PUTTING THE CHEMICALS BACK IN "MULTIPLE CHEMICAL SENSITIVITY"

preface, highlights, summary

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.

PUTTING THE CHEMICALS BACK IN "MULTIPLE CHEMICAL SENSITIVITY"

Ontario 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*

Preface, Highlights, Summary -- TABLE OF CONTENTS

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

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

Note: the complete text is highly referenced. Evidence for the points included in this summary as well as the list of references will be found there.

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, indeed, 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)