

**Information on MULTIPLE CHEMICAL SENSITIVITY  
as a component of Myalgic Encephalomyelitis**

**Margaret Williams (updated) February 2012**

There are many thousands of papers on multiple chemical sensitivity (MCS), most of which are available on the internet.

Multiple Chemical Sensitivity is a well-documented component of myalgic encephalomyelitis (ME) / chronic fatigue syndrome (CFS).

Multiple Chemical Sensitivity is classified in the World Health Organisation's International Classification of Diseases (ICD-10) at T78.4 (Allergy, Unspecified).

Of note is the fact that the brochure from Healthcare at Home Ltd includes Total Allergy Syndrome, the most severe form of MCS, as a condition for which they provide NHS Homecare. They advertise themselves as the UK's leading provider of home healthcare, with over 100,000 patients each year. Their services are paid for by the NHS and by private medical insurers, as well as by self-funding patients.

ME has been classified in the WHO ICD-10 as a neurological disorder since 1969, currently at ICD-10 G93.3 under "Disorders of Brain".

The term "chronic fatigue syndrome" (CFS) is used as an alternative name but it is coded only to ME at G93.3, hence the use of the term ME/CFS.

Throughout the ME/CFS literature there is extensive reference to allergies and hypersensitivities to foods, normal household chemicals, perfumes, petrol and therapeutic drugs.

It is important to be aware that certain psychiatrists who work for the insurance industry have hi-jacked the term "CFS" to mean a somatisation (mental/behavioural) disorder consisting of "chronic fatigue" or tiredness that they believe is caused by aberrant illness beliefs and deconditioning, into which they have repeatedly tried to subsume ME, inverting the acronym and referring to their own construct as "CFS/ME". As these psychiatrists are advisors to Departments and agencies of State, it is this acronym that has been adopted by official bodies, giving rise to considerable confusion

as well as loss of due benefits to claimants, as mental disorders receive lower rates of State benefit and are excluded from insurance cover.

Since 2003 ME/CFS has been classified in the Read Codes used by all UK General Practitioners as a neurological disease at F286. (In the Read Codes, the code "F" relates to neurological disorders and should not be confused with the code "F" in the ICD, which relates to mental and behavioural disorders). Allergy Unspecified is classified as Read Code SN53.

From its launch on 10<sup>th</sup> March 2005 by the Department of Health, the UK National Service Framework for chronic neurological disorders has included ME/CFS.

The UK Department of Health (DoH) accepts ME/CFS to be a neurological disorder; for example:

- (i) the letter dated 11<sup>th</sup> February 2004 from Lord Warner, Parliamentary Under Secretary of State, Department of Health, to the Countess of Mar refers to the ICD classification:: *"The Department accepts that...chronic fatigue syndrome is indexed to the neurology chapter and fatigue states to the mental health chapter"*
- (ii) the letter of 8<sup>th</sup> November 2007 (reference PO00000245876) from Ann Keen MP, Parliamentary Under Secretary of State, stating: *"The WHO classifies CFS/ME as a neurological disease...We have long recognised the WHO classification of CFS/ME"*
- (iii) the letter of 24<sup>th</sup> November 2009 from Mrs Lorraine Jackson, Senior Policy Manager at the DoH, to the Director General of the Association of British Insurers which states: *"The Department of Health accepts the World Health Organisation's (WHO) classification of CFS/ME as a neurological condition of unknown cause"*
- (iv) Lord Darzi, Parliamentary Under-Secretary of State, Department of Health, is on record in Hansard (2<sup>nd</sup> June 2008) stating: *"My Lords, I have acknowledged that CFS/ME is a neurological condition....the Government has made it clear that they consider that CFS/ME should be classified as a neurological condition....I will encourage the Royal College of General Practitioners to look at the WHO classification, which, as I said earlier, is that it is a neurological rather than a mental condition"*
- (v) on 12<sup>th</sup> September 2011, Paul Burstow Minister of Health, reaffirmed the Department of Health's position: *"The Department classes CFS/ME as a long-term neurological disease of unknown cause"*

- (vi) Lord Freud, Minister for Welfare Reform, stated in a letter dated 21<sup>st</sup> November 2011 to the Countess of Mar: *“The Department of Health has indicated that they have ‘always relied on the definition set out by the World Health Organisation in its International Classification of Diseases (ICD) under ICD code G93.3, subheading Other Disorders of the Brain’. The DWP is in agreement with this view....Therefore, for the avoidance of doubt, I can be clear that the Department (ie. the DWP) does not classify CFS/ME as a mental health disorder”.*

**It has been known since at least 1992 that ME/CFS/MCS patients have an immune system that responds over-emphatically to environmental or internal stimuli and that aspects of the immune reaction may not be stoppable even after an insult is over (WK Cho & GH Stollerman; Hospital Practice 1992:221-245).**

It is essential to recognise that MCS involves multi-system and multi-organ damage brought about by a wide variety of chemicals and that a key aspect of MCS is the development of cross-sensitivity which results in sensitivity to compounds to which there has been no previous exposure (the “spreading phenomenon”). This makes the life of an MCS patient very uncertain. Patients with MCS must live in a protected environment with scrupulous attention to every detail of their life in order to avoid becoming severely ill at any time. The systems most involved are the neurological, immunological, endocrinological, musculo-skeletal, gastrointestinal, cardiovascular and respiratory systems.

People who have MCS as an additional component of ME/CFS are internationally recognised as being amongst the most severely affected.

### **Major textbooks on MCS**

The decisive medical textbook on MCS by Professor William Rea was published by CRC Lewis Publishers (New York) in four separate volumes:

Chemical Sensitivity (Vol I): Principals and Mechanisms (1992)

Chemical Sensitivity (Vol II): Sources of Total Body Load (1994)

Chemical sensitivity (Vol III): Clinical Manifestations of Pollutant Overload (1995)

Chemical Sensitivity (Vol IV): Tools of Diagnosis and Methods of Treatment (1997).

There are two other important textbooks:

Chemical Exposures: Low Levels and High Stakes. NA Ashford, CS Miller  
Pub: Van Nostrand Rheinhold, New York, 1991. ISBN 0-442-00499-0.

Environmental Medicine in Clinical Practice. H Anthony, S Birtwistle, K Eaton, J Maberley.  
Pub: BSAENM Southampton 1997 ISBN 0-9523397-2-2.

**Three important papers merit due attention:**

One notable paper is entitled "A review of multiple chemical sensitivity" by RA Graveling et al (Occup Environ Med 1999;56:73-85). Dr Graveling is Head of Human Sciences at the University of Edinburgh and his report was commissioned by the UK Health and Safety Executive; **the conclusions were that the evidence suggests that MCS does exist and most strongly supports a physical mechanism involving sensitisation of parts of the mid-brain, and that certain chemicals are able to directly penetrate areas of the brain and exert an effect at doses much lower than previously considered possible.**

Another is "Multiple Chemical Sensitivity : A 1999 Consensus" (Arch Environ Health 1999;54:3:147-149). One of the 34 signatories was Professor Leonard Jason, a highly-respected scientist well-known to the international ME/CFS community. In summary, the Consensus was that MCS is defined as "*a chronic condition with symptoms that recur reproducibly in response to low levels of exposure to multiple unrelated chemicals and improve...when incitants are removed (and) requiring that these symptoms occur in multiple organ systems*".

