI would have been a text-book laboratory for the synergistic effects of chemical and non-chemical stressors.

The tragic story of what happened to the claims of illness made almost entirely by young people, a majority male, who were strong and fit when they deployed is fairly well known. The early institutional counter response denied chemical impacts and relied instead on a psychogenic notion of stress. Implicit in that model was a characterization of the victims as psychologically weak or deficient, which then encouraged stigmatization. In keeping with this approach, early treatment attempted to fix the victim's mind and ignored the body, generally to no effect other than frustration and despair. To make matters worse, "for many veterans, the reliance on a stress model, with the VA [Veteran's Administration]'s accompanying cognitive behavioral treatment trial, represented a form of delegitimization" (Brown et al., 2012, p. 94). This strategy is very familiar to people with MCS.

In the last 15 years especially, discoveries related to detoxification abilities linked to genetic polymorphisms regarding enzymatic capacities, brain damage that can be seen only with the most advanced forms of imaging and a series of other diagnostic techniques tracking parameters familiar to us from the study of MCS (and other conditions) have helped to better illuminate the multiple and interacting causes and their outcomes. It is now very widely acknowledged that the chemicals unique to that war were responsible for the physical ailments, including neurological, that have been its legacy (e.g., White et al., 2016; Ahmed et al., 2022, Haley et al. 2022).

Can all these toxicological factors be measured precisely to the point of absolute certainty with respect to which toxicant was present and caused which illness? Perhaps a few can, such as those tracked in the Haley et al. 2022 study. But many cannot. The previously cited experience of researchers working in population and individual chemical exposure studies was repeated in the words of several of Brown's (2012) experts. One said: "We are never going to get the exposure models down because I think the exposures are too diverse" (p. 99). Another told Brown: "War, like any other social experience, is very complex and it's hard to deal with complexity in a fashion that we're familiar with"(p. 99). Despite this reality-imposed limitation, conclusions must be drawn so that help may be provided.

In the process of learning about Gulf War Illness, a shift in the definition of "stress" took place for many genuinely seeking to understand and support the sick veterans rather than shield institutions or industries from criticism or liability. As in parallel fields, the concept of stress has been broadened to fully encompass physical hardship and environmental exposures alongside and interacting with psychological and socioeconomic stressors. Further, in this case, psychological stressors, once thought to be individually based, have been tied overwhelmingly to impinging social factors (e.g., chemical warfare, fear of enclosed spaces imposed by others) rather than to mental or emotional weakness.

So, while a clearer picture emerges with respect to how certain physical defenses such as the blood-brain barrier can be weakened by a synergy of stresses, it equally becomes clear that psychosocial stress alone does not produce the symptom clusters of Gulf War Illness, including MCS. Without the chemical exposures of Gulf War 1, the chemical sensitivity among veterans would not have developed.

The field of Gulf War Illness studies shows why it is not accurate to counterpose toxicological to biopsychosocial factors when conceptualizing MCS. But it also shows why in chemical sensitivity, the toxicological factors need to be understood as determining, even as they are considered part of a more complex mix of stressors.

Since the early 1990s, significant numbers of Gulf War veterans, first responders sickened in the 2001 World Trade Center attack, and oil workers injured in many oil spills have sought the assistance of environmental physicians for treatment that has helped to improve their health status when cognitive behavioral therapy failed them.

There are many other lessons in this experience that are beyond the scope of this commentary to explore. It is worth noting that the notion that MCS is a women's disease is not, ipso facto, true in the sense that when the toxicological stressors are severe enough, even large numbers of healthy young men succumb. And it is worth noting that GWI clearly knocks anxiety out as a credible contender for causation.

# PART 8: SOCIALLY DETERMINED STRESS IN CHRONIC MCS EXACERBATES ILLNESS

# PART 8: SOCIALLY DETERMINED STRESS IN CHRONIC MCS EXACERBATES ILLNESS

## 8.1 INTRODUCTION

Having reviewed the specific types of stress - from emotional and socio-economic to physical and toxicological – in the onset of chemical intolerance, and having underlined that we need to understand their synergistic effects, without losing sight of their particular impacts and roles in specific types of illness, we now turn to an examination of multiple types of stressors in the life of the majority of people with chronic MCS.

This analysis will demonstrate that it is the unbearable weight of real existential dangers that causes fear and vigilance in MCS, not the "anticipation of danger" attributed to an anxiety disorder and somatoform illness, per the INSPQ report. It will illuminate the choices that our government's inaction makes in their neglect of MCS, and how lack of knowledge and psychogenic bias among physicians create massive, socially determined stressors undermine health and hinder recovery. The point to consider is that once these stressors have been identified, social measures to reduce them for people with MCS can be easily achieved with the right program of health and social supports that are easily within reach of government policy and health system action – if we choose that path.

## 8.2 FROM GROUPS TO INDIVIDUALS: SILICONE BREAST IMPLANT RECIPIENTS

We now want to move from the lessons provided from studying large, occupational groups such as those in the Masri et al. article to the lives of *individuals* with MCS. These individuals, as we know, are mainly women, and after onset, however it occurred, they are left to deal with terrifying new symptoms without any kind of public or institutional support.

It is perhaps helpful to review another group from the Masri et al. (2021) study in this regard: women who underwent silicone breast implants. This group were unique in that they were all female, had not been aggregated on the basis of a common site, and had experienced exposure as a result of an internal foreign chemical substance rather than as a result of external ambient chemicals encountered through respiration and skin contact.

Although their manufacturers marketed these implants as safe, Masri et al. write that

> [f]ollowing surgical implant operations, numerous physicians have reported multisystem symptoms among a subset of patients closely resembling chronic fatigue syndrome and chemical intolerance [35]. Importantly, silicone may leach slowly from intact breast implant membranes [36] producing inflammatory and immunological responses [37, 38]. The chemical composition of implants varies greatly and may include metals that migrate into surrounding tissue [39]. Processing aids and peroxides also have been used to aid the curing process for implant gels. A causal link between breast implant illness (BII) and symptoms is supported by reports that implant removal can reverse symptoms in 40–60% of patients [40].

> Brawer (2017) [41] summarized his observations of over 500 breast implant recipients by stating that "Prior to implantation these patients manifested no adverse reactions to perfumes, room fresheners, deodorants, hairsprays, cleaning agents, cigarette smoke, exhaust fumes, carpeting, fabric dyes, adhesives, caulking, glues, stain removers, detergents, dry cleaning products, paints, lacquers, insecticides, pesticides, and printing resins." After their systemic illness became established, they subsequently began to experience nausea, dizziness, and headaches on exposure to nearly all of the above. Brawer [41] also noted a "profound similarity" between TILT[/MCS] and four decades of his own observations. (Implant patients, paragraphs 1, 2)

The individual women all had a direct, identifiable source of chemical leaching; the improvement of symptoms on removal of that source took place in up to 60 percent of cases. Anxiety, which might or might not have been an issue for these women—did not cause their symptoms. We do not know for a certainty why as many as 40 percent of women did not recover. We may speculate that they may have retained a body burden of the triggering chemicals and/or the damage done may have required additional therapeutic input to correct and/or it may have become irreversible.

As well, we may surmise that, like the other members of the subgroups who developed MCS in the other seven clusters discussed, whatever the stress levels of their lives had been prior to developing MCS, those levels radically increased afterward. And since stress features so prominently in the INSPQ report as a causal factor for anxiety, which in turn "explains" MCS, it is important to understand this issue in the overall picture of MCS chronicity. It is the matter to which we now turn.

## 8.3. INTRODUCING POST-ONSET CHRONIC STRESS IN LIFE WITH MCS IN THE ONTARIO 2013 STUDY

Having taken a look at adverse chemical impacts, clearly exacerbated by stress in the Gulf War example, we have identified the importance of relevant stress impacts beyond those of an individual's temperament and personal history.

Certainly, Masri et al.'s (2021) study of eight different cohorts helps us understand the determining role of chemical stressors involved in MCS onset in subsets of people facing major exposures over relatively short periods of time, and in resulting long-term illness. It helps us understand that while other types of stress as well as possible genetic factors may increase susceptibility, they alone do not cause MCS onset – chemical exposure must also be present.

We also need such studies in relation to post-onset MCS among disparate individuals – the majority of people who make up the MCS population. Therefore, we now want to take this expanded template of stressors – personal, social, physical, toxicological – and apply it to that subject. Had we a robust literature of substantive epidemiological research that already examined the weight of physical, toxicological, social and interpersonal stressors in chronic MCS,

the results would certainly help shed light on what stress factors including and beyond chemical exposure could predispose, enable, or exacerbate MCS.

Some literature that touches on these subjects exists but is admittedly scant, and includes work by Pamela Gibson (Gibson 1993, 1997, 2006; Gibson & Lindberg 2007, Gibson et al. 2011) and Julienne Lipson (Lipson 2004, Lipson & Doiron 2006). In the grey literature, we also have the rich qualitative study from Ontario, cited frequently throughout (Burstyn & MEAO, 2013, pp. 59-166). This study, originally undertaken as a needs assessment, also describes important aspects of a massive new stress burden that arrived for its participants after they began living with MCS. This study was not engaged by the INSPQ authors. We repeat now that no analysis or definition of MCS can be complete without including the experience of those who live with it through existing literature and, due to the scarcity of such literature, through additional outreach to advocacy organizations, leading clinicians and patients themselves.

In the Ontario study, to determine "gaps and deficiencies" in care and support – our mandate from the Ministry of Health – we used the template of the World Health Organization's social determinants of health to query our participants. We canvassed fairly broadly for participants in different regions of the province. Our participants ranked their severity as moderate to severe. More information about the study methodology as well as direct quotes to support our summary are available in Appendix 3, where readers will find a small but illustrative selection from the many verbatim reports from larger study. Since no new policies, programs or sites have yet been created, we think the experiences of these participants remains relevant and current today.

An important feature of the invisibility of MCS is that, as we have learned, it seems that no person who does not have MCS or lives with someone who does has the faintest idea of how difficult life becomes after onset, especially when severity attains moderate to severe levels – the levels of our study participants – and financial resources are constrained, which is usually the case.

In short, our study revealed that people with moderate to severe MCS experienced an extraordinarily heavy burden of new, extrinsic, and chronic stressors that arrived on top of already existing illness and other "garden variety" stressors. We found that this new burden comprised many massive new difficulties in navigating the most ordinary channels of life. Unsurprisingly, many participants expressed many difficult feelings that followed, including loss, sorrow, grief, frustration, anger and rejection, as well as fear of imminent dangers both chemical and socioeconomic. At times, some participants felt depression, sometimes hopelessness, and sometimes despair. We also found that the MCS participants showed an amazing determination to find meaning and joy in life despite these stressors. We heard no mention of anhedonia (the inability to feel pleasure mentioned in the INSPQ report[58]). And a thorough search of the Ontario study revealed only one mention of pre-onset, or even post onset, "anxiety," the word a participant used to describe her feelings about the dangers of an imminent hospital visit. Our

[58] "Anhédonie" (Messages clés, p. 1) translated in the English version of the Key Messages, p. 2 as "inability to feel pleasure." The English version did not use the technical term.

view is that these feelings are entirely rational given the normal hospital environment. There were no mentions of anxiety disorder.

Our study is not the first to find a lack of anxiety disorder among MCS patients, especially pre-onset. Kutsogiannis and Davidoff, 2001 as cited in Marshall et al. (2010) wrote that

> 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." (pp. 17, 18, emphases added)

We queried many categories of experience, and some the categories of post-onset stress that emerged were ranked by participants as even more significant than others to the extent that several of these required whole chapters of their own in the report. These included:

- financial impacts
- gender issues
- interactions with physicians and the health care system, and
- a meta-stressor that crossed all queried domains, namely stigmatization.

Stigmatization merited some dedicated words in both reports of the Ontario Task Force on Environmental Health (2017, 2018). The white paper accompanying Ontario's Ministry of Health Task Force on Environmental Health 2017 report observed, again with notable understatement:

> Patients with lived experience, clinicians, and researchers have all experienced and/or observed the social stigmatization that affects patients with the conditions. This is arguably particularly acute for patients with ES/MCS. . . . stigmatization may increase the risk of anxiety, depression and other psychological symptoms that, in turn, can be mistaken as causes rather than effects of the diseases themselves. (Hu et al., 2017, p. 47)

One additional note before we delve into the material itself: During and after reading this highly condensed inventory of post-onset stressors readers are asked to consider whether the worry and fear people with chronic MCS regularly experience as a result of the multiplication of stressors in their lives is indeed what the INSPQ report framed as a neurotic and irrational "*anticipation of danger* i.e., feeling a persistent, excessive and inappropriate concern about one's day-to-day activities," (Summary, p. 3), the result of an "illness belief system" (Rapport complet,

p 644) and "phobic avoidance" [59] (Rapport complet, p. 642, translated). Or are these feelings rational and natural responses to these recurring stressors, and the impossible dilemmas and hardships they create. Readers are also asked also to remember the effects of this chronic stress, as all chronic stress, on "neural, cardiovascular, autonomic, immune and metabolic systems" (McEwen, 2008) and the double jeopardy of the combination of chemical and non-chemical stressors (Barrett & Padula, 2019) in affecting overall health and well being.

Readers are also asked to consider to what extent the new, post-onset stressors are likely to exacerbate illness, impede stabilization and retard recovery at a time when de-stressing is needed, and how much better post-onset outcomes would be if we, as a society, improved these conditions, which is very much within our grasp if we wish to make it so.

Readers are also asked to keep in mind the major lesson of the previously discussed Whitehall study: the Whitehall authors did not understand stress as a mental illness, or, indeed as an issue that can be solved by individual action. Most people with chronic MCS could make great strides in improvement, including for some, even a return to normal, with appropriate, effective treatment including a safe place to live, and reduction of stress to normal levels. But for the great majority who do not have the financial means to achieve these conditions, absent such support from our public systems their stressors cannot be made to disappear by their individual action. This is why we call key health determinants "social."

We begin with a note on the overall burden of stress that arrives with chronic MCS.

## 8.4 WHO DETERMINANTS OF DISABILITY, EMPLOYMENT, INCOME SECURITY, HOUSING, FOOD, CLOTHING AND TRANSPORTATION

Disability: First, participants reported that though they were disabled, both in body and in law, they felt invisible and denied. They reported that with their unavoidable encounters with the everyday chemicals now found in every setting, they were disabled by symptoms that we can map on to some or all of the "cutaneous, allergic, gastrointestinal, rheumatological, endocrinological, cardiological and neurological" systems in our working definition and as noted by Damiani et al., (2021). This meant living with a high and disabling degree of poor physical health and accompanying fatigue simply from carrying out daily activities. Different chemicals, alone or together and over differing durations, had different degrees of impact, ranging from a matter of hours to a matter of days, weeks, or even months. New "crashes"—deterioration from one degree to another—were not uncommon. Certain chemicals (solvents and pesticides) were frequently mentioned as causing extremely painful and disabling symptoms that made even the smallest of daily tasks difficult or impossible. The few who had had appropriate care for exposures reported on what a difference that care made. They also reported on how dispiriting it was to know care could be, but was not geographically and/or financially accessible, nor covered by private insurance. The disabling consequences of MCS were, indeed, legion.

[59] "L'évitement phobique est courant chez les personnes SCM…" p. 642

Second, participants found that publicly provided disability programs were very deficient when it came to covering their needs. As a result, many people were permanently going without essential medical supports, including prescription drugs and assistive devices such as air and water purifiers, and experienced tremendous inequality relative to recognized disabilities. Physician assistance is required to obtain disability benefits but was often difficult or impossible to obtain. Many participants reported a lack of support from physicians as especially impactful, ranging from procrastination when writing letters to refusal to assist. (More on physicians below.)

Income security, employment, and working conditions: Participants without private means or established pensions—the great majority, almost all women—reported grave financial impacts on them and their families, describing these as ongoing and frequently causing enormous strain (Appendix 3). Some participants were struggling to survive on social assistance. Others had incomes above the official poverty line, whether through private means, the income of spouses, a middle-class job, a pension, or part-time work. Yet, they reported, they did not have sufficient resources to adequately meet their health needs, which ranged from safe food to housing to health care, none covered or subsidized through public resources. Given the need to cover all health care and support privately, for all too many, even those with middle-class incomes could not take care of personal and family needs when MCS struck.

Job loss due to illness onset and/or a lack of disability accommodation was a central feature of life for the majority of participants and an enormous stressor. Some participants' employers had refused to accommodate them because they did not believe participants were really sick or could be made sick in ways the employees described. Some employers had taken actions that isolated and undermined participants and made it impossible for them to continue working. A number of study informants had succeeded in continuing to work but faced major complex obstacles that remained ongoing, not easily resolved, and boded ill for continued employment. Some participants expressed the desire to continue to work but were unable to due to a lack of supportive accommodations. Some participants got sick because of hazards in the workplace but lost their jobs anyway, sometimes for punitive reasons and often with no compensation. A number of people reported unrealistic pressures for re-employment from family and physicians due to lack of understanding of the condition.

Participants noted that job loss during prime working years without income protection and health benefits seriously affected their present and future income (savings, pensions). Many were left without any savings or insufficient pensions, had been reduced to extreme poverty and feared for their futures, since no safe social housing or long term care existed (and still does not exist).

Participants reported that insurance benefits were extremely difficult or impossible to obtain, and the process of seeking them often became injurious in itself. Some insurers exhibited bullying, discriminatory or other harmful behaviours. In many cases, insurance companies that did not recognize these conditions as illnesses or disabilities put the onus on people who were ill to prove that they deserved insurance or compelled them to take psychotropic medications that

were very harmful. Some participants were cut off prematurely from disability payments. Lack of coverage for essential health and medical needs was a constant, and in these ways, insurers exacerbated illness instead of assisting sufferers.

Even as onset of MCS usually resulted in disability and income loss, the cost for appropriate treatment skyrocketed because this now had to be paid for privately. We identified this as a "crushing burden" (Appendix 3) for many as well as a major inequity and barrier to necessary care for all.

Housing and healthy physical environment: A safe place to live, therefore, safe housing, is the core component of stabilization and improvement for people with chronic MCS. This is because it allows for the avoidance of triggers for long periods every day and above all, at night, and hence offers a resting state to a damaged central nervous system and a struggling, often deficient immune system. Whereas the INSPQ report seems to consider avoidance a neurotic behaviour, it is the absolute minimum prescription by MCS doctors, and participants in this study strongly endorsed it. They reported great improvement in both reactivity and overall health when able to achieve it, and terrible consequences when they were not. Ann McCampbell, a New Mexico physician who provides care for people with MCS writes

> Many people with MCS have lost everything – including their health, homes, careers, savings, and families. They are chronically ill and struggle to obtain the basic necessities of life, such as food, water, clothing, housing, and automobiles that they can tolerate. Finding housing that does not make them sicker, that is, housing that is not contaminated with pesticides, perfume, cleaning products, cigarette smoke residues, new carpets or paint, and formaldehyde-containing building products, is especially difficult. Many people with MCS live in cars, tents, and porches at some time during the course of their illness. (McCampbell, 2001)

*In this context, housing insecurity emerged as a massive problem and top stressor*. For all participants, achieving this medical need required multiple moves of domicile, depleting, exhausting and costly. Those with means made major expenditures in either a new house purchase and/or in non-toxic house furnishings, building material and alterations, and mold remediation to create a safe environment, though these efforts often resulted in great financial hardship and extended physical suffering. Others did not have the means for such major changes and encountered painful, often insurmountably difficult challenges in finding rental accommodation. All participants were highly stressed by housing issues, and some were bankrupted. They reported that both the unsafe housing and the massive stressors in addressing this matter undermined their health and made their MCS worse—in the case of apartment dwellers, the situation was much worse than for those able to find and afford single-family units.

Participants noted with great distress that there is no access to any type of safer housing for this group in any form, be that market-value housing, social housing, supportive housing, emergency shelters, acute care, assisted living, or long-term care and palliative facilities. All noted that

should their situations worsen, either in terms of health or financial viability they would literally have nowhere to go.

Food insecurity: Participants identified food insecurity as a very serious issue for themselves and others with ES/MCS. They identified the following issues: not being able to afford food; not being able to obtain or afford medically indicated food or medically tolerated food (such as organic and gluten free), with resulting adverse health outcomes; supermarket environments where chemicals from everyday products made every shopping excursion an illness-inducing episode and they found that vegetables and fruit were chemically-laden dangers. Not having consistent support, familial or otherwise to prepare and serve meals and clean up afterward when levels of illness made this difficult for them was an added difficulty. Participants pointed out that since many had severe food allergies and sensitivities and/or were not considered eligible for food assistance, they were not able to use Meals on Wheels. And since effective poverty was high among sufferers, many did not have the private means to purchase healthy food or food services. For some, this situation reached extremely dire straits.

Clothing and home furnishing insecurity: One little known but very stressful consequence of severe MCS is long-lasting reactivity to new clothing and shoes.

> You can't have what other people take for granted, like family, friends, socialization, clothing. Lately I order most of my clothing from the Sears catalogue. I guess it's not so lately that everything comes through China and it is soaked in formaldehyde. . . . With my current partner we've taken cotton clothing and washed it in everything and soaked it in vinegar, just washing and washing and washing. . . . After about a year of washing and washing and soaking, then you can wear something. Claire MCS (Appendix 3)

The challenge of new materials with their preservatives, pesticides, dyes, tanning materials, and adhesives can be very difficult. Buying all organic clothing is very expensive and not always possible, and even then, sometimes dyes or chemicals picked up in transport can trigger flares. The repeated washing of new clothing—a tiring, energy-intensive, and expensive process—releases clothing chemicals into the air and, if done in a winter-closed house, can trigger bad flares. Certainly, those with severe MCS end up wearing and patching clothing until it disintegrates, which adds to their sense of social pariah-hood. With respect to shoes, they may wear them for years, even if the fit is no longer good, because breaking in new shoes becomes impossible. This can lead to injuring feet and undermining healthy mobility.

Transportation: Another major stressor for MCS participants is finding a car with a safe interior. This is extremely difficult, even when affordable and some had given up. But riding public transportation had become impossible for most due to ambient fragrances and petrochemical by-products. Since at that time (and still today) no Wheel Trans vehicles were free of fragrances or petrochemically linked substances, participants could not use disability transportation. Trips, especially longer ones, induced serious setbacks. Not being able to get to essential services, purchase necessities, or visit family and friends were also identified as massive stressors.

Education: Some participants had been doing post-secondary or graduate education when onset occurred; others wanted to undertake new education that would allow them to work from home rather than in an unsafe workplace. One participant reported a good experience with a university in accommodating her need; most expressed great frustration about attending school, in the pre-COVID context when some institutions did not allow on-line attendance. Unfortunately, significant numbers of people with moderate to severe MCS are also sensitive to electromagnetic frequencies and could not undertake extended study online, though this was not a complete barrier to all. Still, many participants expressed fear about their financial viability without new marketable skills.

## 8.5 WHO DETERMINANTS OF SOCIAL ENVIRONMENTS, SUPPORT NETWORKS AND HEALTHY CHILD DEVELOPMENT

Problems in basic family relationships: In the context that participants noted of medical, professional, and societal misinformation and stigmatization, many participants said their families found the realities of MCS difficult to understand, accept, and cope with. That lack of medical explanations and support was deeply stressful for sufferers and family members alike. Participants noted that relationships with their own parents and siblings were often highly stressed. Even for families that did fully accept the diagnosis, dealing with the consequences was often very difficult. Participants reported that the condition placed serious strains on all marriages and terminal strains on many. Numerous participants noted how critical the help of spouses and family was and how difficult it was to cope with this condition on one's own, especially with the "new normal" financial constraints.

Social safety and personal support services: Participants pointed out that publicly provided, condition-competent nursing, physiotherapy and personal support services, available for other groups, were missing for those with ES/MCS. Not being able to access homecare with safe providers or even at all was extremely stressful for those who needed it. This was particularly acute as all were very affected by the lack of caregiving from friends outside the family, the adverse health effects of ambient air and condition-illiteracy in hospitals, and the lack of long-term care beds. Participants identified this type of deficiency as a great isolator and poor-health exacerbator.

Healthy childhood development undermined: Participants noted that MCS created very serious problems for parenting children and providing healthy child development conditions. The MCS parent participants indicated that they were not able to parent their children as they would have liked. For some, children became caregivers who carried burdens disproportionate to their years or capacities, which caused their parents to worry about impacts on their children later in life, a source of sorrow and worry for the parents. They concluded that children suffer when parents suffer and vice versa.

Supports for family caregivers absent: Participants noted that the lack of available supports for family members was a very serious problem. Lack of homecare, respite care, child care, caregiver care—especially when these services could not be purchased privately—put a high burden of

stress on family caregivers, reduced their ability to help, and placed a heavy burden of worry, sadness and loneliness on people with MCS.

## 8.6 WHO DETERMINANTS OF DISCRIMINATION, GENETICS, PERSONAL CARE PRACTICES AND COPING SKILLS

Gender-related issues in the culture: Participants noted that identities and gender roles were strained in family and social life, and sexist attitudes were evident, especially in physicians (more below). A number of women spoke about the difficulties of dependency caused by having MCS. Many women spoke about the sexist perception that their illness was not real or serious but rather a result of female physiology, "hormones" or a tendency to complain. Gender related issues in daily life and health care were such frequent and affecting experiences that an entire chapter in the report had to be devoted to them. (We too have devoted a dedicated section, Part 6, to women, in our case in relation to toxicological factors and MCS.)

A number of men spoke about the strains that being sick put on their gender identity. Losing the ability to be the breadwinner featured centrally in their comments. Some also identified strains in having what was perceived as a woman's condition. Some women also spoke about the way in which the perception of the conditions as women's problems created sexist perceptions of male sufferers.

Systemic discrimination: As noted above and elaborated below, the cultural perception that MCS is a sort of hypochondria or a disavowed mental illness, most often depression, was experienced as a deep form of systemic discrimination, a particularly ugly form of ableism, because it denied the disability and punished those who had it. The generative locus of this stigmatization, in the view of all participants, was the medical system, on which more presently.

Genetics: We have already mentioned (Part 2.6) that the investigation of genetic issues, particularly to do with detoxification capabilities, is an area of lively enquiry. At this time, there is a robust hypothesis – if not yet full evidence – that those with deficiencies in this type of genetic heritage are at considerably greater risk of developing MCS than others. More research is needed, but certainly, if an individual has this issue, getting MCS will be more likely and getting rid of it or significantly attenuating more difficult in the chemicalized world we live in. Physicians as a rule (except MCS specialists) showed no awareness of this dimension.

Personal care practices and coping skills: We include this determinant before the social determinant of "access to health services of a decent quality" because we have now shown through an examination of other areas of life how difficult and even impossible it is for many people with MCS to actually follow through alone with the necessary "personal care practices" they need to stay strong, healthy, and minimally reactive. Given these often-insurmountable issues – stressors, in fact– extraordinary coping skills are required, and they demand an energy and accessibility to resources that often cannot be achieved without substantial financial means, adding yet another source of stress –"I know what I have to do, but I can't do this!"—to the others mentioned. The picture that emerged showed that personal skills could not compensate

for the complete vacuum in social, financial, disability and medical supports. Certainly, this was in keeping with the conclusions of the Whitehall study.

This whole cluster of social determinants could be made better by access to decent medical care. Instead, by and large, in these patients' experiences, medical interactions were, most often, additional and very difficult stressors.

## 8.7 WHO DETERMINANTS OF ACCESS TO HEALTH SERVICES OF A DECENT QUALITY

"Getting health care makes me sick:" The consensus view of the participants: Life is difficult. This is true for everyone. But one thing that Canada did many years ago in order to reduce existential anxiety, health inequities, and, therefore, stress was to adopt the principle of universal health care; and one thing that most Canadians know is that they will be able to access reasonably timely, competent, and compassionate health care. It is difficult for most Canadians, therefore, to even imagine what it is like for people who have serious, even life-threatening disease but, in reality, possess none of the health care rights of others, as we shall soon see. Participants in our study spent so much time on various aspects of this issue that several distinct chapters and sections of the report had to be devoted to it and the recommendations that arose from it. The "disempowering and horrible experience" (Appendix 3) that MCS participants described as their ongoing reality vis-à-vis the public health care system and doctors was a massive stressor in their lives, second only to housing.

This is not to say that participants were not responsive or grateful when they did receive good care. Those who had been able to access care by knowledgeable physicians (usually those off OHIP, the Ontario health insurance program, often out of country) or, if more limited, from supportive physicians (within OHIP) reported extremely positive experiences. Participants who had benefited from the care of physicians trained in MCS dubbed these experiences as "miraculous" (Appendix 3) and "life saving" (Appendix 3). We offer some of their words in the concluding section of this commentary – Part 10 – to show how effective and life changing educated, appropriate care can be.

However, the negative experiences of participants with physicians and the health care system were described as stressful in the extreme and outnumbered positive experiences many times over, demonstrating a number of consistent and recurring patterns.

As we begin this discussion of medical stress for MCS patients, it is important to point out that the experience of our study participants with Ontario doctors was validated by the findings of the "Healthcare Practitioner Consultation" contained as Appendix F in the final report of the Ontario Ministry of Health Task Force in Environmental Health, *Care Now* (Ipsos Public Affairs, 2018). This report contains the results of a canvass of 10 primary care and 5 specialist Ontario physicians regarding their knowledge of and attitudes to ES/MCS, ME/CFS, and FM. To broadly summarize the findings: while none felt knowledgeable or comfortable with any of the conditions, a number believed that there was "science" on FM and so thought it possible this was a "real" illness. They also thought that "some science" was beginning to emerge on ME/CFS,

and there were those who were open to thinking about it differently. Nevertheless, many thought there was "no science" on ES/MCS – demonstrating a complete ignorance of existing research – and most were not able to think of it as a real clinical entity; instead they thought of it as a psychological disorder.

