

MULTIPLE CHEMICAL SENSITIVITY

A NOVEL DISEASE MECHANISM

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Public Submission To The National Casemix And Classification Centre
For Inclusion Of Multiple Chemical Sensitivity Under A Novel Classification Of Diseases
Title Chapter: Environmental Diseases In The International Classification Of Diseases
Version 10 Australian Modification (ICD-10-AM)

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CONSIDERATIONS FOR THIS SUBMISSION

Multiple chemical sensitivity has been in the public domain and in medical literature for over half a century. There is clear evidence that the incidence of MCS in the population is significant and probably increasing resulting in major public health and disability access impacts. The lack of recognition surrounding MCS has contributed to profound human suffering. The associated financial and personal costs are enormous.

Recent advances in the scientific understanding of MCS, particularly credible proposals for aetiological biochemical mechanisms, warrant its inclusion in the International Classification of Diseases and Related Health Problems as an entirely new disease entity under the novel Title Chapter: Environmental Diseases.

EVALUATION CRITERIA

Edition

There are no prior editions of ICD-10-AM which index MCS.

There are no prior editions of ICD-10-AM which index Title Chapter: Environmental Diseases.

In 1996 the International Program on Chemical Safety (IPCS), which is supported by the World Health Organisation, in collaboration with several German government agencies for health and environment, held a conference on MCS – the Berlin Workshop. Participation in the event was by invitation only. The non-government organisation representatives were all full time employees of BASF, Bayer, Monsanto and Coca Cola. The US industry representative, who was invited to present the US perspective, was the director of the corporate financed Environmental Sensitivities Research Institute (ESRI), an organisation well known to promote psychogenic claims on MCS and to have very limited involvement with objective MCS research. Several participants in the conference, including the Bayer representative, were directly involved in a major lawsuit involving “wood preservative syndrome”, attributed to pentachlorophenol. There were no MCS community representatives and no independent MCS researchers directly involved. The meeting heard strong criticisms of doctors involved in assisting patients with MCS.

The meeting concluded that MCS should be renamed “Idiopathic Environmental Intolerance” (IEI). In subsequent comments to the media and at scientific meetings some workshop participants defined the word idiopathic as “self-originating” rather than “of unknown aetiology” and erroneously claimed that IEI had been adopted by WHO. A letter of objection from 80 prominent scientists and independent MCS researchers was sent to IPCS, which then issued a notice saying that WHO had “neither adopted or endorsed a policy or scientific opinion on MCS”. Despite an IPCS embargo on publication of the Berlin Workshop report, so-called consensus recommendations later appeared in *Regulatory Toxicology and Pharmacology* (Anonymous 1996). Notably this paper had already been published in a previous edition of *Regulatory Toxicology and Pharmacology*, together with MCS

symposium proceedings sponsored by ESRI, well before the Berlin Workshop had occurred (Ashford and Miller 1998).

These circumstances set the stage on MCS for at least a decade or more. Subsequently the term IEI was adopted widely by government agencies, medical institutions, and researchers in the erroneous belief that the term had been endorsed by WHO.

Correspondence from WHO representatives, in association with this submission to the National Casemix and Classification Centre, indicates the Berlin Workshop concluded there was no evidence that MCS is a single disease. WHO's coding instructions given to date are: "For causes of death, all health conditions stated to be due to multiple chemicals (or specified ones) will be coded to X49 in the International Classification of Diseases. X49 refers to accidental poisoning by and exposure to other and unspecified chemicals and noxious substances. For illness not leading to death (overwhelming majority of cases) you would code the appropriate disease or symptom, in conjunction with the X49" (Madden 2011).

X49 does not include MCS, nor is it sufficient to encapsulate the medical complexities associated with MCS.

In 2000 Germany became the first country to formally recognise MCS by its inclusion in the German version of the International Statistical Classification of Diseases and Related Health Problems, ICD-10-SGB-V.

Germany has classified MCS as:

T78 Allergie

T78.4 Allergie, nicht näher bezeichnet

1;T78.4;;;MCS [Multiple-Chemical-Sensitivity-Syndrom]

1;T78.4;;;Multiple-Chemical-Sensitivity-Syndrom [MCS]

(Deutschen Institut für Medizinische Dokumentation und Information 2000)

Several countries, including Austria, Luxembourg, and Japan have followed the German model in recognising MCS as a physical disease associated with unspecified allergy (ASQUIFYDE 2011).

A discussion of the century-old medical conflict arising over the exact definition of allergy appears in Ashford and Miller's academic text "Chemical Exposures Low Levels and High Stakes" (1998). In Europe, the definition of allergy is quite broad and does not necessarily require the presence of IgE antibodies. However, in the USA and Australia allergy is strictly defined on laboratory tests indicating the presence of IgE antibodies to specific antigens. Objections to the German model have been made on the basis that MCS is not an IgE mediated disease (Donohoe and Immig undated).

The classification T78.4 for MCS is not acceptable in Australia. In 2003 submissions to the National Centre for Classification in Health proposing the inclusion of MCS under allergy in ICD-10-AM were rejected on advice from the Australasian Society of Clinical Immunology and Allergy.

Priority

The recognition of MCS should be considered an urgent commonwealth health priority.

There are clearly documented links between MCS and:

- Musculoskeletal conditions, fibromyalgia, arthralgia, myalgia, muscle twitching, asthenia, arthritides,
- Asthma, reactive airways disease, wheeze, dyspnoea,
- Cardiovascular health, arrhythmias, ectopic beats, tachycardia, bradycardia, asystole, angina, cardiac infarction, hypertension, orthostatic intolerance, thrombophlebitis, thrombocytopenia, vasculitis,
- Mental health, depression, anxiety, panic disorder,
- Obesity, compulsive eating disorder, and
- Injury prevention, chronic symptoms of MCS can be reduced or prevented through chemical avoidance as a primary treatment modality, evidence suggests that early onset MCS can be reversed and prevented from becoming chronic if the chemical incitants are removed sufficiently early, numerous researchers and inquiries into MCS have recommended prevention strategies.

Given that many of the chemicals associated with MCS are known carcinogens this factor also links to:

- Cancer control.

MCS is associated with endocrine disorders, obesity and eating disorders, and may therefore be linked to:

- Diabetes mellitus.

DRG and DRG?

The prevalence of MCS is significant. Indexing MCS will likely impact on diagnostic related group codes.

Stats and Stats?

South Australian population studies show 1% of respondents report being medically diagnosed with MCS, while 16% report hypersensitivity to common chemicals. Around 6% report “serious” health problems due to perfume, household and workplace chemicals and vehicle exhaust. The study concluded that 1% is an underestimation and that some people in the larger 16% group have symptoms more aligned with MCS.

In New South Wales nearly 3% of adults report a medical diagnosis of chemical sensitivity, while around 24 % report unusual intolerances to common chemicals. NSW child health studies have found 2.1% of children aged 2-15 years medically diagnosed with chemical sensitivity, with 7.5% sensitive to chemical odours or smells.

International studies indicate between 1% and 6% of industrialised populations have been medically diagnosed with MCS, with between 16% and 33% reporting unusual chemical hypersensitivity. Many researchers consider that the hypersensitive group are at increased risk of chronic symptoms associated with MCS.

Capturing chemical injury statistics associated with MCS through ICD-10-AM would alter the national morbidity statistics and may have some influence on mortality.

Currency

Research-based data on MCS has increased significantly, particularly in the last decade, but this information is not generally well known in health care services where misinformation about MCS is entrenched. The commonly held medical view that MCS is an entirely psychological phenomenon cannot be supported by any independent evaluation of the data.

Given:

- the well documented temporal link between chemical exposures and the initiation of MCS,
- the identification of the nitric oxide / peroxynitrite positive feedback cycle (NO/ONOO, to be discussed further in this submission) in maintaining elevated levels of NMDA as a proposed biochemical aetiology in MCS,
- the identified common action of chemicals associated with MCS in increasing levels of NMDA,
- the failure of psychogenic advocates to provide an objective review of the available literature on MCS,
- the rejection by science of the dualistic mind/body paradigm,
- the lack of credible evidence to support the assumption that an anxiety-based belief system in patients and their doctors causes somatoform disorders in MCS,
- the clear conflicts of interest amongst promoters of a psychogenic aetiology for MCS, either as manufacturers of chemicals associated with MCS or as expert witnesses in MCS liability trials,
- the documented genetic factors associated with MCS, and

- the long history of false psychogenic attribution in medicine,

The position that MCS is an entirely psychological condition does not stand up to scrutiny (Pall 2009b).

These psychogenic claims:

- threaten the maintenance of public health,
- contribute greatly to the mistreatment and suffering of patients with MCS, and
- impede the application of restorative justice in compensating victims of chemical injury, which is a key aspect of MCS prevention.

HISTORICAL PERSPECTIVE

The first descriptions in the medical literature of what is now commonly called multiple chemical sensitivity are attributed to Theron Randolph. In a series of abstracts published in the *Journal of Laboratory and Clinical Medicine*, Randolph described multiple allergic-type symptoms associated with exposure to industrial solvents, liquid fuels, pesticides, vehicle exhaust, gas and oil fumes, chemical food additives, pharmaceuticals, and cosmetics (Randolph 1954 a-f).

Since that time the condition has been given various names including environmental illness, environmental sensitivities, chemically acquired immune deficiency syndrome (chemical AIDS), environmental maladaptation syndrome, conditioned odour response, 20th century illness, the petrochemical problem, and total allergy syndrome (Ashford and Miller 1998).

In 1987, in an attempt to define diagnostic criteria, Cullen offered the following case definition:

Multiple chemical sensitivities (MCS) is an acquired disorder characterised by recurrent symptoms, referable to multiple organ systems, occurring in response to demonstrable exposure to many chemically unrelated compounds at doses far below those established in the general population to cause harmful effects. No single widely accepted test of physiologic function can be shown to correlate with symptoms. (Cullen 1987)

In 1999 Bartha et al proposed the following six consensus criteria for the definition of MCS, five of which had been identified in 1989 via a multidisciplinary survey of 89 clinicians and researchers with broad experience but widely diverse opinions of MCS:

[1] a chronic condition [2] with symptoms that recur reproducibly [3] in multiple organ systems [4] in response to low levels of exposure [5] to multiple unrelated chemicals and [6] improve or resolve when incitants are removed. (Bartha et al. 1999)

In 2005 Lacour et al., conducted a literature review of symptom profiles and clinical presentation, using the search terms multiple chemical sensitivity, multiple chemical sensitivities, multiple chemical sensitivity syndrome, MCS, idiopathic environmental intolerance, and IEI, which included some overlap with other functional entities such as chronic fatigue syndrome and fibromyalgia. The study concluded that the diagnostic criteria for MCS be extended to include “exposure-related non-specific complaints of the central nervous system”. (Lacour et al. 2005)

Frequently described as a controversial or unexplained condition, the formal recognition of MCS has been severely hampered by the fact that, while many of its symptoms resemble allergy, it is not consistent with the current medical understanding of allergy and is not a primary immunological or true allergic reaction as an IgE mediated response.

Despite the historical lack of medical understanding of the underlying mechanisms of MCS the disease affects large numbers of people worldwide. International studies indicate that between 1% and 6% of industrialised populations have been medically diagnosed with MCS (Bartha et al 1999, Caress and Steinemann 2003, Fitzgerald 2008, Kreutzer et al. 1999, Sears 2007, Silberschmidt 2005).

A much larger percentage, between 12% and 33%, report unusual hypersensitivities to common chemicals (Bartha et al. 1999, Caress and Steinemann 2003, Fitzgerald 2008, New South Wales

Department of Health Survey Program 2003, Sears 2007, Sorg 1999). Some researchers consider that individuals in this larger group may be at increased risk of developing chronic symptoms of MCS (Ashford and Miller 1998).