The third is Psychogenic Origins of Multiple Chemical Sensitivity Syndrome: A Critical Review of the Research Literature by AL Davidoff and L Fogarty (Johns Hopkins, Baltimore). Arch Environ Health 1994;49:5:316-325. The authors consider the psychogenic hypotheses put forward by certain psychiatrists and conclude:

*"Current studies investigating psychogenic hypotheses of the MCS syndrome are methodologically problematic and their conclusions questionable....Disorders based on endocrine, nervous and immune systems often result in multiple organic system complaints that are difficult to diagnose....the presence of multi-system complaints does not constitute evidence for psychogenic causation".*

The Chemical Injury Information Network produces a list of published reference papers on Multiple Chemical Sensitivity.

**Other important books which refer to allergies and hypersensitivities include:**

- Myalgic Encephalomyelitis and Postviral Fatigue States by A. Melvin Ramsay (second edition); Gower Medical Publishing, 1988, ISBN 0-906923-99-9 (the first edition, Postviral Fatigue Syndrome: The Saga of The Royal Free Disease, was published in 1986, ISBN 0-906923-96-4)

- Food Allergy and Intolerance. Brostoff J, Challacombe SJ (eds); Bailliere Tindall, London, Philadelphia, 1987
- Food Intolerance. Ed: John Dobbing. Bailliere Tindall, 1987
- The Body at War. John Dwyer. Unwin Hyman, 1988. John Dwyer, Professor of Medicine at the University of New South Wales, writes: *“There is no longer any doubt that the syndrome is primarily organic, not psychological. Patients with classical symptoms of CFS almost always have reduced numbers of immunoregulatory cells in their blood”* (page 198) and *“A number of patients claim to be extremely sensitive to the environment and the numerous chemicals found in foods, drugs etc. **Most people with CFS do not have extreme sensitivity to chemicals but those who do are even more incapacitated than patients for whom fatigue and changes in mental function predominate”*** (page 206). ISBN 0-04-320225-X
- MCS is specifically referred to in the seminal textbook on ME (The Clinical and Scientific Basis of Myalgic Encephalomyelitis Chronic Fatigue Syndrome. Ed: BM Hyde et al; Nightingale Research Foundation, Ottawa 1992. This 724-page major textbook is the compendium of presentations given by international experts at the First World Symposium on ME/CFS held at the University of Cambridge, UK, 9-12<sup>th</sup> April 1990. ISBN 0-9695662-0-4
- Allergies feature in a book written for patients and their physicians entitled Chronic Fatigue Syndrome by Jay A Goldstein published by The CFS Institute, Beverly Hills, CA.1990 ISBN 0-9625654-0-7
- MCS is mentioned as a known component of ME/CFS in the textbook on ME (Postviral Fatigue Syndrome. Ed. Professors James Mowbray and Rachel Jenkins. John Wiley & Sons, Chichester, 1991). ISBN 0 471 92846 1
- Allergies are mentioned in Betrayal by the Brain: The Neurologic Basis of Chronic Fatigue Syndrome, Fibromyalgia Syndrome, and Related Neuronal Network Disorders by Jay A Goldstein published in 1996 by The Haworth Medical Press, New York, ISBN 1-56024-981-1
- MCS is addressed in the standard medical textbook on environmental medicine (Environmental Medicine in Clinical Practice. H. Anthony et al. BSAEM 1997). ISBN 0-9523397-2-2
- The existence of allergies in ME/CFS is referred to in an over-view (Chronic Fatigue Syndrome: A Biological Approach) edited by Patrick Englebienne & Kenny

De Meirleir, CRC Press 2002, this being a detailed and technical medical textbook. ISBN 0-8493-1046-6

- MCS is mentioned in Chronic Fatigue Syndrome and the Body's Immune Defense System by Roberto Patarca-Montero published in 2002 by The Haworth Medical Press. ISBN 0-7890-1530-7
- A detailed exposition of MCS is the subject of chapter 50 ("Multiple Chemical Sensitivity") by Professor Malcolm Hooper in a well-received textbook entitled Psychiatry: An Evidence-based text by Professor Basant Puri and Dr Ian Treaden (published by Hodder Arnold Publication, 2010); Hooper also contributed chapter 49 entitled "Overlapping multi-system, multi-organ illnesses/syndromes" which includes ME/CFS, MCS, Gulf War Syndrome and organo-phosphate poisoning. Reviews of this textbook include the following: *"...the text is so well-written that I became engrossed in some chapters, reading as a book"* (BMA Medical Book Awards, 2010); *"This book will provide a solid reference source which can confidently take its place next to its more established rivals"* (The Psychiatrist); *"I was very very pleased to find to find the chapter on ME/CFS in this book to be a real gem. Overall this is a superb book and I would recommend it to anyone studying for their MRCPsych exams"* (Martin Eden, who states that he bought the book to revise a few basic concepts before applying for a liaison psychiatry post in Edinburgh). ISBN 978 034 0950060

Books written primarily for the lay reader are incorporated within the chronological list below.

### **Historical perspective of MCS**

For an historical perspective of MCS and an alphabetical bibliography of over 600 referenced scientific articles, editorials, books, book chapters and reports on or directly related to Multiple Chemical Sensitivity (MCS) from 1945 to September 1999, see the document compiled by Albert Donnay of MCS Referral and Resources, 6101 Gentry Road, Baltimore, Maryland 21210, USA ("Bibliography of all scientific articles, editorials, books, book chapters, reports on or directly related to Multiple Chemical Sensitivity disorders", available online).

Starting in 1984 until it ceased publication in 2002, The Medical Information Services of The British Library Document Supply Centre produced quarterly updates of CATS (Current Awareness Topics) on ME/CFS and MCS from the peer-reviewed medical journals.

In relation to MCS, attention must be drawn to the seminal work of two of the world's leading experts, namely Martin Pall, Professor Emeritus of Biochemistry and Basic Medical Sciences, Washington State University and his work on NO/ONOO -- the nitric

oxide (NO) and peroxynitrite (ONOO) cycle in the mechanism of MCS, the biochemical cycle being elevated in patients with ME/CFS and related diseases -- and Mohamed Abou-Donia, Professor of Pharmacology, Cancer Biology & Neurobiology, Duke University Medical Centre, North Carolina and his work on chemical disruption of the blood brain barrier.

### **Major Reports on allergies / hypersensitivities / effects of chemicals**

MCS is documented in the report of The National Task Force on ME/CFS/PVFS 1994, published by Westcare, Bristol, which was supported by the Department of Health.

Risk Assessment of Mixtures of Pesticides and Similar Substances: Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. Chairman: Professor I Hughes. FSA; September 2002.

“ALLERGY – the unmet need”; Royal College of Physicians, 2003. In her Foreword, Professor Carol Black, President of the RCP, said: *“In the UK over the last twenty years, the incidence of common allergic diseases has trebled, giving this country one of the highest rates of allergy in the world. In any one year, 12 million people in the UK (one fifth of the population) are now likely to be seeking treatment for allergy....In publishing this report, the Royal College of Physicians aims to put allergy higher on the healthcare agendas of the Department of Health and planners and managers....These proposals require urgent action”*.

In his Preface to the report, Stephen Holgate, MRC Clinical Professor of Immunopharmacology, School of Medicine, University of Southampton, said: *“In drawing attention to the high and ever-increasing prevalence and complexity of allergy, the disease burden this creates, and the lack of any cohesive approach to delivering an adequate clinical service within the NHS, this report highlights the unmet needs of the many patients who suffer from allergy, and the impaired quality of life they endure....the time has come to make a determined effort to improve clinical services for patients with allergic disease in the UK”*.

The report referred to food allergy and intolerance, to the increased complexity of allergies and to multi-system allergic disease and stated: *“Primary Care Trusts therefore need to be made aware of the burden of allergic disease and alerted to their responsibilities to provide the resources to meet these needs”*.