Uneducated physicians discriminated against MCS patients because they believed the disease to be a mental illness: Participants looking for health care found the great majority of family and specialist physicians to be completely uneducated about MCS, assuming it was some type of hypochondria or mental illness. The participants reported attitudes of negativity, neglect, disrespect, dismissal, spoken disbelief, and explicit disparagement—in other words, of profound discrimination and stigmatization. *Patients ranked this perception of MCS as a psychological disorder as the number one barrier to care and the number one stressor in patient-physician interactions.*

Physicians' negative attitudes affected all institutional systems: Participants keenly expressed their awareness that physicians are the key decision-makers, legitimizers, and gatekeepers to the larger, publicly funded health care system, and they define "legitimate" health problems. Their ability to understand and assist with MCS and their attitudes toward the people who suffered with it were absolutely central to the experiences of people within the larger health system as well as the social support systems. Therefore, access to and the attitudes of medical personnel were ranked very high as sources of important support (positive experience, rare) or serious stress (negative experience, the rule). For a number of participants, negative experiences with medical and nursing care included both physical and emotional trauma. "This can be a very disempowering and horrible experience" (Appendix 3), said one informant, and others agreed.

Physicians' lack of education resulted in no care or actual harm: Virtually all participants felt that there was no health care for them or that what was offered was often harmful and even abusive. On a few occasions, patients encountered behaviours from physicians that were physically harmful and/or intentionally performed.

> I would say 90 percent of my experiences with all of those [physicians] have been unpleasant or unsupportive. Dismissal too, like if I said, "I can't take this medication" or "I can't do that." . . . My doctor called me non-compliant once because I knew I reacted to what they had prescribed. So finally I said, "Okay, I will take that," and I broke out into an angry raised body rash. And I went to her office, and I said, "I took your medication." And she looked at me and panicked. Because she wasn't listening to me, I finally took the medication, knowing what was going to happen to me, just to show her that what I was saying was the truth and was real. Hope (Appendix 3)

Disability related problems: Participants were often refused referrals to other physicians, letters to employers and insurance companies, and explanations to family members and other caregivers (all behaviours with which patient support organizations had been familiar prior to this study). As well, when such practices and attitudes prevailed among physicians, they were

also prevalent among other providers (e.g., nurses and other health and social support personnel).

The three main stress-generating failures of physicians: Linked to attitudes and beliefs, participants identified the most stressful physicians' failures as:

- Lack of safe clinical sites and the refusal to accommodate chemical sensitivity, a potentially life-threatening condition, in providing safe medical treatment of any kind, in providing safe air quality in medical facilities, or in changing personal grooming habits to become fragrance free. This set of stressors was equally applied to the other health professionals patients needed, such as psychotherapists, chiropractors, acupuncturists, massage therapists, dentists, but because medical care is essential when life and limb are in danger, lack of access and the difficulty—often impossibility—of achieving medical access were the most stressful.

- Failure to diagnose in a timely fashion, to diagnose at all, or to diagnose in a fashion that assisted the development of a helpful care plan. In fact, for the great majority, getting an accurate diagnosis was very difficult and took years of consulting multiple family and specialist physicians. This led to physical deterioration and social stresses with friends and family. Participants confirmed that it was impossible to be referred out of province or country for treatment even when such treatment was available in other jurisdictions but not accessible in Ontario.

- Lack of treatment, erroneous treatment, or refusal to take MCS into account in addressing co-morbid conditions. Specialist physicians were identified as completely ignorant of MCS. A number of participants reported experiences of prolonged and severe symptoms followed by a reluctant diagnosis and sometimes the announcement that there was no medical help for the problem.

Physicians' negative attitudes fostered deep distrust and fear: As a result of these negative experiences, many MCS sufferers expressed a deep distrust and even fear of physicians as a group, which was highly stressful to patients, and to physician-patient interactions. Many participants with MCS said that they developed a fear of medical services and avoided trying to access even critically needed emergency and acute care services. During a serious flare—which can easily happen in hospitals—many with MCS become speech impaired, and the stress of trying to negotiate disability accommodation in the face of anger and disbelief, even as deterioration worsens moment by moment, has turned hospitals into danger zones and emergency attendance into a nightmare for many.

> I've had a lot of trouble accessing language for many years now, so there were more than a few misunderstandings. . . . And I couldn't clear them up because I couldn't find the words and I didn't have the energy. It took so much energy to move my hand where it needed to go and to merely think, to come up with a complete sentence, to find words

> which I often got wrong, when people made assumptions it was impossible to try and correct it. Linda (Appendix 3)

Private payment of medical care is prohibitive and heartbreaking: Finally, though not least consequentially, the stresses of having to pay for all MCS-appropriate health care privately, especially for the majority who could not afford this care (or even access it geographically), were often intolerable, and many participants went without any such care as a result. The lack of help, even as patients were aware that it could be provided if their government cared about them, contributed greatly to demoralization and feelings of social abandonment.

## 8.8 SUMMING UP MASSIVE NEW STRESS BURDENS WITH CHRONIC MCS

To re-iterate, the INSPQ report states that

> [C]hronic anxiety is an element common to all of the syndromes studied, and its main feature is the anticipation of danger i.e., feeling a persistent, excessive and inappropriate concern about one's day-to-day activities. A number of factors may be involved, e.g., an individual's temperament, personal history and psychosocial makeup. The severity of the syndrome depends on its duration and the comorbidity that MCS patients frequently experience, i.e., chronic fatigue syndrome, electromagnetic hypersensitivity, fibromyalgia and depression, etc. (Summary, Results, p. 3)

Keeping in mind that effective care and a safe residence would reduce the burden of chronic stress immensely for the vast majority of people living with MCS, we would recast the INSPQ's take on anxiety as follows: the negative affective symptoms from recurring exposures create ongoing episodes that can involve depression and anxiety, among other neurological symptoms. However, the stupendous psychological, physical, socioeconomic and medical stressors of life with MCS are the result of extrinsic realities, not of "personal temperament" or "personal history."[60]

Indeed, it is worth reiterating the essential lessons of the Whitehall study, namely that stress is caused by a combination of high demand and low control and that the imbalance between demands and control predict a range of illnesses.

MCS chronicity, especially absent adequate financial resources, creates an unbelievable accumulation of new problems – high demand – without any available solutions – low control – and inevitably, this creates a phenomenal amount of stress. These new problems create a logical fear for basic security and day-to-day survival. The ubiquity of chemical hazards turns MCSers into "aliens on their own planet," a phrase they often use, and of necessity increases vigilance and concern in seeking to avoid exposures serious enough to provoke suffering and qualitative

[60] Words in quotes in this sentence are from the INSPQ Summary, Results, p. 3.

worsening ("crashes"). True avoidance is impossible to achieve for the vast majority of MCS sufferers, so these responses are natural, logical and responsible, not neurotic.

Can the continuous stress associated with these feelings and judgments impact physical and mental health and thereby impede improvement or recovery? The Adverse Childhood Experiences Study (1998), Whitehall (ongoing), McEwen (2008), Barrett & Padula (2019), among many others, all say that this type of stress predicts illness, and we know this from virtually every other disease. So, in the affirmative, this stress, which can only be solved by socially organized solutions, can seriously impede improvement and recovery from MCS. Reducing it can accelerate these.

Further, while the association of chronic pain with depression and anxiety has been well known for some time, new research suggests that there is also a strong link between trivialization or denial of the experience of pain—especially by physicians—and those two emotions. New studies by faculty at the Texas A&M University's Department of Psychological and Brain Sciences and Institute for Neuroscience show that the denial of pain triggers shame, which they found to be a direct and reliable precursor to depression (Boring et al., 2021). As a write up about the Boring et al. article notes

> Having one's pain invalidated by others—whether by friends, family, or medical professionals—predicted greater feelings of shame, and in turn, elevated symptoms of depression. Notably, these effects were consistent among men and women, except for pain invalidation from doctors which was trending in the same direction but not significant among men" (Ellwood, B., 2022, paragraph 7).

How much more powerful is the negative effect of pain denial—the dominant experience of those with MCS—when in addition to the dismissal of pain, it is actually punished through stigmatization, neglect and the ubiquity of pain triggers?

It is noteworthy that many of the qualitative study participants described how much they would love to have condition-literate therapists and a safe place to receive psychological support to help process the feelings arising from the unbelievable stressors of their new lives, including the recurring effects of denial, and that the lack of counselling and psychotherapy was, in itself, an additional stressor.

## 8.9 PSYCHOLOGICAL AND NEUROLOGICAL THERAPEUTIC MODALITIES FOR MCS

We are aware of the great strides that have been made in understanding the power of the brain both to hurt and to heal. The accelerating research using advanced neuroimaging and other modalities to clarify biological processes related to emotions and behaviours was noted in the Ontario Ministry of Health Task Force on Environmental Health evidence white paper (Hu et al., 2017). We end Part 8 with the following discussion.

Since the approach of psychoneuroimmunology appeared in the early 1980s, there has been a greater emphasis on the "mind-body" connection, but it has tended to emphasize the directionality of mind-to-body rather than to equally include the body-to-mind direction, a direction that is of paramount importance in MCS. We think this is the central reason that classical talk therapy has never proved effective in resolving MCS. It is also likely the best explanation for the fact that anxiolytics, where they are able to be metabolized, may temporarily reduce symptom severity, but do not banish chemical intolerance.

As well, while we found one case of successful anti-depressant use (Andiné, 1997) suggesting there may be a small subset of persons with MCS due to depression, as a rule anti-depressants have not been successful in resolving MCS, and in one well-known study, patients ranked them at the top of list for those treatments they found more harmful than helpful (Gibson et al., 2003, Results, Quantitative data, p 1499 and Table 4, p. 1502). By contrast, in Gibson's study, "[t]he results show primarily that a safe living space and chemical avoidance are reported by patients to be the most efficacious treatments for chemical sensitivity." (Discussion p. 1503)

The roots of cognitive behavioural therapy—often suggested by psychotherapeutic practitioners not familiar with MCS, and elements of which are incorporated in the newer "limbic-" or "brain-retraining" methods—go back to the mid-20th century. Cognitive behavioural therapy has been used very widely to treat a great variety of mental/psychological disorders but has proven itself to be a useful therapeutic treatment only for some (Hoffman et al, 2012).[61] So far it has achieved no documented success for curing chemical intolerance, even if it has been shown to sometimes have ancillary benefits. Its checkered history with ME will be briefly touched on in the next section

Cognitive behavioural therapy has also been combined with mindfulness training. For example, in a small trial, Hauge et al. (2015) sought to measure an eight-week course of mindfulness-based cognitive therapy with MCSers to understand the

> impact of MCS on daily life, symptoms, and reactions following chemical exposures. Secondary outcome measures included the Brief Illness Perception Questionnaire (BIPQ) and the anxiety and depression subscales of the symptom checklist 92 (SCL-92). Participants were assessed at baseline and post treatment, and at follow-up periods of 6 and 12 months. (Abstract, Methods)

[61] From Hoffman et al., 2013: "… a representative sample of 106 meta-analyses examining [cognitive behavioural behaviour therapy] for the following problems: substance use disorder, schizophrenia and other psychotic disorders, depression and dysthymia, bipolar disorder, anxiety disorders, somatoform disorders, eating disorders, insomnia, personality disorders, anger and aggression, criminal behaviors, general stress, distress due to general medical conditions, chronic pain and fatigue, distress related to pregnancy complications and female hormonal conditions. Additional meta-analytic reviews examined the efficacy of CBT for various problems in children and elderly adults. The strongest support exists for CBT of anxiety disorders, somatoform disorders, bulimia, anger control problems, and general stress" (Abstract; emphasis added).

In their abstract, Hauge et al. reported their results as follows:

> We found no effect of [mindfulness-based cognitive behavioural therapy] on the primary outcome, nor did we find an effect on levels of depression or anxiety. We did, however, find positive changes in illness perceptions, which were sustained at 12-month follow-up. . . . Overall, these results suggest that [mindfulness-based cognitive behavioural therapy] does not change overall illness status in individuals with MCS, but that [mindfulness-based cognitive behavioural therapy] positively changes emotional and cognitive representations. (Abstract, Results and Conclusions)

In other words, it can help to cope with feelings about being sick, certainly a good thing; but it does not change the illness itself.

Beyond cognitive behavioural therapy, with the elaboration of the concept of neuroplasticity, several approaches that seek to mobilize the capacity of the brain to build new, healthy (unsensitized) neural pathways have appeared in various limbic/amygdala-retraining approaches. Testimonials to their power can be found on the websites of their practitioners, notably Ashok Gupta in England and Annie Hopper in Canada. Where they have helped affect complete resolution of chemical sensitivity symptoms – many testimonials are posted to that effect – they are very impressive. But it must be clarified that these approaches have not achieved that goal for many others, even if, in many cases, some significant relief from anxiety, depression, and/or other affective states may have taken place (at least for some intervals). And for yet another group, they have resulted in deterioration.

Research on what factors account for better and worse results from these interventions is badly needed. What percentage of people with MCS are helped or not, we do not know. We do not know how specific co-morbidities and risk factors, including body burden, brain injury, active chronic infections, and even genetics, as well as other conventional diagnoses, were present or absent in those achieving a range of outcomes, from total success to total failure. Nor do we know what other therapeutic measures, including obtaining safe housing, were already undertaken by those who succeeded with these programs, before or during the practice periods, so to what extent these other measures were co-factors or even leading factors in recovery. Careful assessment case by case must be exercised with these programs as well, and as noted at the outset of this paragraph, research on all these factors is badly needed.

We note as well that these programs require significant initial financial output, enormous time investment and intentional, far-reaching measures of stress reduction, all of which objectively limit the number of people who can undertake them in today's context. Because even if every person were subsidized for the fees to access these "brain retraining" programs, as long as most people with chronic MCS carry the extraordinary burdens of so many of the stressors described above, most will net get better. True stress reduction means reduction across the board, in physical and toxicological stressors as well as interpersonal, familial, financial, medical, and cultural stressors during a recovery period.

So, in our experience, severity and duration most depend on these multiple factors in combination with the extent of the damage done in onset. Improvement depends on whether or not good clinical care, safe residence, and minimal stress on all fronts, are present.

Psychoneurological modalities can be helpful and should be offered in clinical programs. But this does not mean they can replace the need for safe homes, safe medical sites and the diagnostic and treatment programs for the key biophysical factors that in turn would have positive impacts on the brain. They cannot take the place of disability accommodation rights and supports.

And so, to end where we launched Part 7, it is not correct or useful to counter pose biopsychosocial factors to toxicological ones, let alone discard toxicological factors. Rather it is critical to address them all, each in the right proportion and manner, underlining the centrality of toxicological factors in the specific syndrome and disease process of MCS, and in appropriate relation to the others while also recognizing the adverse and amplifying effects of psychosocial factors.

# PART 9: MYALGIC ENCEPHALOMYELITIS (ME) AND LONG COVID – WHAT CAN WE LEARN?

# PART 9: MYALGIC ENCEPHALOMYELITIS AND LONG COVID – WHAT CAN WE LEARN?

## 9.1 DISPUTING THE CONTENTION THAT CHRONIC ANXIETY LINKS ALL THE CONDITIONS LISTED IN THE INSPQ REPORT

We would like to reassert here one of the central points this commentary illustrates: the complexity of MCS cannot be reduced to one emotion in one region of the brain (limbic system) in one organ system of the body. In Part 9, we illustrate that the same is true for myalgic encephalomyelitis (ME) – referred to in the INSPQ report as "chronic fatigue syndrome." We also issue a warning against the application of this reductionist approach to long COVID. We will address what is currently being done in research on ME as well as what the clinical treatment guidelines say—in other words, we will highlight the problems in the anxiety causation theory as it applies to ME.

We will not undertake a similar effort for fibromyalgia (FM), although one could be taken. We do not agree with the chronic anxiety causation for FM either – exciting new research continues to reveal interesting and novel findings, including one in which fibromyalgia symptoms were passively transferred from fibromyalgia patients to mice, revealing "a pivotal role for autoreactive IgG in the pathophysiology of [fibromyalgia]" (commentary by Tracey, K.J., 2021; research article by Goebel, A. et al., 2021) – hardly explainable by an anxiety disorder. For FM too though, many factors impede progress for treatment and cure. Like MCS and ME, the majority of those who suffer from FM are women, and debate continues as to FM's merits as a real disease (Bernstein, 2016). Likewise, we will not specifically deal with electromagnetic hypersensitivity, even though it so often accompanies MCS as well as being a very difficult condition in its own right. We cannot tackle all the other conditions that the INSPQ puts into the chronic anxiety basket, namely post-traumatic stress disorder, depression, somatization disorder, phobias, and panic disorder as primary diagnoses. But we can take a closer look at ME.

## 9.2 TERMINOLOGY: MYALGIC ENCEPHALOMYELITIS (ME)

The INSPQ report refers to "chronic fatigue syndrome." We assume this signifies ME/CFS or, our preferred terminology, ME, for myalgic encephalomyelitis. The term "ME" is increasingly used to describe the disease, including in Canada by the Canadian Institutes of Health Research-funded ICanCME Research Network.[62] The combined term ME/CFS is in wide use by, for example, agencies in the United States, such as the National Institutes of Health and the Centers for Disease Control, and it is in much of the research literature worldwide. Chronic fatigue syndrome is being used less and less commonly. We will use the term ME unless quoting directly from a source that uses another term.

We want to be clear that ME is not the same as the chronic fatigue that can accompany a variety of other clinical entities, including MCS reactions to chemicals. At times in the INSPQ report, it is

[62] ICanCME stands for Interdisciplinary Canadian Collaborative Myalgic Encephalomyelitis [Research Network].

unclear as to whether the disease (chronic fatigue syndrome) or the symptom (chronic fatigue) is being referenced. Both are used.

Further, we would like to point out that one of the conclusions of the major, ground-shifting 2015 US Institute of Medicine report on ME/CFS (see Part 9.3.1) was that the term "chronic fatigue syndrome" resulted in stigmatization and trivialization and should not be used as the name of the illness (p. 60).

## 9.3 MYALGIC ENCEPHALOMYELITIS IS WIDELY ACCEPTED AS A BIOMEDICAL DISEASE

Let us start by describing what ME is, using words from a recent publication of the European Network on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (Nacul et al., 2021).

> [ME] is characterized by intolerance to efforts expressed by profound or pathological fatigue, malaise, and other symptoms aggravated by physical or cognitive efforts at intensities previously well-tolerated by the individual. Intolerance to efforts may be experienced immediately or typically be delayed for hours or a day or more after exertion and is associated with slow recovery. This marked and prolonged exacerbation of symptoms . . . is termed post-exertional malaise (PEM) and may last several days.
>
> Other key symptoms include unrefreshing sleep, cognitive impairment, orthostatic intolerance, and pain, including muscle and joint pain and headaches. The symptoms are persistent or recurrent over long periods of time and lead to a significant reduction in previous levels of functioning. (Section 1.2 The Population Burden of the Disease and the Need for Better Recognition)

Today, the ME field of study is marked by the following features:

- biomedical, not psychogenic, mechanisms are primarily researched;
- research is conducted across a great many disciplines;
- chronic anxiety does not fit as a universal causative mechanism; and
- current treatment guidelines/recommendations reflect this research.

### 9.3.1 Research in etiology and mechanisms is ongoing and promising

In 2015, the Institute of Medicine (now the National Academy of Medicine) put out a very important and influential report entitled *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness* looking at research evidence related to ME symptoms and manifestations. It concluded that "ME/CFS is a serious, chronic, complex, and systemic *disease* that frequently and dramatically limits the activities of affected patients" (p. 209, emphasis added)

It is well beyond the scope of this commentary to go into all the ME-related research reviewed in the report. However, given that the INSPQ report seems to single out one study on chronic

fatigue syndrome dealing with the hypothalamic-pituitary-adrenal axis (Cleare et al., 2005), it is worth pointing out that the Institute of Medicine (2015) report contains an extensive section dealing with that axis and neuroendocrine abnormalities, which concludes that "evidence is insufficient to conclude that any specific neuroendocrine abnormalities cause ME/CFS, or that any such abnormalities either uniformly differentiate those with ME/CFS from individuals with other illnesses or distinguish a subset of ME/CFS patients" (p. 157).

As noted by Unger et al. (2016), the Institute of Medicine was not the only authoritative agency in the United States reporting on ME around that time:

> The National Institutes of Health (NIH) held a Pathways to Prevention workshop, drawing similar conclusions [to the Institute of Medicine] about the biology of ME/CFS, and the Agency for Healthcare Research and Quality prepared a review of published literature on diagnosis and treatment (16, 17). (Addressing ME/CFS, paragraph 1)

Biological abnormalities found in ME and possible pathophysiologic mechanisms continue to be actively investigated by researchers from a number of fields. Long-time Harvard professor, senior physician at Brigham & Women's hospital in Boston and researcher, Anthony Komaroff, well known for work related to ME, summarized some of the research in a 2019 article in the respected *Journal of the American Medical Association*. To paraphrase him, something is definitely wrong in these patients; there are a great number of biological abnormalities showing up in research, including in the central autonomic nervous system, metabolic changes, immunologic changes, and provocation studies (physical, postural (orthostatic), and cognitive), and unifying models are being proposed. The unifying models Komaroff mentioned do not include chronic anxiety, but they do draw upon the work of Naviaux et al. (2016), the distinguished researcher cited in our Part 2.5.2.

In drawing attention to many of the same abnormalities Komaroff mentioned, Missailidis et al. in their 2019 study "Pathological Mechanisms underlying Myalgic Encephalomyelitis/Chronic Fatigue Syndrome" called ME/CFS "a clinical puzzle" (Introduction, paragraph 6) that "demands a concerted biomedical investigation from disparate fields of expertise" (Abstract). A 2019 study by Natelson et al. looking at CFS and co-morbid medical and psychiatric diagnoses specifically noted that "[o]ur data suggest that depression and/or anxiety are independent disease processes from CFS" (Discussion).

Exciting new research aimed at solving this puzzle is appearing all the time, including a study in preprint authored by a strong team from Ian Lipkin's lab at the Center for Infection and Immunity at Columbia University (Che et al., preprint 2021). This research suggests the presence of "a series of interconnected metabolic alterations in people with ME/CFS [reduced levels of plasmalogens, for one] that may contribute to the pathogenesis of ME/CFS" (Conclusion) – again a promising use of metabolomics, as has happened and needs more funding for in FM and in MCS (which we alluded to in Part 2.6). Lipkin has made many contributions to global public health and is informally known as "the virus hunter," although his work goes well beyond viruses.

He is just one of many well-known and distinguished researchers engaged in ME research, with more entering the field on a year-by-year basis.

### 9.3.2 ME research needs remain vast

Despite many interesting and diverse hypothesis papers and the new research undertaken, there are still parts of the clinical puzzle missing. Much more research is clearly needed. But if pieces are still missing, the vast majority of researchers and clinicians and certainly patients understand this does not equate to a psychogenic paradigm. It simply means those pieces still need to be found.

One such need is subtyping/subgrouping within the condition (a need, as we have previously pointed out, that is present in MCS studies as well). It is key to ensuring that groups under study actually have the same condition. Studying a heterogeneous group of people for underlying mechanisms can confuse any research results (a frequent flaw in much of the MCS research cited in the INSPQ report though it was beyond the scope of this paper to undertake full methodological criticisms).

This is one reason why, when the National Institutes of Health decided to undertake a ME/CFS clinical study, they limited it to people with a post-infectious onset meeting multiple consensus criteria. Only one paper from the study has been published to date, a qualitative study giving the results of a focus group describing the experience of post-exertional malaise and recommending, given the wide diversity of experiences in how the malaise was triggered and presented, that even further subtyping in future research would be helpful (Stussman et al., 2020). More information about the study can be found at https://www.nih.gov/mecfs/nih-me-cfs-clinical-study.

More papers from the study are expected and awaited with great anticipation. A recent update by #ME Action reported on the study and included responses from the principal investigator and clinical director at NIH, neurovirologist Avindra Nath (#ME Action, May 4, 2022). As #ME Action note, Nath's work appears in top journals and he is frequently cited. Nath is quoted as saying "The study will help patients and should move the field forward in a big way." Specifically, in reference to the upcoming paper, Nath noted, "I have never written a paper of this huge magnitude in my life."

Fortunately, in some ME studies there already has been subgrouping, and examples of ways this has been done are listed in the O'Boyle et al. 2021 conceptual paper focusing on how best to conceive the research needed for public health planning and clinical interventions: "symptom presentation (15); co-morbidities (16); genetic traits (17, 18); metabolomics (19); and disease duration (16) (20)." These subgroupings have "enabled an initial alignment of disease stage, clinical phenotype and potential pathophysiological mechanisms (14)" (The Natural History of ME/CFS). O'Boyle et al. continue their analysis by suggesting a different type of subgrouping of ME/CFS patients, that is, by stage of disease progression. As they note,

> reframing along the lines of disease progression could help with defining the distinct stages of disease . . . to accurately describe the pathological mechanisms taking place therein. With a better understanding of these mechanisms, management and research can be tailored specifically for each disease stage. (Abstract)

The paper also raises other issues that apply to all research in this area (and equally to research on MCS, as we have noted): the importance of prospective cohort studies and longitudinal studies in general and the need for large studies. Additionally, an important research need is for the replication of studies. Many small studies have shown some very promising and interesting results, but until they are replicated, outstanding questions remain.

Finally, the need for research funding is great, and this, as we have previously noted, is across the board in the conditions with which we have the most familiarity: ME, FM and MCS. Research into these conditions has been very underfunded, MCS even more than the others. The situation in Canada was clearly pointed out by Hu et al. (2017). Recently published work in the United States related to ME and the gender disparity in the funding of diseases confirms the currency of this situation there (Mirin et al., 2020; Mirin, 2021). These are also illnesses with a high degree of disease burden. We addressed the consequences of such underfunding related to MCS research in Parts 1 through 3.

### 9.3.3 Treatment guidelines contradict a chronic anxiety causation theory

The disease of ME is characterized by post-exertional malaise. In many cases, it is known to be a post-infective and, usually, a post-viral condition. It seems logical that if the infection precedes onset of ME and anxiety comes later, anxiety is unlikely to be the cause of ME. Further, as with MCS, anxiety and depression come to some, not all, both as part of a package of neurological symptoms and as a result of the difficulties of living with the disease.

The US Centers for Disease Control and Prevention has a landing page of its website devoted to Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. One of the subsections of this page is for treatment [and symptom management]. The webpage states, in the part dealing with Depression, Stress, and Anxiety,

> adjusting to a chronic, debilitating illness sometimes leads to other problems, including depression, stress, and anxiety. Many patients with ME/CFS develop depression during their illness. When present, depression or anxiety should be treated. Although treating depression or anxiety can be helpful, it is not a cure for ME/CFS.

Indeed, the most up-to-date treatment guidelines are far removed from what would be recommended for a disease caused by chronic anxiety. Best clinical practices for diagnosing and managing ME/CFS developed by 21 members of the US ME/CFS Clinicians Coalition were published in *the Mayo Clinic Proceedings Journal* (Bateman et al., 2021). These best practices are based on recent research into ME, including the Institute of Medicine report. They include information about diagnostic criteria, co-existing conditions, and alternative diagnoses to

consider; suggestions for clinicians on interview questions, physical examination, and testing; and pharmacological and non-pharmacological treatments. There is a section called "Outdated Standard of Care" that includes information as to why cognitive behavioural therapy and graded exercise therapy can be harmful and are no longer recommended:

> In the past, CBT [cognitive behavioural therapy] and GET [graduated exercise therapy] were studied and recommended for ME/CFS on the basis of the disease theory that "the symptoms and disability of CFS/ME are perpetuated predominantly by unhelpful illness beliefs (fears) and coping behaviors (avoidance [of activity])," leading to considerable deconditioning. [53, 108]
>
> *However, GET and CBT studies have been widely criticized for their methodology, inadequate tracking of harms, and a disease theory that conflicts with the evidence of multisystem biologic impairment.* [4, 108-110] (p. 2871) (our emphasis)

It is lamentable that this caution would need to be included, but it underlies how pervasive and embedded the underlying and mistaken belief in the psychological basis of ME has become.

On October 29, 2021, the United Kingdom's National Institute for Health and Care Excellence (NICE) published a new guideline for the diagnosis and management of ME/CFS. The guideline was developed "using the best available research and working with people who are affected by ME/CFS and professionals who treat and support them" (Information for the Public, ME/CFS: the Care you should expect, paragraph 3).

(As an important aside, and relevant to our concluding recommendations, this process – using the best available research and working with people who are affected by a condition and the professionals who treat and support them – is a lesson for all provincial health ministries in Canada going forward to develop definitions and guidelines for MCS.)

As Peter Barry, consultant clinical advisor for the UK National Institute for Health and Care Excellence and chair of the guideline committee, noted, "This guideline . . . recognizes that ME/CFS is a complex, chronic medical condition that can have a significant effect on people's quality of life" (para. 4). As such, the guideline deals with how to manage or improve symptoms of the disease, and for this, energy management is key.

The NICE guideline recognizes that ME is complex and requires a whole team of healthcare professionals to provide care. The ME/CFS specialist teams "consist of a range of healthcare professionals with training and experience in assessing, diagnosing, treating and managing ME/CFS. They commonly have medically trained clinicians from a variety of specialisms (including rheumatology, rehabilitation medicine, endocrinology, infectious diseases, neurology, immunology, general practice and paediatrics) as well as access to other healthcare professionals specialising in ME/CFS. These may include physiotherapists, exercise physiologists, occupational therapists, dietitians, and clinical or counselling psychologists" (ME/CFS Specialist

Team, Box 3). It is understood that general practitioners continue have important roles including in ongoing care, as well as in recognizing the condition in the first place.