In South Australia, where 1% of the population have been medically diagnosed with MCS, Fitzgerald (2008) concluded that “Since there are no diagnostic or clinical guidelines for MCS in Australia, it is possible that the 1% MCS prevalence is an under-reporting, and that some chemically hypersensitive individuals have symptomology more aligned with that of MCS cases.” This conclusion is highly likely to apply worldwide.

MCS is associated with multiple diverse symptoms often described as non-specific. Symptoms and their severity vary widely from one individual to the next.

MCS can result in extreme disability and loss of function, particularly in severe cases. An evaluation of population studies by Sorg (1999) concluded that “the prevalence of severe MCS in the United States is 4% with greatly reduced quality of life for the patient”. A population study in Atlanta, Georgia, by Caress and Steinemann (2003) found that nearly 2% of respondents had lost their jobs due to chemical hypersensitivity.

It has been roughly estimated that the annual cost of MCS in the USA alone is a staggering US\$ 444 billion, including lost productivity, and that the global cost of MCS is perhaps four times that amount (Pall 2009a). This financial estimate in no way accounts for the many personal losses and profound human suffering that is caused by MCS, a tragic disease which can be prevented.

In 2005 the South Australian Parliament’s bicameral Social Development Committee tabled the findings of its Inquiry into MCS in the Legislative Council. The inquiry concluded:

MCS can be a debilitating condition that causes great hardship for many sufferers, their partners and families. The Committee acknowledges the many individuals with MCS who came forward to share their very personal accounts. It is clear from these accounts that MCS is very real and that many individuals experience considerable suffering, particularly in light of the lack of recognition surrounding this condition. (Social Development Committee 2005)

A growing number of jurisdictions internationally, including Australia and New Zealand, recognise MCS as a legitimate disability requiring reasonable accommodations under equal opportunity legislation (Environmental Risk Management Authority 2002, Human Rights Commission 2010, Social Development Committee 2005).

The Canadian Human Rights Commission has published two seminal papers relating to environmental sensitivities, their medical recognition, disability accommodations, and prevention (Sears 2007, Wilkie and Baker 2007).

MCS is not considered with regard to risk evaluation in chemical regulation, although attempts have been made in Australia to identify research priorities and better understand MCS from a regulatory perspective (National Industrial Chemicals Notification and Assessment Scheme (NICNAS) and the Office of Chemical Safety and Environmental Health (OCSEH) 2010).

A variety of aetiological mechanisms have been proposed for MCS including:

- Vascular mechanisms whereby arterial spasm and haemorrhage results in reduced blood flow, altered function, pain, oedema, and possible necrosis of affected organs (Rea 1975, 1979).
- Limbic kindling/neural sensitisation, which proposes that olfactory-limbic-temporal neural pathways respond more easily to chemical signals or insults in those areas of the brain that are “kindled” by previous chemical exposures, genetic predisposition, stress and other factors (Bell 1990).
- Immunological dysregulation, altered T-cell ratios, T-lymphocyte activation, and cytokine production (Ashford and Miller 1998).
- Biochemical mechanisms involving nutritional deficiencies, defective enzyme detoxification pathways, and increased free radical production (Ashford and Miller 1998).
- Psychogenic mechanisms, mass psychogenic illness (Ashford and Miller 1998), behavioural conditioning (Bolla-Wilson et al. 1988, Shusterman et al. 1988), iatrogenic influences whereby medical professionals who offer practical and psychological support, and confirm a physiological aetiology for MCS, promote somatoform disorders in their patients (Black 1995).
- Toxicant induced loss of tolerance (TILT), proposed by Miller (1997), is described as a two phase phenomenon commencing with initiation due to high level or chronic low level chemical exposure, followed by loss of tolerance to chemicals, foods and pharmaceuticals previously tolerated, and triggering of symptoms. Miller proposed that TILT represents a new mechanism of disease which parallels germ, immune and cancer theories of disease but was unable to explain the exact mechanism. He hypothesised that tolerance breakdown may involve a variety of mechanisms, including neural sensitisation and genetic polymorphisms, acting together and mimicking addiction (Miller 2000).

None of these aetiological proposals, alone or combined, are sufficient to fully explain MCS.

In 2001 Pall identified six vicious biochemical positive feedback loops resulting in elevated levels of nitric oxide and its oxidant product peroxynitrite as a proposed aetiological mechanism underlying chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivity and post traumatic stress disorder (Pall 2001). Pall refers to this mechanism as the NO/ONOO (pronounced “no/oh-no”) cycle and has proposed that it represents an entirely new disease paradigm (Pall 2009a).

1 ICD ENTITY TITLE

A New Classification of Diseases – Chapter Title: Environmental Diseases

On the basis of the convincing nature of the research-based evidence, this submission proposes that an entirely new entity Chapter Title, Environmental Diseases, be included in ICD-10-AM.

It is not the intention of this submission to elaborate extensively on the work of Professor Pall. The consistency of his explanation of the biochemistry proposed to be associated with MCS speaks for

itself. Pall's publication *Multiple Chemical Sensitivity: Toxicological Questions and Mechanisms*, is the most extensively referenced review of MCS to date and appears as Chapter XX in the prestigious publication *General and Applied Toxicology, 3rd Edition*.

General and Applied Toxicology, 3rd Edition is the first port of call for academic researchers, industrial researchers, regulatory professionals, and advanced students looking for timely and authoritative information in the field. Due to the increase in public and media interest in exposure to toxic substances, this provides an indispensable general reference source for general physicians, lawyers, law enforcement agencies, information resource facilities, and members of the general public (Wiley and Sons 2011).

Pall's clarification of the NO/ONOO cycle with respect to MCS explains many of the unexplained mysteries and questions that have plagued the medical understanding of MCS for decades. Not only does it provide a highly cogent reason, backed by many years of extensive research, for the numerous and variable individual symptom presentations in patients with MCS, it also explains how these symptoms are driven by biochemical reactions at a local tissue level, and how multiple seemingly unrelated chemicals play a role in initiating MCS and, once the disease is established, up-regulating the NO/ONOO positive feedback cycle, resulting in further symptom triggering.

1.1 Name

Multiple Chemical Sensitivity (MCS)

This submission proposes the inclusion of MCS as a new entity in ICD-10-AM.

2 CLASSIFICATION PROPERTIES

2.1 Parents

The proposed parent code for MCS is the new Chapter Title: Environmental Diseases.

2.1.1 ICD-10 Code for Unchanged Categories

Consideration of MCS in Existing ICD-10-AM Codes

Chemicals identified as initiating and triggering symptoms of MCS and also up-regulating the NO/ONOO positive feedback cycle are:

- Pesticides: organochlorine, organophosphorous, carbamate, and pyrethoid,
- Organic solvents,
- Carbon monoxide,
- Mercury,

- Hydrogen sulphide.
(Pall 2009b)

It is therefore appropriate that MCS be considered with respect to existing ICD-10-AM classifications:

Chapter XIX

Injury, poisoning and certain other consequences of external causes (S00-T98)

Toxic effects of substances chiefly non-medicinal as to source (T51-T65)

- T52 Toxic effect of organic solvents
 - T52.0 Petroleum products
 - T52.8 Other organic solvents
 - T52.9 Organic solvent, unspecified
- T56 Toxic effect of metals
 - T56.1 Mercury and its compounds
- T58 Toxic effect of carbon monoxide
- T59 Toxic effect of other gases (aerosol propellants)
 - T59.2 Formaldehyde
 - T59.6 Hydrogen sulphide
- T60 Toxic effect of pesticides
 - T60.0 Organophosphate and carbamate insecticides
 - T60.2 Other insecticides

Chapter XX

External causes of morbidity and mortality (V01-Y98)

Other external causes of accidental injury (W00-X59)

Accidental poisoning by and exposure to noxious substances (X40-X49)

- X46 Accidental poisoning by and exposure to organic solvents
- X47 Accidental poisoning by and exposure to other gasses and vapours (carbon monoxide, motor vehicle exhaust gas, utility gas)
- X48 Accidental poisoning by and exposure to pesticides
- X49 Accidental poisoning by and exposure to other and unspecified chemicals and noxious substances (glues and adhesives, metals including fumes and vapours, paints and dyes).

2.2 Type

Disease

MCS can be classified as a disease on the basis of:

- The diverse clinical symptomatology in multiple organ systems exacerbated by low level chemical exposures,
- multiple laboratory and test abnormalities,
- the biochemical mechanisms shown by medical research to exist in the NO/ONOO positive feedback cycle and their proposed aetiological link to MCS,
- the general course of the disease as a chronic yet fluctuating condition with various levels of associated disability,
- chemical avoidance as a symptomatic treatment modality and an essential component in down regulating the NO/ONOO cycle,
- the identification of associated genetic markers, and
- its relationship with environmental chemicals shown to drive the NO/ONOO positive feedback loop.

Injury

MCS can be considered an injury on the basis that it occurs as a result of chemical exposures.

External Causes

MCS can be considered in External Causes on the basis that environmental chemical exposures may cause chemical injuries resulting in MCS.

Reasons for Encounter

If MCS is indexed as an Environmental Disease, as proposed, the situations for which a patient with MCS might enter the health system include all of those currently described in ICD-10-AM.

- Known diseases,
- Symptoms or complaints,
- Requests for preventive or diagnostic services,
- A request for treatment,
- To receive test results, or
- Administrative purposes.

2.3 Use and Linearization

The new entity MCS can be used at all levels of health care employed by ICD:

- Primary Care
- Clinical
- Research

With linearizations in:

- Morbidity
- Mortality
- Other

And speciality adaptation in:

- Environmental Medicine

2.3.1 Linearization Parent

The proposed linearization parent category is Environmental Diseases.

Environmental Diseases

Multiple Chemical Sensitivity

3 TEXTUAL DEFINITION

3.1 Print Textual Definition

MCS is defined clinically on the basis of the 1999 (Bartha et al.) consensus criteria as a [1] a chronic condition [2] with symptoms that recur reproducibly [3] in multiple organ systems [4] in response to low levels of exposure [5] to multiple unrelated chemicals and [6] improve or resolve when incitants are removed.

3.2 Detailed Definition

MCS typically incorporates four different population groups with chemical hypersensitivity.

- Industrial workers.
- Residents located close to chemically contaminated geographical areas.
- Occupants of tightly sealed and air conditioned buildings, including office workers and school children.

- Individuals with an atypical history of hypersensitivity reactions to chemical products, pesticides, building and renovation materials, pharmaceuticals and consumer products.

These populations are not demographically homogenous and their chemical exposure histories may differ substantially. A common feature of their medical history is multiple variable symptoms, lasting for a significant period of time, in multiple organ systems, including generalised complaints of the central nervous system such as headache, fatigue, cognitive dysfunction, memory and concentration difficulties, depression and irritability, in response to a widely diverse range of chemicals. The symptoms improve, or resolve entirely, when the chemical incitants are removed.

A chemical exposure history will sometimes reveal specific events associated with the onset of symptoms such as exposure to pesticide treatments, renovations and remodelling, installation of new carpet, workplace relocation, or changes in workplace or residential exposures. A single high level chemical exposure may not always be identified. Multiple low level exposures need to be considered.

The onset of MCS occurs in two phases – initiation of symptoms followed by a broadening of sensitivities. Symptoms often commence over a relatively short period, perhaps weeks or months, after which multiple symptoms in multiple organ systems are triggered by exposure to very low levels of chemicals found commonly in the environment. The types of chemicals triggering symptoms often broaden over time. Sensitivities to a wide range of foods and pharmaceuticals are commonly present. Sensitivity to light, touch, sound, odours and electromagnetic fields are also reported.