House of Commons Health Committee Report: “The Provision of Allergy Services”, Volumes I and II, Sixth Report of Session 2003-2004. Like the RCP report, this substantive report found that the prevalence of allergy has increased greatly and rapidly in recent years, with the biggest increases coming in areas of serious and complex allergy. Members found it *“staggering”* that there is only one allergy consultant per 2

million people in the UK. The report was critical of PCTs: *“Primary Care Trusts seem not to recognize a problem and are certainly not commissioning additional allergy services (no service, no data, therefore no problem seems to be their reaction)”*.

“CHEMICALS IN PRODUCTS”: Royal Commission on Environmental Pollution; Twenty-fourth Report, 2003. Chaired by Sir Tom Blundell FRS., F Med Sci.

Variability and Uncertainty in Toxicology of Chemicals in Food, Consumer Products and the Environment: Committee on Toxicology of Chemicals in Food, Consumer Products and the Environment. Chairman: Professor I Hughes; FSA, March 2007.

**There are also significant reports from other countries, for example:**

- Memorandum from US Department of Housing and Urban Development on MULTIPLE CHEMICAL SENSITIVITY, April 14, 1992. MCS has been recognized in the USA by the Departments of Justice, Housing, Urban Development and Education since 1996. In particular, the US Department of Housing specifically recognises MCS as a disability granting those afflicted full protection of federal housing laws for the disabled
- US Information for Physicians (1996). Chronic Fatigue Syndrome. Information for Physicians. Issued in September 1996 by The National Institute of Allergy and Infectious Disease, National Institutes of Health (NIH), US Department of Health and Human Services: *“Many CFS patients have a history of allergies years before the onset of the syndrome...Sometimes patients report a worsening of allergic symptoms or the onset of new allergies after becoming ill with CFS.....Allergies are common in people with CFS...(there is a) high prevalence of allergies in the CFS population....many patients are extremely sensitive to drugs”*.
- The Australasian Medical Association Guidelines for Physicians (1997). Clinical Guidelines on the Evaluation of Prolonged Fatigue and the Diagnosis and Management of Chronic Fatigue Syndrome. Produced by a Working Group convened by The Royal Australasian College of Physicians, December 1997 and published by The Medical Journal of Australia.
- A Report on Multiple Chemical Sensitivity The Interagency Workgroup on Multiple Chemical Sensitivity; August 1998: Executive Summary; Background and Historical Review; Epidemiologic Considerations; Theories of Causation and Mechanisms; Potential Tools for Future Research Studies (Use of Biomarkers in Studying MCS); Public Health Issues in Medical Evaluation and Care of MCS Patients; Key panels, Workshops and Reports; Recommendations; Federal Actions; Findings and Recommendations (Overview); References (approx 168 references); Abbreviations; Annex of Research Suggested by Expert Reviewers

- Multiple Chemical Sensitivities Under Siege Dr Ann McCampbell, Chair, MCS Task Force of New Mexico, November 2000
- Proceedings of the First International Environmental Illness Conference, 18<sup>th</sup> – 19<sup>th</sup> May 2001, Ottawa, Canada. This Conference examined Environmental Illness (EI) from the perspective of the medical management of the EI patient, including how to meet patients' needs for accommodation and a healthy environment. Environmental illness includes multiple chemical sensitivity (MCS), Chronic Fatigue Syndrome (CFS), Fibromyalgia (FM) and Gulf War Syndrome (GWS). Speakers included Dr Gerald Ross, Professor Tang Lee, Dr Gunnar Heusar and Professor Nicholas Ashford.
- "Multiple Chemical Sensitivity (MCS): Guidelines for South Australian Hospitals", Government of South Australia, May 2010. This report was produced in response to the Social Development Committee Parliamentary Review of MCS that was based on national and international literature. The referenced report lists common chemical incitants, common symptoms, requirements relating to hospital admission of patients with MCS, appropriate modification of the hospital environment including training of hospital staff to avoid symptom exacerbation and the need for special dietary requirements and medication.

### **International Conferences and Symposia on MCS**

There have been many such conferences including the Fifth BASENM international conference at the University of Oxford in 1998 and the Royal Society of Medicine (Section of Clinical Allergy) symposium on "A critical look at the immunology of (ME)CFS" also held in 1998, at which speakers included Professor Denis Wakefield, Professor of Pathology, Director of Immunology & Immunopathology, Prince Henry Hospital, New South Wales; Professor Nicholas Cohen, Department of Microbiology and Immunology, University of Rochester, New York; Professor AW Rook, Department of Bacteriology, UCL Medical School and Dr William Weir, Consultant Physician and ME specialist, then at The Royal Free Hospital, London.

### **The following papers and textbooks and books provide important information about MCS; for ease of reference, some extracts are included because they are illustrative**

As well as published medical reference papers, there are a large number of books which refer to allergies as being a component of ME/CFS.

Furthermore, the many worldwide patients' support groups make a point of referring to the high prevalence of allergies and hypersensitivities in ME/CFS in their newsletters, journals and literature, including information packs that are sent out to doctors.

### **1970**

Encephalomyelitis resembling benign myalgic encephalomyelitis. SGB Innes. Lancet 1970:969-971

*“Could it be that enteroviral infection, in predisposed or previously sensitised subjects, sets in train some process, say of an allergic nature, which accounts for the similarity of symptoms and the chronic relapsing course? We do not know if the ‘allergic process’ is entirely self-perpetuating”.*

### **1976**

Special Article: Benign Myalgic Encephalomyelitis or Epidemic Neuromyasthenia. AM Ramsay. Update, September 1978:539-542

*“In Edinburgh in 1970...Innes suggested that the enteroviral infections had triggered off an allergy”.*

### **1977**

Enhancement of IgE-Mediated Histamine release from Human Basophils: Role of Interferon.

S Ida, J Hooks et al. The Journal of Experimental Medicine 1977:145:892-906

### **1978**

Allergy to food and chemicals: the scope of the problem. S Todd. Nursing Times March 1978:438-441

Food Allergy: Fact or Fiction? R Finn, HN Cohen. Lancet Feb 1978:426-426

### **1979**

Diagnosing Food and Chemical Susceptibility. WJ Rea. Continuing Education, Sept 1978:47-59

The Environmental Aspects of Ear, Nose and Throat Disease. Part 1. WJ Rea. JCEORL & Allergy July 1979:41-57

The Environmental Aspects of Ear, Nose and Throat Disease. Part 2 WJ Rea. ORL & Allergy Digest Sept 1979:41-55

### **1980**

Food Allergy and Intolerance in 100 Patients - Local and Systemic Effects. MH Lessof, DG Wraith et al. Quarterly Journal of Medicine, New Series XLIX 1980:195:259-271

Your house can make you sick Alfred V Zamm. In: Why your house may endanger your health. Alfred V Zamm and Robert Gannon; pub. Simon & Schuster, New York 1980

### **1981**

Viruses as Nonspecific Modulators of Immunological Reactivity. BF Semenov. Acta Virol 1981:25:122-128

Intestinal Permeability in Patients with Eczema and Food Allergy. PG Jackson, MH Lessof et al. The Lancet June 13: 1981:1285-1286

Late-onset atopic eczema and multiple food allergies after infectious mononucleosis. R St C Barnetson et al. British Medical Journal 1981:283:1086

### **1982**

The Immunology of Allergy. In: Disease and the Environment. Ed. AR Rees, HJ Purcell. Proceedings of the Inaugural Conference of the Society for Environmental Therapy 1981:65-78

Hypersensitivity to Mains Tap Water in Adults: its Clinical Features and Treatment. CWM Wilson. Nutrition and Health 1982:1:85-91