In the NICE guidelines, psychological conditions and symptoms are not specifically called out but are dealt with as they would be for any medical illness. They are certainly not seen as causative. As with the US ME/CFS clinicians' document, special negative mention is made of both CBT [cognitive behavioural therapy] and GET [graduated exercise therapy], with a note that the therapies (as defined in the document) *should not be used.*

Another important document published in 2021 was the European Network on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome's expert consensus on diagnosis, service provision, and care of people with ME/CFS in Europe (Nacul et al., 2021). It was their description of ME that we quoted at the beginning of this section. The recommendations are very much in line with those from the United States and the United Kingdom and came from 55 European clinicians and researchers from 22 countries, informed by people with ME.

### 9.3.4 Medical community needs to abandon idea that ME is psychosomatic

In spite of the biomedical research ongoing and already undertaken, the contention that ME is psychogenic in origin continues to arise. In Ontario, as recorded by the Ipsos Public Affairs Healthcare Practitioner Consultation (commissioned by the Ministry of Health and Long Term Care for the Task Force on Environmental Health and looking at all three conditions), previously cited, a number of the physicians interviewed "admitted that they had been skeptical in the past, but had changed their opinion and attitudes in light of new scientific literature and years of personal experience treating patients affected by these conditions." (2018, p. 9) The Ipsos report writers also noted that "[p]articipants acknowledged that the lack of definitive scientific evidence on the conditions' etiology, physical presentation and treatment led to believability or 'legitimacy' issues." (p. 8) We comment that these physicians did not seem to be at all up to date on research, but rather had an impressionistic and misinformed idea of the available science.

This reality – that so many physicians are completely unaware of important research, be it in ME, MCS and even In FM – is a fundamental problem for these conditions. Important, ground-breaking research has been and is being done, but if physicians, individually and in their associations, do not read and absorb it and if medical schools do not teach it, it has little impact.

Other examples of the long-standing belief in the psychogenic nature of ME are not hard to find. As noted by Pheby et al. (2021) in an editorial entitled "Turning a Corner in ME/CFS Research," contained in a special Issue -- *ME/CFS: Causes, Clinical Features and Diagnosis* -- in the journal *Medicina*,

> many doctors refuse to accept that ME/CFS is a genuine clinical entity, and ascribe it instead to a variety of psychiatric diagnoses. A major cause of doctors' disbelief in ME/CFS is the 1970 paper by McEvedy and Beard in the BMJ, which determined that the 1958 Royal Free epidemic of ME/CFS was 'epidemic hysteria' [2]. . . . The weaknesses in

> the McEvedy/Beard paper . . . should be sufficient to consign the hysteria hypothesis to the dustbin of history, where it belongs. (paragraph 2)

An article by Underhill and Bailloid (2021) contained in the same *Medicina* special issue specifically "confirms that ME/CFS is an organic disease and repudiates the hypothesis of it being a psychosomatic illness" (Conclusions).

As to whether many of the conditions grouped by the INSPQ report are connected and whether the underlying pathophysiological mechanisms are the same or shared,[63] we are aware that there is scientific literature that theorizes on this matter. Belying the simplistic approach taken in the INSPQ report—that is, one pathophysiologic mechanism across a wide diversity of conditions is the key mechanism in all of them—this literature is not at all settled; as demonstrated by Lacourt et al. (2013), various researchers are arguing pro, con, and both. It may well turn out that some mechanisms are the same while other mechanisms are different, for this is the case with symptoms.

Further, it should be noted that while MCS, ME, and FM frequently co-occur, they also each frequently occur with other physical and mental health conditions (Parlor, 2009). In other words, people with a wide range of other conditions can also have any of these illnesses, just as people with arthritis can also have a heart condition and/or depression.

## 9.4 LONG COVID: ENTER A NEW CHRONIC, COMPLEX POST-INFECTIVE ILLNESS

### 9.4.1 A new, ME-like illness is now epidemic and visible

Stepping away from the basket of conditions listed in the INSPQ report, it is worth bringing attention to the new condition known as long COVID or, in the research community, confusingly as post-acute sequelae of COVID-19 (PASC), the post-Covid-19 condition (PCC) or post-acute COVID-19 syndrome (PACS). The definition of and diagnostic criteria for this condition are "not yet well established." (Ontario Public Health, April, 2022) Neither, obviously is the name. We will stick with long COVID.

After two years of the COVID-19 pandemic, a very large number (5 to 30 percent) of those who developed COVID-19 are facing a confounding and at times terrifying set of symptoms that look a great deal like ME (Razak et al., 2021). As noted, estimates of prevalence vary considerably, and it is difficult to come to a specific figure. However, in any scenario, the numbers would be substantial. As well, "[c]are for patients with PACS [long COVID] will likely place added stresses on the health care and social support systems, including increased emergency department visits,

[63] The specific conditions that are captured by this type of grouping is ambiguous. As well, the terminology used differs. Here are some examples: medically unexplained symptoms or medically unexplained physical symptoms; nonspecific, functional, and somatoform symptoms (NFS); somatoform disorders (in the DSM-5 as "somatic symptom disorder"; in the ICD-11 as "Bodily Distress Disorder"); functional somatic syndromes; Persistent Physical Symptoms; and Central Sensitization Syndromes.

outpatient care, inpatient care and rehabilitation involving multidisciplinary teams. (58-61)" And there will be a need for funding for further study, across a wide range of research needs, as well as for supporting multidisciplinary models of care. (Ontario Public Health, April 2022, Conclusions and Public Health Implications, p. 20). We return to these needs, expressed here for long COVID, but identical to the needs for MCS, ME and FM in our Part 10.

According to several important research commentaries, it is thought likely that at least some of the pathophysiology of the long COVID condition overlaps with other post-infectious fatigue syndromes and ME (Komaroff & Lipkin, 2021; Paul et al., 2021; Proal & VanElzakker, 2021; Choutka et al., 2022). The need for additional research to investigate the validity of this hypothesis has also been noted. A number of long COVID patients are, depending on their symptoms, their duration and severity, now meeting the case criteria for ME and are being diagnosed as such.

Very central to long COVID are neurological symptoms, including anxiety and depression. Al-Aly et al. (2021) documented this phenomenon in *Nature*:

> Our high-dimensional approach identifies incident sequelae in the respiratory system, as well as several other sequelae that include nervous system and neurocognitive disorders, mental health disorders, metabolic disorders, cardiovascular disorders, gastrointestinal disorders, malaise, fatigue, musculoskeletal pain and anaemia. (Abstract)

It is worth noting that a 2022 preprint study out of Québec looking at the effect of long COVID on healthcare workers by Carazo et al. received quite a bit of media attention. It demonstrates how serious this condition may be among the healthcare workforce and the implications this may have for the delivery of healthcare, including after the pandemic. Also worth noting, the May 26, 2022 first person account in *Healthy Debate* by Toronto emergency physician, Jennifer Hulme, "Long COVID – A public health crisis taking out women at the height of their lives," while written specifically about long COVID, illustrates so many of the points we have made during this commentary, including dealing with the unknowns and medical ignorance, the toll the disease takes on health, hopes and dreams and the particular burden placed on women, for instance. While this article specifically mentions the now evident similarities with ME, all the larger factors are true for MCS as well.

As in MCS, FM and ME, in long COVID we see a complex condition in which interacting bodily systems are highly disturbed—in this case, indisputably as a result of an infectious episode. Other recent studies also point to disturbed immunological markers and hypothesize that remnants of virus are continuing to trigger inflammation or autoimmune antibodies have been triggered. As well as discussing these two hypotheses (virus reservoir/remnants and autoimmunity), Jan Choutka of the University of Chemistry and Technology (Prague), Viraj Jansari and Akiko Iwasaki of Yale and Mady Hornig of Columbia in their 2022 paper, "Unexplained post-acute infection syndromes," published in *Nature Medicine*, discuss two additional hypotheses (for a total of four) -- dysbiosis/reactivation (dysregulation of the microbiota-gut-brain axis) and tissue damage. We note that similarly to what we have posited for MCS, these hypotheses are

not mutually exclusive and, as they note, could exist in combination. In the review article "The immunology and immunopathology of COVID-19," (Merad et al.) published in 2022 in *Science*, the same four hypotheses for long COVID appear, perhaps not surprisingly as Akiko Iwasaki is one of the co-authors.

What is not often suggested at this point is that this complex condition is the result of chronic anxiety, even if anxiety is one component of the sequelae of the acute infection and merits treatment once it appears.

### 9.4.2 Raising the alarm: Will Long-COVID be psychologized?

It is, however, worth cautioning that viewpoints can change for the worse as well as for the better. Indeed, Hunt et al. (2022) described just such a situation and warned against what has occurred with ME:

> We emphasise that the greater aetiological certainty around Long Covid relative to ME/CFS, alongside prevalence and dynamics associated with a public health crisis, may help ensure appropriate framing and ethical treatment of Long Covid patients. However, we also note that socio-political dimensions of health and illness have played a role in the psychologizing of ME/CFS, and we caution that Long Covid may be susceptible to a parallel process of politicisation. We argue that Long Covid can currently be conceptualised as sitting at a crossroads and that learning lessons from mistakes made with ME/CFS could ensure that Long Covid does not follow a similar path. (Introduction, paragraph 3)

Writing in *The Guardian*, Mariani (2022) had the following to say, much of which is relevant to what has taken place with MCS, ME and FM.

> The way physicians discuss relatively unknown, unestablished conditions can quickly become dyed into the wool, codified among general practitioners and specialists and understood as red flags delineating what conditions might not actually be biological illnesses at all – and therefore best avoided or referred to a psychiatrist.
>
> When presented with a condition they know little about, or worse, a cluster of symptoms they've never encountered before, many doctors have historically done one of two things. Either they've psychologized the malady, attributing it to a psychiatric cause – hysteria, conversion disorder, somatization – or they've assured the patient that there's nothing actually wrong with them, and they just need to relax and rest.
>
> "A real thing that happens in medicine a lot of times is that when we don't understand something," said David Lee, an ER physician at NYU, "we just try to explain it away rather than accept that, 'Hey, maybe we just don't understand this.'"

> Or, as Harvard pulmonary physician Jason Maley put it, "I think that there's definitely a risk, if there isn't a rigorous description of a condition, for people to assume it's not real, or it's anxiety, or it's not a big deal."
>
> The term now routinely employed to describe this phenomenon is gaslighting. (paragraphs 37-41; emphasis added)

## 9.5 CONCLUDING REMARKS

MCS, FM, and ME have all have been subject to claims over the years that they are psychogenic in origin. We do not agree with this claim nor do the people for whom we advocate and who are very greatly impacted by the repercussions of this erroneous view. Fortunately we are joined in this viewpoint by many researchers and clinicians working with MCS. Part 9 has dealt with ME and shown that chronic anxiety as the linking cause is not in accordance with ME research, nor is it supported by treatment guidelines. Further, lumping these conditions together under the umbrella of chronic anxiety causation effectively erases their specific identity, which is extremely counterproductive for purposes of diagnosis, treatment, research and prevention.

Research on ME, taking place in many fields, almost invariably comes to the conclusion that much more research is needed and that the condition is complex and multi-system. And importantly, more and more, there is an understanding that one single mechanism is unlikely to explain all pathophysiological processes and that even within an individual condition, subgrouping is needed—not everyone with the condition is the same. Likewise, with both FM and MCS, it is unlikely that one single mechanism will explain their complexity. But, as with MCS, this recognition of the need for more research, should not be taken as an excuse to withhold appropriate treatment, as outlined in continually updated guidelines.

Long COVID is a newly recognized and yet-to-be understood condition. There are already signs that in spite of its known origin, its complex presentation and multi-system impact may soon be met by some in the same way as have MCS, FM, and ME, that is, it must be psychological. The impacts of such a conclusion would be immense, as we have seen for MCS, FM, and ME, at the individual and societal levels, resulting in widespread suffering and massive economic impact on society due to a lack of research, treatment, education, and support.

According to Ryan (2021), "Finding a health professional who accepts and understands post-viral illness is akin to tracking down a unicorn with a medical degree" (paragraph 4). Ryan has lived with ME for years and has felt the consequences of physician ignorance even despite the great strides made in ME research. Our qualitative patient study (Burstyn & MEAO, 2013) and our referenced study of attitudes of Ontario physicians (Ipsos Public Affairs, 2018) show that there are doctors who continue to think ME is a psychological disorder. The INSPQ report can only reinforce this embedded medical error. We need something better.

# PART 10: RECOMMENDATIONS FOR MOVING FORWARD

# PART 10: RECOMMENDATIONS FOR MOVING FORWARD

## 10.1 SETTING THE STAGE FOR CARE

We opened this extended commentary and counterargument with two quotes, asking readers to consider which version of MCS causation they find most persuasive – chemicals or chronic anxiety. We now hope that the references we have cited and the experiences we have brought to bear from clinical insights and patient experience have provided convincing support for our account of MCS. This we have summarized in the following description, first introduced in Part 1. Please read it carefully, as each word is important, deliberately chosen and consequential. We present it here in point, rather than paragraph, form to facilitate that reading.

- MCS is a multi-system, recurrent, environmental disorder that flares in response to different exposures (i.e., pesticides, solvents, toxic metals, fragrances, cleaning products, cigarette smoke, certain foods, drugs/medicine, mold and other vehicles of exposure) at concentrations that do not provoke such symptoms in other people.

- MCS is characterized by neurological, immunological, cutaneous, allergic, gastrointestinal, rheumatological, cardiological and endocrinological signs and symptoms.

- MCS is a widespread condition and the majority of people who live with it (approximately 70 percent) are women, though a significant minority are men.

- Onset, which may happen slowly over time or rapidly, begins on exposure to a particular chemical or mixture of chemicals (including bio and well as synthetic toxicants) that commonly affect the immune system and/or nervous system, such that MCS appears to be primarily a neuroimmune disease process.

- This chemical exposure interacts with one (or both) of these systems [immune and nervous] in a way that renders individuals intolerant to subsequent exposures, which are then experienced as triggering or flaring events.

- After the initial onset, some new triggering events may result in “crashes” - additional worsening to qualitatively greater degrees of severity that are not easily reversible without intervention.

- Affected individuals no longer tolerate everyday exposures to a wide range of structurally diverse substances at levels that never bothered them previously, including ingestants, inhalants, implants, and skin contactants.

- Many previously tolerated foods and drugs may trigger symptoms. At times, onset is not observed or reported immediately, and the phenomenon of "masking" can obscure MCS and delay diagnosis.

- MCS ranges in severity.

- Early, milder stages are often erroneously perceived to be allergies, require adjustments and avoidance, but go undiagnosed.

- Moderate to severe MCS involves greater intensity and duration of symptoms.

- Severe MCS brings very intense reactions, great physical suffering and can be life-threatening for some people when exposed to some chemicals. Major efforts to avoid triggers are required, making life in the ambient air of chemically-laden everyday environments unsustainable.

- This is how MCS disables those affected.

- When co-morbidities are present – often the case – overall health is further compromised, and additional barriers are encountered.

- MCS is usually responsive to significant degrees to appropriate measures and treatments, and becomes worse without these.

We have provided our extended critique of the INSPQ report's conclusions, adduced the evidence and offered our counter description because we are convinced that if the conclusions of the INSPQ report become the basis for policy and implementation, heath programs, disability policy, public health policies and research directions, in any jurisdiction, erroneous, indeed dangerous, consequences will unfold, creating major setbacks in place of advancements. It is for this reason, that we fully support the campaign and letter by the Association de la santé environnementale du Québec (ASEQ/EHAQ) for the report to be withdrawn. This letter addressed to Québec's Minister of Health and Social Services, Hon. Christian Dubé is found as Appendix 5.

Accordingly, and in a positive spirit of moving forward, we now want conclude by focussing on practical next steps – the type that people living with MCS need the most. And in this spirit, we agree with the following important conclusions from the INSPQ report.

> … [T]he chronic biological disturbances observed with this syndrome, the severity of the symptoms experienced, the social and professional repercussions, and the high prevalence of MCS in the population, qualify it as a real health issue. Given that those suffering from MCS are, to varying degrees, genuinely ill and that their condition would justify appropriate medical and social support; the authors favor the establishment of

> centres of expertise specializing in MCS, as well as the continuation of the scientific monitoring of this syndrome. (Key Messages p. 2)

We have no doubt that MCS is a "real health issue" with severe symptoms, social and professional repercussions and wide prevalence. We strongly favour the "establishment of centres of expertise specializing in MCS" provided they are safe sites delivering appropriate care; and we strongly support serious funding for "the continuation of the scientific monitoring of this syndrome."

The outstanding questions are: what case definition of MCS will prevail, what will be delivered in these proposed dedicated centres of expertise and what research will be funded and prioritized? These are the questions we take up in this concluding portion of our document.

## 10.2 PRACTICAL CONCLUSIONS

From the point of view of people who live with MCS in every province, those persons to whom our public services are meant to respond but do not at present, what is most needed today are strategically focused processes to respond, on the ground with real services, to provide:

### 10.2.1 Medical needs

To be clear: there is not a large enough body of peer-reviewed literature to, on its own, guide the creation of a comprehensive, effective, appropriate program of clinical care. But there are networks of physicians who have been providing care that is outcomes-based and comprises both promising practices and established conventional medical practice (in pharmacological and anti-infective areas, for example). This means that to create effective care in Canada, physicians who practice this medicine, and the knowledge they have amassed and translated into the educational offering of their associations, will need to be the primary sources for the following efforts:

> Develop the case definition and clinical guidelines, including the appropriate roster of effective diagnostic and treatment services in clinical programs. Utilize the examples of the best clinical programs available, not the conclusions of the INSPQ report, to establish clinical care across the continuum of care (primary, specialist, hospital, long term and end-of-life care).
>
> Develop a plan for dedicated centres of service that also provide interprofessional care, so those with MCS can access more than just physician services in a safe site.
>
> Recruit expert clinicians practicing state-of-the art environmental medicine and with established clinical track records from Canada and internationally (to augment the limited expertise available here). Integrate expert patient advocates fully into this process.

Ensure that safe air quality as a medical requirement is part of clinical services, both in dedicated centres, and available to patients when in attendance in larger health care settings. In regard to health facilities, Damiani and colleagues acknowledge the grave difficulties of MCS patients in encountering unsafe air quality when they seek out healthcare. Specifically, they arrived at agreement on a number of items related to what they call the 'hospitalization domain" and underline the importance of breathable air in clinical spaces, through a number of methods including

> "… MCS ambulatory [clinic] should be far from sterile processing facilities, laundries, waste rooms or any sources of internal and external MCS triggers. Solvents, pesticides and herbicides or any other potentially toxic chemical agent dispersions should be avoided in the external area adjacent to the MCS [clinic]." (3.4.1 Hospital Environment)

As fully addressed in the Ontario reports, we would extend this medical need and this approach to all clinical spaces, and see this principle codified into clinical guidelines because without access to care, care is effectively not available.

Ensure that chemically-safe housing is understood as a medical requirement, enshrined in case definitions and guidelines; and a disability and housing right validated by physicians. Safe housing includes homes, shelters, social and assisted housing where people with MCS can breathe safely and recover from a world saturated in common chemicals. In this sense, MCS safe housing should be classified as a medical device, not only as protection against the elements. There is more about housing below and in Appendix 6.

### 10.2.2 Disability needs and rights

Create, educate about and enforce recognition of MCS as a disability, and determine what that means in terms of relevant rights and entitlements with respect to accessibility and equity in health care coverage. Just as accessibility means ramps and elevators for those who are mobility-impaired, accessibility will mean breathable air for those with MCS, a requirement that will also greatly improve the health of workmates and schoolmates, and, indeed, medical staff and social service providers. Where accessibility may be deemed not possible – in manufacturing and retail spaces, for example, and even in multi-unit dwellings if landlords refuse or are unable to make modifications – accepted guidelines for compensation in terms of financial assistance need to be adopted as policy so that every individual does not have to fight for this right on their own, over and over again. As well, many social assistance entitlements and programs now available to all other Canadians, including medical device and pharma care subsidies, are needed.

### 10.2.3 The special case of MCS-safe medical housing

A few additional words about housing are necessary, because it is so central, and yet so difficult to achieve and so thoroughly abandoned by government at all levels. In the Ontario 2013 business case and its supporting reports, the need for safe housing as the first and constant requirement for stabilization and well-being for those with MCS was addressed at length. Its importance was reflected in the proposed staffing complement for the centre of excellence, which included a housing department with an initial full-time position to initiate housing solutions. We note that Canada has declared that people have a right to housing, and to accessible housing (van den Berg and Appendix 6). However poor or sick a person may be, Canadians believe, and our laws declare, that citizens have a right to protection from the elements, even if only a roof over a bed in a shelter for the homeless. But this right simply does not exist in reality for people with MCS, anywhere along the housing continuum. The cost of a safe home today far exceeds the means of many who need it to survive. Therefore, we strongly support the call of the *Association de la santé environnementale du Québec* (ASEQ/EHAQ) for a national MCS housing program and have appended their letter as part of Appendix 6. As we have, they also call for safe medical facilities and safe schools. In Ontario, the need for safe air in new clinical facilities was addressed by an architect's report for safe health care facilities.

Government supports for safe housing can– and ought to – support a variety of projects along the "housing continuum":[64] loans or bursaries for private home modification; government subsidized new-build market value single-family homes and market-value rental homes (see Appendix 6, which includes the model of the Zurich project); subsidized housing units in all-MCS multiple family dwellings; MCS- dedicated spaces for assisted living-units (which could be co-located in the same MCS buildings) and safe long term care facilities. Aside from seven MCS-dedicated units built decades ago in Barrhaven, a suburb of Ottawa, there is not one MCS-dedicated housing unit, let alone building or development, in Canada. This has forced some people to commit suicide or seek medical assistance in dying (MaID). With approval and funding, ASEQ-EHAQ's in-process housing project in Québec could quite rapidly be brought to fruition and serve as an excellent example of safe MCS housing for the rest of the country.

## 10.3 MOVING FORWARD FROM LITERATURE REVIEWS

In our view, then, if there are to be any new literature reviews, they must be geared to supporting and accelerating these main operational goals. No more 8-year literature reviews; no more decades-long study processes divorced from action recommendations. Further, given the gaps in the existing peer-reviewed literature, new reviews of relevant literature going forward must include the relevant educational curricula of environmental medical associations,[65] selected for the process by knowledgeable clinicians practicing at the leading edge of care,

[64] CMHC https://www.cmhc-schl.gc.ca/en/professionals/industry-innovation-and-leadership/industry-expertise/affordable-housing/about-affordable-housing/affordable-housing-in-canada

[65] Minimally, the American Academy of Environmental Medicine https://www.aaemonline.org/ and the International Society for Environmentally Acquired Illness https://iseai.org/

defined as that which provides complete and comprehensive care for MCS, in which psychoneurological care is only one component.

To be crystal clear: Just because the INSPQ report does not take us in the right clinical direction, it must not be used to justify holding back the development of clinical approaches, programs, and services on the correct basis or to continue to take no action to make disability rights meaningful. These processes need to proceed post-haste so that those living with MCS can receive the full rights to health care to which Canadian citizenship entitles them, and soon, not in some far off and unforeseeable future. There is enough clinical and expert patient experience to do this; what is needed is the will to design and implement a plan and the modest sums to fund it.

How can this come about?

## 10.4 FEDERAL SUPPORT FOR PROVINCIAL/TERRITORIAL ACTION IS URGENTLY NEEDED

At this time, every province and territory must fend for itself in moving forward on MCS definition, guideline development, care capacity and accommodation. For many reasons, this has so far lead to paralysis, at least since two modest efforts in the mid-1990s (in Nova Scotia and in Ontario) were made, but not extended. To continue to leave each province or territory to develop its own case definition and clinical guidelines on its own would certainly entail a great deal of wasteful duplication, and worse, would inevitably result in important inconsistencies and inequities in care across the country – witness the divergence in the Alberta, Québec and Ontario reports. However, the worst outcome (other than implementing the version of MCS espoused in the INSPQ report) is the status quo: no action at all, due to the complexity and contested nature of MCS, and the evident approach of provincial officials and medical associations to simply ignore it no matter how serious and widespread it becomes.

With these factors still placing a drag on provincial/territorial-level action, it is time for the federal government to pro-actively provide support and accelerate desperately needed change, in the direction of the highest practice standards. In a collaborative effort, Health Canada, as the lead but also the Public Health Agency of Canada, the Canadian Institutes of Health Research and the Canadian Housing and Mortgage Corporation should take the following steps:

1. Sponsor an international colloquium of leading practitioners (providing comprehensive care) and expert patient advocates, tasked with developing a consensus definition and guidelines, including for safe clinical spaces and affirming the medical need for safe housing. The Alberta report (p.76) recognized that consensus among international experts and among organizations was needed; we can't wait forever for others to develop this. Work with the Canadian Medical Association to bring its positions on MCS understanding and care provision into the present day, to dissolve the outdated medical attitudes that prevail from the centre of the Canadian medical establishment.

2. Share the case definition and guidelines results with the provinces and territories, and provide adequate, ear-marked funding incentives to assist them to take customized steps to operationalize these in appropriate polices, programs, clinics and personnel within their own health and social services sectors.

3. As a key component of MCS capacity, provide funding or co-funding for the creation of three needed tiers of care. Dedicated funding would rapidly accelerate provincial/territorial action and should be flowed as start money, with future operational funding eventually becoming a provincial/territorial responsibility.
    - First, centres of excellence in major cities. Affiliated to teaching hospitals and universities but with medical autonomy so as to provide promising practices, these would provide expertise for the most difficult cases, develop curriculum for medical and other health provider schools, be physician support resources for partnering regional clinics and individual practitioners, and collaborate with government officials as needed to move the whole agenda forward. Funding for such centres, from the federal government, would be a powerful and effective incentive to take action. All clinical spaces in such centres would be scent and chemical free.

    - Dedicated regional and local clinics are needed because, in addition to a commitment to make needed care available close to home, MCS patients simply cannot travel long distances or stay in ordinary accommodation. Local clinics could solve the problem of funding mechanisms by paying physician salaries instead of fee for service. They could provide interprofessional care with the specific health professions identified by Ontario patients as critical to health and well being (such as chiropractic, acupuncture, naturopathy, massage and psychotherapy) working in an MCS safe setting.

    - A third tier of providers—specially trained family physicians – can be spread across provinces with regional and a central facility for support and referral. Compensation mechanisms, including changing diagnostic and service codes, would be needed for them and would also be important for all primary care providers, as incentive and recognition.

4. Create and fund Research Chairs, based on the Canada Research Chairs program and ensure they are cross-appointed to leading universities and the provincial centres of excellence, to drive basic, clinical and epidemiological research on MCS. This would be a powerful measure in establishing MCS as a dynamic and important field of study and securing it institutionally. At least two of these Research Chairs should be established in an expeditious manner.

5. Launch an MCS-safe, CMHC-led federal housing project, including all relevant components along the "housing continuum of care." In 2016, the federal government provided almost $1.7 billion to support over 536,000 households living in social

housing.[66] Provinces and territories administer 80% of the agreements with social housing providers. CMHC administers the remaining 20%. This program should rapidly be expanded to include MCS individuals, who have been marginalized in both physical, financial and even medical (e.g. long term care, end of life care) ways.

The government of Canada has a serious responsibility to over 1.1. Canadian citizens to provide material assistance to provinces to bring about needed and overdue action. Because we have no system of care for MCS, it is not a matter of provinces or territories simply filling in "gaps" in care, but rather creating new systems from scratch. Federal help for such an undertaking via the steps delineated above is clearly justified. A coordinated appeal from provincial and territorial health ministers to the federal government would be very helpful in this respect, but regardless, the relevant federal ministries and agencies must show meaningful leadership now. And for leadership to be meaningful it needs real dollars for the right initiatives.

## 10.5 PROVINCIAL/TERRITORIAL ACTION DOES NOT NEED TO WAIT FOR FEDERAL ASSISTANCE

That said, in the absence of federal government action, all these proposals can be implemented by provinces on their own initiative, and the designs and templates developed in Ontario can certainly assist, if only to provide thought pieces for each jurisdiction. Whatever the process, MCS patients have been asking for recognition and care since the 1970s, and delaying action for another decade or two while more "study" takes place is not acceptable – in any part of the country. If, as may be the case, Québec feels it is so distinct in its needs that it wants to be entirely independent, then it will need to find ways to move beyond the erroneous conclusions of the INSPQ report to create effective and appropriate polices and services in the immediate future.

As an important informational point, Ontario patient advocate organizations do not consider either the BC Women's Hospital Complex Chronic Diseases program (which is mandated to treat ME, but not MCS as a primary diagnosis) or the Nova Scotia Integrated Chronic Care Service (which appears to have very limited set of clinical services based largely on psychoneurological and social work approaches) to have adequate clinical programs for MCS. The social and psychological supports they offer are very helpful, and should be incorporated into new clinical programs. (And, as we have already noted, the Environmental Health Clinic at Women's College Hospital in Toronto provides diagnosis only.) But reproducing this limited complement of services in new centres while omitting the important components of the clinical programs needed and offered in full MCS clinics (e.g. Environmental Health Center-Dallas, and as briefly outlined below) would leave the MCS population neglected, sick and betrayed. The selection and/or training of clinicians for new centres must be undertaken so as to be able to provide a full complement of service and with the meaningful recommendations of expert patient advocates.