There may be a history of multiple medical consultations to investigate non-specific complaints.

Physical examination is often unremarkable. Standard laboratory analyses may show no or few significant abnormalities, however, more specialised tests will reveal multiple anomalies in multiple organ systems (Ashford and Miller 1998).

Six vicious positive feedback biochemical cycles up-regulating levels of NMDA and involving nitric oxide and peroxynitrite – the NO/ONOO cycle – have been proposed as an underlying aetiological mechanism in MCS (Pall 2009b).

MCS has no known cure. Symptoms are highly variable and fluctuate significantly over time. Most patients never fully recover. Medical management of MCS should focus on avoidance of chemicals, foods and pharmaceuticals that trigger symptoms, and reducing levels of NMDA through the use of anti-oxidant dietary supplements, although other agents including pharmaceuticals may be available. It also incorporates identification and treatment of any underlying infection, stress reduction, and symptomatic relief treatment (Ashford and Miller 1998, Pall 2009a; 2009b).

An understanding and empathic approach that offers support and encourages self-management rather than cure is recommended as part of a positive, long term therapeutic relationship (National Industrial Chemicals Notification and Assessment Scheme (NICNAS) and the Office of Chemical Safety and Environmental Health (OCSEH) 2010).

4 TERMS

4.1.1 Synonyms

Alternative terms for MCS in common usage include:

- Acquired intolerance to solvents,
- Chemical acquired immune deficiency syndrome (chemical AIDS),
- Chemical injury and sensitivity,
- Chemical intolerance,
- Chemical sensitivity/sensitivities,
- Conditioned odour response,
- Environmental illness,
- Environmental maladaptation syndrome,
- Environmental sensitivities,
- Gulf War syndrome,
- Idiopathic environmental intolerance,
- Multiple chemical sensitivity syndrome,
- Petrochemical problem,
- Sick building syndrome,
- Total allergy syndrome,
- Toxic encephalopathy,
- 20th century disease, and
- other.

4.2 Inclusion terms and base inclusion terms

Chronic fatigue syndrome, electromagnetic hypersensitivity, post traumatic stress disorder, and fibromyalgia can be considered as co-morbidities with MCS.

4.2 Exclusion terms and base exclusion terms

MCS can be considered for exclusion from the German ICD-10-SGBV model expressed in:

T78 Allergie
T78.4 Allergie, nicht näher bezeichnet
1;T78.4;;;MCS [Multiple-Chemical-Sensitivity-Syndrom]
1;T78.4;;;Multiple-Chemical-Sensitivity-Syndrom [MCS]

Classification under allergy is not consistent with the conventional Australian medical understanding of allergy as an IgE mediated response.

5 BODY SYSTEM /BODY STRUCTURE DESCRIPTION

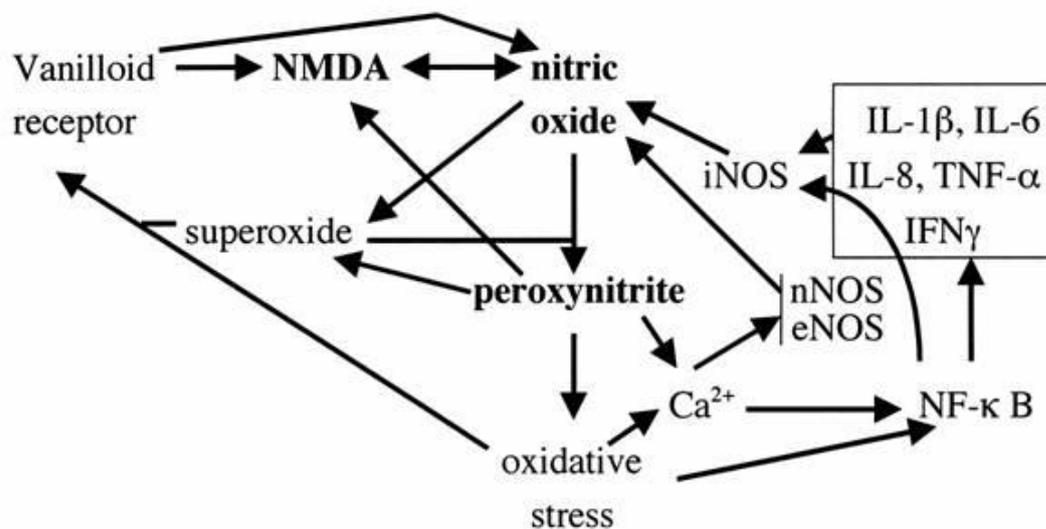
5.1 Body System

A Novel Biochemical Disease Mechanism

This submission proposes that MCS represents a novel body system description occurring at a biochemical level within body tissues - the NO/ONOO positive feedback cycle.

Professor Pall explains:

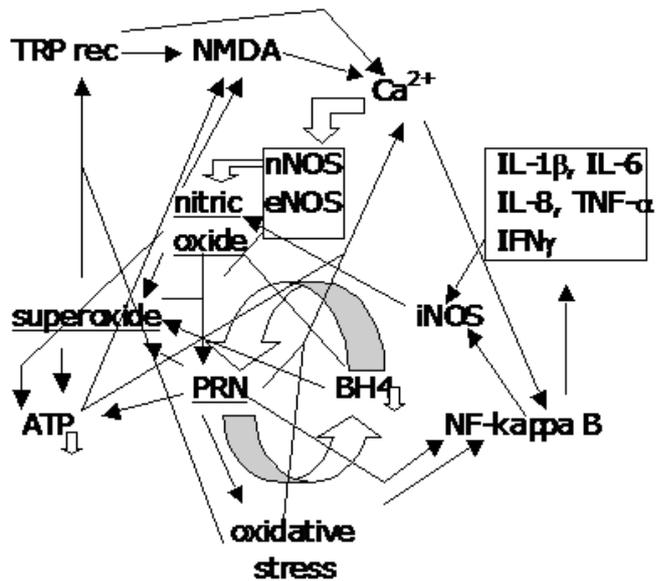
Figure 1



The vicious (NO/ONOO-) cycle diagram

Each arrow represents one or more mechanisms by which the variable at the foot of the arrow can stimulate the level of the variable at the head of the arrow. It can be seen that these arrows form a series of loops that can potentially continue to stimulate each other. An example of this would be that nitric oxide can increase peroxynitrite which can stimulate oxidative stress which can stimulate NF-kappaB which can increase the production of iNOS which can, in turn increase nitric oxide. This loop alone constitutes a potential vicious cycle and there are a number of other loops, diagrammed in the figure that can collectively make up a much larger vicious cycle. The challenge, according to this view, in these illnesses is to lower this whole pattern of elevations to get back into a normal range. You will note that the cycle not only includes the compounds nitric oxide, superoxide and peroxynitrite but a series of other elements, including the transcription factor NF-kappaB, oxidative stress, inflammatory cytokines (in box, upper right), the three different forms of the enzymes that make nitric oxide (the nitric oxide synthases iNOS, nNOS and eNOS), and two neurological receptors the vanilloid (TRPV1) receptor and the NMDA receptor (Pall 2011a).

A more detailed elaboration of this positive feedback system offers an explanation of the exquisitely high level of sensitivities observed in response to very low level chemical exposures.



The vicious (NO/ONOO-) cycle diagram incorporating BH4, TRP receptors, and ATP.

Central to the figure are the reciprocal interactions between peroxynitrite, abbreviated as PRN and tetrahydrobiopterin (BH4) depletion. Also indicated is the ATP (energy) depletion produced by the impacts of peroxynitrite, superoxide and nitric oxide on mitochondrial function. Symptoms of MCS are generated by elevated levels of nitric oxide and/or other important consequences of the proposed mechanism, i.e. elevated levels of peroxynitrite or inflammatory cytokines, oxidative stress, elevated NMDA and TRPV1 receptor activity, ATP and BH4 depletion and others (Pall 2011b)

5.2 Body Part – Anatomical Site

The NO/ONOO cycle occurs at a biochemical level within the body. The chemical reactions involved are not highly tissue specific. Varying diffusion concentrations of nitric oxide/peroxynitrite across all body tissues accounts for the wide variety of symptoms associated with MCS (Pall 2001).

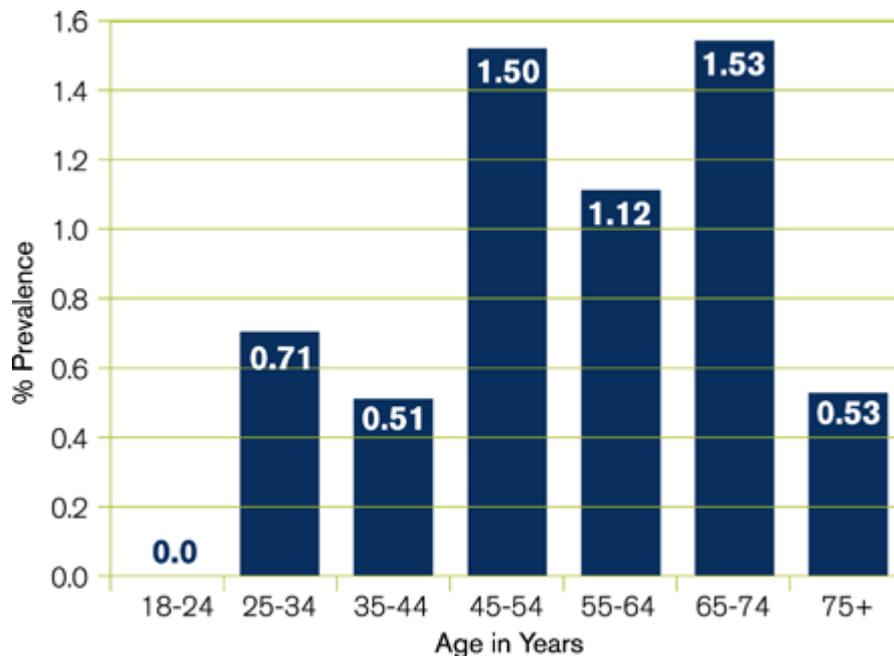
6 TEMPORAL PROPERTIES

6.1 Age of Occurrence & Occurrence Frequency

Age

MCS can affect both children and adults of any age, although the onset typically occurs in mid-life.

Age distribution data from South Australia suggest a late onset Gaussian-type distribution curve for MCS, although this survey did not include adolescents and children.



(Fitzgerald 2008)

In 2007-2008 a New South Wales a population health survey report on child health found 2.1% of children aged 2-15 years had been medically diagnosed with chemical sensitivity, while 7.5% were sensitive to chemical odours or smells (New South Wales Department of Health 2010).

Gender

Predominance of MCS among Women

Women are significantly more likely to acquire MCS than men. Approximately 60% to 80% of people diagnosed with environmental sensitivities are women (Sears 2007).

Occurrence Frequency

Population Studies of MCS

International population studies reveal that MCS is very common, with between 1% and 6% of people medically diagnosed with the disease. There is an even greater incidence of unusual chemical hypersensitivities within the general population that is estimated to be between 12% and 33% (Bartha et al 1999, Caress and Steinemann 2003, Fitzgerald 2008, Meggs et al 1996, New South Wales Department of Health 2002, Sears 2007, Silberschmidt 2005, Sorg 1999). It is thought that the larger hypersensitive group may be at increased risk of developing chronic symptoms of MCS (Ashford and Miller 1998).