Food Intolerance: A Major Factor in the Pathogenesis of Irritable Bowel Syndrome. VA Jones, P McLaughlan et al. The Lancet 20 Nov 1982:1115-1117

The Role of Allergy in Arthritis, Rheumatism and Polysymptomatic cerebral, Visceral and Somatic Disorders: A Double Blind Study Marshall Mandell et al. J of IAPM July 1983:5-16

Book / The Mile-High Staircase Toni Jeffreys. Hodder & Stoughton 1982. ISBN 0-340-279907

### **1983**

Food and Chemical Sensitivity. JJ McGovern, JA Lazaroni et al. Arch Otolaryngol 1983:109:292-297

Total allergy syndrome: what evidence can be established? N Mike, P Asquith. Proceedings of 2<sup>nd</sup> Fisons Food Allergy Workshop, pub. The Medicine Publishing Foundation, Oxford, 1983:79-83

Ecological hazards in the hospital setting. Vicky Rippere. Bethlem & Maudsley Gazette 1983:31:2:9-10

### **1984**

Myalgic encephalomyelitis. Cory Matthew. New Zealand Medical Journal 1984:782.

*"Many myalgic encephalomyelitis patients also experience food and chemical intolerances, and are often therefore unusually sensitive to the side effects of drugs".*

Adverse reactions to foods. DH Allen, R Loblay et al. The Medical Journal of Australia Special Supplement, Sept 1984:S37-S42

Myalgic encephalomyelitis and the general practitioner. JC Murdoch. New Zealand Family Physician Winter 1984:127-128

*"In the long term sufferer, patients are often anxious to identify food and chemical allergies".*

### **1985**

The postviral fatigue syndrome – an analysis of the findings in 50 cases. PO Behan, WMH Behan, EJ Bell. Journal of Infection 1985:10:211-222

*“Our clinical impression, however, is that there is a high incidence of atopic illness in patients with this syndrome”.*

Evidence for Active Epstein-Barr Virus Infection in Patients with Persistent Unexplained Illness: Elevated Anti-Early Antigen Antibodies. James F Jones et al. Ann Int Med 1985:102:1:1-7

*“These screening tests do not preclude an abnormality in immune function in these patients...previous alternative diagnoses in these patients have included antibody negative lupus erythematosus and allergic diathesis”.*

Persisting Illness and Fatigue in Adults with Evidence of Epstein-Barr Infections. Stephen E Straus, G Tosato et al. Ann Int Med 1985:102:7-16

*“By all regards...many of these patients appeared to be neurotic. However, our detailed studies have uncovered a series of subtle yet objective organic abnormalities in these patients. Importantly, nearly all of the patients studied had increased T cell mediated suppression...which showed increased numbers of OKT4 positive (helper-inducer) cells”.*

Gut and Joint Disease. (News Bulletin & Allergy Forum) C Carini, J Brostoff. Annals of Allergy 1985:55:624-625

What is the current state of knowledge of ecological illness or total allergy syndrome? Is there an immune basis to this condition? J Brostoff. British Medical Journal 1985:290:1884

The New Chemical Victims. Ecological Illness Law Report, 1985:3: 4-5:16-20

Book / Better Recovery from Viral Illness. Darrel Ho-Yen. Dodona Books, Inverness, 1985  
ISBN 0 9511090 1 4 (second edition 1987; third edition 1993)

Book / Clinical Ecology – the treatment of ill health caused by environmental factors. G Lewith & J Kenyon (University of Southampton). Thorsons 1985 ISBN 0-7225-1102-7. The chapter entitled “Chemical Sensitivity” concludes: *“Total allergy is getting more common, so a recognition of its existence is of some importance for us to be able to find out anything more about this life-threatening condition”.*

**1986**

Correlation between allergy and persistent Epstein-Barr virus infections in Chronic-Active EBV infected patients. George B Olsen, James F Jones et al. J All Clin Immunol 1986:78:308-314

*“Eighty percent of patients with CA-EBV (ie CFS / ME) demonstrate clinically significant IgE mediated allergic disease, including...food and drug reactions. The data indicate that patients with CA-EBV have...a high association with hypersensitivity states...percent positive responsiveness to allergens is consistent with the high degree of allergy observed in these patients”.*

Immunological and Clinical Aspects of Food Allergy. J Brostoff, GK Scadding. Adv. Med. 1986:21:286-302

Specific allergen-induced Epstein-Barr nuclear antigen-positive B cells from patients with Chronic Active EBV infections. George B Olson, James F Jones et al. J Allergy Clin Immunol 1986:78:315-320

*“Patients in this study have significantly increased (1) responsiveness towards specific allergens, (2) responses towards greater numbers of allergens (3) increased numbers of IgE-positive T cells and B cells.... and (6) elevated serum IgE levels than do patients with mild or moderate allergic disease alone. Patients...demonstrate an increased incidence of allergies and symptoms, indicating various neurologic disorders”.*

Book / Recent Advances in Clinical Nutrition Ed: Wahlquist M & Truswell A. pub. John Libby, London 1986; chapter on Food Intolerance pp 169-177 by RH Loblay, AR Swain.

Book / Postviral Fatigue Syndrome: The Saga of Royal Free disease. A. Melvin Ramsay. Gower Medical Publishing 1986 ISBN 0-906923-96-4 (second edition Myalgic Encephalomyelitis and Postviral Fatigue States published 1988 ISBN 0-906923-99-9).

Book / ME: Post-Viral fatigue Syndrome and how to cope with it. Celia Wookey. Croom Helm 1986 (chapter on immunology pp 31-32). ISBN 0-7099-3672-9.

## **1987**

Environmental Illness: A Disorder of Immune Regulation. AS Levin, VS Byers. Occupational Medicine Oct-Dec 1987:669-681

Environmental Illness. William J Rea, 1987:207-214

The Worker With Multiple Chemical Sensitivities: An Overview. MR Cullen. Occupational Medicine State of the Art Reviews 1987:2:4:655-661

IgE complexes in food allergy. C Carini et al. Annals of Allergy 1987:59:110-117

Transcript of Presentation by Mark Loveless, specialist in Infectious Diseases, Oregon; ME/CFIDS Conference 4-7<sup>th</sup> November 1987.

Myalgic encephalomyelitis- how to care for a sufferer. UK ME Association Leaflet 1987

Laboratory Diagnosis of Food Intolerance. DLJ Freed. In: Brostoff and Challacombe, Bailliere Tindall 1987

Chronic Epstein - Barr Virus Infection. James F Jones, Stephen E Straus. Ann Rev Med 1987:38:195-209

*"...the clinical observation that most of these individuals report or demonstrate...allergic disease (at) an uncommonly high prevalence rate".*

The Epstein-Barr Virus and Chronic Fatigue. Irving E Salit. Clinical Ecology 1987 / 88:V:3:103-107

*"Patients...tend to tolerate medications very poorly and many have a history of allergies including drug allergies".*

The 'Chronic, Active Epstein-Barr Virus Infection' Syndrome and Primary Fibromyalgia.  
D Buchwald,  
DL Goldenberg, JL Sullivan, AL Komaroff. Arthritis & Rheumatism 1987:30:10:1132-1136

*"A history of allergies was reported by 64% of patients".*

## **1988**

Viruses and neuropsychiatric disorders. JF Mowbray. JRSM 1988 81:311-312

*"...the possibility that temporary viral infection might produce a permanent change leading to disease. When the disease presents, the virus might not be present so that Koch's postulations for the disease would not be fulfilled.... We are then considering a group of disorders in which there may be an inherited genetic predisposition...to disease occurrence if infection is present, associated with some other environmental factor (which) may be chemical. There is much talk of a symbiosis between a virus infection and food intolerance in patients with the postviral fatigue syndrome. There is a natural tendency to reject such a 'fringe medicine' approach...There are, however, simple examples of similar concatenation of infection and environment, where the cause is known".*