[66] CMHC information https://www.cmhc-schl.gc.ca/en/professionals/industry-innovation-and-leadership/industry-expertise/affordable-housing/about-affordable-housing/affordable-housing-in-canada

## 10.6 DISABILITY RIGHTS CANNOT BE REALIZED WITHOUT MEDICAL SUPPORT

As Canadians with laws and policies on human and disability rights, we have asserted the importance of clearly recognizing MCS as a disability by ensuring those who have it are able to realize all the rights and entitlements such a status confers on Canadian citizens, including laws and guidelines for disability-appropriate MCS accommodation (Wilkie & Baker, 2007; Sears, 2007). People with MCS can make great contributions to their families, their communities and the economy. But this can only happen if their disability is accommodated and supported. Experience shows that in order to obtain these supports, physician assistance, including advocacy is required. And physicians as a group (with important individual exceptions) have shown that they won't provide such assistance unless they feel comfortable as gatekeepers, which will only happen when they have in hand a case definition that is accepted into clinical practice.

From this point of view, were the definitions of the INSPQ report of MCS as an anxiety and somatoform disorder to be adopted as policy, disability recognition and accommodation would – at least according to our reading of the implications of such conclusions – suffer far-reaching adverse consequences. In particular, the characterizations of MCS as psychogenic and trigger substances as "harmless" are potentially very harmful to implementing safe air quality needs in homes, clinical sites of all kinds and schools, as well as, where possible, in workplaces. And this type of accommodation is the pre-condition to recognizing and assisting with the medical and disability dimensions of MCS. For this, however, two basic, critical pieces are needed.

## 10.7 MEDICAL EDUCATION AND PROVINCIAL FUNDING MECHANISMS ARE THE LEVERS THAT WILL CHANGE THE WORLD

To make both clinical care and disability recognition possible, it is clear that timely and proactive measures to develop state-of-the-science curriculum to teach basic MCS to all physicians is urgently need. Curriculum for family physicians and specialists is badly needed, but who will be able to design and deliver this? We also need additional, specialized training for those who want to work specifically with MCS patients in centres of expertise and help to educate other physicians. Government recognition and medical education – ideally, created by meaningful federal and/or provincial government initiatives and incentives – would create de facto protection for MDs and incentives strong enough to permit them to build care capacity, encourage basic and clinical research, and greatly enhance the reservoir of research and patient outcomes.

Simultaneously, funding mechanisms must be pro-actively established, ranging from salaries for physicians and staff within dedicated centres so that the long consultations needed particularly early in the diagnostic and treatment phases are compensated; to changes to the health system codes, creating recognized categories and sufficient time for diagnostic and treatment services. There are many physicians who want to expand their scope of practice to include environmental medicine and MCS patients, but cannot do so without adequate remuneration, currently

impossible to receive. Once such remuneration is established and education made available, physicians will be able to turn their wishes and intentions into everyday medical practice.

## 10.8 ONTARIO STUDIES HAVE MUCH TO OFFER THE FEDERAL GOVERNMENT AND OTHER PROVINCES

As noted, given the urgency of helping this large, growing and profoundly excluded population, it seems wasteful and unproductive to mount another huge literature review exercise, especially one not specifically guided by a focus on creating clinical care capacity and establishing meaningful disability measures in health and social service systems. We now have two Canadian survey reports (Québec and Alberta) and from elsewhere smaller, more targeted documents that are focused on clinical issues, such as the Damiani et al. (2021) review, which we have frequently mentioned, and the Rossi and Pitidis (2017) review, referenced frequently in the Alberta report. Moreover, the decade-long Ontario process has a lot to offer on other fronts going forward.

From the collection of the research reports and business case document for an Ontario Centre of Excellence in Environmental Health, affiliated regional/local clinics and special training for primary care practitioners, the business case document provides a detailed blueprint for how to create this network. It was commissioned by Ontario's Ministry of Heath, and can be a very helpful document for other provinces, and the federal government as well. The following reports can be downloaded from http://recognitioninclusionandequity.org/resources/ .

- The qualitative needs identification study – referenced frequently in this commentary, and available in the larger report, *Recognition, inclusion and equity – The time is now: Perspectives of Ontarians living with ES/MCS, ME/CFS and FM* (Burstyn & MEAO, 2013) contains extensive needs identification research that remains relevant, as well as a detailed proposal for a model of care and a care delivery system. Importantly, the larger report includes extensive recommendations and design proposals for the integration of disability policy and programs as well. (Québec's enlightened integration of health and social services provides in effect the best launching pad for creating new services and policies. This is because MCS requires integrated, aligned action on health and disability fronts at the same time.)

- The model of care – promising practices within a research framework – is also elaborated in *Chronic, Complex Conditions: Academic and Clinical Perspectives* (Molot 2013).

- The business case document is a stand-alone blueprint for the care delivery system, *Recognition, inclusion and equity: Solutions for people living in Ontario with ES/MCS, ME/CFS and FM – The Business Case Proposal*. It provides a template for staffing, building and costing both a central centre of expertise and affiliated regional clinics, as well as

initiating a program of primary care provider education and support – all in a sequenced implementation plan.[67]

- Finally, available from the architect (Main Street Studio, David Fujiwara[68]) guidelines for modest, safe renovations to retrofit or adapt safe clinical spaces in which to receive MCS patients.

It bears repeating that all this work is predicated on a biophysical-toxicogenic understanding of MCS.

Major component parts of the 2013 design were taken on board by the reports of the Ontario Ministry of Health Task Force on Environmental Health. The reports - *Time for Leadership,* 2017; *Care Now*, 2018. These reports include some additional useful proposals for processes to develop clinical guidelines, communities of practice and practice tools. These can be found via links at https://www.health.gov.on.ca/en/public/programs/environmentalhealth/.

## 10.9 THE ECONOMIC ARGUMENT FOR CREATING A COST-SAVING NETWORK OF APPROPRIATE CARE COMES FROM PATIENTS WHO HAVE BENEFITED FROM EXPERT PHYSICIAN CARE

We have explained that we are advocates who have worked for a long time to enable the establishment of a central centre of excellence, dedicated regional clinics, and special training for family physicians for MCS, ME, FM, and their often-associated co-morbidities in Ontario. We therefore welcome the recommendation to establish centres of expertise in Québec. The determining question for patient outcomes, however, is what kind of expertise is meant and needed.

In Part 8 and in the Appendix 3 excerpts from the Ontario qualitative patient study, we offered MCS patient descriptions of their highly negative experiences with public health care providers—physicians, mostly, but some nurses as well. “A horrible and disempowering experience” (Appendix 3) was how one participant put it, summing up the great majority of all MCS participants’ experiences.

However, in their frustrating and often futile search for effective care, as the Ontario business case, the INSPQ report and the Alberta report point out, MCS patients use physician services at higher rates than the norm, seeking care for MCS-related multi-system health problems in our public systems. So, patients are undergoing seemingly endless frustration and even trauma that results in very poor outcomes. Just one example, from the patient’s perspective:

[67] All the original reports – research reports and business case itself – are available at http://recognitioninclusionandequity.org/resources/
[68] http://mainstreetstudio.ca/

> My doctor … had me go to maybe a dozen specialists, a neurologist, a gastrointestinal specialist, another neurologist for fibro, my dentist. . . . Everybody, each of the specialists had their take of what was wrong with me, but none of them connected it to MCS. . . . I was diagnosed at the Environmental Health Clinic. **Betty** (Appendix 3)

At the same time, our governments are paying a great deal of money – more than $150 million annually in Ontario, according to the 2013 research – for useless or even harmful physician utilization even as patients are stressed and deteriorating. This is a lose-lose situation for all concerned that has been going on for decades.

In the literature that frames MCS as a psychological disorder, we invariably read words to the effect that patients have normal laboratory finds and are unresponsive to treatment. This is the version of MCS that continually appears as a justification for government inaction. But what kind of diagnostic tests and what kind treatment are we talking about? When uninformed and inappropriate care is provided, of course patients are unresponsive, because their physicians entirely miss the key issues and the key treatments. This would be the case for any disease or condition. When appropriate testing and treatment is provided, wonderful things happen.

This was demonstrated in the 2013 patient needs identification study. So, to address the type of expertise and clinical programs that would end up helping patients and reducing physician and testing utilization costs, we want to offer just a few comments from that study (Burstyn & MEAO, pp. 97-101) from participants who were fortunate enough to find and were able to afford knowledgeable medical care. The improvements in their outcomes and quality of life speak for themselves, as do the tremendous responsiveness and appreciation of the patients.

> Dr. A's treatment worked! . . . After the IV I could talk. I wasn't slurring my words anymore. . . . Also, she impressed me because she asked me how I felt. . . . In my experience with doctors, I've never met a doctor before that really cared about the patient. . . . She's a wonderful person, a wonderful doctor. **Shan** (p. 99)

> I've had a few positive experiences with health care people. Notably, first of all, Dr. M., the environmental physician. **Robert** (p. 98)

> I went to the LAMP occupational health program. . . . It's the Lakeshore Area Multiservice Project. It's the only Community Health Centre that has an occupational component, and there was a new addition built on designed specifically for people with chemical sensitivity. So, the docs there are excellent, and the program is excellent. I also came to the clinic when Dr. F. was here, and so my diagnosis was confirmed. **Hillary** (B, p. 99)

> Dr. A. is a miracle in my books. She tells you the truth in the first place, and in the second place, she gives you alternatives that, if you go on the internet, you can find them. **Sharon** (p. 99)

Today, for the vast majority of MCS patients, expert care like this is impossible to obtain. There are very few physicians in very few places that even offer it, and they often have long waiting lists. Travel requirements are often impossible, and private payment is prohibitive. Therefore, our health care systems are paying the wrong doctors in the wrong places at the wrong times for the wrong diagnostics and treatments, and patients and taxpayers are getting terrible outcomes. This will not change unless and until the right care in the right places becomes for the right diagnostics and treatment become part of our health care system.

To determine what types of care and support ought to be provided by the much-needed centres of expertise, we once again refer to our needs-identification process (Burstyn & MEAO, pp. 27, 208, 209). Here, in addition to expert medical care, both primary and specialist, patients identified five additional health disciplines as essential for maintaining day to day life. The patient-identified list of clinical needs looked like this, and it is worth noting that these are services available at the Environmental Health Centre- Dallas, and included in Nathan's book (2018) of clinical tests and treatments.

- Safe clinical spaces, for consultation and for treatment, in primary, acute and emergency settings
- Expert, respectful and comprehensive medical care that addresses each individual's medical unique combination of needs
- Physiotherapy, chiropractic, massage, acupuncture, nutrition
- Detoxification supports
- Psychological and mind-body supports
- Peer self-management activities
- Family support activities
- MCS necessary assistive devices (water and air purification)

From the few patients who were able to access comprehensive, state-of-the-art care, and also drawing on clinical experience, new centres of expertise will need to adopt the kind of medical approaches widely in use among environmental physicians and bring these into the public health care system. Clearly, then, this would mean an expansion from our current offerings in the provision of diagnostic and treatment procedures – and would need net new funding mechanisms for these. By now the list of issues for which capacity is needed is familiar but bears repeating:

- Toxic body burdens (heavy metals such as mercury and lead, pesticides, solvents, mycotoxins)
- Brain injury, with appropriate imaging; cognitive and motor problems, both with chemical exposures and ongoing
- Chronic, even subclinical infections (bacterial, viral, fungal, parasitic);
- immune system component strength, (e.g., T-cells, immunoglobulins, mast cell activation)
- Hypoxia, melatonin deficiencies, addressing problems in the blood-brain barrier

- Gut dysbiosis, digestive, and nutritional deficiencies
- Food allergies, other allergies, histamine levels
- Hormonal disorders
- Genetic polymorphisms and
- Cognitive and affective symptoms.

As disabled persons with specific accessibility and accommodation needs and expenses, our patients also identified their needs for appropriate social supports, also requested in the ASEQ-EHAQ letter:

- Safe housing: social, assisted, shelters – a top priority of qualitative importance.
- Condition-educated, fragrance-free personal support workers, lab technicians and nurses for personal hygiene, mobility needs, laundry, cleaning, shopping, maintenance as well as nurses and lab technicians for health-related issues such as blood draws.
- Food security for safe foods
- Safe transportation (appointments, necessities, social and family needs)
- Support services to family caregivers: education, peer-group, respite care
- Support services to sick parents with children; support services to parents with sick children
- Income support services (social assistance, ODSP, WSIB, etc.), especially for private health care and safe-housing rent.

Once again, we want to re-iterate a point that cannot be stated too often: New centres should provide condition-literate psychotherapeutic services and be able to prescribe anxiolytics and anti-depressants, always being conscious that lower doses, or in some case, none can be used due to an individual MCS patient's decreased ability to metabolize such drugs. But if the intent of the INSPQ report and its anxiety-causation thesis would be to limit the treatment of MCS and its underlying conditions to these psychological approaches, rather than expanding care to include the above biomedical-toxicological components, this would be fundamentally wrong. It would contribute to the current erroneous and stigmatized status of MCS patients as well as potentially causing them actual medical harm.

Additionally, if the clinicians in these new centres took the approach that avoidance is a neurotic symptom that should be proactively abandoned, a possible interpretation of the INSPQ report's conclusions; and that the need for avoidance should be ignored in clinical sites and disability accommodation, then the foundational rule of medicine—"first do no harm"—would be seriously violated.

## 10.10 CLOSING WORDS

It is time to acknowledge that care for those with MCS, as well as for a host of new and complex illnesses that have arisen in the chemical age requires a paradigm expansion and the inclusion of

new ways of practising medicine, new tests, new treatments, new system codes, and new (if only via renovation) facilities. “The system” has not been able to help to date, and sometimes it has perpetuated harm. Therefore, solutions will not be found within the system as it currently exists. Solutions will only be possible if the “the system” is changed and improved. This requires a leadership role for government, as well as a consciousness change in medical associations’ outdated and erroneous ideas of MCS.

The INSPQ report states that it “is intended for physicians and healthcare professionals who will encounter MCS cases, for researchers in this field, and for MCS patients and their families” (Key Messages, p.2) Given the stigma and ignorance around MCS, linked to an erroneous and embedded belief that it is a psychological disorder, and given the fresh support this report provides to that view, we do not understand how it could possibly help any of these groups. It seems to us it would do a great deal of damage on every front.

On the other hand, an awareness campaign that correctly portrays MCS as a complex, environmentally-linked condition that can be extremely painful and disabling in many ways, including with neurological impairments (among which anxiety is one symptom) – is badly needed. Explaining that we can incorporate testing and treatment of MCS that would improve individual health and family and community well-being into our health care system would make sense, and it would finally make first-class citizens of those who struggle to live with MCS.

We understand that this explanation would unavoidably raise the question of the safety of many of the chemicals present in our everyday life, even at the unspecified normal or weak concentrations cited in the report – an unintended consequence of our chemical age. This is a challenge, but it is posed by the entire epidemiology and toxicology of chemically-linked disease, not just MCS. We understand, perhaps better than many others, the complexities and challenges involved in facing this issue across a number of government departments. But without action, things will only get worse, including in the continual rise in numbers of those with MCS.

Policy-makers and many other interested parties are starved for information about MCS. We worry that if the INSPQ report, read in a search for enlightenment, were to be taken up by officials in Québec and elsewhere, it could seriously set back the entire environmental health, women’s health, and disability agendas for a long time to come. It would be tragic if Québec were to be the agent of such a historic defeat.

As this is a matter of national and international concern and urgency, we add to our hope for new efforts and a change of direction in Québec another hope: that Health Canada and Environment Canada finally take seriously the 1.1 million Canadians diagnosed with MCS and offer leadership and substantial funding to provincial health care systems in the ways described above. And we hope that provinces, while urging the federal government to provide targeted funding, do not wait any longer to act.

In the meantime, people are very sick and without care or support. And it is a matter of human health and disability rights that those who have already developed MCS should be afforded

access to safe, effective, and appropriate care, just as those who have other diseases—often environmentally linked or caused—are recognized and treated. The time for action is now.

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The Whitehall Study

"A long-term cohort study of British [male] civil servants that was started in 1967. The aim of the first phase was to explore the relationship of cardiovascular disease to stress, social status, individuals' location in the hierarchical administrative structure of the civil service, access to and use of leisure facilities, and numerous other social and behavioral variables. This is summarized at http://www.workhealth.org/projects/pwhitew.html [Note: Link does not work]. The second phase focused on stress, perceived status, and self-esteem [and was expanded to include women]. The progress of this study of work and health is reported at http://www.ucl.ac.uk/whitehallII/ These studies and others have demonstrated the importance of social and psychosocial factors as determinants of health."

Taken from the Oxford Reference -- Quick reference https://www.oxfordreference.com/view/10.1093/oi/authority.20110803122305785

For a good overview of the Whitehall project and results, in graph form, also see: https://sheffieldequality.files.wordpress.com/2012/11/the-whitehall-studies.pdf.

And see https://www.ucl.ac.uk/epidemiology-health-care/research/epidemiology-and-public-health/research/whitehall-ii
The above link directs you to a list of publications by year e.g., from 1991, explaining the study and some conclusions, including "… Healthy behaviours should be encouraged across the whole of society; more attention should be paid to the social environments, job design, and the consequences of income inequality."
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# APPENDICES

# APPENDIX 1 – INFORMATION ABOUT THE SIGNATORIES TO "PUTTING THE CHEMICALS BACK IN MULTIPLE CHEMICAL SENSITIVITY"

Principal writer: Varda Burstyn
Assisted in writing and editing by: Maureen MacQuarrie
Ontario Ad Hoc Environmental Advocates Group: Bev Agar, Ted Ball, Varda Burstyn, Mike Ford, John Doherty, Izzat Jiwani, Denise Magi, Maureen McQuarrie, Scott Simpson, Adrianna Tetley

| Name | About |
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| Varda Burstyn | Varda Burstyn is a life-long environmentalist, an award-winning author and a consultant who has worked and published in environmentally-related health issues since the late 1980s. She has also been a volunteer board member with a number of environmental organizations, including Greenpeace Canada and the Environmental Health Association of Ontario. Since 2008, Varda Burstyn has been working with non-profits, patient advocates and the Ontario government to meet the health and social service needs of the nearly one million Ontario residents with chronic, co- morbid, environmentally-linked illnesses, initially bringing together a collaborative of advocates and providers who obtained ministry funding for the major study process for an Ontario Centre of Excellence in Environmental Health business case. She worked as the lead consultant on that project and was a founding member of the Ontario Task Force on Environmental Health. She advised extensively on the implementation report awaiting action at this time. She is currently a member of the board of the Chemical Sensitivity Foundation (US). |
| Maureen MacQuarrie | Maureen MacQuarrie was a member of the Ontario Task Force on Environmental Health. She is a lawyer and policy advisor who was forced to stop working in 2001 due to ME. She has been an advocate for those with ME and other related health issues and has used her strong analytic skills in background documents and to raise issues with policy makers. Maureen is the editor of Eleanor Stein MD's 2012 self-management manual "Let your light shine through: Strategies for living with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, Fibromyalgia and Multiple Chemical Sensitivity" as well as Dr. Stein's more recent, "More Light" and is a collaborator on Valerie Free's "Lighting up |

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| | a Hidden World: CFS and ME. Maureen is a member of the Steering Committee for the ICanCME Research Network as well as on its clinical care working group. |
| Bev Agar | Bev Agar, who was an alternate member of the Ontario Task Force on Environmental Health, was forced to retire early from her teaching position and move out of Toronto due to a lack of accommodation for serious ES/FM/ME. She has fought long and hard for accessibility and accommodation, advocating at the policy level and helping many individuals craft their legal battles for disability rights. She has also worked to raise environmental health and MCS awareness in a number of organizations, ranging from local citizens groups to national federal departments, convincing them to make specific policy changes. Bev is optimistic that positive change will occur so that everyone can reach their full potential and live barrier-free lives, free of discrimination. |
| Ted Ball | Ted Ball has a wealth of top-level government experience after 15 years as a Chief-of-Staff and Senior Policy Speechwriter to Ministers in the Bill Davis Government — where he participated in the development of a $1.5 billion Industrial Strategy; in provincial constitutional Premiers' Conferences; in health policy reforms in mental health and long term care — as well as playing a role as Chief-of-Staff during two provincial budgets in the Ministry of Finance. For the past twenty years, Ted has been the CEO of Quantum Canada, later Quantum Transformation Technologies, a leading-edge capacity-building company with systems thinking tools for strategy execution and for designing complex adaptive systems for integrated healthcare services delivery. Quantum also offers their Patient Experience Design Methodologies to design the "seamless patient experience" across the continuum-of-care across a delivery system, or across the silos within an organization. Ted has served as strategy coach to CEOs of Teaching Hospitals/ Community Hospitals/ Deputy Ministers/ and the Secretary to Cabinet in the Government of Ontario. He has worked on environmentally-linked illnesses as a volunteer lobbyist, MEAO Board member, and as Co-Chair of the Environmental Health Business Case Study and as an active Social Media advocate who weekly engages thousands of readers on his passionate arguments for patients with MCS and the other environmentally-linked illnesses. |

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| John Doherty | John has spent nearly 25 years as consultant working with healthcare, housing organizations and other agencies to be more effective and focussed in serving their local communities. He has been actively involved in the process to create a centre of excellence in environmental health over many years, serving as the co-chair of the OCEEH interim steering committee. He has volunteered for many non-profit organizations, in various roles, including, for many, as chair of their board of directors. John was elected as a Trustee with the Toronto Board of Education for nine years during which he focused on finances, human resources and improving access to the school system. He was chair of the Board of Greenpeace Canada for seven years, the leading environmental organization in Canada. During that time, Greenpeace campaigned with indigenous leaders in Alberta on the long term health impact of the tar sands on community health. As a Board member and Chair of the Toronto Environmental Alliance, TEA worked to highlight the impacts of environmental degradation on communities in Toronto and how to engage local residents in the fight for a cleaner, healthier environment. |
| Mike Ford | Mike Ford, who served as a member of the Ontario Task Force on Environmental Health, is a Toronto-based bilingual professional songwriter, musician, and educator with 25 years of experience in the entertainment industry, as well as 15 years of experience creating and delivering artistic, socially-focused educational programs across Ontario. As a caregiver, he has seen the incredible difficulties and obstacles that MCS presents, in terms of physical pain and debilitation, housing, day-to-day functioning, threat of exposures, health care challenges, financial hardship, and legal ordeals. Mike has repeatedly seen how vastly short society falls in terms of providing understanding, guidance, help, and healing to those suffering from the effects of toxic environmental exposure. |
| Izzat Jiwani | Izzat Jiwani, PhD, was a member of the Ontario Task Force on Environmental Health, and a co-chair of its Care working committee. She is a member of ICanCME Research Network on its clinical care working group. She has been a post-doctoral fellow with the Research Chair in Governance and Transformations of Health Care Organizations and Systems (University of Montreal). Izzat has published on, among other topics, Canada's chronic disease management systems and a comparative study on Ontario and Quebec's primary care |

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| | models. She is a health and social policy analyst and a researcher with broad experience in the public sector that includes the Ontario Ministry of Health and Long Term Care in the Strategic Health Policy division and a qualitative research on the status of palliative care in AKDN hospitals in six developing countries. As a caregiver to a family member with debilitating ME and MCS, Izzat has witnessed how a young well-educated professional with much to contribute to society is severely hampered by lack of knowledgeable clinical care professionals and supportive social care systems. As a social scientist, she supports that in the current milieu of emerging and changing scientific knowledge, public policies must be informed by research inclusive of promising practices and the patient experience in order to effectively improve the lives of those with chronic complex illnesses such as MCS and ME. |
| Denise Magi | Denise Magi is President of The Myalgic Encephalomyelitis Association of Ontario (MEAO), an organization supporting, representing and bringing awareness to the medical conditions of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), Fibromyalgia (FM) and Environmental Sensitivities/Multiple Chemical Sensitivity (ES/MCS). In the public sector, Denise has a long and extensive work experience as a legal assistant and in the library sciences. Denise has been on various steering committees including the initial steering committee that developed the business case proposal for the Ontario Centre of Excellence in Environmental Health, which seeks to establish a patient-centred model of medical care and system of service delivery for patients with ME/CFS, FM and ES/MCS, as well as other environmentally-linked medical conditions. She is dedicated to the cause of establishing a patient-centred health care delivery system to help Ontarians living with environmentally-linked medical conditions. She would like to ensure that the recommendations of the business case proposal and the aligned recommendations of the Task Force on Environmental Health be implemented as fast as possible. Denise was also a member of the Task Force on Environmental Health. She is a patient with personal knowledge of ME/CFS, FM and ES/MCS and is a long standing volunteer and health advocate. |
| Scott Simpson | Scott Simpson is a long-time patient advocate, including for patient safety, ensuring the patient's voice and perspective is meaningfully involved in policy, research and treatment. |

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| | Scott worked with Dignitas International, a Canadian medical humanitarian non-governmental organization, to increase access to life-saving HIV medications and health care in Malawi, Africa. Domestically, Scott worked in HIV counseling intervention programs at Toronto Metropolitan University, and is the co-author of two published papers about their findings. He is also a co-author of a published article on patient safety for ME and long COVID. Scott is co-founder of the advocacy organization Millions Missing Canada, part of the Millions Missing international collaborative. Scott is also an Executive Committee member of the Interdisciplinary Canadian Collaborative Myalgic Encephalomyelitis (ICanCME) Research Network. Scott is a founding member of the Patients for Patient Safety Alliance Canada; hosts the Medical Error Interviews podcast; and provides counseling to people living with medically marginalized diseases like MCS. Scott has been living with HIV since 1998, and with ME since 2012. |
| Adrianna Tetley | Adrianna Tetley has over 40 years experience in advocacy, public administration, community development, governance and policy development. Between 2004 and 2020 Adrianna was CEO of the Alliance for Healthier Communities, an organization that represents community governed interprofessional primary health care organizations including community health centres in Ontario. In 2011, advocates with environmentally linked conditions, approached the Alliance to sponsor a grant from the Ministry of Health to develop a business case for an Ontario Centre of Excellence in Environmental Health. In partnership with Ted Ball, Adrianna co-chaired the Steering Committee for the business case.This began the over 11-year journey in becoming a strong advocate for a system of care for people living with ME/CFS, FM and ES/MCS. Upon retirement from the Alliance, Adrianna continues her commitment in a volunteer capacity as treasurer on The Myalgic Encephalomyelitis Association of Ontario (MEAO) an organization that represents environmentally linked complex chronic conditions, including ME/CFS, FM and ES/MCS. Her priority is to ensure that the recommendations of the business case proposal and the aligned recommendations in the Taskforce on Environmental Health reports be implemented with appropriate funding as soon as possible. |

# APPENDIX 2 – LIMITATIONS, UNCERTAINTIES AND DATA GAPS IN THE MCS LITERATURE: APPLICABLE COMMENTS FROM THE ALBERTA REPORT

The following points, made by the Alberta report with respect to the literature they reviewed, seem to us also to have relevance to the literature the INSPQ report reviewed.

In the INSPQ report, as in the literature reviewed in Alberta, "some studies reviewed involved less than 10 subjects, while others had hundreds."(Alberta, p. 77) Many different study designs were used, making it difficult to compare their results. And, as already noted by us, and noted also by Alberta, longitudinal studies were largely missing. The Alberta report states: "This is a significant gap, as such studies are useful in assessing the causal influences on disease states."(p. 78)

The following verbatim discussion points of some of the limitations, uncertainties and data gaps in the literature reviewed in the Alberta report appear to us to have a significant degree of relevance to the literature reviewed by the INSPQ report. We provide them for informational purposes, other points can be found in the Alberta report itself:

- There is a lack of experimental studies that evaluate multiple doses (e.g., 3 or more) of irritants or odorous VOCs. As a result, it is not clear if there is a dose-response relationship apparent for MCS, particularly in relation to olfactory processing and neurological sensitization/neurogenic inflammation. However, it is recognized that these types of studies could be challenging to complete in sensitive individuals. (p. 78)

- There is a limited amount of information involving MCS and controlled exposure to chemical mixtures. The challenge studies included typically evaluated exposure to one chemical at a time. However, chemicals are present within indoor and outdoor environments as mixtures. It is not known if the observed responses in the MCS subjects (or lack of responses) would change when another chemical is added to the mix? What would the nature of this effect be - additive, synergistic, less-than- additive and why? These are dilemmas which impact conventional toxicological risk assessments and are also applicable to MCS. (p. 78).

- For the olfactory and neurological sensitization studies, there were notable differences in the mode of delivery of odorants or chemicals to subjects. Some studies involved nasal mask, a nasal olfactometer, chamber studies (with and without nose plugs), scratch and sniff or "Sniffin Sticks' tests, and aerosolized vapours. There were also no clear, objective measures of exposure consistently used in the studies. This lack of consistency in administration contributes to the overall gap of knowledge regarding dose-response. For these studies, it was also not always clear as to which of the observed effects were physical or psychological. (p. 78)

- As a result of the various study designs, there is some variability in how long study subjects were permitted to become acclimatized or adapted to their study environment, and how their individual sensitivities were managed before, during and after the study. This variation could have affected study outcomes. (p. 78)

- There is a lack of clarity and consistency with respect to comorbidity with other conditions and medication use. As discussed in Section 3.6, several overlapping conditions have been identified for MCS. While many studies did adjust for such variables, due to the vague nature of some of the diagnoses for these conditions, it is not clear how accurate these adjustments have been and how they could have influenced the MCS study data across endpoints. (p. 79)

- The atopic or allergy status of subjects was not always determined consistently in the studies. Until the relationship (if any) of allergy and immune dysfunction and MCS is more refined, the variability that could result in the data as a result of people both with and without allergies or atopic conditions being included in study populations is not known. (p. 79)

- The potential role of memories of previous exposures to odours and the determination of familiar vs. novel, sweet vs. pungent or foul and emotions attached to these sensations may contribute variability to symptom profiles of MCS. It is likely that individuals would vary greatly with respect to emotions attached to odours, and thus their responses would also vary. Within a clinical study context, these factors (memory, emotional responses) are likely challenging to manage and document. (p. 79)

- For the most part, the studies evaluated… were focused on one area (e.g., immune effects, genotype, phenotype, olfactory processing, etc.), perhaps with psychological symptom scoring also being considered. There is a lack of MCS studies that evaluate more than one biological mechanism at a time. (p. 79)

# APPENDIX 3 – FINDINGS IN "COMMUNITY VOICES" FROM THE QUALITATIVE NEEDS IDENTIFICATION SURVEY, ONTARIO 2013

To provide further corroboration of the MCS patient experience in general, and to support Part 8 of this current document, here is a (very) small selection of excerpts from a qualitative study by Varda Burstyn, M. Ann Phillips, PhD., Paula McKweon & Erica Halapy, MSc. "Community Voices" (Part 3) and "Special Issues" (Part 4) 59-166, in Burstyn, V. & MEAO (2013) Recognition, inclusion and equity – The Time is Now: Perspectives of Ontarians Living with ES/MCS, ME/CFS and FM, prepared for the Steering Committee of the Ontario Centre of Excellence in Environmental Health Business Case Project and the Ontario Ministry of Health and Long-term Care 2013. [69]

This was a qualitative needs identification report addressing the current state (survey of patients' experience, needs, gaps in services); special analysis of women's, children's, stigmatization issues; in-depth exploration of model of care and delivery; in-depth discussion of issues in barrier removal across government and the public sector.