In the USA MCS has been medically diagnosed in 2% to 6% of adults, while 16% to 33% report that they are unusually or especially sensitive to everyday chemicals. Among Gulf War veterans who

were deployed 15% report chemical sensitivity, three fold the incidence of chemical sensitivity in un-deployed veterans (Bartha et al 1999).

In Canada in 2003 the prevalence of medically diagnosed MCS was 2.4% in people aged 12 years or older and 2.9% in people aged 30 years or older (Sears 2007).

Less information is available on the prevalence of MCS in Europe. In Demark in 2005 it was assumed to be around 1% (Silberschmidt 2005).

Prevalence data for MCS in Australia are consistent with international findings. In South Australia around 1% of population survey respondents report being medically diagnosed with MCS, while around 16% report chemical hypersensitivity (Fitzgerald 2008). In New South Wales nearly 3% of adults have been medically diagnosed with chemical sensitivity, with nearly 25% reporting sensitivity to chemical odours (New South Wales Department of Health 2003). The prevalence of medically diagnosed chemical sensitivity (2.1%) and odour sensitivity (7.5%) in children in New South Wales NSW is noted above. No other Australian jurisdictions have undertaken chemical sensitivity studies in children.

The actual incidence of MCS in New Zealand is unknown. Based on international findings it was assumed in 2002 to be less than 1% (Environmental Risk Management Authority 2002).

South Australia's population study found an average of 6% of respondents reported that their health was "seriously affected by exposure to ... perfume, traffic pollution, household chemicals, workplace chemicals" (Fitzgerald 2008). This figure is entirely congruent with the recorded 6% prevalence of medically diagnosed MCS in California (Bartha et al 1999), where medical knowledge of MCS has been assessed to be higher than other jurisdictions (Ashford and Miller 1998). These data add weight to the South Australian study's premise that "Since there are no diagnostic or clinical guidelines for MCS in Australia, it is possible that the 1% MCS prevalence is an under-reporting, and that some chemically hypersensitive individuals have symptomology more aligned with that of MCS cases" (Fitzgerald 2008). This conclusion is also likely to apply in other countries where medical knowledge of MCS is poor.

Medical testimony to the Social Development Committee (2005) reported that the incidence of MCS in the Australian community is increasing.

For many years people with MCS have been sincerely attempting to alert authorities to the public health implications of their illness. In 2001, in a study of self-care in MCS, the author noted a message of warning from people with MCS: "We are the canaries in the coal mine; what has happened to us will happen to many others unless we clean up our environment" (Lipson 2001).

6.2 Developmental Course / Stage

MCS Initiation and Broadening of Sensitivities – A Two Phase Process

MCS has been observed to occur as a two-phase phenomenon commonly initiated by a single high level exposure or multiple low dose exposure to chemicals. Following initiation, chemical sensitivities then broaden over time and result in symptoms being triggered by a diverse range of

chemicals, foods and pharmaceuticals (Johnson 2000, Pall 2009a; 2009b, Rea 1992, Sorg 1999, Ashford and Miller 1998, Miller and Mitzel 1995).

The classes of chemicals associated with initiating MCS are the same as those that trigger symptoms once the disease is established (Pall 2009a).

In the vast majority of cases MCS is a chronic, incurable condition with symptoms that are highly variable in nature but most often permanent (Pall 2009a). Although many people may experience some improvement in their condition over extended periods of time, very few return to the level of well-being and function enjoyed prior to the onset of MCS (Ashford and Miller 1998).

Longitudinal patient studies have been recommended by the Australian government's scientific review of MCS to further understand the course of MCS (National Industrial Chemicals Notification and Assessment Scheme (NICNAS) and the Office of Chemical Safety and Environmental Health (OCSEH) 2010).

Recovery and Prevention

There have been some reports of patients with early onset MCS who have recovered, provided that they avoid further problematic chemical exposures (Hileman 1991). This suggests that the chronic symptoms of MCS are preventable (Ashford and Miller 1998).

Numerous investigations have made recommendations on MCS prevention strategies.

7. SEVERITY OF SUBTYPE PROPERTIES

Severity Scales

Environmental Exposure and Sensitivity Inventory (EESI)

The Environmental Exposure and Sensitivity Inventory (EESI) offers a standardised approach to measuring chemical sensitivity in the research and clinical settings. The instrument is a self-rating scale to assess;

- Symptom Severity
- Chemical (Inhalant) Intolerances
- Other Intolerances (e.g. foods, medications, alcohol)
- Life Impact, and
- Masking (a measure of ongoing chemical exposures).

It is both accurate and useful, individually or collectively, in a variety of applications including the selection of chemically sensitive subjects for research, assessment of chemical sensitivity in various study populations, cross comparison of groups studies by different investigators, pre- and post assessment of therapeutic interventions, clinical evaluation of complex patients who report

intolerances, and teaching medical residents and students how to evaluate patients for chemical sensitivity and MCS.

Using a scale from 1-100 for Symptom Severity and Chemical Intolerance, and 1-10 for Masking, with cut-off points in each category, patients can be categorized into three risk categories for MCS – “very suggestive”, “somewhat suggestive” and “not suggestive”.

Risk criteria			
Degree to which MCS is suggested	Symptom Severity score	Chemical Intolerance score	Masking score
Very suggestive	≥ 40	≥ 40	≥ 4
Very suggestive	≥ 40	≥ 40	< 4
Somewhat suggestive	≥ 40	< 40	≥ 4
Not suggestive	≥ 40	< 40	< 4
Problematic	< 40	≥ 40	≥ 4
Problematic	< 40	≥ 40	< 4
Not suggestive	< 40	< 40	≥ 4
Not suggestive	< 40	< 40	< 4

Consideration of all EESI categories, including Other Intolerance and Life Impact scales, allows chemically sensitive patients to be distinguished between other sick patients and controls with relative reliability.

More complex analyses can be obtained using altered high or low cut off points in each category together with a multiple logistic regression equation (Miller and Prihoda 1999a).

A shortened version of the test, the Quick Environmental Exposure and Sensitivity Inventory (QEESI), enables researchers and clinicians to more easily facilitate history-taking of patients with chemical sensitivity and related conditions (Miller and Prihoda 1999b).

The Chemical Odour Sensitivity Scale (COSS) is a tool both for assessing self-reported chemical odour sensitivity as a vulnerability marker and for screening for MCS (Bailer et al. 2006)

8. MANIFESTATION PROPERTIES

8.1 Signs and Symptoms

There is an extensive range of symptoms associated with MCS. Based on the results of a literature review, Labrage and McCaffey (2000) identified over 150 MCS-related symptoms. Sorg (1999) lists a total of 41 different symptoms, although many of these only occur in a minority of patients. Those most commonly reported in MCS are linked with the central nervous, gastrointestinal and respiratory systems (Ross 1992).

Percentage Prevalence of Symptoms Reported for MCS (Ross 1992)

Symptom	Prevalence (%)
Headache	55
Fatigue	51
Confusion	31
Depression	30
Shortness of breath	29
Arthralgia	26
Myalgia	25
Nausea	20
Dizziness	18
Memory problems	14
Gastrointestinal symptoms	14
Respiratory symptoms	14

Patient data from the Nova Scotia Environmental Health Centre, a publicly funded Canadian facility specialising in environmental illness treatment and research, commonly featured fatigue, difficulty concentrating, forgetfulness and irritability (Joffres et al., 2001). As noted previously, it has been proposed that these generalised complaints of the central nervous system represent a sentinel diagnostic feature of MCS (Lacour et al 2005).

Symptom severity scores are known to be higher in women than in men (Joffres et al 2001).

In the vast majority of cases chronic symptoms are variable but permanent and occur on a daily basis (Ashford and Miller 1998). Symptoms triggered by chemical exposures vary from mild to life-threatening, depending on the level of associated severity and the organ systems affected.

Thrombosis and asystole in response to chemical exposures have been reported (Reed Gibson 2005).

8.2 Investigation Findings

Investigations conducted on patients with chemical injury and sensitivity show evidence of:

- Abnormal SPECT brain scans showing reduced blood flow to the frontal, temporal and limbic areas and reduced uptake of contrast medium in the early phase of injection,
- Changes in brain PET scans,
- Neurological abnormalities in nerve conduction, EEGs, evoked potentials,
- Hypothalamic-pituitary-adrenal axis dysfunction,
- Impaired neurocognitive/neuropsychological function,
- Autonomic dysfunction, including orthostatic intolerance,
- Abnormal ECG, tachycardia, frequent ectopic beats,
- Reactive airways disease associated with the release of inflammatory substance P and neurogenic inflammation,
- Adrenal cortisol changes with frequent deficiency,
- Protein deficiency with greatest deficiency in detoxification-related amino acids,

- Changes in Phase II detoxification following challenge, with deficiency of glutathione and superoxide dismutase and increase of lipid peroxides and other free radicals,
- Changes in cell membrane lipid composition to a pro-inflammatory status,
- Pancreatic digestive enzyme (chymotrypsin) deficiency,
- Intracellular essential mineral deficiency,
- Reduced antioxidant function,
- Increased markers for oxidative stress,
- Altered energy metabolism,
- Nutrient deficiency, the most prevalent being B 12,
- Secretory IgA deficiency with frequent parasites and/or Candida,
- Immune abnormalities, altered T-cell and B-cell function, reduced NK cell function, auto-antibodies, and
- Alterations in porphyrin metabolism and related enzyme deficiencies, (Ziem 2001, Ziem and McTamney 1997, Pall 2009a)

9. CAUSAL PROPERTIES

This submission proposes that MCS is caused by metabolic, environmental, occupational and genetic factors.

9.1 Aetiological Type

Metabolic

The primary proposed metabolic factor in MCS is the NO/ONOO positive feedback cycle.

Environmental

The primary environmental factors are chemical exposures.

Occupational

Occupational chemical exposures are frequently associated with MCS (Pall 2009b, McKeown-Eyssen et al 2001, Ashford and Miller 1998).

9.2 Causal Properties – Agents

Chemical Agents

Chemical exposures temporally associated with symptoms of MCS are:

- Pesticides: organophosphorous, organochlorine, carbamate and pyrethroid,

- Organic solvents,
 - Carbon monoxide,
 - Hydrogen sulphide, and
 - Mercury.
- (Pall 2009a; 2009b, Ashford and Miller 1998)

A review of pesticide poisoning data from the US Environmental Protection Agency found reports of chemical sensitivity associated with multiple chronic symptoms following exposure to the organophosphate pesticide chlorpyrifos (Blondell and Dobozy 1997).

Household exposure to synthetic pyrethroids has been linked to chronic symptoms and long term disability consistent with MCS (Kolaczinski and Curtis 2004).

9.3 Causal Mechanisms

All of the above chemicals and chemical classes have been shown to elevate NMDA activity, a key driving factor within the NO/ONOO positive feedback cycle (Pall 2009a; 2009b).

Exposure to organophosphate pesticides, as the initiating event in MCS, results in significantly greater symptom severity compared to organic solvent exposure in renovation and remodelling materials as the initiating event. This comparison indicates a physiological basis for MCS (Miller and Mitzel 1995).

Dunstan et al (1995) have reported elevated levels of serum organochlorines in chronic fatigue syndrome patients suggesting that recalcitrant organochlorines may play an aetiological role in CFS. Rea et al (2002) have found evidence suggesting a role for hormone deregulation from exposure to chlorinated compounds in chemically sensitive patients.

Proponents of a psychogenic aetiology for MCS sometimes justify their position on inconclusive data from MCS provocation studies, where patients are intentionally exposed to chemicals in a controlled environment in order to assess sensitivity reactions. A systematic review of these studies revealed a number of methodological weaknesses and shortcomings with the conclusion that the role of psychological factors in MCS had been over-stated (Goudsmit and Howes 2008).