The Myalgic Encephalomyelitis Syndrome. JC Murdoch. Family Practice 1988:5:4:302-306. Pub. Oxford University Press

*“Many patients with this syndrome...have had chemical toxicity diagnosed.... many patients with long-term symptoms develop food sensitivities”.*

Allergy and the Chronic Fatigue Syndrome. Stephen E Straus, Janet Dale et al. J Allergy Clin Immunol 1988:81:791-795

*“This article summarises recent studies of the syndrome and emphasises our assessment of one of its more common manifestations, allergy. Many patients report inhalant, food or drug allergies. Allergies are a common feature of patients with the chronic fatigue syndrome. Among the features of this syndrome is a high prevalence of allergy, an allergy that appears to be substantial, both by history and by skin testing”.*

Postviral Fatigue Syndrome. PO Behan, WMH Behan. Crit Rev Neurobiol 1988: 4:2:157-178

*“A variety of immunological abnormalities were detected, including abnormal T4 / T8 lymphocyte subset ratios, dysfunction of natural killer cells, abnormal proliferation of B cells and decreased IgG concentrations”.*

Chronic Fatigue Syndrome and Chemical Overload. RA Buist. International Clinical Nutrition Review 1988:8:4:173-175

Poor sulphoxidation ability in patients with food sensitivity. GK Scadding, R Ayesch et al. British Medical Journal 1988:297:105-107

Environmental Illness. WJ Rea. 1988:207-214

New Light on Chronic Fatigue Syndrome. Robert A Buist. J Orthomolecular Med 1988:3:3:146-149

Systemic Mast Cell Disease. William D Travis et al. Medicine. Williams and Wilkins 1988:345-368

Ecological Illness Law Reports. Ed. Earon S Davis, June 1988:5:1-2

Book / The Body at War John Dwyer. Unwin Hyman 1988. ISBN 04-320225-X

Book / Chronic Fatigue Syndrome: The Hidden Epidemic Jesse A Stoff & Charles R Pellegrino  
Random House, New York 1988. ISBN 0-394-56956-3

### **1989**

Treatment of Patients with Chronic Fatigue Syndrome. Nelson Gantz & Gary Holmes.  
Leading Article. *Drugs* 1989;36:6:855-862

*“Several authors have detected histories of atopy and high frequencies of skin test reactivity to selected allergens, suggesting an allergic mechanism may play a role in the aetiology of the disease. Multiple other immunological abnormalities have been noted....the importance of such abnormalities...may serve as markers for a subset of patients....who have measurable immunological abnormalities”.*

Thoughts on the management of myalgic encephalomyelitis. Michael Jenkins. *British Homoeopathic Journal* 1989;78:6-14

*“There do seem to be considerable overlaps between the presentations of ME, post-viral fatigue syndrome and multiple allergies....multiple allergies to foods and less often to inhalants are quite common”.*

Postviral syndrome --- how can a diagnosis be made? SJ Bowman, J Brostoff, S Newman, JF Mowbray. *JRSM* 1989;32:712-716

*“The 89 full responders were divided into five groups...group 2 patients had a specific diagnosis (of) food allergy”.*

The Chronic Fatigue Syndrome: Definition, Current Studies and Lessons for Fibromyalgia Research.

AL Komaroff & D Goldenberg. *J Rheumatol* 1989;16:19:23-27

*“Myalgic encephalomyelitis...is similar in most respects to the other chronic fatigue syndromes...on medical history, the only clearly striking finding is a high frequency of atopic or allergic illness (in about 50 - 70%).... On immunologic testing, we and others have found evidence of subtle and diffuse dysfunction”.*

The relationship between viral infections and onset of allergic diseases and asthma. VB Busse. *Clinical and Experimental Allergy* 1989;19:1-9

Chronic Fatigue Syndrome. GH Ross, JA Monro. CMAJ 1989:140:361

Chronic Fatigue Syndrome. GH Ross, WJ Rea, AR Johnson. CMAJ 1989:141:11-12

Chemical Sensitivity in Physicians. WJ Rea, GH Ross et al. Clinical Ecology 1989:6:4:135-141

Diseases of Food Hypersensitivity. DD Metcalfe. The New England Journal of Medicine 1989:321:4:255-257

Chemical hypersensitivity: A chemically-induced immune system disorder. The UKOPRP; Chemical hypersensitivity, 1989

Mast cells move to centre stage Linda Gamlin. New Scientist 24 June 1989

Cooking up a storm Linda Gamlin. New Scientist 8 July 1989

Another man's poison Linda Gamlin. New Scientist 15 July 1989

Wining Workplace Litigation: what you must know to represent your client's interests effectively.

Earon S Davis. The North Carolina Academy of Trial Lawyers, 1989

Winning Workplace Litigation: Chemicals in the Environment: MULTIPLE CHEMICAL SENSITIVITY.

Earon S Davis. Ecological Illness Law Report October 1989

Book / Understanding ME. DG Smith. Robinson Publishing, 1989. ISBN 1 85487 019 X

Book / Why M.E.? B Dawes & Damien Downing. Grafton 1989. ISBN 0- 586-20666-3

Book / Living with ME. Charles Shepherd. Cedar 1989 (William Heinemann Ltd) ISBN 0-434-11156-2

Book / M.E. Postviral Fatigue Syndrome. Anne Macintyre. Unwin Hyman 1989 ISBN 0-04-440318-6

Book / M.E. What is it? Mike Franklin & Jane Sullivan. Century 1989 ISBN 0-7126-2966-1

Book / The Complete Guide to Food Allergy and Intolerance Jonathan Brostoff & Linda Gamlin Bloomsbury 1989 ISBN 0-7475-0242-0

Book / Overload: Beating ME, the Chronic Fatigue Syndrome Jacqueline Steincamp

pub. Cape Catley Ltd, New Zealand 1988 (subsequently published by Fontana / Collins 1989). ISBN 0-00-637478-6

## **1990**

CD8 Deficiency in Patients with Muscle Fatigue Following Suspected Enteroviral Infections (Myalgia Encephalitica). JR Hobbs, JF Mowbray et al In: Protides of the Biological Fluids. Jan 1990:36

*"It is also clear that acquisition of T cell deficiency, particularly of the CD8 subset, can itself impair immune regulation and predispose to atopy not previously experienced by the patient. Three of the criteria are sufficiently frequent to suggest they should become part of the routine screening of such patients, and these are a subnormal level of CD8 lymphocytes...What seems to be especially related to the ME symptoms in our clinically selected patients is a failure to show the expected rise and normalisation of CD8 numbers.... In the present study, the patients show a 40% incidence of both clinical and laboratory evidence of atopy.... It has been shown that T cell deficiency, particularly of the suppressor subset, can predispose to atopy, which can indeed be acquired by patients without a genetic family history".*

Muscle versus brain: chronic fatigue syndrome. AR Lloyd. Conference Report from international conferences on CFS in Los Angeles, USA and Cambridge, UK. Med J Aust 1990:153:5:530-534

*"Dr Rob Loblay discussed the relationship between CFS and intolerance to food substances....he stressed that these substances...appear to be an important precipitant of symptoms in patients with CFS.....Carefully designed, double blinded challenges...showed that a significant minority (34%) of patients benefited from dietary modification".*