This in-depth and substantive patient study informed the detailed design of a system and model of care, also described at length in the same document. This system was then adopted by the business case itself - Recognition Inclusion and Equity - The Time Is Now: Solutions for Ontarians Living with ES/MCS, ME/CFS and FM – which was intended to provided a blueprint, including costing for departments and functions, for staffing, for rental of physical sites and safe retrofitting for MCS patients, and for a modest lodge to provide safe accommodations for patients who had to consult specialists and/or receive treatment in Toronto.

These and other related documentation are available at:
http://recognitioninclusionandequity.org/resources/

The methodology section can be found at the end of this appendix.

## WHERE DOES ANXIETY-INDUCING STRESS COME FROM FOR THOSE LIVING WITH MCS?

In Part 8 "Socially determined stress in chronic MCS exacerbates illness," the new stressors that accompany post-onset MCS were described, as tightly as possible and with few patient words. The severe, even extreme chronic stressors post-onset that become part of everyday life almost immediately, especially with severity have in no way been factored in, either in the INSPQ report or the cited literature that seeks to track and explain the mechanisms of chemical sensitivity.

[69] This and its companion section "Special Issues" can now be found as a stand-alone document at the webpage address on our cover, http://recognitioninclusionandequity.org/inspq-mcs-report-critique/
or within the original full report, Recognition, inclusion and equity – The time is now: Perspectives of Ontarians living with ES/MCS, ME/CFS and FM, Varda Burstyn and MEAO, 2013
http://recognitioninclusionandequity.org/resources/

Yet, if stress is a contributing factor – as it is in all disease, and as the INSP report insists with respect to MCS – the levels of stress in the lives of those living with MCS who cannot access appropriate treatment or safe ways to live in the world must be taken into account in understanding the nature of severity and duration.

As noted, we have in Ontario a rich source for information on the chronic stress of daily life with MCS in Canada in an in-depth qualitative study undertaken in 2011 and submitted in 2013 to inform the business case commissioned by the Ontario Ministry of Health for what was then called the Ontario Centre of Excellence in Environmental Health. The methodology of this study and a discussion of its participants can be found at the end of this appendix. Twenty-three mostly female participants with MCS as a primary diagnosis were interviewed and a number of others who had co-morbidities with ME/CFS and FM are also included in our selection here.

Since no actual changes have been enacted to date in the social and medical conditions in Ontario – despite a lot of study and discussion – and since this study's findings echo and deepen the findings of the shorter scholarly studies, we can assume that the findings of this study still hold today. The full original study report numbered about 300 pages and the summary for the supporting report for the business case numbered about 110 pages. What follows is of necessity a highly condensed account. Still, it should be highly informative. The picture that emerges – of layer upon layer upon layer of new stress that is not resolvable on an individual level – should, we hope, adjust the input for the discussion of stress and anxiety in post-onset MCS, and ensure that the framework of further investigation takes these realities into account.

The quote excerpts from the report begin below, the page numbers of the quotes reference the pages in the original document. Many of these quotes have been used in our commentary with the general reference to Appendix 3.

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## 1. OVERAL IMPACTS ON HEALTH, FAMILY, FRIENDSHIPS, FINANCES AND MOBILITY: "CHRONIC, COMPLEX, DEBILITATING AND DISABLING, NEGATIVELY AFFECTING EVERY ASPECT OF LIFE."

With respect to the overall impacts MCS has on wellbeing, family life, friendships and social integration – key factors in the social determinants of health and in stress levels most participants said that they lived a normal life before onset of these conditions and were active and healthy.

> Well, I was a healthy young woman, and very strong and fit, and in high school I was a majorette and on several sports teams, so that shows you the level of activity I took part in. Nancy ME FM MCS p. 87

> Once upon a time, I was a Critical Care Nurse and full of dreams and very active in my community, and volunteering with kids on the street and the homeless, and driving our

> seniors to Church, had a boyfriend - just living life in the fast lane, I guess. Mary Lou ME FM MCS. p.87

Then, after onset, while the extent of the impact on individuals varied to some degree, participants unanimously confirmed MCS to be chronic, complex, debilitating and disabling, negatively affecting every aspect of life. At the severe end of the gradient, the impacts of these conditions were compared to effects of stroke, to the effects of chemotherapy, to late stage HIV-AIDS or severe arthritis. They noted that, especially without medical care, duration is long, even life-long, and severity of illnesses is often extreme. This study confirmed that these conditions are chronic and serious – with all that means for stress levels. It also confirmed that symptoms could occur for years - up to 17 years in our study - before diagnoses were made.

For the MCS participants, clear trigger processes or specific events were evident. ES/MCS participants identified that chemical events in their work places and personal spaces, including offices, dwellings and cars, were triggers for symptoms. In addition to chemical toxic exposures, flu or other infections and physical injuries were also mentioned.

> It all happened as a result of exposure to incorrectly mixed adhesive chemical to repair a windshield in my vehicle. I started getting symptoms within about fifteen minutes of being in my vehicle. Things started to go weird and life … went to hell in a hand basket …It wasn't until I saw Dr. B. that she diagnosed the FM and chemical sensitivity and the toxic brain injury. Sandra MCS FM p. 69

> It's been about half my life that I have had chemical sensitivities, multiple chemical sensitivities. … I think what happened was when I was young I had a major inner ear infection. Then I went to the hospital; I had surgery; I had tubes put in and I had them taken out. Then I started having the asthma attacks in the fall. Then, when I was in my early 20s – I was in nursing school actually – that's where it started. I started to have reactions to chemicals and perfumes and things around – the cleaners and stuff. I couldn't even continue in the class. I had moved to Montreal and there I found out that it could be this multiple chemical sensitivities. Petra MCS p. 69

Participants reported that both the physical and emotional challenges of day-to-day life could be staggeringly difficult as they struggled to deal with their post-onset 'new normal'. Here are informant comments on that struggle. Keep in mind that many people live with two or three of these conditions at once.

> You can't have what other people take for granted, like family, friends, socialization, clothing. Lately I order most of my clothing from the Sears catalogue. I guess it's not so lately that everything comes through China and it is soaked in formaldehyde. … With my current partner we've taken cotton clothing and washed it in everything and soaked it in vinegar, just washing and washing and washing… After about a year of washing and washing and soaking, then you can wear something. … I moved to the country on the advice of my doctor. Then the air quality has deteriorated over [there during] the time

> I've been unwell so that, you really can't go anywhere. … I'm more polluted now, than in my house in the city, 'cause you have the wind off the water. It's really a Catch-22. Claire MCS, p. 71

> I can't eat food from a supermarket because that's all contaminated with fragrances and laundry product residue. So I need non-supermarket sources of organic food. I must prepare my own food. Mixed, packaged foods have too many sources of contamination. Even at the farmers' market, I bought organic cabbage rolls because, you know, their vegetables were really good for me. I'm eating the cabbage rolls and I can taste dish detergent in them, so I asked, 'Well, what do you wash your dishes with?' 'Oh, we use Palmolive.' I said, 'Well it's in your cabbage rolls. LMS MCS, p. 71

Most participants had left jobs and ordinary workplaces behind, but some were still trying. They found it very difficult.

> You know, going to work just about does me in every day. I don't have much energy at the end of the day, you know, coming home, making supper, doing the domestic duties. The fatigue and the brain fog have been most difficult and the emotional aspect. Dealing with, coming to terms with, the fact that this is the way it is, when intellectually I am somewhere else and my body kind of betrays me. I think of all the things I could be doing if I did not have this limitation and that causes incredible despair for me. Hope MCS, p. 72

Whether employed or not, most informants said they experienced great emotional as well as physical hardship. They noted that the most ordinary life events can trigger setbacks if they involve certain types of chemical stressors, making it difficult simply to live in the world as it is. It was not uncommon for sufferers to seriously consider suicide. Those who had who had endured the trauma of these severe illnesses said they felt as though they and their lives are discontinuous with their previous selves.

> The main diagnosis, I don't know what is worse; I have been diagnosed with toxic brain injury, MCS and FM. … I couldn't work and I couldn't stand all the smells and everything in Stouffville so I had to sell my home – I was living in a little cottage that belonged to some friend of mine up here and then they let me live in it and were trying to help me with research and stuff. … in November of 2002 … I was probably so suicidal because I thought that the rest of my life was going to be spent in a little cottage by the river where it was freezing cold with a composting toilet, by myself in pain, which wasn't an option. … The whole experience changed me psychologically so much, I lost myself, I died. The real Sandy basically died with this and this person that is left now is a totally new invention, I don't even recognize myself in the mirror. Sandra MCS FM, p. 72

Negative social attitudes that are "uncaring, dismissive and discriminatory." (p. 72) The physical hardships and barriers participants experienced were coupled with and made worse by what they described as "very widespread negative social attitudes that are uncaring, dismissive and discriminatory." Almost all participants in the study described a feeling of being invisible, to

community and society, and to health and social service providers. Lack of respect, exclusion and discrimination in the health and social support systems, they suggested, set the stage and the tone for the treatment of sufferers in work and social life. Many study participants described shunning behavior from peers and family. Many people feared this stigma so intensely that they had tried to hide their illness from family and peers.

> Even though I live in the country, on my street a lot of IT people are moving in, and last year my neighbour had a router going through my bedroom window. I had to get a professional in to do a reading on it, and forward it to my neighbor and it was a really bad feeling. I used to be friendly with this neighbour and no longer. You become, you become isolated and worse than isolated, you actually become hated. **…** What I would like to see is publicity, that this is real, so that I would have a family, that I wouldn't be shunned. Shunning was an old fashioned method of really killing people. It was kind of like with voodoo. If your whole tribe is against you, you die. The only way shunning wouldn't be so prevalent would be through the media. Claire MCS, p. 73

As a result of these attitudes, many informants reported resisting their diagnosis and continuing to 'push through' - with many harmful effects resulting.

> At the beginning I didn't believe there was such a thing as chronic fatigue. I just thought those people were lazy. … When my doctor first told me that was what I had, I said, 'That's yuppie flu.' And I said, 'There's no such thing and I haven't got it and there's no way I'm taking time off.' Joan ME FM MCS, p. 74

Participants without private means or established pensions reported grave financial impacts for them and their families, describing them as "ongoing, frequently devastating, financial impacts" (page 84) (more on this presently).

Indeed, in the noted context of professional and societal misinformation and stigmatization, participants said their families often found the realities of the conditions difficult to understand, accept, and cope with. Lack of understanding by family members was deeply stressful for sufferers and family members alike. Even for families that did fully accept the diagnoses, dealing with the consequences was often very difficult. Participants reported that the condition placed serious strains on all marriages and terminal strains on many. Numerous participants noted how critical the help of spouses and family is; and how difficult it is to cope with these conditions on one's own.

Problems in parenting, and other family members: The participants noted that MCS created very serious problem problems for parenting of children. The MCS parent participants indicated that they were not able to parent their children as they would have liked to. For some parents, children became caregivers who carried burdens disproportionate to their years or capacities. They concluded that children suffer when parents suffer, and vice versa.

> My younger son lived with me all that whole time. He is seriously affected (cries) because, for instance, he couldn't have his friends over. All his friends wore Axe or something that is definitely a no-no. I can't be exposed to that. So his social life was definitely changed…. He had to worry about his mother a lot more, because his mother was in pain, because his mother was fatigued, he didn't know if his mother was going to die. Don't forget he was maybe twelve when I was disabled. … most of his teenage years I've been in arbitration and human rights so … he was [not] immune to that, he had to get the side effects. These are very serious emotional and physical demands on our family. Elva MCS FM ME, p.76

Participants noted that Relationships with their own parents and siblings of sufferers were often stressed.

> I've lost touch … even family that lives a two-hour drive away. I can't attend those events because of the driving. I can only drive myself about 15, 20 minutes. But to be in a car for an hour is my max before it interferes with the rest of the week. So, I haven't seen certain family members for a long time. Sophie FM ME MCS (p. 76)

Participants notes that the lack of available supports for family members is a serious problem and an inequity in service. Lack of homecare, respite care, child care, caregiver care - especially when these services cannot be purchased privately - puts a major stress on caregivers.

Gender-related issues: These were addressed by all participants. They noted that identities and gender roles were strained in family and social life, and sexist attitudes were evident. A number of women spoke about the difficulties of dependency caused by the conditions.

> I was never that type of woman before this illness. I was very strong and capable and it's been a real learning experience being the dependent, because this wasn't my personality nor how I felt about myself or anything. Claire MCS (p. 77)

Many women spoke about the sexist perception that their illnesses were not real or serious, but rather a result of women's physiology or tendency to complain. (An entire chapter was devoted to this finding in the original document).

A number of men spoke about the strains on their gender identity of being sick. Losing the ability to be the breadwinner featured centrally in their comments. Some also identified strains in having what was perceived as a 'woman's condition.' Some women spoke about the way in which the perception of the conditions as 'women's problems' created sexist perceptions of male sufferers.

For participants who did not already have a partner, dating or finding a mate was made very difficult with these conditions.

Friendships and community life: One participant described friendships and community life as "a disappearing act." (p. 77) Friendships and social support networks were always negatively affected. Isolation was the norm.

For all, social and community life as a whole had been strongly negatively impacted, and in many cases completely eliminated. Isolation, including severe isolation, had been the frequent result. Some participants notes that a lack of belief in the reality of the conditions and an absence of compassion was part of the loss of friendships for some. Participants noted that Isolation affects couples and families too, not just those directly afflicted.

> I had friends that don't bother with me anymore because it takes too much effort to be with me because there are a lot of rules attached to what you can smell like, what you have to do for two or three days before you come and see me. They fell by the wayside. … I don't have a social life. Sandra MCS FM (p. 78)

ES/MCS participants said their social lives were restricted by the ubiquitous presence of everyday chemicals. Some felt that because of their needs, people experienced them as an imposition. Some felt their needs were not perceived as legitimate. For many, being social in 'normal' circumstances was impossible, or exacted a very heavy price. It was not uncommon for ES/MCS sufferers to experience hostile behaviour from friends or acquaintances who rejected the reality of MCS. Friends who did understand and continued to care become very precious.

Financial impact and enormous strain. With respect to financial impacts, participants spoke of enormous strains. Some were struggling to survive on social assistance or, in one case, a disability pension. Others had incomes above the official poverty line – whether through private means, the income of spouses, a middle-class job or a pension –yet reported they did not have sufficient resources to adequately meet their health needs - ranging from food and housing to health care. For all too many, even middle-class incomes could not take care of personal and family needs when the MCS struck.

> Honestly right now, I don't have enough money this month to buy the rest of my supplements. I have to wait for another eight days until my cheque comes in, but for those eight days I am going to be without my cough pill. If I had money I could follow my regimen more and that has been a problem for me, running out of money to follow what I need and that causes inconsistency in my body. Hope MCS social worker, p. 83.

Job loss due to illness onset and/or lack of disability accommodation was a central feature of life for the majority of informants. Some participants' employers would not accommodate them because they did not believe their employees were really sick. Some employers took actions that isolated and undermined their employees and made it impossible for them to continue working. A number of study informants had succeeded in continuing to work but faced major and complex obstacles that remain ongoing and are not easily resolved. Some participants expressed the desire to continue to work but were unable to, due to lack of provision of supportive accommodations to suit the needs of their conditions. Some participants got sick because of

hazards in the workplace, but lost their jobs anyway, sometimes for punitive reasons, often with no compensation. A number of people reported unrealistic pressures for re-employment due to lack of understanding of the conditions.

Participants pointed out that job loss during working years without income protection and health benefits affects future income (pensions) as well as present income, and many were left without any. Others struggled to get by.

> It has been incredibly difficult financially, because the insurance company that will end up settling with me has denied any kind of responsibility for the toxic injury. So I had just been on my own trying to muddle through and operating on CPP disability for a number of years, and now with CPP and old age. Sandra MCS, p. 85.

Study participants reported that the financial impacts of these conditions, combined with an absence of publicly-funded care and support, ranged from very considerable to crippling. Significant, ongoing, often devastating was how we termed it (p. 74). Extreme financial difficulties combined with lack of social supports result in great stress, including emotional distress, for many people. (This theme was a constant in all areas surveyed.)

Participants reported that insurance benefits are extremely difficult to obtain for many and the process of seeking them often becomes injurious to those already very sick. Some insurers exhibited bullying, discriminatory and other harmful behaviours. In many cases, insurance companies that did not recognize these conditions as illnesses or disabilities put the onus on people who were ill to prove that they deserved insurance, or compelled them to take medication or perform physical 'therapies' that were very harmful to them. In these ways, insurers exacerbated illness instead of assisting sufferers. Some participants were cut off prematurely from disability payments. Lack of coverage for essential health and medical needs

> Why are only the pharmaceutical company medications subsidized? My $200 worth of supplements a month isn't. The next person on ODSP [Ontario disability support program] who takes $200 worth of pharmaceuticals, doesn't have to pay for them. LMS MCS, p. 86.

Even as onset of MCS usually resulted in disability and income loss, the cost for appropriate treatment, uninsured privately or publicly, had to be paid for privately. This was identified as a "crushing burden" by many; and for all, a barrier to necessary care and a major inequity.

Participants found that publicly-provided disability programs were very deficient when it came to covering the needs of people with MCS. These programs have never been revised to include coverage for the special needs of people living MCS. As a result, many people were permanently going without essential medical supports, and experienced tremendous inequality relative to comparator groups. Physician assistance is required to obtain public benefits, but was often difficult or impossible to obtain. Many informants reported lack of support from physicians, ranging from procrastination to refusal to assist.

Housing – the special stressor of ES/MCS. Housing insecurity emerged as a massive problem for those with ES/MCS. Having a chemically-safe supportive housing is a medical need requiring multiple moves and major expenditures in house furnishings and alterations to create a safe environment. Most participants had a stressful history of multiple moves. These moves are very expensive because they involve repeated moving and repairing costs, and not infrequently, the repeated loss of equity in property. Many people with ES/MCS are bankrupted by this process, and their health fundamentally compromised.

Participants noted that there is no access to 'safe housing' for this group - be it in emergency shelters, market value housing, supportive housing, assisted living or long term care and palliative facilities. This creates a nightmare scenario for many, one that can repeat many times over years.

MCS participants ranked the issue of housing insecurity as the single greatest stressor and most urgent need; and also as the greatest inequity and barrier to accessing health supports, among them many grave inequities and barriers documented in this study. (This issue is addressed n detail in Chapter 20 of the original document).

> That was a terrible journey. …It progressively became worse as I deteriorated. But … the City of Toronto Housing, when they got letters from my doctor saying I needed to be transferred, and even to the point where the doctor said I was concerned even about my life, that I could I die in … the available housing ... Because I didn't fit into their criteria that was, like cancer, they said the only thing they could do was put me on the waiting list which is ten years, that I couldn't get special consideration for transfer. … I was ... being kept in relapse because I couldn't get to a place where I could be stable. So that was psychologically really awful, being in relapse and knowing that you don't have to be. ... It's been very sad. Almost every avenue where I've needed support or help, the initial and continued response was no response that helped me get a foot up. MaryLou ME FM MCS (p. 90)

ES/MCS 'avoidance' of triggers: This is a critical strategy, and improves quality of life and – severity dependent – productivity as well. But participants explained that it is complicated, demanding and expensive, and a stressor in its own right.

> The water filtration installed here wasn't sufficient for me to use the kitchen sink to wash my clothes in, so I had do them in the bathroom through the double shower filter, and the bending ruined my back. After a year, they finally put in a second carbon for the whole house filter (instead of a pre-filter,) so now I can wash my clothes standing up.. However, after I washed my facemask, my skin felt like it was burned. It just went red for about a week from using it. I'm still going to have to use the drinking water filter, which has an extra filter, to wash my facemask. … I had to use bottled water before moving here. … I couldn't wash the clothing off my back except for with the bottled water. I had to drink and cook with it too. I couldn't afford to get water filtration installed. One of the

> women at the spring water filtration place gave me a couple of dollars off the bottles, she was really helpful and supportive with my orders, buy it was insanely expensive and prevented me from doing many things I needed to be able to do (like have clean clothing and bedding). LMS MCS (p. 90)

Food insecurity: participants identified food insecurity as a serious issue for themselves and others with ES/MCS. They identified the following issues as stressors: not being able to afford food at all; not being able to obtain or afford medically-indicated food or medically-tolerated food (such as organic and gluten free), with adverse health outcomes; supermarket environments where chemicals from everyday products make every shopping excursion an illness-inducing episode; not having any consistent support to prepare and serve meals, and clean up afterward when levels of illness made this difficult for them. Participants pointed out that since many have severe food allergies and sensitivities, and/or are not considered eligible for food assistance, they are not able to utilize Meals on Wheels. And, since effective poverty is high among sufferers, many do not have the private means to purchase healthy food or food services.

> For eating I get one meal a day and the rest of my meals are on Ensure, cold soup or water. I ran out of Ensure so I have a banana for breakfast and have water for lunch and at night I have a dinner. That is basically what my life looks like now. I keep telling people I need fourteen hours of personal support work but they say no, that ten is the limit. That is the very unpleasant part. … I am shocked, that even my family doctor doesn't have the power to convince them that I need convalescent care or higher care. Even one hour with the PWS is not enough for all the eating, changing and the cleaning. It just runs out. I have 15 minutes to eat and she has to sometime hand-feed me because I am too weak or it is too painful to eat. TJ FM ME MCS (p. 91)

> I haven't been able to get eggs for two years because the delivery guys carrying eggs with date stamps and the dye gets into the eggs and affects me. There's some basic foods that I can't get delivered now. Linda MCS (p.91)

Social safety and personal support services: Participants pointed out that CCAC-provided, condition-competent personal support services, available for comparator groups, are missing for those with ES/MCS, and are urgently. Not being able to access home care, at all, or with safe providers, was extremely stressful.

> Right now, I am totally stuck in bed. … My family doctor and I are frustrated with CCAC – they don't really listen to what I need. They only give ten hours for someone that has no family support and is bed-ridden. Basically I get a diaper changed every 24 hours -- I am going to try not to cry here. I have to sit in my urine, which is very uncomfortable to sit in urine for 24 hours and wait for someone to come and change me. For eating I get one meal a day. ... That is basically what my life looks like now. I keep telling people I need fourteen hours but they say no, that ten is the limit. TJ FM ME MCS (p. 92)

> The first visit has to be in the office, then they'd decide if they can do a home visit after. They're not open to Skype or anything like that. They don't have a fragrance-free office, and they said they can't guarantee safety for a home visit, and they won't even do the home visit unless I come into the office. 'What we can offer you is an appointment to come in to see us where we'll discuss it.' I said, 'so you're offering me a chance to become completely disabled and possibly not be able look after myself … you're offering me a chance to be assaulted, basically.' LMS MCS (p.92)

> So life has become extremely difficult for me, trying to get food in here and trying to manage. I tried to get home help, you know, through CCAC, and I was interviewed over the phone about a year and a half ago – it totally exhausted me. And they said, yeah, there'd be a social worker calling you… I think it was six to eight months later, she called. And she came for an interview to my home… So yep, she interviewed me, and I said, 'well, do I qualify for some home healthcare? Like, I need somebody to help do my laundry or do something around here for me.' And she said, 'oh yeah, you qualify, but there's a waiting list of 1000 people.' Can you imagine? Nancy ME MCS FM (p. 92)

Transportation: this, it turned out, was another major stressor for participants with ES/MCS, since at present no public transport or Wheel Trans vehicles are free of fragrances and other petro-chemically linked substances. Trips, especially longer ones, can induce serious setbacks, but lack of a personal vehicle is not uncommon. So not being able to get to essential services or to visit family and friends was also identified as a major stressor.

## 2. GETTING HEALTH CARE MAKES ME SICK – HEALTH CARE SYSTEM STRESSORS FOR PEOPLE LIVING WITH MCS

'*…A very disempowering and horrible experience.'* (p. 104)

Life is challenging – that's a truism that applies to everyone. But one thing that Canada did many years ago is to adopt the principle of universal health care; and one thing that most Canadians have to ease existential uncertainty is the knowledge that they will be able to access reasonably timely, competent and compassionate health care. It is difficult for most Canadians, therefore, to even imagine what it is like for people who have serious, even life-threatening, disease but none of the health-care rights – in practice – of others. So much time was spent by study participants on the various aspects of this issue for them, that several distinct sections of the report had to be devoted to them. The"disempowering and horrible experience" that MCS participants related vis-a-vis health care is a massive stressor in their lives.

Study participants who had been able to access care by knowledgeable and even supportive physicians did report some positive experiences with them – "a miracle" (p. 97) "and "life saving," (p. 98) validating the benefits of competent, appropriate care. However, their negative experiences with physicians and the health care system outnumbered their positive experiences many times over, affirming a number of consistent and recurring patterns of negative

interactions and experiences with health care professionals. These were described as stressful in the extreme.

> I would say ninety per cent of my experiences with all of those [physicians] have been unpleasant or unsupportive. Dismissal too, like if I said, 'I can't take this medication' or 'I can't do that,' … my doctor called me non-compliant once, because I knew I reacted to what they had prescribed. So finally I said 'okay, I will take that,' and I broke out into an angry raised body rash. And I went to her office, and I said, 'I took your medication.' And she looked at me and panicked. Because she wasn't listening to me, I finally I took the medication, knowing what was going to happen to me, just to show her that what I was saying was the truth and was real. Hope MCS (p. 105)

> Every one of us has a non-evident, or invisible, disability. You can't say, 'my arm is broken. Please stop hitting my broken arm.' Doctors have a responsibility to become knowledgeable about things that are difficult, things that are not curable. … Refusal to do that is negligence. It is abuse. Hilary MCS (p. 105)

Disrespect, dismissal, spoken disbelief and explicit disparagement: The great majority of consultation participants found beliefs among physicians that MCS is a mental illness and/or hypochondria. Linked to these beliefs, common physician attitudes included disrespect, dismissal, spoken disbelief and explicit disparagement; even, on a few occasions, behaviours identified by patients as physically harmful and/or intentionally performed.

> I find that in the medical system there is a de-legitimization of this condition ES/MCS and there is a dismissal, and you are pathologized in a negative sense and psychologized. … They need to understand that this is a legitimate condition, and disability, because that was one of the most disparaging experiences for me when i reached out for help. Hope MCS (p. 106)

Participants were refused referrals to other physicians, letters to employers and insurance companies, explanations to family members and other caregivers - all behaviours with which patient support organizations were familiar with prior to this study. As well, when such practices and attitudes prevailed among physicians, they were also prevalent among other providers (e.g., nurses, other health and social support providers).

Patients identified the three worst outcomes of these attitudes as

- First was the failure to diagnose - timely fashion, or at all, or in a fashion that assisted the development of a helpful treatment and care plan.
- Second was the lack of treatment, or erroneous treatment, or refusal to take MCS into account in addressing co-morbid condition.
- Finally, there was the refusal to accommodate chemical sensitivity, a life-threatening condition, in providing safe medical treatment, safe air quality in facilities or safe air quality with patients through changing personal grooming habits.

Above and beyond the conditions themselves, chronic infections were mentioned as frequently missed by Ontario physicians, and very consequential to overall health. Diagnoses were made by GPs and by specialists and sometimes by nurse practitioners. Often primary care providers had no idea what their patients are dealing with.

> I was diagnosed in the states through Dr. S. with a blood infection and was treated for that on a long-term antibiotic course. And lo and behold, my fibromyalgia, which wasn't even responding to narcotics, started minimizing. Mary Lou ME FM MCS (p. 109)

Even with an accurate diagnosis, most individuals did not have access to appropriate health care. When this occurred, it resulted in harm to patients.

Lack of physician knowledge frequently led to harmful interventions. Lack of established system-wide clinical guidelines and familiarity by physicians creates deficiencies in treatment, and not uncommonly, conflicting messages to patients, which is very stressful. Participants noted that very few physicians understand that for many, MCS includes problems in metabolizing pharmaceutical substances. The physicians were reluctant to believe patients when they explained this and at times compelled patients take harmful medication. This was experienced as extremely stressful.

> I had three or four mini strokes and went to a local GP who i had seen now and then, but he had no clue of any of this. And he gave me a prescription for Lipitor, saying, 'oh well, you'll have to be on this now, because of the strokes.' Well, I think after one or two pills at the most, I had a very extreme reaction that attacked all my muscles. I could barely walk, and I wasn't feeling like I couldn't walk at that time. I was pretty strong at that time. Nancy FM ME MCS (p. 110)

Negative effects of diagnosis as mental illness or hypochondria: as already noted (and as such a frequent and ubiquitous theme that the report devoted a whole chapter to it), almost universally, participants' encountered physicians and other health professionals who diagnosed and treated the conditions as affective or non-existent disorders, with very negative consequences for patients. The MCS participants encountered the belief among medical doctors that their health problems were 'in their head' in the sense of a being psychological or affective disorders, either depression or somatization, or, indeed, a form of hypochondria. This had many adverse outcomes – all of it tremendously stressful in both emotional and physical ways.