MCS is sometimes described as sensitivity to irritants, smells and odours. But this description is not consistent with the evidence. Doty (1994) has observed MCS related sensitivity reactions in people with no sense of smell (anosmia). Joffres et al (2005), Millqvist and Lowhagen (1996) and Millqvist et al (1999) have documented sensitivity reactions to chemicals while subjects wore nose clips. Hillert et al (2007) found lowered olfactory centre responses, rather than higher, in cerebral imaging of subjects with MCS compared to controls. These studies do not support the proposal that sense of smell plays a major role in MCS. Based on these and other findings Pall (2009b) has concluded that "We are looking at a response to chemicals, many of which have odours, not a response to odours".

9.4 Genomic Linkages

There is compelling evidence with very high levels of statistical significance that six genetic factors involved in the metabolism and detoxification of organic solvents and related compounds, and pesticides, also play a role in susceptibility to MCS (Pall 2009b).

Genetic Polymorphisms Influencing MCS Susceptibility

Gene	Study	Function – Chemical Metabolism	Comments
PON1	H,M	Detoxification of organophosphorous toxicants including pesticides	
CYP2D6	M	Hydroxylation of hydrophobic compounds	May be expected to increase activity of strictly hydrophobic solvents on the TRPV1 receptor
NAT2	M,S	Acetylation	May produce more or less activity, depending on substrate
GSTM1	S	Provides reduced glutathione for conjugation	Should increase detoxification and excretion
GSTT1	S	Glutathione conjugation	Should increase detoxification and excretion
UGT1A1	M&S	Glucuronidation, leading to increased excretion	

H=Haley et al 1999; M=McKeown-Eyssen et al 2004; S=Schnakenberg et al 2007; M&S= Müller and Schnakenberg 2008.

(Pall 2011b)

All of these genetic polymorphisms exhibit gene X environment interactions, influenced by chemical exposures in specific populations, resulting in variable patterns of genetic susceptibility within those populations. It follows from these genetic studies that, together with evidence for the temporal associations of MCS initiating chemical exposures, the role of toxic chemicals in MCS is undeniable (Pall 2011b).

9.5 Risk Factors

Other risk factors, apart from chemical exposures, that are associated with MCS initiation are:

- Psychological stress/abuse.
- Infection.
- Physical trauma, notably involving the head and neck.

(Ashford and Miller 1998, Pall 2009a)

There is substantial evidence that all of these stressors increase levels of NMDA (Pall 2009a; 2009b).

10 FUNCTIONING PROPERTIES

Disabilities arising from MCS vary substantially but have implications across all areas of the International Classification of Functioning, Disability and Health lists b, d and e.

Levels of functioning, disability and health are often associated with the frequency and intensity of environmental sensitivity reactions, although there is not always a direct relationship. Some individuals who are seriously and permanently disabled in numerous areas of functionality and participation may only experience mild environmental sensitivity reactions; while others who experience severe and disabling sensitivity reactions can maintain general functionality, health and well being provided that environmental symptom triggers can be minimised or avoided.

Chemical exposures not only cause the impairments associated with MCS, they also act as barriers to participation in industrial culture (Reed Gibson 2009).

10.1 Impact on Activity and Participation Relating to the ICF d List

MCS has potential impacts in all areas of the ICF d list.

10.1.1 Understanding

In an evaluation of patients with chemical injury and sensitivity using the Wechsler Adult Intelligence Scale-Revised and the Halstead-Reitan Neuropsychological Battery (which includes assessment of problem solving, judgment, abstract reasoning, concept formation, mental flexibility and mental efficiency), more than 50% of subjects scored within the range for neurocognitive impairment. In addition, 48% of subjects reported visual changes, most commonly blurred vision associated with chemical exposures (Ziem and McTamney 1997). Impaired reading and mathematical ability are also reported (Ashford and Miller 1998).

10.1.2 Communication

In an evaluation of patients with chemical injury and sensitivity 46% of subjects scored within the impairment range in the Speech Sounds Perception Test, 58% experienced slurred words or difficulty finding words, while changes in hearing were reported by 32% of subjects (Ziem and McTamney 1997).

10.1.3 Mobility

MCS has significant overlap with both chronic fatigue syndrome and fibromyalgia, with between 75% and 80% of MCS patients meeting diagnostic criteria for the other two conditions, respectively (Buchwald and Garrity 1994). Muscle discomfort/spasm and joint discomfort are reported in 49% and 52% of MCS subjects, respectively; 49% experience coordination difficulties, 29% tremor and

shaking, and 33% muscle twitching (Ziem and McTamney 1997). Fatigue and musculoskeletal pain are consistently amongst the most commonly reported complaints of MCS patients (Ross 1992).

With regard to transportation, apart from the disadvantages caused by reduced physical mobility, chemicals in common products such as pesticides used in public parks and roadside maintenance, personal fragrances, cleaning and deodorising products, and vehicle exhaust form major disability access barriers to transport, notably with respect to public transport (Reed-Gibson 2009).

10.1.4-7 Self Care – Domestic Life – Interpersonal Interactions and Relationships - Life Activates – Social Participation

Reed Gibson et al (1998) have conducted exploratory social research to assess social supports in chemical injury and sensitivity. An examination of 305 persons with MCS was done using The Personal Resource Questionnaire 85 (PRQ 85).

Part 1 of this instrument looks at 10 life situations where assistance might be needed in the previous six months, and gathers information on the person's resources and their satisfaction with those resources.

Part 2 is a 25 item scale based on five dimensions;

- Worth – the indication that one is valued,
- Social Integration – that one is part of a group,
- Intimacy – the provision for attachment/intimacy,
- Nurturance – the opportunity for nurturance, and
- Assistance – the availability of information, emotional, and material help.

Subjects in the sample had been unwell for an average of 15 years.

PRQ85 scores were lower than those found in healthy populations but similar to samples with chronic illnesses such as diabetes mellitus and multiple sclerosis. Participants reported experiencing considerable difficulties in the previous 6 months regarding support needs and satisfaction with support.

Using an adapted environmental illness disability instrument, participants were asked to self-rate the severity of their disability using a four-point scale.

The category guidelines for the four levels of disability were:

Mild:

Able to work. Frequently has many symptoms, some of vague nature. May find petrochemicals and other environmental exposures such as cigarette smoke to be unpleasant or produce discomfort but able to work effectively.

Moderate:

Able to work at home or with controlled environment at work place. May have to use gas mask or charcoal mask and air purifier filter system. Exposure to inciting agents causes acute symptoms which may alter functional capacity.

Severe:

Unable to work effectively, even with environmental control, using avoidance, masks or filters. On some days, may be able to work 30 to 60 minute shifts several time a day if in a very controlled environment. Reacts to many chemicals such as insecticide, formaldehyde, perfume, petro-chemicals, etc. and has severe mental and physical symptoms which may or may not clear. Public exposures such as church or shopping are not tolerated. Visitors to home must clean up significantly. Requires a clean room, carpet-free, cleared of inciting agents, special heating and air filtering. Needs natural fibre clothing specially laundered.

Totally Disabled:

Requires assistance to function in rigidly controlled home environment. Reactive symptoms have spread to virtually all environmental agents including chemicals, foods, pollens, and moulds. Has mental and physical symptoms that are incapacitating, although frequently not structurally described. Total and very restrictive environmental control required in home and vehicle. Cannot tolerate others who have outside exposures with even small contamination of clothing or hair with odours. Has difficulties with virtually everything in environment.

The study results found that participants self-rated as mild (12.8%), moderate (31.1%), severe (39.3%), or totally disabled (15.7%).

Women accounted for 80% of respondents. Nearly 60% of respondents were either married or living with a partner. Perceived social supports correlated positively with having a partner. Women reported higher levels of social support than men. There was some suggestion that men with MCS may be more stigmatised and less able to access support than women.

Many respondents reported feeling extremely isolated from their family, especially where family members had been asked to be chemical free. Respondents reported that family members did not understand chemical sensitivity (15%), refused to stop wearing perfume (12%), did not believe that the respondent had a physical illness (7%), and refused to discuss MCS (3%). Respondents were excluded the from family gatherings (2%), called a malingerer (2%) or hypochondriac (2%), verbally abused (2%), refused visits (2%), subjected to target humour (1%), excommunicated entirely (1%) and deliberately exposed to chemicals (1%).

A little over half of the respondents reported contact with a community-based support group, although this did not correlate directly with a higher level of perceived social support. There were weak correlations between severity of condition and high support group contact.

Access to community services, public outings, shopping, and other public contacts were diminished due to the need to avoid chemical exposures. Travel by aeroplane and automobile was restricted, thereby confining respondents to small geographical areas. The application of psychiatric labels for MCS left respondents isolated from spouses, family, friends, and especially doctors. Fragrances worn by helping professionals often limited access to medical care (Reed Gibson et al 1998).

A further qualitative study by Reed Gibson et al (1996) examined life disruption in chemical injury and sensitivity. MCS was associated with reported difficulty in employment, finances, quality of available medical care, access to public spaces and resources, relationships, and with considerable personal distress.

In 2005 Reed Gibson et al looked at disability induced identity changes in people with MCS. Themes identified included loss of a stable familiar personality, loss of self-positioning, emotional suppression to meet others' expectations, life disruption, forced personal growth, spiritual discovery, and identity reconsolidation. The authors found these experiences to be congruent with other delegitimized illnesses (Reed Gibson 2005).

10.2 Contextual Factors Relating to the ICF e List

People with MCS encounter numerous complex difficulties with respect to environmental factors. The following are just some examples of the problems that arise.

Products and Technology

Personal Consumption

MCS is often associated with sensitivities to foods that are commonly consumed on a daily basis by the general population. Consequently people with food sensitivities do not have access to many foods that are routinely available and frequently require alternative, rare and often expensive food sources. Food availability is further restricted due to chemical food additives, chemicals used in food processing and packaging, agricultural pesticide residues in foods, and persistent organic pollutants present in the food chain, notably in fish, such as mercury, organochlorines, polychlorinated biphenyls, and their breakdown products.

Sensitivity to pharmaceuticals in MCS can restrict the use of medications, particularly in severe cases.

The presence of chemicals in most retail outlets is a further access barrier to these services.

Personal Use in Daily Living

People with MCS report sensitivity reactions to plastics, fabrics, clothing, furniture, and many other articles for personal use. Often these products are manufactured using chemicals associated with MCS or are actively treated with formaldehyde, pesticides, fragrances, and other toxics.

In a well publicised case in South Australia over 60 ambulance officers reported allergic-type reactions to new uniforms ranging from mild discomfort and itching to life-threatening anaphylactic shock. At least one officer developed severely disabling MCS. The offending substance was thought to be a dye or detergent (Wheatley 2007).

Personal indoor and outdoor mobility and transportation

Reactions to plastics and other synthetic materials used in personal mobility and transportation are problematic.

Products for communication

Reactions to electromagnetic fields are reported by people with MCS, thereby restricting the use of mobile and cordless telephones, and other wireless-based connectivity technologies.

Design, construction and buildings products and technology of buildings for public and private use

Volatile Organic Compounds in Indoor Air

Newly constructed, tightly sealed, and air-conditioned buildings present serious MCS-related public health and disability access problems. Contemporary building design and construction materials have been identified as one of the major contributing factors for both the initiation of MCS and for triggering symptoms once the disease is established. New building, remodelling and renovation products containing volatile organic compounds have been identified as a major contributing factor to MCS (Ashford and Miller 1998).

Attempts have been made in Australia to identify chemicals of concern in indoor air and to maximise mandatory fresh air exchange volumes, but MCS was given only the briefest consideration and dismissed as unproven (Environment Australia 2001).