The chronic fatigue syndrome: a return to common sense. AM Denman. Postgrad Med Journal 1990:66:499-501

*"A high incidence of concomitant atopic disorders may prove to be a useful diagnostic point".*

A New Manifestation of Seminal Fluid Hypersensitivity. N Mike, G Bird, P Asquith. Quarterly Journal of Medicine New Series 75 1990:276:371-376

## **1991**

Defining the Chronic Fatigue Syndrome. Gary P Holmes. Rev Inf Dis 1991:13:1:S53-S55

*“Preferably, patients with CFS who have such abnormalities might be considered a subset of the larger group: ie. persons with CFS who have immune dysfunction”.*

History of the Chronic Fatigue Syndrome. Stephen E Straus. Rev Inf Dis.1991:13:1:S2-S7

*“There is little doubt that classic allergy and atopy are inexplicably prevalent in CFS. In a recent study, a high proportion (50%) of patients with CFS were found to be reactive to a variety of inhalant or food allergens when inoculated epicutaneously in the classic manner. In the healthy population, reactivity rarely exceeds 15-20%”.*

Symptoms and Signs of Chronic Fatigue Syndrome. AL Komaroff & D Buchwald. Rev Inf Dis 1991:13:1:S8-S11

*“The patients’ medical histories reveal one clearly striking finding: a high prevalence of atopic or allergic illness (for 40 - 70%).*

Review of Laboratory Findings for Patients with Chronic Fatigue Syndrome. D Buchwald & A Komaroff. Rev Inf Dis 1991:13:1:S12-S18

*“In fact, allergies are a common feature of patients with CFS” (citing refs 11,13,51,52).*

Chronic Fatigue Syndrome in Northern Nevada. Sandra Daugherty, Daniel Peterson et al. Rev Inf Dis 1991:13:1:S39-S44

*“Our investigations have...produced evidence of ...a decrease in CD8 suppressor cells with resulting elevation of the ratio of CD4 to CD8 cells”.*

Fatigue: Definition and Management. Ivan Barofsy & Marcia West Legro. Rev Inf Dis 1991:13:1:S94-S97S

*“Allergies...may predispose a person to the development of CFS following an immunologic assault”.*

Food allergy and pelvic pain. BA Gbolade, R Jackson. Journal of Obstetrics and Gynaecology 1991:11:457

Notes on ME/CFS (myalgic encephalomyelitis, chronic fatigue syndrome). Australia & New Zealand ME Society (ANZMES) leaflet 1991

Postviral Fatigue Syndrome -- Laboratory Abnormalities. Dedra Buchwald. In: Postviral Fatigue Syndrome. ed. Rachel Jenkins & James Mowbray. John Wiley & Sons, Chichester, 1991

Multiple Chemical Sensitivity. Special Report. B Hileman (Washington). Chemical & Engineering News  
July 22 1991:26-42

*“(MCS) is increasingly being recognised in government regulations and the courts...MCS has been legitimised in a number of federal and state government regulations...People with MCS are also recognised as disabled under the Fair Housing Act of 1988...The Social Security Administration also recognises MCS...The number of chemicals the victims respond to is equally wide, ranging from pesticide residues to vehicle exhaust; household cleaners; perfumes...fomaldehyde in new clothing; fumes from gas stoves; off-gassing of paints, glues, and carpets in new construction; emissions from carbonless copy paper, laser printers and newsprint. Most of these triggering agents are irritants or neurotoxins, and many are mixtures of volatile organic compounds...Initially, most patients respond to just one type of chemical exposure, but usually their sensitivities spread to a wider range of agents. In many, sensitivities also expand to include common foods that they used to be able to eat...The chemical industry ...and the medical insurance industry have added fuel to this debate. Understandably, they have taken a strong interest in this issue because the trace levels of chemicals that allegedly cause illness are orders of magnitude lower than current regulatory levels...Clearly the economic stakes in this issue are very high (as) the chemical industry...could be faced with many more thousands of very costly law suits”. The Report records the words of a Professor of Pharmacology at George Washington University Medical Centre who was diagnosed with MCS: “the multiplicity of things that could provoke symptoms continued to frighten and amaze me”. The Report notes that: “the ratio of helper (T4) to suppressor (T8) lymphocytes are altered in the immune system of patients with MCS patients....Severely affected MCS patients may have difficulty leaving their homes because of the multitude of chemical exposures they encounter....These patients are ill and deserving of compassion, understanding, and expert medical care”.*

Review by John M Balbus Kornfeld: Chemical Exposures: Low Levels and High Stakes. NA Ashford, CS Miller. (pub) Van Nostrand Rheinhold, New York, 1991 The New England Journal of Medicine April 9 1992:1032

USA: Multiple Chemical Sensitivity. JB Sibbison. The Lancet Jun 15 1991:337:1469-1470

***“There is no specific treatment for this MCS syndrome, whose existence is widely acknowledged”.***

Action Against Allergy Newsletter number 41: April 1991

Book / The Disease of a Thousand Names David S Bell. Pollard Publications, Lyndonville, New York 1991

Book / Chemical Exposures: Low Levels and High Stakes. NA Ashford, CS Miller. pub. Van Nostrand Reinhold, New York, 1991

## **1992**

Considerations for the Diagnosis of Chemical Sensitivity. William J Rea, Alfred R Johnson et al; In: Biologic Markers in Immunotoxicology; National Research Council (U.S.) Subcommittee on Immunotoxicology: 1992:169-192; National Academy Press

Advancing the understanding of multiple chemical sensitivity (MCS): Overview and recommendations from an AOEC workshop. KM Rest. Toxicology Ind. Health / Jul-Aug 1992:F(4):1-13

Chronic Fatigue Syndrome. WK Cho & GH Stollerman. Hospital Practice 1992:221-245

*“The numerous attempts to elucidate the pathogenesis of chronic fatigue syndrome are evoked by the names....chronic Epstein-Barr virus infection and total allergy syndrome (twentieth century disease). It is known that such patients are remarkably likely to have a history of atopy pre-dating the onset of chronic fatigue syndrome (50-83%). **Patients may have an immune system that responds over-emphatically to environmental or internal stimuli...aspects of the immune reaction may not be stoppable even after an insult is over**”.*

Plasma and Cerebrospinal Fluid Monoamine Metabolism in Patients with Chronic Fatigue Syndrome: Preliminary Findings. MA Demitrack, Stephen E Straus et al. Biol Psychiatry 1992:32:1065-1077

*“Patients with chronic fatigue syndrome are reported to have a higher incidence of allergic conditions. Indeed, it has been speculated that heightened allergic responsiveness may be a risk factor for the development of the syndrome. In particular, the diverse clinical and immunological features have been argued to reflect an ongoing state of immune activation”.*

What causes ME? David Freed. Interaction: The Journal of ME Action 1992: No.11

Reactions to food additives. MH Lessof. Journal of the Royal Society of Medicine 1992:85:513-515

Hypersensitivity to environmental factors. Journal of the Australian and New Zealand ME Society 1992

Advancing the understanding of multiple chemical sensitivity (MCS): Overview and recommendations from an AOEC workshop. KM Rest. Toxicology Ind. Health / Jul-Aug 1992:F(4):1-13

Multiple Chemical Sensitivity (MCS): Hazards in 1992. Hazards Publications Ltd, Sheffield S1 1FQ, UK

Memorandum from the US Department of Housing and Urban Development on MULTIPLE CHEMICAL SENSITIVITY, 14<sup>th</sup> April 1992

Book / Running on Empty. Katrina Berne Hunter House Inc. USA 1992 (subsequently published by Bloomsbury, London) ISBN 0-7475-2138-7