MCSers fear medical services and those who are severely ill will avoid medical services, even critically-needed emergency and acute care services. L Because of the physical dangers posed to patients by a lack of knowledge about and safety for MCS in medical settings, and lack of knowledge of care protocols, those with this condition were extremely aversive to health providers and health sites.

> I actually was in touch when I was in Toronto with EMS, because the thought of having to call an ambulance scared the hell out of me, because if the people are scented or there's

> scent whatever, then I would just be sicker and then I couldn't speak for myself, which is the most frightening thing to think about … then I'd experience what other people have experienced in hospitals, which is being put in a psych ward. In Toronto I got sick… from truck exhaust under my window, ended up a couple days later with a kind of stroke called time blindness. And there was no way I was going into a hospital because … they spout the scent-free line but it isn't. Betty MCS (p. 113)

> I've had a lot of trouble accessing language for many years now, so there were more than a few misunderstandings …and I couldn't clear them up because i couldn't find the words and I didn't have the energy. It took so much energy to move my hand where it needed to go and to merely think, to come up with a complete sentence, to find words which i often got wrong, when people made assumptions it was impossible to try and correct it. I just gave up and waited, hoping for a better opportunity to arise. Now [that housing is safe] I'm starting to get more language back. Linda MCS (p.113)

Participants identified the extremely – at time unbelievably – high levels of stress involved in living with MCS in today's world. They equally identified how stressful it is not to be able to find or access psychotherapists and counselors who have training in MCS and can provide the psychological support needed by MCS patients to survive.

> The stress! The crises that one goes through and so on, result in a lot of stress. Through some of those crisis periods I wanted to get some support, counseling, somebody to talk to, but I didn't have anyone. And the efforts that I made to do that were for the most part frustrating and fruitless. … Even though counseling agencies sometimes say that they deal with all kinds of issues, they largely are uneducated and uninformed. Rob ME MCS (p. 112)

## METHODOLOGY

A criteria-based sampling method was used to select participants from among those who completed an initial questionnaire. The goal was to select participants from a broad range of circumstances, seeking representation from:

- As many parts of the province as possible and from both urban and rural areas
- All adult ages
- Men in addition to women as they experience the conditions less frequently
- The three conditions based on their relative proportions among the Ontario population according to the 2010 Canadian Community Health Survey
- Individuals with varying levels of disease severity, and
- Individuals experiencing the conditions for varying lengths of time
- Caregivers, who were eligible to participate on behalf of individuals with the conditions.

We did have imperfections (addressed in the full-length compilation). But we can say with confidence that we were successful enough to generate a wealth of valid, illuminating themes and findings.

THE QUESTIONNAIRE

The development of the questionnaires went through a collaborative and iterative process among the researchers, a member of the Institute for Social Research at York University (John Pollard) and the President of the National ME/FM Action Network (Margaret Parlor). In addition, the interview and focus group questions were pre-tested with seven individuals from the target population. This allowed individuals affected by the conditions under study an opportunity to provide feedback on the survey tools and methods. Further modifications to the questions and format were made based on their feedback before the protocols were finalized. The final interview questionnaire is shown here.

MEAO PATIENT QUALITATIVE INTERVIEW QUESTIONS

About You

1. Tell me about yourself, your experience of being ill, your main diagnosis and other health problems. Probe: What has been difficult or challenging for you?
2. How long have you been ill, who made your diagnosis, where and when?
3. What have you done to get yourself better? Probe: What types of health care and other supports and services have you used?

Health and Social Supports

4. Can you describe any supportive or positive experiences you've had while seeking health care or social or legal supports since your illness, at onset and currently? Probe: Any experiences with your physician, specialists, with social workers, insurance or disability?
5. Can you describe any unpleasant or unsupportive experiences you have had while seeking health care social, legal and other services since your illness, at onset and currently? Probe: Any experiences with your physician, specialists, with social workers, insurance or disability?
6. Have you had any unmet needs while seeking health care, social, legal or other services since your illness, at onset or currently? Probe: Unmet needs would be services that you would have liked to have available to you but found that they were not
7. How much of an understanding did your various physicians and other health professionals have of your condition?
8. Has your employer/workplace been supportive of you during your illness?
9. What impact has your illness had on your family and caregivers?

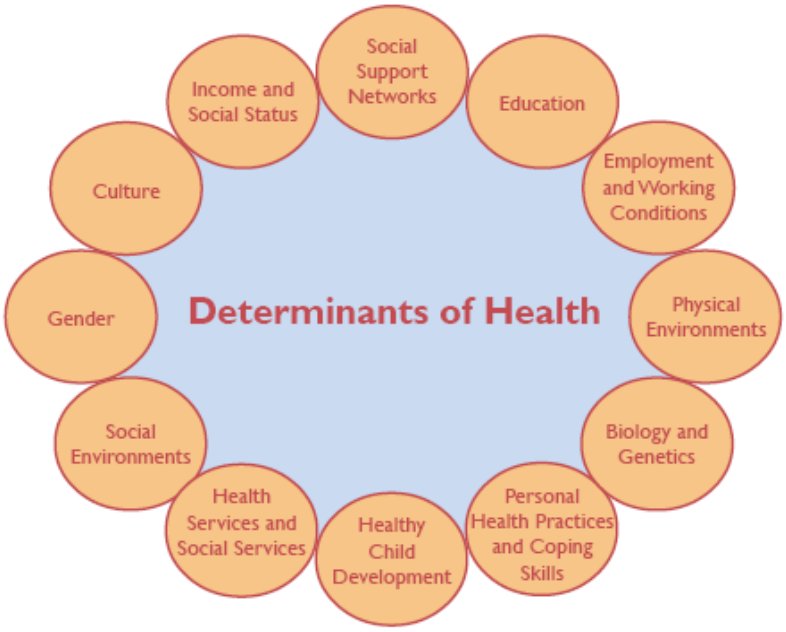
10. What impact has your illness had on your relationships with your friends and social support networks?
11. Have your health care providers, or the social, legal and other services assisted or made it easier for your family and care-givers to support you? Probe: Have they made it more difficult for them to do so? How so?
12. How has being a woman [or a man] affected your experience of your illness and of seeking health care?
13. Have you felt any prejudice, lack of respect and/or discrimination within the health care system, social, legal and other services? Probe: If yes, can you elaborate on your experience.

Solutions and Changes

14. Do you have any suggestions about what could be changed in terms of health care and the health care system to improve your life and your health and make life better for your family and caregivers?
15. Do you have any suggestions about what could be changed in terms of social, legal, insurance, disability, workplaces, and any other services to improve your life and your health and to make life better for your family and caregivers?
16. If you were designing an ideal system of care that would address most your illness related needs and the needs of your family and caregivers, what would that system include?

SOCIAL DETERMINANTS

The Determinants of Health identified by the World Health Organization (WHO)




Source: WHO 2013

This oft-cited WHO diagram condenses the cumulative wisdom of decades, and illustrates that health is the result of multiple dimensions. If even one of these is badly damaged, there may be negative health outcomes. If some or many of these dimensions fare poorly, there will almost certainly be negative outcomes. And if most of these dimensions are in trouble, so will be the populations who endure that trouble. Such is the population of people with the CELCs, at this time.

The main WHO determinants were ordered in this report to better identify the social determinants that most affect our populations - and to the extent possible, their priority or dependencies, though these are dynamic, complex and intertwined.

These are the fourteen issues we queried our community about, and address in the findings and subsequent recommendations -- Disability (having it; societal recognition through accommodation, law, custom); Income security, employment and social status; Food insecurity; Housing insecurity; Health services; Social safety support networks - involve services that address; family and social inclusion/exclusions; friendships; community involvement; isolation; emotional/psychological wellbeing; Gendered issues; Physical environment; Education

The dimensions of biology and genetics and early childhood development were not addressed by this study, but are discussed by John Molot in *Chronic complex conditions: Academic and clinical perspectives*.[70] Participants were encouraged to speak about their experiences in terms of gender, and the larger social/environmental context.

[70] J. Molot, MD, *Chronic complex conditions: Academic and clinical perspectives* (Ontario Centre of Excellence in Environmental Health, 2013). The clinical submission to the Ministry of Health and Long Term Care, supporting the Ontario Centre of Excellence Business Case Proposal.

Demographic characteristics of the 56 patient informants: Most participants were middle-aged (ages 40-69), with the majority (41.1%) being aged 50-59. The sample included some participants aged 30-39 and aged 70 and older, but did not capture anyone younger than age 30. The large majority of participants were women (85.7%), although 8 males did participate in the study. All regions of Ontario were represented with most participants residing in Toronto and Central Ontario (53.6%) followed by Eastern Ontario (32.1%). Those residing in urban settings represented the majority of the sample (92.9%).

Characteristics associated with people's diagnoses of ES-MCS, FM and/or ME-CFS: The majority of consultation participants had a main diagnosis of ME-CFS (44.6%) followed by FM (32.1%) and then ES-MCS (23.3%). Almost half of the participants in this study (48.2%) had multiple diagnoses. Only one participant in the sample had been suffering for less than five years, while 37.5% had experience symptoms for 20 years or more. The majority of participants (55.4%) rated the present severity of their main diagnosis somewhere in the moderate range (5-7 on a scale of 1-10). When rating their severity when they felt their worst, there was a shift towards the severe range (8-10 on a scale of 1-10) with the vast majority (91.1%) with a rating in this range. Only one participant rated their worst severity in the milder category of 1-4.

Connections to organizations and the broader ES-MCS, FM and ME-CFS communities: Participants were asked if they belonged to an organization such as the MEAO, National ME/FM Action Network or the Environmental Health Association of Ontario. Over half of participants (57.1%) belong to such an organization. Similarly, over half (58.9%) of participants belonged to a support group, either in person or online, that is related to one of the conditions. The proportion of those who did not belong to a related organization or support groups (approximately 40%), is still sizable. When asking participants how many other people they know with these conditions, almost half (44.6%) indicated they knew 20 or more people; 3.6% did not know anyone else, while 17.9% knew only 1 or two other people. The vast majority of people have access to internet at home, which can facilitate connectedness to health related information, organizations and communities.

# APPENDIX 4a – THE CHEMICAL MANUFACTURERS ASSOCIATION'S (CMA) "ENVIRONMENTAL ILLNESS BRIEFING PAPER" 1990

The paper (which begins on the next page) was reproduced in a reprint in BEST of the Reactor, edited by Susan Molloy, 1990, pages 171 - 181. Discussed in Illness and the Environment: A Reader in Contested Medicine. Ed Steve Krohl-Smith, Phil Brown and Valerie J. Gunter New York University Press, New York (1997).

We have not reproduced the CMA document's Appendices.

> From the following Chemical Manufacturers Association's briefing paper "Environmental illness patients generally lead troubled lives and have genuine problems in coping with family, work and life-style pressures. They often eagerly accept environmental illness as the explanation for their condition…" (page 224 here)
>
> "Because environmental illness is a health issue, the only people who can legitimize it are physicians, and they have not. Should environmental illness arise as an issue, a coalition with the state medical association is absolutely necessary."(page 237 here)

We start with our introductory comments -- Our society now has long experience with the intervention of commercial interests when the evidence of illness from their products threatens their profits. Whether the issue is smoking or pesticide use, or any number of other substances or practices that clearly have proven harmful to humans and fellow creatures, commercial interests have often intervened in ways geared to powerfully undermine the credibility of those who suffer from the products of their commercial practice. These battles are major and ongoing every day, fought by scientists and environmentalists against corporations with profits to lose.

ES/MCS (originally called 'Environmental Illness') has been no exception. The difficulty is that the commercial propaganda promoted by the then-Chemical Manufacturers' Association, (now, American Chemistry Council) left a harmful lasting legacy - the myth that people with ES/MCS are emotionally troubled, not physically sick - while the vast majority of those who have adopted this belief have no notion of its origin. It is our opinion that by denying the harms suffered by ES/MCS 'canaries' - harms that, unlike the slow and hidden progression of hidden cancers, for example, are acute and immediate and excruciating - the chemical industry effectively succeeded in whitewashing many of the chemicals that today have either been banned, or are under siege by those fighting for the interests of future generations and the biosphere. Some of the most ubiquitous of those chemicals have been documented in popular books such as *Slow Death by Rubber Duck* and *The Body Toxic*.[71]

[71] Rick Smith & Bruce Lourie, Slow Death by Rubber Duck: The Secret Danger of Everyday Things, Counterpoint, 2011. Nena Baker, The Body Toxic: How the Hazardous Chemicals of Everyday Things Threatens our Health and our Well-being, North Point Press, New York. 2009

From the Best of the Reactor introductory commentary -- In 1990 CMA lobbied for approximately 175 member companies, and supported twenty full-time lobbyists in Washington, DC. The CMA was in the process of establishing a Political Action Committee to enable contributions to the campaigns of political candidates. The paper below was circulated to physicians associations, insurers, governments and other businesses. Today, the CMA has a new name - the American Chemistry Council.

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The CMA'S Environmental Illness Briefing Paper

## Executive Summary

Known variously by more than 20 names, among them, chemical hypersensitivity syndrome, total allergy syndrome and 20th century disease, "environmental illness" is a subject of controversy within the field of medicine and an object of considerable public attention. For many patients, environmental illness has become the explanation for a combination of symptoms for which they've found no other acceptable explanation.

According to a small group of clinicians from a medically unrecognized specialty called "clinical ecology" or "environmental medicine," millions of people in this country suffer from environmental illness. Practitioners of environmental medicine report that the medical cause of their patients' conditions is a depressed immune system. These clinicians attribute their patients' symptoms which typically include headaches, fatigue, depression, anxiety and digestive problems primarily to exposure to trace amounts of virtually all synthetic chemicals found in food, water, air, clothing and everyday surroundings. In short, environmental medicine specialists believe their patients are severely "allergic" to the world they live in to the extent that many of them cannot function in society.

There is no doubt that these patients are ill and deserving of compassion, understanding and expert medical care. However, nationally known experts in the fields of allergy, immunology and internal medicine say the assertion that environmental illness is a legitimate disease is unproven. Elaborate testing of the immune systems of these patients almost always indicates normal immune functions, and they rarely have increased infections.

And only rarely are their symptoms supported by physical findings or laboratory tests. In addition, review of both the methods of diagnosis and treatment used by environmental medicine specialists have shown no convincing evidence that their patients have unique, recognizable symptoms or that their treatment procedures are any more effective than placebo treatment.

Environmental illness patients generally lead troubled lives and have genuine problems in coping with family, work and life-style pressures. They often eagerly accept environmental illness as the explanation for their condition and undertake the costly life-style changes including moving to

new environments and eliminating all synthetic agents from their homes that are part of treatment.

Despite unsubstantiated evidence, environmental medicine specialists and their patients persistently advocate that environmental illness exists. What they have failed to prove in the scientific arena, they are attempting to legitimize in the media, in the legislature, and in the courts. The important elements of human interest stories, human suffering, controversy, testimonials, and novelty, have provided natural stories for the media.

Legislative initiatives have so far failed to legitimize environmental illness, but it would not be difficult for legislators to misperceive the goals of environmental medicine as medically legitimate. And lawsuits, of which several are currently pending, could multiply.

The label of environmental illness is a misdiagnosis and condemns these patients to the life of an outcast with little hope of cure. It is essential that their described symptoms be taken seriously. These patients deserve the best medical evaluation and treatment consistent with established medical principles.

It is not the legitimacy of the patients that is in question, but the alleged environmental cause. Failure to recognize this critical difference can result in enormous costs to the patient, to industry and to society.

"Environmental Illness" Background "Environmental illness" has no single, accepted definition. However it may be described as a diagnosis that ascribes a broad range of common substances in the environment. Proponents allege that these symptoms are triggered particularly by contact with trace amounts of chemicals in our food, water, air and daily surroundings.

Symptoms are typically multiple, subjective and unsupported by physical findings or laboratory tests. Headaches, fatigue, depression, anxiety and digestive problems are some of the common initial complaints.

Those physicians who diagnose environmental illness call themselves "environmental medicine specialists." (Formerly they called themselves "clinical ecologists.") Environmental medicine is very controversial. There is no residency training in environmental medicine and the certifying board for its practitioners is not recognized by the American Board of Medical Specialties.

Furthermore, the American Academy of Allergy and Immunology, the California Medical Association and the American College of Physicians have taken the position that the tenets of environmental medicine are unproven (Refer to Appendix D).

## Diagnosis and Treatment

Practitioners of environmental medicine generally diagnose environmental illness by performing "provocation testing," which consists of exposing subjects to various mixtures of test substances

at progressively higher concentrations. The testing is variously done by inhalation, injection or placing the test solution under the patient's tongue. If any symptoms occur, the test is positive.

Subsequently, part of the subject's therapy consists of injection of the offending agents in lower concentrations. This "neutralization therapy" has no proven or even logical medical or scientific rationale to support it, according to the medical community. Provocation testing and symptom neutralization bear some superficial resemblance to skin testing for allergies and allergy shots for desensitization but are actually quite different. (Refer to section on Allergic Diseases, p. 9.) No reputable medical organization accepts provocation testing combined with neutralization therapy as having scientific meaning.

Independent "provocation testing" of environmental illness patients, for example, has resulted in equal numbers of positive tests from placebo solutions and from solutions of substances to which they allegedly were sensitive. [Terr, A. I., 1987. In Allergy: Clinical Ecology. Insights in Allergy. 2(5).]

Another part of an environmental illness patient's treatment is to avoid the common substances that purportedly make them ill. This could include living in environments totally free of modern synthetic materials, such as rooms or trailers with metal or porcelain surfaces; elaborate air filtration; and diets free of all additives, preservatives, or contaminants. This approach obviously renders the individual unemployable.

In short, there is no consensus on the proper diagnosis, treatment or even existence of environmental illness as a single, proven medical condition. The hypotheses of environmental medicine practitioners are medically unproven and have been rejected by professional medical organizations. In addition, the treatments, which are extremely expensive, have not verifiably helped patients any more than placebo therapy would.

### "Environmental Illness" Impacts

Environmental medicine specialists and other advocates are well organized and effective at representing environmental illness as a recognized medical condition affecting millions of people in this country. These advocates are working hard to legitimize environmental illness. Environmental illness already affects the patients who accept it as a legitimate disease. Should environmental illness advocates succeed in their efforts, it would also impact society and many industries.

For the patients, the unproven tests used to diagnose environmental illness may in fact lead to misdiagnosis of a true medical illness. Because environmental illness cannot be clearly diagnosed by clinical criteria, environmental illness specialists use the history of presumed environmental exposure as the basis for diagnosis.

This belief in itself can be psychologically crippling. Indeed, some patients view themselves in a hostile world, surrounded by chemicals that make them chronically ill and physicians who do not care. Often, their life becomes centered totally around their disease. Coping becomes stressful

and living needs become costly as these individuals change their life-styles to avoid all chemicals. They are determined to consume only organic foods grown without insecticides, sprays and fertilizers.

They may use only items made of glass, porcelain, stainless steel and untreated animal or plant fabrics (cotton, linen, silk, wood and leather). Often, this results in social isolation, difficulty within the community and unemployability.

The primary impact on society would be the huge cost associated with the legitimization of environmental illness. Up to now, environmental illness and the associated testing and therapy have not been eligible for coverage under such programs as medical insurance plans, Social Security disability, Medicare and Workers' Compensation. But proponents of environmental illness are now trying to legislate the legitimacy of environmental illness.

Although they have not been successful, it would not be difficult for legislators to misperceive environmental illness as medically legitimate and fail to recognize the potentially enormous cost that could accrue. Environmental illness advocates believe they are entitled to a number of sources of financial support. Among them:

- monetary damage for increased illness resulting from exposure;
- monetary damages for existing fear of contracting future illness;
- disability benefits from private insurance policies and Social Security;
- reimbursement for medical costs;
- Workers' Compensation payments;
- a variety of workplace protections (from termination, demotion, pay cuts, etc.);
- rehabilitation services; and
- financial assistance for alteration of living space.

Environmental illness forces nearly succeeded in accomplishing their goal in Maryland in 1988. They proposed legislation and it came close to being passed before informed health professionals became aware of it and managed to transform a bill legitimizing the diagnosis of environmental illness into a resolution to study the issue. The resulting study basically called environmental illness an unresolved issue; however, further actions by the legislature in Maryland on this issue seem unlikely in the near future.

Proponents of environmental illness have drafted "fill-in-the-blank" model legislation in an attempt to accomplish their aims. Such legislation could pop up in any state at any time. A carbon copy measure in California passed, but Governor Deukmejian vetoed it after the California Medical Association intervened.

The impact, however, would not be restricted to the chemical industry. Commonly used chemicals are found everywhere, in the home, the workplace, outdoors, shopping malls, and even hospitals. Potentially affected industries include the textiles, clothing, lawn care products,

household cleaners, dry cleaners, paints and solvents, perfumes, hair treatment products, plastics, paper and many other consumer goods industries.

There is also the threat of lawsuits. Litigants seeking redress for personal injury allegedly resulting from exposure to toxic substances are numerous now. Should environmental illness be recognized by legal or judicial decree, these suits would only multiply. Toxic torts create special problems for the defendant in the best of circumstances. It is scientifically impossible to ever prove a negative, the nonexistence of something.

Plaintiffs typically allege effects at very low exposure levels that are only known to be caused at much higher exposure levels. Often, only the presence of nearby chemicals, rather than true exposure, is documented. Or they allege that health effects were caused by substances not known to cause those effects.

Suits involving environmental illness are further complicated by the lack of a definition of environmental illness. In the eyes of environmental medicine practitioners and their patients, almost any symptom could be caused by exposure to almost anything. But most physicians do not agree with the environmental illness advocates. For example, Dr. Abba Terr, an immunologist at Stanford University Medical School, summarizes environmental illness in a chapter of a recent book reviewing multiple chemical hypersensitivity:

> The concept of multiple chemical hypersensitivities as a disease entity in which the patient experiences numerous symptoms from numerous chemicals and foods caused by a disturbance of the immune system lacks a scientific foundation. Published reports of such cases are anecdotal and without proper controls. There is no convincing evidence for any immunologic abnormality in these cases. Diagnostic methods have been shown to be unreliable. Diagnosis, treatment and theoretical concepts underlying the purported disease are not consistent with current immunologic knowledge and theory. As defined and presented by its proponents, multiple chemical hypersensitivities constitutes a belief and not a disease.
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> [Terr, A. I., 1987. Multiple Chemical Sensitivities: Immunologic Critique of Clinical Ecology Theories and Practices. In "Occupational Medicine State of the Art Reviews: Workers with Chemical Sensitivities", ed. M. R. Cullen, Vol. 2(4):693. Philadelphia, Hanley and Belfus.]

## Supporting Material: Theories of Etiology

Proponents of "environmental illness" ascribe many symptoms to exposure to numerous common substances in the environment. Although these can include natural chemicals, more often the symptoms are attributed to low level chronic exposure to synthetic chemicals. Most recently, environmental illness proponents have postulated that exposure to such chemicals causes a malfunction of the immune system that results in sensitivities not only to the chemicals to which the patient has been exposed but also to chemicals he may encounter in the future.

In the eyes of its advocates, almost any symptom can be attributed to environmental illness. But laboratory tests on patients who believe they are suffering from environmental illness have shown normal or inconsistent results.

Some of the patients who believe they have environmental illness also have symptoms characteristic of psychosomatic illness. [Terr, A. I. 1986. Environmental Illness: A Clinical Review of 50 Cases. "Archives of Internal Medicine". 146:145- 149. Stewart, D. E. et. al. 1985. Psychiatric Assessment of Patients with "20th Century Disease" in "Canadian Medical Association Journal". 133:1001 - 1006.]

Others have a variety of symptoms that do not fit any known medical disease. These latter patients should be investigated further with well designed scientific studies rather than being stigmatized by unproven illness that might hinder further medical investigation.

## Allergic Diseases

Environmental illness advocates have borrowed much of their terminology from the fields of allergy and immunology. This can be very confusing since there are legitimate allergic diseases that are well accepted and documented by the medical profession.

Environmental illness advocates claim that sensitization to one chemical may cause a spreading phenomenon in which the patient becomes allergic to many chemicals. True allergies do not behave this way. If a patient is sensitized to one chemical, they are sensitized only to that chemical and perhaps to a few other chemicals that are structurally almost identical. New sensitizations must occur before the patient will react to different chemicals.

Documented allergic diseases are caused when an individual develops an exaggerated IgE response to environmental, drug or microbial antigens. IgE is an immunoglobin protein that circulates in the blood and brings about allergic responses; other immunoglobins are involved less frequently. Typically, allergies do not affect everyone exposed to the substance. Minute amounts of the offending agent may cause symptoms in a person who is sensitized or allergic to the substance. But not all chemicals are capable of causing allergies.

Allergic individuals characteristically give rapid responses in skin testing, have high sum IgE levels and often have increased blood and tissue concentrations of eosinophilic leukocytes; an eosinophilic leukocyte is a specific type of white blood cell.

Symptoms are subjective changes perceived and described by the patients while signs are objective physical findings observed by the physician. Allergic symptoms typically involve the skin, the respiratory tract or the gastrointestinal tract. The following statements are generally true:

- Food allergies may cause vomiting, cramps and diarrhea.
- Skin reactions cause hives, which are large blisters or red, itchy rashes.

- Respiratory allergies are either of the hay fever type which involves the nose causing sneezing or nasal congestion, or the asthma type, which involves the lungs and the lower respiratory tract causing difficulty in breathing.
- A severe generalized allergic reaction known as anaphylactic shock may have symptoms of a drop in blood pressure and spasm of the larynx leading to shock and suffocation.

The location and type of symptoms most often depends on the type of contact with the agent to which the patient is sensitized. For example, contact with poison oak or with poison ivy usually involves the skin and results in a red, itchy rash with small blisters. Firefighters who are exposed to smoke from burning oak or ivy, however, inhale and ingest the smoke and may have symptoms in the lungs, nose and gastrointestinal tract as well. [ Hood, L. E. ed. 1984, Immunology, 2d. ed. 460-462. California: Benjamin/Cummings.]

In contrast to environmental illness, the symptoms of allergic reactions are reproducible. Usually a person who is allergic to an agent has the same type of contact and the same symptoms on each subsequent contact.

## Problems with Medical Testing

The specialty of immunology is one of the newest and most rapidly changing medical specialties. Laboratory tests used to measure a person's immune system function are also relatively new and still evolving. Some of the laboratory tests proponents of environmental illness use to support their position are well established in the medical repertoire. Other tests are new and not accepted by the general medical profession. A few, such as cytotoxic testing, have been declared invalid by federal agencies [ Fed. Reg. Vol. 48, No. 162, August 19, 1983-Notices.] which will not reimburse for performance of these tests.

Environmental medicine specialists often do a large number of screening tests on their patients. Inevitably, one or two tests are abnormal. Individual laboratory results are often compared with ranges of numbers rather than one absolute number. By chance alone, five percent of people tested with no clinical disease will have either "abnormally" high or low laboratory values.

The more tests that are done, the more often the result will be abnormal, simply because of the mathematics involved. Proponents of environmental illness use these abnormal tests as proof that the patient has environmental illness.

The nonstandard test most often conducted by environmental medicine specialists is provocation with neutralization. In provocation testing, subjects are exposed to concentrations of suspected substances either by inhalation, injection under the skin, or placement under the tongue. The occurrences of any symptoms within a short period of time are noted; any symptom is interpreted as a positive test.

Lower concentrations are then given until no symptoms occur. The concentration resulting in no symptoms is termed the "neutralizing dose." Provocation testing is not an accepted practice within the medical community.

Any patient has the right to expect that a qualified person is managing the laboratory in which tests of immune function are being conducted. The patient also has the right to expect that the physician interpreting the test results is qualified. Both the American Board of Pathology and the American Board of Internal Medicine, in conjunction with the American Board of Pediatrics and the American Board of Allergy and Immunology, now have examinations to assess the competence of clinical pathologists, internists and pediatricians conducting diagnostic immunologic tests.

"This certification process was developed to ensure that clinical immunology laboratories are directed by the persons who know the most about conducting such tests, properly applying them in diagnosis, and interpreting the results." [1988. Certification in Diagnostic Laboratory Immunology, "Annals of Internal Medicine". 108: 458-459.]

## Why "Environmental Illness" is Not Science or Medicine

"Environmental illness" lacks credible medical specificity. The symptoms, which are changes perceived by the patients, reported are neither substantiated by clinical signs, which are objective physical indications of illness, nor by laboratory testing of a wide array of body functions. The breadth of isolated symptoms is exceeded only by the number of purported chemical and environmental causes.

Indeed, there is no medical precedence to suggest that any syndrome or disease can be brought on by numerous separate and distinct agents

Proponents of environmental illness assert that environmental illness exists because they have repeatedly observed patients with multiple, non specific symptoms, conceivably arising after a variety of exposures to numerous chemical substances. The heart of the problem lies in their reasoning process and the validity of the data they use to support a causal link.

The basic fallacy in their reasoning is that the observed symptoms may be induced by many other causes. An equivalent example of such erroneous reasoning is that if a rooster crows every morning before sunrise, then the sun rises because roosters crow.

Because a case of environmental illness cannot be defined objectively, control individuals (those without both the "disease" and exposure to the "agent") cannot be defined in order to perform traditional scientific studies. This fact is confirmed by the current scant medical literature on the subject, which only emphasizes collections of cases. Such case studies without controls cannot prove the valid existence of environmental illness but can only assert its existence.