While not directly addressing the problems of MCS, contemporary building standards offer the opportunity to reduce volatile organic compounds in indoor air (Green Building Council of Australia 2010, New Zealand Green Building Council 2008).

The US Centres for Disease Control and Prevention have developed comprehensive practical guidance for improving and maintaining the indoor environment. Concerns include workers with health related complaints whose symptoms improve when they are no longer in the building. Guidance is available with reference to “a variety of contaminants (in the form of gases and particles) from office machines, cleaning products, construction activities, carpets and furnishings, perfumes, cigarette smoke, water-damaged building materials, microbial growth (fungal / mold and bacterial), insects, and outdoor pollutants ... indoor temperatures, relative humidity, and ventilation levels” (Centers for Disease Control and Prevention 2011).

Australia and New Zealand have no comparative guidelines.

Products of Concern

Numerous consumer products contribute to the chemical pollutants associated with MCS.

The following is taken from a population study conducted in Atlanta, Georgia. It identifies some of the commercial products that most commonly trigger symptoms in subjects with MCS.

Product	Percentage of Subjects
Cleaners	88.4
Tobacco smoke	82.6
Perfume	81.2
Pesticides	81.2
Car exhaust	72.5
Salon/barber	60.9
New carpet	53.6
Public parks	52.2
Chlorine/water	39.1
Furniture	39.1
Fresh ink	26.1
Appliances	10.1

What actions of others produce your symptoms and how severe are they?

Barbecue grill	39.1
Others' smoke	33.3
Lawn pesticides	31.9
Laundry	18.8
Running car	14.5

(Caress and Steinemann 2003)

The following is taken from a population study of chemical sensitivity in South Australia. It identifies what percentage of people in the general population report "serious" health problems from common chemical products.

Product	Percentage of Subjects
Perfume	7.1
Traffic pollution	5.3
Household chemicals	5.6
Workplace chemicals	6.2

(Fitzgerald 2008)

Tobacco

Although bans on tobacco smoking apply to many indoor areas, smoking in doorways, access corridors and public areas remains problematic.

Pesticides

Australia has one of the highest rates of per capita pesticide consumption in the world and an almost universal cultural acceptance of the widespread use of pesticide. This situation presents major difficulties for people with MCS in terms of safe access to buildings, gardens, public spaces, and agricultural areas that are treated with pesticides. Similar circumstances apply in New Zealand.

An example of the continuing widespread use of pesticides associated with MCS is the organophosphate chlorpyrifos. Over the last decade or more, in response to new data on health and safety concerns, several reviews of chlorpyrifos have been undertaken by the Australian Pesticides and Veterinary Medicines Authority resulting in bans on its residential use, and the voluntary withdrawal of many chlorpyrifos-based products by manufacturers. However, it is still widely used in agriculture. In 2009 there were 85 registered chlorpyrifos products available in Australia (Australian Pesticides and Veterinary Medicines Authority 2009).

Synthetic pyrethroids are commonly used in household insect sprays and surface sprays.

Fragrances

Modern fragrances in personal care, cleaning, deodorising, and many other products are composed of volatile organic compounds known to be associated with initiating and triggering symptoms of MCS. The ubiquitous use of these products is a serious matter of public health and disability access concern. Personal fragrances are consistently reported as most frequently triggering symptoms of MCS. In South Australia's chemical sensitivity study over 7% of the population reported "serious" health problems from perfume (Fitzgerald 2008, Caress and Steinemann 2003).

International efforts are being made to control the use of fragrances in public institutions and other shared spaces. Similar strategies are slowly being adopted in Australasia.

Natural Environment and Human Made Changes to Environment

Climate

People with MCS often do not tolerate rapid temperature changes or temperature extremes (Ziem and McTamney 1997).

Light

Sensitivity to light, both natural and artificial, is reported. Artificial light sources that generate electromagnetic fields, particularly fluorescent lighting, can be problematic.

Sound

Sensitivity to ambient sounds is reported, sometimes requiring people with MCS to seek isolated living areas away from common sources of noise.

Support and Relationships

Immediate family, friends

The work of Reed Gibson and associates described above has provided data on the disruptive influence of MCS with respect to family and personal relationships.

Acquaintances, peers, colleagues, neighbours

Interpersonal conflict is a common feature of MCS, particularly in high density housing, due to the ubiquitous use of chemical products in the wider community - fragrances, laundry and cleaning agents, air fresheners, paints and renovation materials, pesticides, combustion heating, etc. This situation is not assisted by the fact that ignorance of MCS is widespread, that MCS is frequently seen as a psychological condition, or that the complaints of people with MCS are simply not believed. MCS accommodation requests are often seen as unnecessary and inconvenient demands (Reed Gibson et al 1998).

People in positions of authority

The lack of formal recognition of MCS by authorities results in major disadvantage and discrimination against people with MCS.

Personal care providers and personal assistants

Good relationships with personal care providers and assistants are dependent to a measurable degree on the extent to which people with MCS are accommodated with respect to their environmental sensitivities (Reed Gibson et al 1998).

Health and health-related professionals

It is well recognised that there has been a prolonged and often vituperous medical dispute, lasting over many decades, regarding the aetiology of MCS which has not assisted the care and welfare of people suffering the disease. Most health care and allied services are relatively inaccessible to MCS patients due to both chemical and attitudinal barriers. Health care services are highly chemicalised environments due to the need for infection control, general hygiene and medical treatments. Conventional health professionals do not usually recognise MCS and are often poorly informed.

There is no training in environmental illness in medical schools. Medical assumptions regarding a psychological aetiology for MCS often prevail, despite the existence of the large body of evidence to the contrary, and also the rejection of the dualistic mind-body paradigm by science (Pall 2009b). Medical services have been noted to be particularly reluctant to accommodate patients with MCS (Governor's Committee on Concerns of the Handicapped 1996). Consequently access to well-informed, supportive medical care is highly restricted for people with MCS.

Doctors in Australia, New Zealand and elsewhere who approach the care of MCS patients from a physiological perspective challenge medically accepted disease paradigms and often face peer pressure, isolation and censure by their colleagues, and investigation by medical insurers. These medical professionals justify their continued patient advocacy with an altruistic moral discourse and an ethical commitment to "truth" (Phillips 2010). Medical services offering informed treatment and care together with adequate disability accommodation for MCS patients are often heavily booked and expensive, or only available in distant locations. However, patients who are able to access this type of care, sometimes known as Environmental Medicine, often report greatly improved health benefits (Reed Gibson 2005).

Conventional medical attitudes towards MCS are slowly changing. In 2010, in response to the Social Development Committee Inquiry into MCS (2005), the South Australian Department of Health introduced Multiple Chemical Sensitivity (MCS) Guidelines for South Australian Hospitals. These guidelines acknowledge the kind permission of Queensland Health to adapt the Royal Brisbane and Women's Hospital MCS guidelines for use in South Australia (SA Health 2010). Despite this acknowledgment the Royal Brisbane and Women's Hospital has apparently not ratified its MCS guidelines and refuses to make them publicly available.

Although MCS hospital guidelines exist in South Australia anecdotal reports indicate that they are not being respected by health care staff. Patients with MCS continue to be subjected to intolerable chemical exposures that threaten their health status and prevent them from accessing hospital-based care. Similar difficulties are reported routinely to community-based MCS support groups throughout the Australasian region.

MCS Hospital Guidelines exist in Western Australia, and include advice on discharge planning and care in the community, but they currently only apply to country regions (WA Country Health Service 2010).

Attempts by MCS community advocacy groups in New Zealand to have Australian MCS hospital guidelines adapted for official use have been rejected by health authorities. Similar circumstances apply in the Australian Capital Territory and the state of Victoria, where MCS hospital guidelines have been under consideration by health authorities but have not been ratified.

With regard to community-based health services in South Australia the Social Development Committee Inquiry into MCS made recommendations that the Department of Health "consider developing appropriate protocols and procedures that enable greater access to health care services for people with MCS" (Social Development Committee 2005). This recommendation was rejected by the state government on the basis that work had already commenced on MCS hospital guidelines (Government of South Australia 2005). Currently the MCS Guidelines for

South Australian Hospitals are not applicable to community-based health care and allied services. Similar circumstances apply across the entire Australasian region.

There is a real and urgent need to ensure that people with MCS are adequately accommodated in health care in order to provide equitable access to services that are considered a basic right under Article 25 of the United Nations Universal Declaration of Human Rights.

Article 25.

(1) Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care and necessary social services, and the right to security in the event of unemployment, sickness, disability, widowhood, old age or other lack of livelihood in circumstances beyond his control.

(General Assembly of the United Nations 1948).

The MCS Society of Australia has published a discussion paper on improving hospital access for people with MCS. The paper offers recommendations and practical guidance on measures such as improving indoor air quality, safer cleaning and disinfection, fragrance-free policy, pest management, furnishings and carpets, MCS patient protocols, and compliance with state and commonwealth disability discrimination acts (Clark 2010).

The Need for Specialist Environmental Medical Units (EMU)

In Australia and New Zealand there are no specialist public health care services for patients with MCS. In Australia two private hospital-based EMUs offered services in the past but both these facilities have been closed for around a decade or more (Social Development Committee 2005). The dedicated medical practitioners who once operated these hospital clinics now provide services from their private consulting rooms.

There is an urgent need in Australia and New Zealand to establish publicly funded specialist health care services for environmental illness treatment and research, similar to that offered by the Nova Scotia Environmental Health Centre in Canada. The following is extracted directly from their website.

Environmental Health Centre

Mission Statement

The Nova Scotia Environmental Health Centre is dedicated to care of people with chronic illness related to the environment; research into causes and effective treatments and education.

Patient Population

The Nova Scotia Environmental Health Centre is a treatment facility for individuals with chronic illness such as Multiple Chemical Sensitivity (MCS), Chronic Fatigue Syndrome (CFS), Fibromyalgia (FM) and other environmentally related conditions.

Treatment Approach

Our treatment approach is holistic and in line with the [Health Canada's 12 Determinants of Health](#). We function through a managed collaborative team. The care team includes a multidisciplinary team of clinicians and the patient.

The centre offers a clean environment to its patients by following a strict [no scent policy](#) with the staff and patients adhering to the use of specific products for personal use.

Understanding that patients need to be treated and research conducted in a clean environment, the physical environment has been carefully designed. Architects worked closely with patients and staff to make sure all aspects of the design, structure and building of the NSEHC provided a clean, safe environment. All materials used in construction of the Centre went through rigorous testing before being used. Consultants, patients, staff and architects worked together to make sure these materials were safe and would not interfere with the testing or research being done at the Centre. A few of our publications give a detailed description of construction strategies adopted and construction materials used in the design and operation of this unique facility.

At the NSEHC, we offer optimal care for the patients by emphasizing the following goals:

- Provide validated testing and treatment for environmental sensitivities.
- Patient education.
- Disseminate knowledge through publications, conferences and newsletters
- To research environmental sensitivities in close collaboration with affected individuals, health care professionals and research scientists.
- To advise provincial and national agencies working to develop policies related to recognizing, preventing and treating environmental sensitivities.

(Nova Scotia Environmental Health Centre 2011).

Attitudes

Improving attitudes towards MCS through education programs is vital.

Individual attitudes

Much has already been described above regarding the impacts of individual attitudes towards MCS, both the positive and negative. Even in circumstances where families, friends and others may not fully understand MCS, a supportive and accepting attitude towards people with MCS significantly improves their quality of life and ability to engage with society.

In South Australia the Social Development Committee (2005) recommended that the Department of Health “coordinate the dissemination of information on MCS to a wide range of organisations and groups including medical practitioners, local Councils, and the general public”.