### **1993**

Clinical presentation of chronic fatigue syndrome. AL Komaroff. Ciba Foundation Symposium 173: Chronic Fatigue Syndrome. John Wiley, Chichester 1993:43-61

*“On past medical history, the only clearly striking finding in our studies is a high frequency of atopic or allergic illness (in approximately 50 - 80%, in contrast to a background prevalence of about 10% in the population at large.....Immunological studies suggest that in CFS, the immune system is in a state of chronic activation”.*

Chronic Fatigue Syndrome: Influence of Histamine, Hormones and Electrolytes. L Dechene. Medical Hypotheses 1993:40:55-60

Hypersusceptibility to chemicals: risk factors for neurological disease? Editorial: A Williams. Journal of Neurology, Neurosurgery, and Psychiatry 1993:56:943-946

Immunologic, Psychological and Neuropsychological Factors in Multiple Chemical Sensitivity. Gregory E Simon et al. Ann Int Med 1993: 19:2:97-103

### **1994**

Summary and Perspective: Epidemiology of Chronic Fatigue Syndrome. Paul H Levine. Clin Inf Dis 1994: 18:1:S57-S60

*“It has been noted for a number of years that a history of allergies appears to be an important risk factor for CFS, **and the spectrum of illnesses associated with a dysregulated immune system now must include CFS”.***

Simultaneous measurement of antibodies to Epstein-Barr Virus, HHV6, Herpes Simplex Types 1 & 2, and 14 Enteroviruses in Chronic Fatigue Syndrome: is there Evidence of Activation of a Non-specific Polyclonal Immune Response? Farrin A. Manian. Clin Inf Dis 1994;19:448-453

*“As has been noted in other investigations, a high percentage (60%) of patients with chronic fatigue syndrome in this study reported an allergy to drugs or other substances”.*

Comparison of Patients With Chronic Fatigue Syndrome, Fibromyalgia, and Multiple Chemical Sensitivities. D Buchwald, D Garrity. Arch Intern Med 1994;154:2049-2053

*“67% of subjects with CFS reported an exacerbation of their symptoms following exposure to air pollution, cigarette smoke, solvent fumes or perfumes. Disability among our patients with CFS, FM and MCS was substantial. In Australia, CFS represents a loss to society of \$59 million per year”.*

Effective Allergy Practice (1994). Report of the British Society for Allergy and Environmental Medicine with The British Society for Nutritional Medicine. A Document on Standards of Care and Management for the Allergy Patient. Ed: HM Anthony, S Birtwistle, J Brostoff, D Freed, N Williamson et al (BSAENM)

Psychogenic Origins of Multiple Chemical Sensitivity Syndrome: A Critical Review of the Research Literature. AL Davidoff, L Fogarty (Johns Hopkins, Baltimore). Arch Env Health 1994;49:5:316-325

*“Current studies investigating psychogenic hypotheses of the MCS syndrome are methodologically problematic and their conclusions questionable....Disorders based on endocrine, nervous and immune systems often result in multiple organic system complaints that are difficult to diagnose....the presence of multi-system complaints does not constitute evidence for psychogenic causation”.*

Book / The Canary and Chronic Fatigue. Majid Ali. Life Span Press, New Jersey, USA 1994

ISBN 1-879131-04-8

## **1995**

High incidence of antibodies to 5-hydroxytryptamine gangliosides and phospholipids in patients with Chronic Fatigue Syndrome and Fibromyalgia Syndrome and their relatives: evidence for a clinical entity of both syndromes. R Klein, PA Berg. Europ J Med Res 1995/1996:1:21-26

*“Chronic fatigue syndrome and fibromyalgia syndrome also demonstrate similar immunological abnormalities such as...allergic / atopic reactions”.*

Clinical management of chronic fatigue syndrome - Physiology. DJ Clauw. Journal of CFS 1995:1:3/4:185-190

Unexplained Illness: the mind versus the environment. MJ Radcliffe, P Ashurst, J Brostoff. Journal of the Royal Society of Medicine 1995:88:678-679

## **1996**

The Neuroimmunology of Chronic Fatigue Syndrome. Lucinda VS Scott, Timothy G Dinan. Journal of Chronic Fatigue Syndrome 1996:2:4:49-59

*“An increase in peripheral turnover of 5-HT may explain the heightened allergic responsiveness as well as the musculoskeletal pain seen in CFS”.*

Chronic Fatigue Syndrome. Information for Physicians. Issued in September 1996 by The National Institute of Allergy and Infectious Disease (NIAH); National Institutes of Health (NIH), US Department of Health and Human Services.

*“Many CFS patients have a history of allergies years before the onset of the syndrome...Sometimes patients report a worsening of allergic symptoms or the onset of new allergies after becoming ill with CFS.....Allergies are common in people with CFS....(there is a) high prevalence of allergies in the CFS population....many patients are extremely sensitive to drugs”.*

Chronic Fatigue Syndrome as a Delayed Reaction to Chronic Low-dose Organophosphate Exposure.

PO Behan. Journal of Nutritional & Environmental Medicine 1996:6:341-350

Recognition of Multiple Chemical Sensitivity by Federal Authorities. A Donnay. Pub. MCS Referral & Resources, Baltimore 1996.

Potential animal model of multiple chemical sensitivity with cholinergic sensitivities. Overstreet DH,

Miller CS et al. Toxicology 1996:111:1-3:119-134

Book / Surviving M.E. Joyce Fox. Vermillion (Random House UK Ltd). ISBN 0-09-181472-3

Book / Osler’s Web: Inside the Labyrinth of the Chronic Fatigue Syndrome Epidemic.

Hillary Johnson. Crown Publishers Inc. New York 1996 ISBN 0-517-70353-X

## **1997**

Clinical Crossroads – A 56 year old woman with Chronic Fatigue Syndrome. AL Komaroff. Beth Israel Deaconess Medical Centre Clinical Conference. JAMA 1997;278:14:1179-1188

*“In addition to the symptoms included in the case definition, many patients with CFS also frequently report...intolerance of pharmaceuticals that affect the central nervous system....The more pertinent question to ask...is whether objective biological abnormalities can be found more often in patients with CFS. The medical literature of the past decade indicates that there are indeed such abnormalities...It is now evidence that this illness is not simply an imaginary one, nor the result of anxiously amplifying normal bodily sensations....Many patients with CFS have experienced atopic symptoms since childhood, and the atopic symptoms often flare in CFS”.*

Draft Clinical Guidelines on the Evaluation of Prolonged Fatigue and the Diagnosis and Management of Chronic Fatigue Syndrome. Produced by a Working Group convened by The Royal Australasian College of Physicians, December 1997. Published by The Medical Journal of Australia.