Such hypotheses by environmental medicine practitioners are unfocused and scientifically unfounded, and have been rejected by main-stream professional medical organizations.

The data used by the proponents of environ-mental illness is largely invalid. [California Medical Association Scientific Board Task Force on Clinical Ecology. 1986. Clinical Ecology - A Critical

Appraisal. "Western Journal of Medicine", 144:239-245.] Their principle data consists of uncontrolled and unblinded observations of alleged patients improving after therapy. Simply stated, they have not considered classical placebo effect, whereby a small percent of treated individuals will always improve regardless of whether effective therapy was used or not (the good effects of sugar tablets have been known for 2000 years).

Other problems with their information are that appropriate epidemiology cannot be applied, their patient history questionnaires are overly simplistic and biased, and high quality psychological testing of patients is generally avoided.

The scientific dilemma is that well conducted studies (with controls) cannot prove the nonexistence of the "disease" because true science can not prove a negative. Advocates can only assert the existence of a theoretical condition while assailing traditional clinicians and scientists for not having the ability to disprove their theory.

People who have received the label of environmental illness clearly merit the compassion and understanding of the medical and social communities. Emphasis should be placed on proper psychological diagnosis and treatment rather than upon false labels and therapy that can ultimately prolong their impairment.

Because the role of true science is inherently limited, it is the responsibility of reputable scientists and clinicians to emphasize that environmental illness has not been proven to exist.

## Responding to the Media

Because environmental illness is a health issue, its debate is best left primarily to physicians; the chemical industry, for example, should not get overly involved in such debates. Nonetheless, a ready response for media queries is a prudent precaution. Should reporters, editors, news directors or other media question industry about environmental illness, it would be appropriate to respond in a limited way. Steps best taken are:

- Monitor media coverage of the issue.
- Gather relevant background and reference material.
- Identify medical personnel familiar with environmental illness who can speak as experts.
- Informally offer guidance and background materials to reporters, based on their degree of knowledge.

## Workers' Compensation Trends

Legislation already introduced by environmental illness support groups is designed to legitimize environmental illness for disability purposes. Given this thrust, more and more workers' compensation claims are expected. Presently, no state recognizes environmental illness on its list of workers' compensation diagnoses.

Each case would be considered on an individual basis. Since proponents of environmental illness advocate that patients suffering from environmental illness avoid all contact with synthetic chemicals, a diagnosis of active environmental illness could preclude return to work in many jobs.

### Cost Impact

Once workers' compensation claims are settled, the plaintiff often files a toxic tort claim based on product liability theory. At the present time, it is estimated that to defend an average case of this type through a jury trial costs in excess of $200,000 to $300,000. No figures are available on the number of environmental illness cases filed nationwide.

### Expert Testimony

Proof of causation varies greatly from jurisdiction to jurisdiction. For this reason it is impossible to give a short definition that would be accepted by most jurisdictions. However, in each case the plaintiff bears the burden of proof on the issue. Often the plaintiff needs a person accepted by the court as an expert who will testify that there is a cause and effect relationship to a reasonable degree of medical certainty.

The qualifications for being an expert vary from jurisdiction to jurisdiction and even from judge to judge, as does the meaning of "reasonable degree of medical certainty." While there have been a few exceptions, in most cases environmental illness proponents have not been excluded from giving expert testimony.

### State Legislative Summary: History of Legislative Initiatives in Environmental Illness

California: Legislative activity in California began with a bill (AB 3587) introduced in 1981 to primarily set up a "chemical hypersensitivity syndrome advisory committee." It also made provisions for educating those who believed they were environmentally ill about treatment and life-style changes, public education for prevention, and workshops to facilitate exchange between researchers and proponents of environmental illness. The bill passed in both Houses of the California Assembly but was vetoed by Governor Deukmejian.

A second bill (SB 1177) was introduced in 1985. It requested funding for a pilot project to identify those allegedly affected by this syndrome, to develop a clearinghouse for information and advocacy, to provide legal, financial, medical and support services and to conduct and coordinate interdisciplinary conference and research activities on environmental illness. This bill was also defeated.

Connecticut: A public health committee House bill (5191) was defeated in Connecticut in 1987. It would have established a program to study and treat environmental illness at the University of Connecticut Health Center in Farmington.

Maryland: The Maryland Senate drafted and both chambers passed Joint Resolution 32 (1988), which directed the Maryland Department of Environment to conduct a study on the alleged

"chemical hypersensitivity syndrome." [Bascom, R., M.D., M.P.H. 1986. "Chemical Hypersensitivity Syndrome Study." University of Maryland School of Medicine.] While there is no single definition of environmental illness or the problems it is alleged to pose, the study group's mission was to determine if people could be classified as suffering from allergic reactions.

When the study was finished, Maryland's Secretary of the Department of Environment, Martin Walsh, sent an advisory letter to Governor William Donald Schaeffer. In his closing summary of the environmental illness study, Walsh in dictated that "...a great deal more research is needed before there will even be a consensus on a definition of chemical hypersensitivity. It is, in my view, premature to classify environmental illness as a purely environmental problem in the classic sense." (Refer to Appendix E.)

A copy of the Maryland Department of Environment's Report on chemical hypersensitivity syndrome can be ordered from the Maryland Department of the Environment, 2500 Broening Highway, Baltimore, MD 21224 (Fee: $25).

Florida: In 1989, Florida passed a bill creating a registry of people believing they have multiple chemical sensitivities. Creation of such a registry implies that the disease listed is accepted as proven. In this case, this is not true.

Because environmental illness lacks clear definition, the issue could be considered in various state legislative committees. Depending upon the intent of an environmental illness bill, it could be forwarded to Health and Welfare, Labor, Judicial, or Environmental committees. If the proposal focused on alleged allergic reactions, it would be considered by Health related committees; if the purpose of the bill were to review workers' compensation claims rising out of alleged environmental complications, it would be reviewed in Labor or Judicial committees; and, if the proposal asserts environmental concerns then the bill would be sent to Environmental committees.

Legislators and respective staff should be wary of legislation attempting to review and redress the issue of environmental illness or related themes. (The topic is not easily recognizable as it is not consistently addressed by the popular names of environmental illness or chemical hypersensitivity syndrome.) Environmental illness bills should be thoroughly critiqued by members of the medical and legal community prior to legislative action. When considering a bill, legislators should remember that environmental illness is a grey area, one which has not proven its existence in the medical arena and one which has no precedence in state statutes.

## Legislative and Social Goals

Dr. Linda Lee Davidoff, representing the Environmental Illness Support Group, stated in her testimony to the Environmental Affairs Committee of the Maryland Senate, on May 8, 1988, that if Senate Joint Resolution 32, titled "Chemical Hypersensitivity Syndrome" was enacted, "chemically sensitive" people would benefit from:

- access to insurance coverage;

- social services;
- financial assistance;
- vocational rehabilitation; and
- alternate housing.

E.J. Davis, J.D., M.P.H., editor of "Ecological Illness Law Report", Vol. 2(6): p. 3, revealed several specific legal goals of his agenda, several of which follow:

- preventing "improper" employee dismissals and demotions;
- securing and maintaining a "safe" work environment;
- securing financial assistance for the rehabilitation of living space;
- securing coverage under Medicaid or Medicare and various state and federal assistance programs;
- securing workers' compensation payments;
- securing assistance under federal and state protections for disabled;
- securing compensation from companies and individuals responsible for chemical exposures that cause disabling illness;
- securing proper income tax deductions for expenses associated with ecological illness, especially excess costs of remodeling or changing heating systems and organic foods; and
- securing safe environments and food in prisons, mental hospitals, hospitals, and other public and private institutions.

## Overlap With Indoor Air Pollution

Indoor air pollution or "tight building syndrome" is currently a major topic in several regulatory agencies and environmental advocacy groups. Symptoms often resemble those attributed to environmental illness. Among them: headaches, dizziness, drowsiness, nausea, irritations of the skin and upper respiratory tract, anxiety, irritability and other nervous system disorders.

Insufficient provision of fresh air in a building's heating, ventilation and air conditioning system, resulting in a buildup of air contaminants, formaldehyde, pesticides, cleaning materials and others, most often is cited as the cause. However, rarely is a specific agent indicated.

Environmental illness advocates would like society to believe that "sufferers" in indoor air pollution have a form of environmental illness because this would significantly increase the victim population and further legitimize their cause.

## Forming Coalition

Because it has the potential to impact many segments of society, many groups have an interest in placing environmental illness in its proper perspective. Among them:

- medical associations;
- manufacturers and applicators of agricultural and pesticide products;
- personnel, labor relations, etc.;

- food dealers;
- restaurants;
- insurance companies;
- self-insurers;
- soap and detergent manufacturers;
- chambers of commerce;
- lawn care services;
- homebuilders;
- aerospace industry;
- retailers; and
- automobile manufacturers.

Because environmental illness is a health issue, the only people who can legitimize it are physicians, and they have not. Should environmental illness arise as an issue, a coalition with the state medical association is absolutely necessary.

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Appendix A Synonyms for Environmental Illness Allergic Toxemia, Cerebral Allergy, Chemical AIDS, Chemical Hypersensitivity Syndrome, Chemical Induced Immune Dysregulation, Complex Allergy, Ecological Illness, Environmental Hypersensitivity Disorder, Environmentally induced Illness, Immune System Dysregulation, Multiple Chemical Hypersensitivity, Total Allergy Syndrome, Twentieth Century Disease.

Appendix B Environmental Illness Organizations American Academy of Environmental Medicine The American Academy of Environmental Medicine (AAEM) was founded in 1965 as an international association of physicians interested in clinical aspects of environmental medicine. Prior to 1984, they were called the Society for Clinical Ecology (Environmental Medicine). This group changed its name after 1984. The position paper of the Society for Clinical Ecology states that the organization is made up of physicians, who are board certified in a clinical specialty and interested in newer concepts utilizing diagnostic and treatment modalities in treating environmental illness. The 1988 position statement of the AAEM is included in Appendix D of this paper. [AAEM, 10 E. Randolph St., New Hope, PA 18933 (215) 862-4544 or Fax (250) 862-2418]

American Board of Environmental Medicine, Inc. Formal residency training is required for board certification. The board, however, is not recognized by the American Board of Medical Specialties, which is the umbrella organization overseeing specialty board certification of medical doctors in the United States. The American Board of Environmental Medicine, founded in 1988, offers its own examination in the field of environmental medicine. Executive director: Dr. Clifton R. Brooks, M.D., M.P.H., 2114 Martingale Dr., Noran, OK 73072; phone (405) 329-8437

Appendix C Editorial Statement "Clinical Ecology: Environmental Medicine or Unsubstantiated Theory?" Reproduced with permission from the Annals of International Medicine, Kahn, Ephraim; Letz, Gideon, 1989 July; 11 1(2): 104-106).

Appendix D Position Statements: California Medical Association Scientific Task Force on Clinical Ecology, Clinical Ecology -- A Critical Appraisal [Information], reproduced with permission from the "Western Journal of Medicine", 1986 Feb.; 144:239-245)

American Academy of Allergy and Immunology (http://www.aaaai.org/)

American College of Physicians (http://www.acponline.org/)

American Academy of Environmental Medicine (http://www.aaem.com/)

# APPENDIX 4b – MULTIPLE CHEMICAL SENSITIVITIES UNDER SIEGE 2001

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Movies like *Erin Brockovich* and *A Civil Action* depict the true stories of communities whose members became ill after drinking water contaminated with industrial waste. Their struggles clearly show how difficult it is for people to hold corporations responsible for the harm they have caused. Whether individuals are injured by exposures to contaminated air or water, silicone breast implants, cigarettes, or other chemicals, their quest for justice is usually a David versus Goliath battle that pits average citizens against giant corporations.

When confronted with the harm they have caused, corporations typically blame the victims, deny the problem, and try to avoid responsibility for the harm caused. The corporate response to people with multiple chemical sensitivities (MCS) has been no different. People with MCS are made sick from exposures to many common products, such as pesticides, paints, solvents, perfumes, carpets, building materials, and many cleaning and other products. But the manufacturers of these products would rather silence the messenger than acknowledge the message that their products are not safe.

To that end, the chemical manufacturing industry has launched an anti-MCS campaign designed to create the illusion of controversy about MCS and cast doubt on its existence. What has been said about the tobacco industry could easily apply to the chemical industry regarding MCS, that is, "the only diversity of opinion comes from the authors with … industry affiliations (1)."

It is a credit to the chemical industry's public relations efforts that we frequently hear that multiple chemical sensitivities (MCS) is "controversial" or find journalists who feel obligated to report "both sides" of the MCS story, or attempt to give equal weight to those who say MCS exists and those who say it does not. But this is very misleading, since there are not two legitimate views of MCS. Rather, there is a serious, chronic, and often disabling illness that is under attack by the chemical industry.

The manufacturers of pesticides, carpets, perfumes, and other products associated with the cause or exacerbation of chemical sensitivities adamantly want MCS to go away. Even though a significant and growing portion of the population report being chemically sensitive, chemical manufacturers appear to think that if they can just beat on the illness long enough, it will disappear. To that end, they have launched a multipronged attack on MCS that consists of labeling sufferers as "neurotic" and "lazy," doctors who help them as "quacks," scientific studies which support MCS as "flawed," calls for more research as "unnecessary," laboratory tests that document physiologic damage in people with MCS as "unreliable," government assistance

programs helping those with MCS as “abused,” and anyone sympathetic to people with MCS as “cruel” for reinforcing patients’ “beliefs” that they are sick. They also have been influential in blocking the admission of MCS testimony in lawsuits through their apparent influence on judges.

Like the tobacco industry, the chemical industry often uses non-profit front groups with pleasant sounding names, neutral-appearing third party spokespeople, and science-for-hire studies to try to convince others of the safety of their products. This helps promote the appearance of scientific objectivity, hide the biased and bottom-line driven agenda of the chemical industry, and create the illusion of scientific “controversy” regarding MCS. But whether anti-MCS statements are made by doctors, researchers, reporters, pest control operators, private organizations, or government officials, make no mistake about it – the anti-MCS movement is driven by chemical manufacturers. This is the real story of MCS.

## CHEMICAL INDUSTRY

In 1990, the Chemical Manufacturers Association (now the American Chemistry Council) vowed to work to prevent the recognition of MCS out of concern for potential lost profits and increased liability if MCS were to become widely acknowledged (2). It specifically committed to work through physicians and medical associations to accomplish this, stating that it was critical to keep physicians from legitimizing MCS. Unfortunately, this plan has been relatively successful. The industry has enlisted the aid of vocal anti-MCS physicians who promote the myths that people with MCS are “hypochondriacs,” “hysterical,” “neurotic,” suffer from some other psychiatric disorder, belong to a “cult,” or just complain too much. Most of these physicians work for industry as high-paid expert witnesses although their financial ties are usually not disclosed in their journal articles, interviews, or speaking engagements. Therefore, many people, including those in the health care profession, are often led to believe that these physicians’ opinions reflect an honest appraisal of MCS rather than the chemical industry’s agenda. At least one industry expert witness has authored two anti-MCS position papers for prominent medical associations. It is easy to see why these papers are biased against MCS and how by helping to combat MCS in the courts, these position statements are quite lucrative for industry and expert witnesses alike.

## PHARMACEUTICAL INDUSTRY

The pharmaceutical industry is also involved in the effort to suppress MCS. Drug companies, which usually work with the medical profession to try to help patients, are working to deny help for those with MCS. This is extraordinary, but can be explained by the fact that the pharmaceutical industry is intimately linked to the chemical industry. That is, many companies that make medications also manufacture pesticides, the chemicals most implicated in causing MCS and triggering symptoms in people who are chemically sensitive. For example, Novartis (formerly Ciba-Geigy and Sandoz) is a pharmaceutical company that makes and sells the widely used herbicide atrazine (3). This helps explain why a Ciba-Geigy lobbyist submitted material to a New Mexico legislative committee in 1996 opposing all legislation related to MCS and declaring that the symptoms of people with MCS “have no physical origins“ (4). The legislation being

proposed would have, among other things, funded a prevalence study of MCS, an information and assistance program and "800" telephone number, hospital accommodation guidelines, and an investigation of housing needs of people with MCS (5).

Novartis is also a large manufacturer of the organophosphate insecticide diazinon (3), a neurotoxic pesticide currently being reviewed for its safety by the U.S. Environmental Protection Agency (6). The EPA recently banned a related organophosphate pesticide, chlorpyrifos (commonly sold as Dursban), from household uses because of concern about its toxicity, especially to children (7). The pharmaceutical company Eli Lilly used to be a part of DowElanco (now Dow Agroscience), the primary manufacturer of chlorpyrifos (8). Aventis (formerly Hoeschst and Rhone-Poulenc) manufactures the allergy medicine Allegra as well as the carbamate-containing insecticide Sevin (active ingredient carbaryl) (9). Monsanto, known for making Roundup and other herbicides, is a wholly owned subsidiary of a pharmaceutical company called Pharmacia (10, 11). Zeneca manufactures pesticides (12) and pharmaceuticals (AstraZeneca), including drugs to treat breast and prostate cancer, migraine headaches, and epilepsy (13) — illnesses whose cause or exacerbation have been linked to pesticide exposures.

Pfizer and Abbott Laboratories make both pharmaceuticals (14) and pesticides (15), while BASF makes pharmaceutical ingredients and pesticides (16). Even Bayer, famous for making aspirin, manufactures the popular neurotoxic pyrethroid insecticide Tempo (active ingredient cyfluthrin) (17). Novartis, Ciba, Dow, Eli Lilly, BASF, Aventis, Zeneca, and Bayer are all members of the American Chemical Council (formerly the Chemical Manufacturers Association), as are other pharmaceutical manufacturers, such as Dupont, Merck, Procter & Gamble, and Roche (18).

The pharmaceutical industry has been able to spread misinformation about MCS and limit the amount of accurate information received by physicians and other health care providers through its financial influence over medical journals, conferences, and research. It is well known that magazines containing cigarette ads are less likely to publish anti-smoking articles. Similarly, because medical journals rely on pharmaceutical advertisements for funding, they are not likely to publish positive MCS articles. In fact, researchers supportive of MCS have long complained that it is very difficult to get their studies published in the medical literature. Pharmaceutical companies may also influence medical organizations such as the American Medical Association, whose funding relies in large part on the sales of drug advertisements in its journals (19), and the American Academy of Family Physicians, whose major donors are drug companies (20).

Corporate financing of medical conferences has also been shown to bias the information presented (21). Since continuing medical education is becoming increasingly reliant on corporate sponsorship, industry influence over physician education is a growing concern in the medical community (22). Other ways the pharmaceutical industry can influence physicians are also of concern. In a 2000 Journal of the American Medical Association article (23), the author states that "physicians have regular contact with the pharmaceutical industry and its sales representatives, who spend a large sum of money each year promoting to them by way of gifts, free meals, travel subsidies, sponsored teachings, and symposia" (p. 373). The study concludes that "the present extent of physician-industry interactions appears to affect prescribing and

professional behavior and should be further addressed … "(p. 373). This is especially true regarding the effect that the pharmaceutical and chemical industries have had on physicians' professional behavior in response to MCS. Because they do not receive appropriate and accurate information on MCS during their training or from medical journals and continuing education courses, physicians have been largely unprepared to deal with chemically sensitive patients. As a result, their responses to MCS patients have tended to range from dismissive to blatantly hostile. One example of the pharmaceutical industry's direct attempt to present anti-MCS information at a medical conference was at the 1990 meeting of the American College of Allergy and Immunology. Sandoz (now Novartis) was scheduled to sponsor a one day workshop that characterized people with MCS as mentally ill (24). This company was a large manufacturer of pesticides and pharmaceuticals (25), including anti-psychotic, anti-depressant, and sedative medications (14). Therefore, Sandoz stood to benefit both from pesticides being exonerated as the cause of MCS and from people with MCS being treated with psychiatric drugs. As it turned out, people with MCS outraged by the workshop risked their health to protest the event and were able to shut it down (26)…..

The pharmaceutical industry also influences research on MCS. First and foremost, it is not pursuing research on MCS (other than to perhaps fund a few studies to try to discount it), despite being a major source of funding for medical research to help those with other diseases. Secondly, as was evident when the Ciba-Geigy lobbyist opposing funding for MCS research in New Mexico, the industry is not only refraining from doing research on MCS itself but is attempting to block research by others as well. A recent editorial in the New England Journal of Medicine outlined a myriad of ways that financial ties with the pharmaceutical industry may influence physicians (27). "The ties between clinical researchers and industry include not only grant support, but also a host of other financial arrangements. Researchers serve as consultants to companies whose products they are studying, join advisory boards and speakers' bureaus, enter into patent and royalty arrangements, agree to be the listed authors of articles ghost written by interested companies, promote drugs and devices at company-sponsored symposiums, and allow themselves to be plied with expensive gifts and trips to luxurious settings" (p. 1516). In fact, some industries, including the tobacco industry, have paid authors up to $10,000 to publish letters in high-profile scientific journals (28, 29). The author of another New England Journal of Medicine article wrote, "The practice of buying editorials reflects the growing influence of the pharmaceutical industry on medical care" (30). Since these conflicts of interest are increasingly encroaching on the medical profession in general, it is highly likely that some of them apply to physicians opposed to MCS as well.

## ENVIRONMENTAL SENSITIVITIES RESEARCH INSTITUTE

Several nonprofit organizations and trade associations sponsored by the chemical industry are particularly active in opposing MCS. For example, lobbyists for RISE (Responsible Industry for a Sound Environment), a pesticide trade association, and the Cosmetic, Toiletry, and Fragrance Association testify against MCS each year in the New Mexico legislature. The Chemical Specialties Manufacturing Association, which represents companies who manufacture and distribute home, lawn and garden pesticides, antimicrobial and disinfectant products,

automotive specialty products, waxes, floor finish products, and many types of cleaners and detergents, has also submitted anti-MCS comments to the NM legislature (31). And individuals from a lesser-known organization calling itself the Advancement of Sound Science Coalition published an opinion-editorial in two New Mexico newspapers several years ago that was critical of the positive steps being taken by the New Mexico legislature on MCS (32, 33).

The leading opponent of MCS, however, is unquestionably the Environmental Sensitivities Research Institute (ESRI). This corporate-financed nonprofit organization was founded in 1995 specifically to combat MCS. According to MCS Referral and Resources, ESRI was founded to "serve the needs of industries affected by MCS litigation" (34). But since ESRI tends to be secretive about its membership, board members, and activities, it is hard to know exactly who is involved with ESRI and what the organization does. However, it is known that ESRI is primarily supported by its member companies and trade associations, who pay $5000 or $10,000 a year in annual dues (35, 36). It is also known that the past board of directors have included representatives or employees of DowElanco, Monsanto, Procter and Gamble, RISE, the Cosmetic, Toiletry and Fragrance Association, and other chemical companies and trade associations (36).

Although ESRI has in the past claimed to be a scientific and educational organization dedicated to the open exchange of scientific information (37), this is belied by its decidedly anti-MCS views. ESRI's bias against MCS is evident in its fact sheet that claims that MCS is a "phenomenon" that "defies classification as a disease" (38). It appears that this organization's main work consists of disseminating anti-MCS literature, holding anti-MCS conferences, intervening in legal and government affairs, and otherwise trying to impede progress on MCS. And despite its name as a research institute, ESRI has only recently begun to award small MCS research grants. It will be a great surprise, however, if the majority of these studies do not support a psychological basis for MCS.

Besides lacking objectivity, some of ESRI's activities demonstrate questionable ethics. For example, ESRI published an "advertorial," advertisements made to look like legitimate news stories, in newspapers around the country that stated that MCS "exists only because a patient believes it does and because a doctor validates that belief." Then, according to Albert Donnay of MCS Referral in Resources, ESRI anonymously tried to get the American Academy of Family Physicians Foundation (AAFPF) to endorse its anti-MCS brochure (36). Fortunately, the AAFPF withdrew its support for the brochure when ESRI would not put its name on it.

One of the more flagrant misrepresentations in the brochure (39) was the answer "No" to the question, "Is MCS listed as a disability under the Americans with Disabilities Act?" One might consider this an honest mistake if it were not for the fact that an article published at almost the same time by ESRI's then executive director clearly demonstrated he knew better. In the article, he states that "although not categorically noted to be a disability in the body of the law, the ADA [Americans with Disabilities Act] does allow for the consideration of MCS as a disability on a case-by-case analysis that is applied to all other physical and mental impairments" (40). And he also writes that "in 1991, the Department of Housing and Urban Development stated that people suffering from MCS can seek protection under federal housing discrimination laws." It appears

that ESRI was attempting to mislead physicians and the public into believing that MCS is not a covered disability, while its executive director was warning an industry-oriented audience that MCS was a covered disability and offering suggestions for how to defend themselves against a claim.

New Mexico has had direct experience with ESRI representatives and tactics. In 1996, ESRI mailed anti-MCS literature to a state disability agency that was developing a report to the legislature on MCS. Among other things, this material included advice on how to avoid accommodating chemically sensitive employees (41). Then, ESRI staff visited New Mexico in person. The ESRI manager attended a Town Hall Meeting on MCS at which she offered to help the state epidemiologists develop a prevalence study protocol. Shortly thereafter, however, she reportedly told another member of the prevalence study working group that MCS can't be studied because it doesn't exist. This circular reasoning, that you can't prove MCS exists without more study and you can't study it because it doesn't exist, is commonly used by industry lobbyists. A corollary to this is the lobbying strategy of calling for more research on MCS while attempting to block it at the same time.

ESRI's then executive director also visited Santa Fe in 1996. Among other things, he went to a Medicaid Advisory Committee meeting and urged that Medicaid benefits be denied for the diagnosis and treatment of chemical sensitivities, spoke against MCS at a continuing medical education (CME) conference for physicians where he failed to disclose his industry affiliations as required by CME guidelines, and berated the staff at an independent living center for providing a support group for people with MCS. Another ESRI project involved paying a medical journal to publish the proceedings of an anti-MCS conference in its supplement (42). This conference was organized, in part, by a consulting firm that was owned by ESRI's then executive director and supplied expert witnesses to testify against MCS. Later these papers were cited as references to support anti-MCS statements in material ESRI gave to the Ciba-Geigy lobbyist, which she submitted to the legislature. In keeping with its attempts to keep a low profile, however, ESRI did not put its name on the documents that were submitted.

## A ROSE BY ANY OTHER NAME

Even though MCS has gone by that name for over a decade, industry associates would have you believe that it goes by a myriad of other names, so many that it must not be describing anything legitimate. In fact, if an article starts out with a long list of possible names for MCS, you can be almost positive it is going to be critical of MCS. Referring to MCS as a "phenomenon" rather than an illness and using the term "multiple chemical sensitivity syndrome" also tend to be code for "it doesn't really exist" or if it does, "it's all in people's heads." Articles using these names are usually accompanied by other myths and put-downs, such as MCS has no definition, no objective findings, and no known prevalence, and is "only symptom-based," a "belief system," or "chemophobia." People with MCS are also frequently dismissed as having an "unexplained illness," as if they, rather than their physicians, were to blame for not adequately "explaining" it.

Since 1996, however, the chemical industry has taken a bold new approach to the name for MCS. It has made a concerted effort to rename MCS "idiopathic environmental intolerances (IEI)." It is quite clear that its motivation is to get the word "chemical" out of the name. This would be analogous to the tobacco industry trying to change the name of "smokers cough" to "idiopathic respiratory paroxysms." Anything to try to distance the disease from its products.

But despite frequent claims to the contrary by its users, the term IEI has not replaced the name for MCS. Its use, however, has slowly increased over the years in anti-MCS journal articles, industry propaganda, and medical association position papers. Fortunately, the use of the term IEI is like a tracer dye that immediately alerts the reader, patient, or constituent that the person or organization using the term is biased against MCS. The most frequent users of the name IEI are doctors who work for industry as expert witnesses or allegedly "independent" medical examiners, industry-sponsored organizations, and allergy or occupational medicine organizations that have long been critical of environmental doctors who treat people with MCS. While there may be some individuals who innocently use the term IEI, the overwhelming majority who use it appear to be connected to industry in some way.

One of the more outrageous claims that the chemical industry and its associates make is that the World Health Organization (WHO) supports the name change from MCS to IEI. The WHO was one of the sponsors of an International Programme on Chemical Safety (IPSC) workshop on MCS held in Germany in February 1996. This workshop was dominated by industry-associated participants and had no representatives from environmental, labor, or consumer groups. Instead, the non-governmental participants were individuals employed by BASF, Bayer, Monsanto, and Coca Cola (43). It was at this meeting that the decision was made to try to change the name of MCS to IEI.

Besides getting the word "chemical" out of the name, the workshop participants chose to add the term "idiopathic," apparently because they thought it meant the illness was "all in someone's head" rather than of unknown etiology (cause) (44). But lots of "real" illnesses are considered idiopathic, such as idiopathic epilepsy (i.e., epilepsy not resulting from trauma, surgery, infection, or other obvious cause). Still, implying that MCS has no known cause helps the industry. They do not want to be held responsible for their products causing MCS, or for that matter, triggering symptoms in people sensitized to them. It's hard to understand, however, how IEI is much of an improvement over MCS, since the term MCS does not address the cause of the illness either. It is just a good description of the condition, that sufferers are sensitive to multiple chemicals, which is not that different from having multiple "environmental intolerances."

In any case, the WHO issued a statement to the workshop participants after the meeting to try to put a stop to claims that WHO supported the name change from MCS to IEI. It stated that "A workshop report to WHO, with conclusions and recommendations, presents the opinions of the invited experts and does not necessarily represent the decision or the stated policy of WHO." It goes on to say that "with respect to 'MCS,' WHO has neither adopted nor endorsed a policy or scientific opinion" (45). Despite this explicit disclaimer, claims that the World Health Organization supports IEI continue to be made by MCS opponents.