Societal attitudes, social norms, practices and ideologies

Reed Gibson (2005) describes the cultural response to MCS as “almost entirely negative” and has indicted the attitudes and standards of industrialism as the cause of MCS.

In a qualitative interview of 26 subjects Reed Gibson et al (2011) found lack of spatial access as a major factor in limiting the ability of people with MCS to cultivate new relationships. Societal lack of understanding and refusal to accommodate people with MCS interacted with these factors to keep people with MCS isolated in a culture where chemical exposures are common.

Dr Ann McCampbell, MD, Chair of the MCS Task Force of New Mexico, has disclosed a highly sophisticated collaboration of chemical and pharmaceutical industrial interests whose aim is to “create the illusion of controversy about MCS and cast doubt on its existence” (McCampbell 2001).

Pall (2009b) has noted that advocates of a psychogenic aetiology in MCS have clear conflicts of interest and have failed to consider the impacts on humans of chemicals associated with MCS, or to look at animal models associated with MCS, or to offer any objective assessment of the available literature on MCS, and that medicine has a long history of “false psychogenic attribution”.

Social and medical opinions that adopt a dismissive psychogenic attitude towards MCS are extremely unhelpful. Chemical sensitivity reactions occur in people with MCS regardless of the attitudes and opinions of others. MCS is highly unresponsive to curative psychotherapies (Reed Gibson et al 2003).

Numerous commentators have compared MCS with the negligent and scandalous circumstances that have surrounded other public health fiascos such tobacco and asbestos.

Services Systems and Policies

Direct and indirect discrimination against people with MCS is both widespread and firmly institutionalised. Many people with MCS are either unaware of their disability rights under the Australian federal *Disability Discrimination Act*, state-based equal opportunity acts, and the New Zealand *Human Rights Act*, or they simply do not have the personal health, financial resources, and organisational support required to pursue discrimination complaints.

Chemical Regulation

MCS is not considered with regard to risk evaluation in chemical regulation. People in the general community often wrongly assume that regulated chemical exposure standards must apply to everyone and may attempt to justify their discrimination against people with MCS on that basis.

The absence of regulatory action on MCS has widespread consequences, particularly with respect to agricultural and residential pesticide spray drift and residues, the use of organic solvents in building and renovation materials, and the accepted levels of pesticide residues and other chemicals in food.

The Inquiry into MCS in South Australia recommended that consideration be given to “undertaking a review of the adequacy of the current chemical regulatory structure and assessment processes in addressing issues raised by people with MCS with regard chemical use, including the adequacy of health and safety labelling information on chemicals associated with MCS” (Social Development Committee 2005).

The Australian government is currently conducting a review of national chemical regulation – Better Chemical Regulation. However, there has been no indication that this review will consider MCS.

Herbicide

The Inquiry into MCS in South Australia heard evidence that the organophosphorous herbicide glyphosate, the active ingredient in Monsanto’s Roundup, is a chemical frequently identified as causing and triggering the symptoms associated with MCS. Roundup and other glyphosate-based herbicides are used extensively by local governments in Australia and New Zealand to control weeds in roadsides and other public areas.

The Inquiry recommended that Local Governments:

- Establish No-Spray Registers to identify residents with MCS and chemical sensitivities.

That the Department of Primary Industries:

- Encourage the adoption of best practice in chemical use,
- Advise local governments on working with local communities to implement best practice chemical use,
- Ensure local governments clearly understand their legal obligations under Control of Use legislation.

And that the relevant State Government Ministers:

- Lobby the Federal Government to research alternative weed control measures,
 - Ensure the findings of such research are made available to Local Government,
- (Social Development Committee 2005)

None of these recommendations have been fully implemented to date, although work in South Australia is proceeding on No-Spray Registers. Other states and territories in Australia and New Zealand are slowly adopting similar No-Spray Register reforms in response to residents' complaints and growing public concerns. Less than a handful of local governments have ceased using herbicide in street maintenance, an example being Fremantle, Western Australia, where steam treatment is used. A few jurisdictions have attempted herbicide-free maintenance but have returned to herbicide use due to cost concerns.

The official response in Australia and New Zealand to the emerging data on the adverse public health effects of pesticides and herbicides has been very poor. This compares extremely unfavourably with the international response. In Canada, for example, over 120 municipalities have ceased using pesticides (including herbicides) in city maintenance and have placed bans and other restrictions on the private, cosmetic use of pesticides. The legal right of local governments to enact pesticide by-laws has been repeatedly challenged by commercial pesticide interests but consistently upheld by Canadian courts.

A best practice review of international pesticide by-laws aimed at reducing the cosmetic use of pesticides found that education alone was not sufficient to significantly change public behaviour. Reductions in public pesticide use were best achieved through a combination of education, local by-laws and supportive state and federal legislation (Kassirer 2004).

Disability Discrimination Guidelines

In response to reports of people being "affected by sensitivity to chemicals used in the building, maintenance and operation of premises", the Australian Human Rights Commission (2011) included notes on the use of chemicals and materials in its guidelines on access to buildings and services. These notes included references to more extensive guidelines previously developed in the USA by the Job Accommodation Network (see below).

Although the South Australian government has published disability access guidelines to government owned and leased buildings that include questions on MCS (Department for Transport Energy and Infrastructure 2006), compliance with the MCS aspects of these guidelines is virtually non-existent.

No other Australian state or territory has developed MCS disability access guidelines.

New Zealand has no disability access guidelines for MCS. Although MCS is thought to fall within the legislated prohibited grounds of discrimination, the New Zealand Human Rights Commission has advised that this position has not been legally tested (Human Rights Commission 2010).

Similar circumstances apply in Australia, where there is little jurisprudence on MCS, apart from an Australian Capital Territory Discrimination Tribunal ruling which upheld the complaint of a woman with MCS regarding her need for fragrance controls in group therapy (Wilkie and Baker 2007).

The USA's National Institute of Building Sciences, in collaboration with the Architectural and Transportation Barriers Compliance Board, and with MCS community support and advocacy organisations, has produced comprehensive MCS disability access guidelines (National Institute of

Building Sciences 2005). The US Job Accommodation Network, under contract from the Department of Labor's Office of Disability Employment Policy, has published accommodation guidelines for employees with MCS/environmental sensitivities, (DeFreitas Saab 2010a) and fragrance sensitivity (DeFreitas Saab 2010b).

The Canadian Human Rights Commission (2007) has published extensive policy guidance on environmental sensitivities, including: The Medical Perspective on Environmental Sensitivities (Sears 2007) and Accommodation for Environmental Sensitivities: Legal Perspective (Wilkie and Baker 2007).

Access to Restorative Justice

Many people acquire MCS in the workplace or elsewhere as a result of pesticide applications, renovations, remodelling, new buildings, or occupational chemical exposures. The experience of these people is that their injury, and resulting chronic illness and disability, is routinely denied by employers, contractors and insurers. Increasingly they are successfully winning financial compensation but only after a prolonged, costly and exhausting legal struggle. Medical specialists who act as witnesses for the victims of chemical injury are being treated as deviants by their peers and face substantial professional disillusionment and emotional drain (Phillips 2010).

Social Security

People with MCS in Australia and New Zealand are eligible for the disability support pension on a clinical case-by-case basis requiring medical confirmation of their MCS diagnosis and associated disability. This situation presents significant hardships given the lack of recognition of MCS within mainstream medical culture.

Unlike conventionally recognised disabilities, financial assistance to purchase and maintain essential MCS-related disability aids such as air and water filters, oxygen supplies/generators, and absorbent face masks is not provided by social security services in Australia or New Zealand. In addition, public health care services often do not subsidise the numerous and expensive specialist medical tests and treatments required by people with MCS.

In South Australia the Social Development Committee's recommendation "that the State Government's Minister for Disability lobby the Federal Government to consider providing some Federal assistance for essential aides and items to assist people with severe disabilities arising from MCS symptoms in managing their condition" was not supported by state government (Government of South Australia 2005).

Access to Employment

National occupational health safety and welfare standards in Australia and New Zealand do not recognise MCS. Only a handful of private workplaces in Australia have adopted MCS-related

disability access and occupational health and safety guidelines, examples being the Disability Advocacy and Complaints Service SA, the Disability Information and Resource Centre SA, and the AIDS Council of SA. Everyday use of personal fragrances, air fresheners, and toxic cleaning products in the workplace is particularly problematic. Many people with moderately severe MCS, who could work if they were given appropriate accommodation, are excluded from participation in the workforce due to chemical barriers.

A population study by Caress and Steinemann (2003) found that over 13% of people with chemical hypersensitivity had lost their jobs due to chemical intolerance. This represents nearly 2% of the total population.

Access to Education

Children with MCS are particularly disadvantaged with respect to education. A review of literature relating to indoor air quality and building-related health problems in schools found evidence that “sick building syndrome” is commonly reported, and that these symptoms are related to volatile organic compounds (VOC), moulds and microbial VOCs, and allergens (Daisey et al 2003). In Australia and New Zealand government education departments have no formal policies on MCS. Anecdotal evidence suggests that education authorities are generally disinterested in recognising and accommodating MCS. There are reports of parents having to resort to home schooling to educate their MCS-affected children.

Increasingly universities in Australia are attempting to respond to individual disability access requests from students affected by MCS but clear policy guidelines have yet to be developed.

Access to Housing

Reed Gibson et al’s (1998) research describes how many people with MCS live in extreme circumstances and that even their own homes made them sick. Respondents reported living totally housebound for long periods (38%), living in cars (4%), in tents (3%), in trailers or campers (2%), on patios (1%), in cleaned-out garages (1%), in a community of porcelain trailers (1%), and totally outdoors (1%). The inability to live in conventional housing necessitated physical separation even from immediate families.

Similar circumstances exist in Australia and New Zealand where public housing authorities have no formal guidelines on MCS. Although isolated attempts are sometimes made to house individuals with MCS, public housing applicants are often rejected on the basis that they do not technically qualify for the type of housing required. Rental accommodation is particularly uncertain as landlords are generally ignorant of MCS and are often unwilling to accommodate their MCS affected tenants.

Transportation Services

Public transport services in Australia and New Zealand have no MCS disability accommodation guidelines. The widespread use of personal fragrances represents a major access barrier to public transport. Taxi services routinely use chemical-based air fresheners and fragranced cleaning products.

Vehicle exhaust is one of the most frequently reported symptom triggers in MCS.

10.3 Body Functions Relating To the ICF b List

Functional disruptions in MCS across all areas of the ICF b list are well documented in the medical literature (Ashford and Miller 1998, Caress and Steinemann 2003, Pall 2009a, Ross 1992, Ziem 2001, Ziem and McTamney 1997).

Consistent with the diagnostic criteria for MCS (Bartha et al 1999), symptom severity is frequently associated with environmental exposures.

MCS Patient Profiles

The following are based on the results of study profiles of symptoms amongst patients with chemical injury and sensitivity.