## MCS IN COURT

Perhaps the area where the chemical industry is most aggressively fighting MCS is in the courts. This is not surprising considering the fact that ESRI was founded to assist industries involved in MCS litigation. MCS cases commonly involve workers compensation, social security, toxic tort, disability or health insurance, and disability accommodations. MCS can also arise in divorce proceedings, child custody battles, and landlord-tenant and other disputes. In lawsuits where chemical manufacturers are directly involved, for example, when they are being sued for harm caused by their products, it is clear that attacks on the plaintiff's credibility and medical condition, including MCS, come from the manufacturers. It is often unrecognized, however, how much the chemical industry is also involved in suppressing MCS in other lawsuits, through filing of briefs, supplying "expert" witnesses, and distributing anti-MCS literature to attorneys and witnesses.

The chemical industry also seems to have been influential in convincing many judges that MCS testimony should not be allowed in court. They argue that MCS does not satisfy the Daubert criteria for the admission of scientific testimony established by the U.S. Supreme Court in 1993. This ruling eliminated the requirement that expert testimony be "generally accepted" in the scientific community to be admissible and replaced it with the requirement that the reasoning or methodology underlying any proposed testimony merely be scientifically reliable and relevant (46). Thus, the intent of the ruling was to allow testimony on emergent theories of disease even if they had not yet been generally accepted by the medical community. But in the case of MCS, this has backfired. The Daubert ruling, which was intended to make it easier to admit scientific testimony in court, has increasingly been used to block testimony on MCS.

Some judges have ruled that MCS does not satisfy the Daubert criteria, despite the fact that it clearly satisfies at least three of the four factors specified in the Daubert ruling to assess proposed testimony. The Daubert ruling states that the following considerations will bear on admissibility of expert testimony: 1) whether the theory or technique in question can be (and has been) tested, 2) whether it has been subjected to peer review and publication, 3) whether the reasoning or methodology has a known or potential error rate, and 4) whether it has widespread acceptance within a relevant scientific community (46). According to these criteria, testimony on MCS should be admitted because, it "can" and "has" been tested (47), has been subjected to extensive peer review and publication (48), and is widely accepted in the environmental medicine community. The factor regarding potential error rates is largely irrelevant because MCS is a clinical diagnosis that does not rely on tests.

But whether an illness or theory satisfies the Daubert criteria is obviously in the eye of the beholder. A judge in New Mexico, for example, ruled there was not enough published literature on MCS to fulfill the Daubert criteria (49). Yet there are over 600 articles on MCS and related conditions in the published literature, the majority of which support a physiological rather than psychological basis for MCS in a ratio of two to one (48). The judge rejected testimony on MCS even though he thought there would be enough literature in 5 to 10 years for it to satisfy the

Daubert requirements. But if a judge is convinced MCS will be well established in the future, then testimony on MCS is credible and ought to be admitted now. After all, the intent of the Daubert rule is to admit testimony on just such valid emerging theories of disease as this one. In addition, it is unclear how much this judge was swayed by the anti-MCS opinions of the defendant's expert witness, who admitted she relied on material sent by ESRI for her testimony and did not know who funded the organization (50). It is, indeed, unfortunate that the subjective nature of the Daubert criteria has allowed judges to misinterpret them in favor of the chemical industry. This has resulted in many people with MCS being denied disability benefits, compensation for toxic injuries, and reasonable accommodations under the ADA, among other things.

A case in point is a recent ruling by the Massachusetts Supreme Court that rejected MCS testimony in a work-related injury case because the physician's testimony was not based on "reliable methodology," that is, because he did not use a test to diagnose MCS (51). This conclusion was reached even after stating that "a new theory or process might be so 'logically reliable' that it should be admissible, even though its novelty prevents it from having attained general acceptance in the relevant scientific community" and that "in many cases personal observation will be a reliable methodology to justify an expert's conclusion." This is another example of a biased interpretation of the law against MCS. And again we find the chemical industry involved. Though not a defendant in the case, the American Chemical Council (formerly the Chemical Manufacturers Association) filed a "friend of the court" brief against the worker and expressed delight with the court's anti-MCS decision (52).

Finally, there are growing attempts to get medical licensing boards to revoke the licenses of physicians who diagnose and treat chemically sensitive patients. One physician is in a legal battle with the California Medical Board to keep his license, in part, for this reason (53). In an anti-MCS booklet, an author who is known as an industry sympathist, has called for state licensing boards to "scrutinize" the activities of doctors who treat MCS patients. He also stated that he thought "most of them should be delicensed" (54). Trying to put physicians who treat MCS out of practice or harassing them until they quit on their own is an extremely insidious way of trying to get rid of MCS. It is also a threat to the independent practice of medicine by everyone.

## IMPACTS OF MCS

The impact of MCS on individuals and society is huge, both in terms of its potential severity and the number of people affected. Many people with MCS have lost everything – including their health, homes, careers, savings, and families. They are chronically ill and struggle to obtain the basic necessities of life, such as food, water, clothing, housing, and automobiles that they can tolerate. Finding housing that does not make them sicker, that is, housing that is not contaminated with pesticides, perfume, cleaning products, cigarette smoke residues, new carpets or paint, and formaldehyde-containing building products, is especially difficult. Many people with MCS live in cars, tents, and porches at some time during the course of their illness. In addition, people with MCS usually have financial difficulties. One of the most unjust aspects of the anti-MCS movement is that many expert witnesses are paid $500 per hour to testify against people disabled with MCS who are seeking that much money to live on per month.

The impact on society is no less severe. An increasing number of physicians, lawyers, teachers, computer consultants, nurses and other skilled workers who were once productive members of society can no longer support themselves or contribute their skills to society. Their loss of earning power also translates into less money spent in the marketplace and less tax revenues. Deputy state epidemiologist Ron Voorhees of New Mexico estimated in a letter to the governor that the state may be losing 15 million dollars a year in tax revenues due to the decreased earning capacity of those with MCS (55).

And this medical condition is not rare. Prevalence studies in California (56) and New Mexico (57) found that 16% of the respondents reported being chemically sensitive. Additionally, in New Mexico 2% of the respondents reported having been diagnosed with MCS — the more severe form of chemical sensitivities — and in California, 3.5% reported having been diagnosed with MCS and being chemically sensitive. Although women report being chemically sensitive twice as often as men, which contributes to its "hysteria" label, those reporting chemical sensitivities are otherwise evenly distributed with respect to age, education, income, and geographic areas. Chemical sensitivities are also evenly reported among ethnic and racial groups, except for Native Americans, who reported a higher prevalence in both studies.

It should be of great concern to everyone that this devastating and potentially preventable illness is affecting an increasing percentage of the population and disabling a significant portion of the work force. It is affecting people in all walks of life throughout the country and around the world. It is vitally important, therefore, that MCS be squarely addressed and not swept under the rug as the chemical and pharmaceutical industries are trying to get the medical profession and government to do. But ignoring MCS is not only ill-advised, it is inhumane.

## CONCLUSION

MCS is under siege by a well-funded and widespread disinformation campaign being waged by the chemical and pharmaceutical industries. Their goal is to create the illusion of controversy about MCS and cast doubt on its existence. These industries feel threatened by this illness, but rather than heed the message that their products may be harmful, they have chosen to go after the messenger instead. While corporations are only beholden to their stockholders, medicine and government need to be responsive to the needs of their patients and citizens. Unfortunately, industry has convinced many in the medical and legal professions, the government, the general public, and even loved ones of people with MCS, that this illness doesn't exist or is only a psychological problem. As a result, people whose lives have already been devastated by the illness itself frequently are denied appropriate health care, housing, employment opportunities, and disability benefits. On top of this, people with MCS often have to endure hostility and disrespect from the very agencies, professionals, and people who are supposed to help them.

For example, an elderly woman with MCS was forced out of public housing and became homeless when staff insisted on remodeling her apartment, even though she warned them

ahead of time that the new carpet and cabinets would make her too sick to continue living there. The physician of a woman, hospitalized because she was having anaphylactic reactions to all foods, tried to transfer her to the psychiatric ward for "force feeding." A school district fired a chemically sensitive teacher for excessive absenteeism after it failed to provide her with the accommodations she had requested and needed in order to work. A former airline attendant had to camp in the desert and a mother and her small child had to live in their car because they could not find housing that did not make them severely ill. And a man disabled with MCS is unable to obtain vocational rehabilitation services even though he wants to work.

Countless others have failed to find tolerable housing, including a former marathon runner who has lived in her car for 7 years and struggles to fight off frostbite every winter. In another case, a chemically sensitive woman living in her trailer was forced to leave a state park when hostile staff insisted on spraying pesticides while she was there. The park supervisor said that he had seen a television show on MCS which convinced him that he did not have to make accommodations for people claiming to have MCS because it did not exist. The show had featured ESRI's then executive director and portrayed people with MCS as freeloaders and misfits.

Despite the chemical industry's disinformation campaign, however, and its influence over doctors, lawyers, judges, and government, incremental progress is being made with respect to MCS. This is a testament to the strength, courage, dedication, and sheer numbers of people with MCS. In fact, there are so many people becoming chemically sensitive that attempts to ignore or silence them are ultimately doomed to fail. But even though it is just a matter of time before MCS gets the recognition it deserves, each day it is delayed prolongs the suffering of millions of people with MCS and puts millions more at risk of developing it. Therefore, it is essential that those in medicine, government, and society begin to see past the industry disinformation campaign in order to recognize the true nature of MCS and the urgent need to address this growing epidemic.

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## APPENDIX 5 – LETTER OF APPEAL TO HON. CHRISTIAN DUBÉ, MINISTER OF HEALTH AND SOCIAL SERVICES, QUÉBEC

TO THE MINISTER OF HEALTH AND SOCIAL SERVICES QUÉBEC

We support the critical work being done by the Environmental Health Association of Québec. We support their request to remove the INSPQ report on MCS from the INSPQ website and update it.

We must listen to the voices of those experiencing MCS and remove barriers for this disability by implementing fragrance-free and least-toxic solutions immediately. The implementation of these recommendations would benefit not only people with MCS but the health and wellbeing of everyone.

The INSPQ report places even more barriers for these struggling individuals experiencing MCS. Québec must support the protection of human rights and ensure accessibility and protection of individuals with disabilities.

We are extremely concerned about this report and want to know how you will support this community moving forward. We support ASEQ-EHAQ's request to take into account the scientific leadership of experts in the field and:

> recognize MCS as a health condition, and mandate least-toxic solutions and fragrance-free spaces for essential services, especially health care;
>
> withdraw the INSPQ report on MCS from the INSPQ website, and revise and update it in a timely manner, consulting MCS experts, researchers, doctors, groups and people with lived experience of this health condition;
>
> create proper legal, social, and medical support for this population to address stigma and ensure their health and accessibility to broader society;
>
> consult relevant groups and individuals experiencing MCS in order to ensure proper accessibility and social support for this population;
>
> ensure access to appropriate housing and healthcare for all people experiencing MCS;
>
> and support the ASEQ-EHAQ housing project without delay and provide appropriate backing in order to ensure its swift completion to provide housing, health and wellbeing for this disabled population.

We, Ontario advocates, support this appeal and look forward to hearing back from you about your plan to achieve the above within the shortest period of time.

# APPENDIX 6 – SAFE HOUSING, HEALTH FACILITIES AND SCHOOLS

## A.5.1. Safe Housing, a precondition to stabilization and improvement

For those with MCS living in a safe dwelling is a first-line health requirement. Since good indoor air quality is a medical necessity for the chemically sensitive, safe housing is the precondition to stabilization and improvement. There is no more important medical requirement, and no more important disability need.

The Centre for Equality Rights in Accommodation (CERA) joined with the National Right to Housing Network to produce a brochure on implementing the right to housing in Canada. As they note:

> "All levels of government in Canada are bound by Canada's international human rights commitments. The International Covenant on Economic, Social and Cultural Rights (ICESCR) states explicitly that its provisions "extend to all parts of federal states without any limitations or exceptions."
>
> The obligation to ensure the right to housing under international law applies not only to the federal government but also to provincial, territorial and municipal governments, and to all public administrators, tribunals and inter-governmental bodies in Canada. The federal government's legislative commitment to the right to housing in the NHSA [National Housing Strategy Act, 2019] is linked to an existing commitment of all governments in Canada to ensure that their laws, policies, programs and decisions are consistent with the right to housing under international law " p. 6

A Primer on Housing Rights in Canada prepared in 2019 by Ryan van den Berg (and contained in our document's references) also contains a lot of very pertinent information.

Unfortunately, need, right to housing, and right to disability accommodation do not translate to adequate or safe housing.

Blogger and advocate Linda Sepp gives us a first hand look at the need, the difficulties she encountered as well as explaining the difference safe housing has made in her life:

> I was a creative Canadian, and mother of two now adult children, who became disabled and housebound from exposures to toxic chemicals allowed in everyday products and materials. In my case, the "straw that broke" my back was cheap carpeting installed on the floor below me in 1994, years after the hazards of toxic carpets had been known.
>
> After many years of increasing disability and almost losing my life (related to my housing situation in Toronto and what followed), I am now slowly regaining some abilities as a result of finally having safer and affordable housing, housing which was built and maintained as non-toxic as possible specifically for people with MCS/ES. I am not

> subjected to constant indoor exposures from other people's product use here, although what gets used in the neighborhood (laundry products, wood smoke, pesticides, etc) can still have profoundly disabling effects (cognitive and physical) at times, because the air purification devices I have available are not sufficient to replace a human being's need for fresh, clean, unpolluted air.

Her blog post on healing contains more,
https://seriouslysensitivetopollution.org/2012/02/21/healing/

Linda begins her blog post on MCS and Housing, which assembles a lot of useful information in this area, with the following, and it will be very familiar, as we have stated this on a number of occasions:

> "Safe, healthy housing is the number one health-care need of people with Multiple Chemical Sensitivities (MCS), Environmental Sensitivities (ES), and Electrical Hyper-Sensitivities (EHS)."

https://seriouslysensitivetopollution.org/mcs-and-housing/

Another very useful source of information, as well as explanation of the issue comes from Pamela Reed Gibson PhD of James Madison University. Her original monograph is entitled, 'Understanding and Accommodating People with Multiple Chemical Sensitivity in Independent Living.' Chapter 4 of this monograph has been extracted and can be found at the following web address as 'The Housing Challenge in Multiple Chemical Sensitivity." https://www.ei-resource.org/articles/multiple-chemical-sensitivity-articles/the-housing-challenge-in-multiple-chemical-sensitivity/ (accessed May 25, 2022). It too starts out in what will be a familiar way,

> Housing may be the single most crucial element in survival and possible improvement for someone with MCS. Yet it is almost impossible for people with MCS to find places to live that are truly safe for them. Housing may be their most difficult challenge, a challenge greater even than for people with other disabilities. Toxic chemicals such as formaldehyde, and those found in glues, paints, new carpet, and pesticides are commonplace in construction of all types. In addition, it is impossible to control what occurs beyond one's property lines. City dwellers are subject to industrial emissions, vehicle exhausts, toxics used by neighbors such as lawn chemicals, and a myriad of other poisons. Rural dwellers are exposed to farm chemicals that include pesticides, herbicides and chemical fertilizers. (Current housing conditions for those with MCS, paragraph 1)

Assisting ES/MCS sufferers to achieve healthy housing is the most health-effective and, eventually, cost-effective preventive or supportive measure that can be taken.

[At the time of writing in 2013 and currently], however, only seven units of safe social housing (in Barrhaven, Ottawa) have ever been constructed in Ontario (or Canada, for that matter). Turnover is very slow and the waiting list very long, indicating a great need for such housing. Such housing should be understood within the same frameworks as both supportive housing

(mental illness, physical disabilities) and as medical housing (safe breathing envelope.) (Burstyn & MEAO, p. 167)

Aside from seven units in Barrhaven, Ontario, there are no other such developments in any other Canadian jurisdiction. *Highly developed plans for a proposed community with mixed-use housing now exist to be located in the Laurentians outside Montreal (with the Environmental Health Association of Québec http://ecoasisquebec.ca). All that is needed is government support. See the appeal attached here at A.5.5.*

It's time to get started.

### A.5.2 When safe oases can be achieved and other exposure managed, wonderful things happen

- People at mild levels of chemical sensitivity need never 'crash' into more severe stages, or can recover quickly from early 'crashes' when safe shelters exist to allow for safe short-term and emergency housing.

- With permanent housing, those who are already more seriously affected may recover to more mild levels and return to full productivity; or may be able to feel well enough that they can earn a living working from home; and certainly will have a quality of life that is bearable, even with severe ES/MCS when their dwellings support, not harm, them.

- Those who experience symptoms in more toxic environments beyond the home can still be functional parents and spouses at home, minimizing the cascade of negative consequences to families such a disability would otherwise bring.

- Children can recover from exposures in other contexts, or, if needed, have a place where schooling can proceed and a life built despite the condition.

- For elderly or more seriously disabled people, safe supportive/assisted living, long-term care and palliative care facilities – of which there is not one unit or bed at present – mean that daily life can be made bearable, possibly even enjoyable. Those with ES/MCS who live in facilities not adapted to their condition now suffer immensely. Life is shortened either through health stresses or suicide.

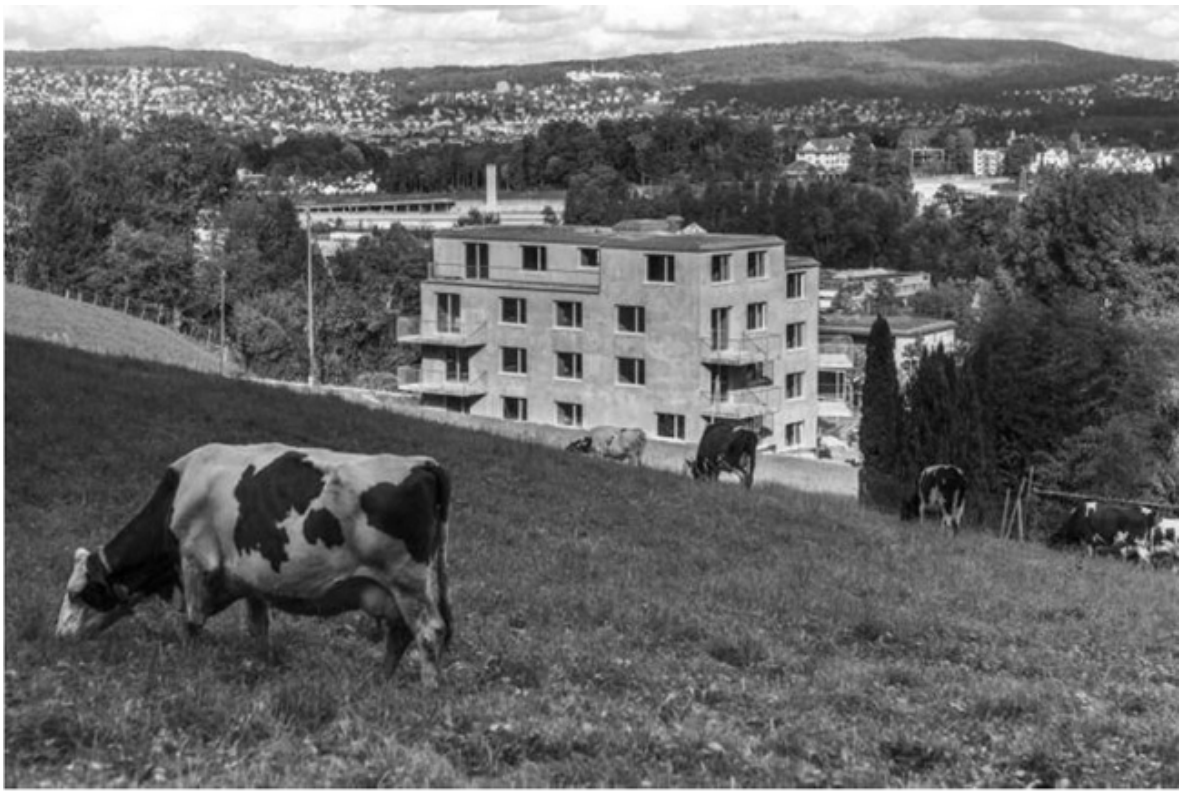
Note: Material above extracted from Burstyn & MEAO, 2013, pp. 166, 167

### A.5.3 Some housing examples

A Swiss multi-story apartment building

In a suburb of Zurich, Switzerland in 2013 a pioneering project was completed. “No smoking, no perfume, no mobile phones: Swiss apartment building provides refuge for the hypersensitive,” read the headline of an article in the Daily Mail, 7 April 2014, in which reporter Sam Webb chronicled the social, financial, design and materials journey undertaken by Zurich city officials in partnership with MCS patients, to help those living with severe chemical sensitivity by providing that most important thing: a safe home.

In an enlightened move, the city of Zurich “made available the land and provided interest-free loans to help finance the £4.1m project,” Web wrote. He quoted Lydia Trueb, a Zurich housing office spokeswoman: “‘We wanted to help these people to have a calm home where they hopefully will be less sick.’” [ http://www.dailymail.co.uk/news/article-2598460/No-smoking-no-perfume-no-mobile-phones-Swiss-apartment-building-provides-refuge-hypersensitive.html The Daily Mail, April 6, 2014, updated April 7, 2014, Sam Webb]



Government assisted multiple-family building for chemically and electromagnetically sensitive people and their families -- Photo credit: Simon Zangger, as found at https://www.eiwellspring.org/multiunit/ZurichHouse.htm

Construction started in March 2012 and ended October 2013. The project has received a lot of attention in German-language media: both radio and television, architectural magazines and even the journal for Swiss physicians. Learn more about all aspects of the project at

https://medicalxpress.com/news/2014-04-swiss-refuge-hypersensitive.html and https://www.eiwellspring.org/multiunit/ZurichHouse.htm

Many more details about the building process can be found at EI Wellspring.

Multi-unit developments, most private, one public, in the United States, visit EI Wellspring at their webpage dealing with multi-unit builds: https://www.eiwellspring.org/multiunit.html

An Arizona public initiative can also be found at the same site: https://www.eiwellspring.org/multiunit/AZPublicHousingProject.htm . To view one of several private developments – out of reach for most with MCS, but modest, simple and a good template – see the Inn of Regina Caeli at *Regina Caeli: a private development of* safe housing near Dallas.

Van living – a last alternative, not recommended and certainly not as a permanent solution, and extremely difficult in Canadian winters, EI Wellspring contains advice for living in a van https://www.eiwellspring.org/saferh/LivingInVan.htm

Unfortunately we know of at least one Canadian, artist Marie LeBlanc who is currently doing that. The link below will take you to an online exhibit that Marie is doing to raise awareness about MCS. As the 'about the artist" description notes, Marie relocates to the southern US desert during the winter months. https://aanm.ca/the-end-of-the-end-of-time/ [accessed May 25, 2022]

### A.5.4 Safe health facilities and schools are critically important

The material below is taken from the 2013 Qualitative study (Burstyn & MEAO, p 177)

By the same token, health facilities, in order to help and not harm must also be places where air quality is safe. Many people with ES/MCS do not seek primary care when they should because they must risk feeling very sick simply to consult their doctor. It is a cruel irony of modern life that hospitals are very dangerous sites for those with ES/MCS. A combination of poor air quality and poor-to-no understanding of the need for safe reception protocols can create a minefield of terrifying proportions. Many people with ES/MCS do not even seek specialist and hospital care when they need these because they are not prepared to risk their health in hospital environments.

For children and youth schools must be places where they are safe enough to learn and develop and come home healthy every night. This is not the case at this time. Above all, the use of no-toxic cleaning products, the banning of pesticides and the vetting of new equipment and furnishings for off-gassing of chemicals in schools would create an 'equal opportunity breathing environment'. Such measures would benefit all children too, for children are much more vulnerable than adults to chemical hazards and deserve to study in a safe place. For chemically

sensitive children, if the school is not safe, then a safe home becomes overwhelmingly important.

### A.5.5 Environmental Health Association of Quebec's demand for housing for the disability of MCS

We (the Advocates) support the **Association pour la santé environnementale du Québec / Environmental Health Association of Québec (ASEQ-EHAQ)** in their 'Demand for housing for people with the Disability of MCS Now' https://aseq-ehaq.ca/en/housing-for-mcs/

Below is a copy of the letter/email being sent to many policy makers and politicians across Canada.

[The incident involving "Sophia," who was granted and availed herself of MAiD, which we have discussed earlier] is not the only incident; several other instances of MAiD have been brought to our attention for the same reason: **Lack of Housing**. The solution to a housing crisis for people experiencing MCS cannot and should not be state-sanctioned death. Safe affordable housing would have prevented these lives from being lost, and must be created to stop additional deaths. MAiD cannot be used as the elimination of disabled people instead of providing for a social need.

This situation should NEVER have happened and should NEVER happen again. Disabled people across Canada deserve to have their needs met and to thrive, so they can help Canada become a vibrant and inclusive country which will benefit everyone. No one should experience unsafe living conditions or homelessness especially due to unsuitable chemical-laden environments. This email will be sent to the following officials:

Location based– premier
Location based housing minister
Location based disability rights ministers
Prime Minister Justin Trudeau
Carla Qualtrough, Federal Minister of Employment, Workforce Development and Disability Inclusion
Ahmed Hussen, Federal Minister of Housing and Diversity and Inclusion
David Lametti, Federal Minister of Justice

This is the text of the letter/email:

A woman with Multiple Chemical Sensitivities (MCS) who lived in unsuitable housing, which made it inaccessible for her disability, recently lost her life through medical assistance in dying (MAiD), because accessible healthy housing could not be found for her in time. (Accessible, healthy housing for the disability of MCS is free of smoke, fragrances and volatile organic compounds (VOCs) released from many commonly used products. Exposure to these substances

can cause multiple symptoms in multiple body systems. Continuous exposures cause increased disability).

Unremitting exposures to chemicals, fragranced products and smoke from neighbours, caused continuous symptoms of MCS and led to a deterioration of her health. In order to improve her health, and stop these continuous symptoms all she needed was accessible healthy housing. Despite attempts to gain accommodation from her landlord and neighbours, they rejected or inadequately accommodated these requests, sometimes verbally abusing her and blaming her for her disability. She spent years contacting governments for help, looking for safe housing, and pursuing accommodations, but could not find accessible AND affordable housing. Rather than being provided with safe shelter, a basic human need, she was instead cleared for death through MAiD. This sounds like an execution. [I, the letter writer] am calling on you to act immediately to stop this from ever happening again by taking immediate action to find and create accessible and affordable housing for this disabled population so that more people with this condition will not continue to lose their lives.

MCS is a recognized disability by the Canadian Human Rights Commission, protected under the Canadian Human Rights Act, with 1,130,800 people in Canada diagnosed with MCS (Statistics Canada, 2020). The prevalence of this disability is increasing (Statistics Canada 2000 – 2020). Sensitization to chemicals in commonly used products subsequently provoke symptoms in multiple body systems. This is debilitating and often leads to unemployment and severe loss of quality of life. To remain symptom-free and improve their health, people with MCS need least toxic solutions for all aspects of everyday living.

[I, the letter writer] am asking you to act immediately to create accessible and affordable housing for people experiencing MCS. The Accessibility Act promises barrier-free access to full and equal participation in society, yet people with MCS are denied accommodation to remove barriers or to support them from being safe in their own homes. Without action being taken, more people will continue to suffer, as a direct result of the government's failure to act on this crisis. Healthy housing is a medical necessity for people experiencing MCS. The lack of healthy housing for this community was identified as a need in the Ontario Task Force Report on Environmental Health (2018). Yet, to date, no one is listening.

Let this not be passed up as a jurisdictional issue with everyone washing their hands of this urgent problem and passing the buck. We pay our taxes both provincially and federally. It is time you all got together and had a conversation in order to come up with an acceptable solution to a growing and desperate need, while the prevalence of this disability continues to increase (Statistics Canada 2000 – 2020). In the spirit of 'Nothing About Us Without Us', involve the MCS groups and people with lived experience in this process.

This woman is not the only person who faces this housing crisis for people with MCS, and she will not be the last. This crisis should never have happened and should never happen again. People with all disabilities and people with MCS are important and valuable members of our communities and this situation is a disgrace that everyone across Canada should be ashamed of.

Every person deserves appropriate accommodations, and accessible housing. The solution for this housing crisis for MCS, IS NOT Medical Assistance in Dying (MAiD).

[I, the letter writer] am calling for:

1. The government to find and build immediate accessible, affordable housing for people with MCS;
2. Immediate implementation of accessible healthcare policies including fragrance free, no idling, least toxic product use in all healthcare facilities;
3. Immediate action for education on MCS in all learning institutions and especially medical schools;
4. Immediate awareness and education to all support systems including law enforcement, social workers, medical personnel;
5. Fund research on MCS.

The housing that will address this crisis must:

- Be independent living;
- Be free of smoke (wood burning, tobacco, marijuana, vaping), perfumes/fragrances, chemicals from cleaning and laundry including other harmful volatile organic compounds (VOCs), and mold;
- Use only least-toxic solutions for all applications;
- New construction must have only least-toxic materials, and be built in such a way as to constantly off-gas VOCs;
- Not be heated by wood, propane or oil;
- Not be located in a polluted area. It must be away from Industry, farming, golf courses, smoke, and heavy traffic.

If you need more information on how you can build this housing, please contact the Environmental Health Association of Québec at 514 332 4320.

Your action will determine whether or not more people continue to die by MAiD as a direct result of being neglected due to their disability. [I, the letter writer] request a response from you on your actions going forward in this regard, and I look forward to your swift action to stop this senseless loss of life, and prevent others from suffering due to lack of action and lack of housing.