Functional Affect	Approximate Percentage of Subjects
Confusion/inability to concentrate	70%
Unusually low energy and fatigue	70%
Memory problems	68%
Slurred words	58%
Headache	57%
Dizzy and lightheaded	55%
Weakness in body part	54%
Throat soreness, tightness	52%
Joint discomfort	52%
Numbness/tingling	51%
Co-ordination difficulties	50%
Nasal discharge, stuffiness	50%
Muscle discomfort/spasm	49%
Visual changes	48%
Sinus discomfort	47%
Urinary frequency	47%
Chest heaviness/pain	46%
Itchy, watery eyes and nose	43%
Weak voice, hoarseness	43%
Coughing	42%

Chest tightness	41%
Abdominal pressure, cramps, and pain	40%
Unusual thirst	40%
Flushing skin	39%
Tinnitus	35%
Insomnia	35%
Muscle twitching	35%
Sneezing	34%
Changes in hearing	33%
Difficulty swallowing	33%
Other sleep disturbance	32%
Itching, rash, hives	31%
Tremor or shaking	30%
Reduced cold tolerance	30%
Reduced bladder control	26%
Ectopic beats	25%
Rapid pulse	25%
Wheezing	25%
Reduced heat tolerance	24%
Swelling throughout body	22%
Swollen glands	22%
Swelling of ankles	18%
Frequent infections	11%
Flare up of yeast infection	8%
Fever	5%
Spontaneous bruising	4%

(Ziem and McTamney 1997)

The following is taken from the Nova Scotia Environmental Sensitivities Research Centre study of the prevalence of major symptoms, ranked in order of frequency, in subjects drawn from an environmental sensitivity referral centre.

Functional Affect (Symptom)	Percentage Of Subjects
In general	
Difficulty concentrating	95%
Fatigue, very tired, without energy	95%
Tiredness not relieved by rest or sleep	92%
Sneezing/runny or congested nose without a cold	91%
Forgetfulness/poor memory	90%
Irritability	90%
Other headache	88%
Itchy eye(s)	88%
Trouble finding the right words	86%
Need to clear throat	85%

Difficulty making decisions	84%
Stuffy or full sinuses	83%
Muscle pain or ache not related to overexercise	83%
Stiffness in muscles or joints	83%
Feeling light-headed	82%

After exposure

Sneezing/runny or congested nose without a cold	66%
Itchy eye(s)	64%
Difficulty concentrating	54%
Other headache	52%
Burning eye(s)	50%
Hoarse or loss of voice	49%
Stuffy or full sinuses	46%
Forgetfulness/poor memory	46%
Tight chest	45%
Usually acceptable odours were sickening	44%
Fatigue, very tired, without energy	43%
Difficulty making decisions	43%
Trouble finding the right words	43%
Irritability	43%
Feeling light-headed	43%

Top five symptoms scores reported among individuals with environmental sensitivities.

Functional Affect (Symptom)	Occurrence Frequency (Maximum Score Is 12)
------------------------------------	-------------------------------------------------------

In general

Stronger sense of smell	8.8
Fatigue, very tired, without energy	7.4
Tiredness not relieved by rest or sleep	7.4
Less sense of smell than most people	7.0
Usually acceptable odours were sickening	6.7

After exposure

Stronger sense of smell	9.6
Tiredness not relieved by rest or sleep	7.8
Trouble seeing at night	7.5
Bruise easily	7.3
Sensitive to temperature change	7.3

(Joffres et al 2001)

Syncope and thrombosis have been reported anecdotally as a consequence of chemical exposure in MCS (Reed Gibson 2005)

Depression and anxiety are commonly reported in MCS (Ashford and Miller 1998, Pall 2009a). In a population study in Atlanta, Georgia, only 1.4% of subjects with MCS had a prior history of emotional problems before the onset of MCS, whereas 37.7% developed them after physical symptoms emerged (Caress and Steinemann 2003). This supports the conclusion that MCS has a physical not a psychological aetiology (Caress and Steinemann 2003, Pall 2009a;2009b, Ashford and Miller 1998, Winder 2002, Saito et al 2005, Goudsmit and Howes 2008).

Attacks of rage have been reported to occur in response to chemical exposures in MCS (Pall 2009a).

Disruptions in higher level cognitive function, memory and concentration are reported (Ashford and Miller 1998, Pall 2009a).

Hypertension, orthostatic intolerance, and abnormal heart rate and pulse pressure responses to exercise, are commonly reported in MCS and are thought to be related to autonomic nervous system dysfunction (Pall 2009a, Ziem and McTamney 1997, McFetridge-Durdle et al 2009).

Sexual dysfunction is commonly reported (Ashford and Miller 1998)

11 SPECIFIC CONDITION PROPERTIES

11.1 Biological Sex

Gynaecological disorders, dysmenorrhoea, pre-menstrual syndrome, are documented (Mabray 1982/1983; 1983, Ashford and Miler 1998). Endometriosis is anecdotally reported.

11.2 Lifecycle Properties

Both Mabray (1982/1983; 1983) and Rea (1988) have reported infertility in MCS.

12 TREATMENT PROPERTIES

Avoidance of chemicals, foods and pharmaceuticals that trigger symptoms is highly recommended as a fundamental treatment strategy in MCS. This includes avoiding conventional agricultural produce grown with pesticides, and processed foods containing chemical additives (Pall 2009a, Ashford and Miller 1998).

An assessment of the self-reported effectiveness in a range of alternative and conventional treatments found the most effective treatments by many orders of magnitude were:

- maintenance of a chemical-free living space, and
- chemical avoidance.

Air filter and rotation diet are also rated highly (Reed Gibson et al 2003).

A rotation diet requires that related food groups are eaten only once over a period of four to five days to avoid prolonged exposure and subsequent sensitization to naturally occurring food chemicals.

Underlying infections should be identified and treated as effectively as possible. Antibiotic therapy should be approached with caution due to drug sensitivity reactions. However, where antibiotics are tolerated clinical improvements are reported in nearly half of MCS subjects (Reed Gibson et al 2003).

Stress reduction, including avoidance of excessive exercise and psychological stressors, is considered an important aspect of therapy (pall 2009a).

The symptomatic treatment of MCS needs to be approached with the understanding that sensitivity reactions to a wide range of pharmaceuticals are common. Medications should be introduced with caution as anecdotal reports indicate that therapeutic responses to medications can occur at doses far below what would normally be prescribed. Overdose may occur in these circumstances.

Pall's NO/ONOO disease paradigm recommends focussing on treatments that down-regulate the production of NMDA as opposed to simply treating the multiple symptoms of MCS. A summary of potential agents and the basis on which they are recommended appears below.

NO/ONOO- Cycle Summary of Individual Agents or Classes of Agents

Agent or Class of Agents	Clinical Trial Data or Clinical Observation/Anecdotal Reports
Vitamin C (ascorbic acid)	Clinical Trial Data
Tocopherols/Tocotrienols	Anecdotal Reports
Selenium	None
Carotenoids	None
Flavonoids	Clinical Trial Data
Reductive stress relieving agents	Clinical Trial Data
Mitochondrial regeneration agents	Clinical Trial Data
L-Carnitine/Acetyl-L-carnitine	Clinical Trial Data
Hydroxocobalamin/B12	Clinical Trial Data

Folic acid	Clinical Trial Data
Vitamin B6/pyridoxal phosphate	Anecdotal Reports
Riboflavin	None
Other B vitamins	None
Glutathione/glutathione precursors	Clinical Observations
a-Lipoic acid	None
Magnesium	Clinical Trial Data
SOD minerals/zinc,manganese, copper	None
NMDA antagonists	Clinical Trial Data
Riluzole	None
Taurine	None
Inosine/uric acid	None
Long chainomega-3 fatty acids	Clinical Trial Data
Agents that lower NF-kB activity	Anecdotal Reports
Curcumin	None
Algal supplements	Clinical Trial Data
Hyperbaric oxygen	Clinical Trial Data
Minocycline and Other Tetracyclines	Clinical Observations
Creatine	None
Lowered vanilloid activity	None
Carnosine	None
TRH	Clinical Observation
D-ribose	Clinical Trial Data
Ecklonia cava extract	Clinical Trial Data

(Pall 2011c)

Exotoxins predicted to up-regulate NMDA, such as aspartame and mono-sodium glutamate, should be avoided (Pall 2011c).

A number of other professionals in the area of MCS, including Teitelbaum, Nicolson, Cheney, Petrovic, and Ziem have independently developed treatment protocols using similar agents (Pall 2011c).

Pall and Ziem have offered a combined treatment protocol.

Agents from Pall/Ziem Protocol Predicted to Down-Regulate NO/ONOO- Cycle Biochemistry

Nebulized, inhaled reduced glutathione
Nebulized, inhaled hydroxocobalamin (sometime also use sublingual)
Mixed, natural tocopherols including g-tocopherol
Buffered vitamin C
Magnesium as malate
Four different flavonoid sources: Ginkgo biloba extract, cranberry extract, silymarin, and bilberry extract
Selenium as selenium-grown yeast
Coenzyme Q10
Folic acid
Carotenoids including lycopene, lutein and b-carotene
a-Lipoic acid
Zinc (modest dose), manganese (low dose) and copper (low dose)
Vitamin B6 in the form of pyridoxal phosphate
Riboflavin 5'-phosphate (FMN)
Betaine (trimethylglycine)

(Pall 2011c)

Ziem has added three agents: green tea extract, hawthorn extract and acetyl L-carnitine.

Clear and distinct clinical improvements are reported in patients adopting the Pall/Ziem protocol (Pall 2009a).

Research programs for MCS treatments, including clinical trials, are urgently needed.

13 DIAGNOSTIC CRITERIA

Bartha et al 1999 Consensus Criteria

Consensus criteria for MCS were first identified in 1989 via a multidisciplinary survey of 89 clinicians and researchers with broad experience but widely diverse opinions of MCS.

In 1999 Bartha et al proposed the following six consensus criteria for the definition of MCS, the first five of which were identified in 1989.

1. Symptoms are reproducible with repeated (chemical) exposures.
2. The condition has persisted for a significant period of time.
3. Low levels of exposure (lower than previously or commonly tolerated) result in manifestations of the syndrome (i.e. increased sensitivity).
4. The symptoms improve, or resolve completely, when the triggering chemicals are removed.
5. Responses often occur to multiple, chemically unrelated substances.
6. Symptoms involve multiple-organ symptoms.

These criteria are probably the most widely accepted definition of MCS (Pall 2009b). They have been assessed as being effective for making clinical distinctions between patients with MCS and other chronic illnesses (McKeown-Eyssen et al 2001).

The use of these criteria when comparing occupational practice patients and general practice patients produced a high odds ratio suggesting that occupational chemical exposures are a frequent cause of MCS (McKeown-Eyssen et al 2001, Pall 2009b).

Proposed Alterations to the 1999 Criteria

Pall has expressed concern that the 1999 consensus criteria refer to “chemically unrelated substances”. Given that all of the chemicals associated with MCS may act to produce increased levels of NMDA, Pall has suggested that “chemically diverse” is a more accurate description. He has offered the following alteration to the 1999 criteria which would “not change how the case definition is used in practice”:

1. Symptoms are reproducible with repeated (chemical) exposures.
2. The condition has persisted for a significant period of time.
3. Low levels of exposure (lower than previously or commonly tolerated) result in manifestations of the syndrome (i.e. increased sensitivity).
4. The symptoms improve, or resolve completely, when the triggering chemicals are removed.
5. Responses occur to multiple, chemically diverse substances.
6. Symptoms include those derived from multiple organs.

(Pall 2009b)

Pall has also offered the following definition which includes the proposal by Lacour et al (2005) that symptoms of the central nervous system be included as a necessary criterion for the diagnosis of MCS.

1. Symptoms are reproducible with repeated (chemical) exposures.
2. The condition has persisted for a significant period of time.
3. Low levels of exposure (lower than previously or commonly tolerated) result in manifestations of the syndrome (i.e. increased sensitivity).
4. The symptoms improve, or resolve completely, when the triggering chemicals are removed.
5. Responses occur to multiple, chemically diverse substances.
6. Symptoms include those derived from apparent CNS sensitivity, such as chemically elicited headache, fatigue, depression, anxiety, memory and concentration difficulties and confusion and cognitive dysfunction.

(Pall 2009b)

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