Individual differences in neural sensitisation and the role of context in illness from low-level environmental chemical exposures. Bell IR, Klimas NG, Patarca R et al. Environ Health Perspect 1997;105 (Suppl 2):457-466

*“This paper summarises the clinical phenomenology of MCS (and) outlines the concepts and evidence for the olfactory-limbic, neural sensitisation model for MCS....Neural sensitisation is the progressive amplification of responsivity by the passage of time between repeated, intermittent exposures. Initiation of sensitisation may require single toxic or multiple subtoxic exposures, but subsequent elicitation of sensitised responses can involve low or non-toxic levels. Thus, neural sensitisation could account for the ability of low levels of environmental chemicals to elicit clinically severe, adverse reactions in MCS”.*

Chronic Fatigue Syndrome. Mark A Demitrack, N Cary Engelberg. Current Therapy in Endocrinology and Metabolism 1997;6:152-160

*“An abrupt onset precipitated by a stressor (and) exacerbation of allergic responses are characteristic of glucocorticoid deficiency. We suggest that some of the reputed immunologic disturbances in patients with CFS (eg. exacerbation of allergic responses) could also reflect a relative glucocorticoid deficiency”.*

Fibromyalgia, Chronic Fatigue Syndrome and Myofascial Pain Syndrome. Don L Goldenberg. Curr Op Rheumatol 1997;9:125-142

*“Allergies are common in CFS...There was a 73% incidence of atopy in the CFS patients”.*

Neuroendocrine Correlates of Chronic Fatigue Syndrome. A Brief Review. Mark A Demitrack. J Psychiat Res 1997:31:1:69-82

*"...non-specific indices of immune activation reported in CFS (eg. increased allergic sensitivity) may well be secondary to a chronic reduction in circulating cortisol levels".*

Interstitial cystitis: unexplained associations with other chronic diseases and pain syndromes. Alagiri M et al. Urology 1997:49: (5A Suppl):52-57

*"Allergies, irritable bowel syndrome, sensitive skin (and) fibromyalgia were the most common diseases in the interstitial cystitis population. Interstitial cystitis has as yet an unexplained association with certain other chronic diseases and pain syndromes".*

Profile of patients with chemical injury and sensitivity. Ziem G, McTamney J. Environ Health Perspect 1997:105: Suppl 2:417-436

*"It is thought that patients with chemical sensitivity have organ abnormalities including the liver, nervous system (brain, including limbic, peripheral and autonomic), immune system, and porphyrin metabolism, probably reflecting chemical injury to these systems. Laboratory results are not consistent with a psychologic origin of chemical sensitivity. Substantial overlap between chemical sensitivity, fibromyalgia and chronic fatigue syndrome exists: the latter two conditions often involve chemical sensitivity".*

An Expert's Explanations on MCS. I Bell. The CFIDS Chronicle, Winter 1997:91-92

Government Agencies Acknowledge MCS. The CFIDS Chronicle, Spring 1997:49. US Government agencies formally recognized that MCS is a serious problem and a legitimate disability; many States and Government Departments (including the US department of Justice, the Department of Housing and Urban development and the Department of Education) afford sufferers protection under specific laws enacted to safeguard the civil rights of the disabled.

Chemical Sensitivity: Allergic to the 20<sup>th</sup> Century. D Jones. WDDTY. Nov 1997:8:8:1-4

Toxicant-induced Loss of Tolerance – An Emerging Theory of Disease? Claudia S Miller. Environmental Health Perspectives March 1997:105:2:445-453

## **1998**

A critical analysis of multiple chemical sensitivity. Thomas JG. Med Hypotheses 1998:50(4):303-311

*“Multiple chemical sensitivity (MCS) is a chronic condition of irritation and inflammation of sensory organs, gastrointestinal distress, fatigue, and compromised neurological function....MCS is believed to be a disease that spreads between various target organs and is caused by sensitisation to chemicals with very different structures. MCS is often attributed to free radical production and stress, which indirectly causes spreading because of damage to the immune system”.*

Neurally-mediated hypotension and chronic fatigue syndrome. PO Rowe, H Calkins. Am J Med 1998;105 (3A):15S-21S

*“There is a high prevalence of allergic disease amongst those with CFS...both viral infection and allergic reactions to food antigens enhance the excitability of mechanically sensitive vagal afferents...(providing) a potential link between these clinical situations and the development of neurally-mediated hypotension (NMH) in patients with allergy, (suggesting the need) to include general medical management techniques to prevent exacerbations of food and inhalant allergies in those with CFS”.*

Chronic Fatigue Syndrome. A Chaudhuri et al. Proc R Coll Phys Edin 1998;28:150-163

*“...patients often suffer from atopies. There is incontrovertible evidence that CFS patients suffer from atopy more frequently than normal population, for which an aberrant cytokine response is a possible explanation”.*

Chronic Fatigue in Overlapping Syndromes. A Chadhuri, P Behan. CNS. Summer 1998;1:2:16-20

*“The organic nature of CFS soon became apparent from a detailed study of symptoms and neuroendocrine tests. Symptoms of CFS are influenced by specific drugs and anaesthetics that can alter cell membrane ion channel function”.*

Evidence for and pathophysiologic implications of HPA axis dysfunction in fibromyalgia and chronic fatigue syndromes. Mark A Demitrack, Leslie J Crofford. Ann NY Acad Sci 1998;840:684-697

*“Buchwald and colleagues...described a high prevalence of symptoms not previously thought to be characteristic of fibromyalgia, such as recurrent rashes, a history of allergies....Among the principal symptoms of glucocorticoid deficiency (is an) exacerbation of allergic responses”.*

Multiple Chemical Sensitivity (MCS). Chemical Injury Information Network Leaflet 1998.

Allergology: Blimps versus nuts. David Freed. *Lancet* 1998;351:221-222 (Review of the book *Environmental Medicine in Clinical Practice*, ed. Honor Anthony, Sybil Birtwhistle, Keith Eaton, Jonathan Maberly pub. 1997 by The British Society for Environmental and Nutritional Medicine (BSAENM); pp481; £43 ISBN 0-9523397-2-2):

*“‘Environmental Medicine in Clinical Practice’ is the acceptable face of clinical ecology and contains a lot more hard science than you might expect.....(clinical ecologists) do have observations about the many medically unexplained symptoms that tend to be labelled as somatisation or hypochondria....The official line put out by traditionalists that ‘there is no evidence’ for clinical ecology will not do; there **is** evidence, and these authors have presented it”.*

The relationship between chronic fatigue syndrome, fibromyalgia and chemical sensitivity. A Vojdani, P Chopra. Fourth International AACFS Research & Clinical Conference on CFIDS Oct 1998: Abstract page 100

Prevalance and Overlap of Chronic Fatigue Syndrome and Fibromyalgia Syndrome Among 100 Patients With Multiple Chemical Sensitivity. Albert Donnay: Presentation at Fourth International AACFS Research & Clinical Conference on CFIDS Oct 1998, Mass. USA. Abstract page 53

The Relationship between Chronic Fatigue Syndrome, Fibromyalgia, and Chemical Sensitivity A Vojdani et al. (*ibid*)

A Report on MCS -- Background and Historical Review. Article. US Government Web Site 1998.

A Report on Multiple Chemical Sensitivity (MCS): The US Interagency Workgroup on Multiple Chemical Sensitivity was held on 24<sup>th</sup> August 1998 and its Report contains 167 reference papers (see especially Sections I, IV, V, VII, VIII, X [the reference papers] & XI). The Workgroup reviewed the scientific literature pertinent to MCS, considered recommendations from various expert panels on MCS, reviewed past and current federal action, and developed technical and policy recommendations. The Workgroup noted the public health issues and challenges presented by MCS and the need to better inform the health-care community about MCS, stating that patients should not be offered ineffective or potentially dangerous treatments. The Workgroup noted the disruption of homeostasis that resulted from a wide range of exposures and the adverse effects commonly encountered with substances such as cosmetics, petrol/diesel, exhaust fumes, aerosol air fresheners, laundry detergents and solvents present in products such as construction materials, newspaper and other ink-related products, furniture and carpets. Federal agencies have increased their cooperation on MCS issues through sharing current knowledge, development of research

recommendations and co-sponsorship of workshops and conferences and the Workgroup noted that this Report is part of that continuing effort. The Report included selected legal cases and Court decisions which have found that MCS qualifies as a handicap for the purposes of employment discrimination statutes.

## 1999

### Neural sensitisation model for multiple chemical sensitivity: overview of theory and empirical evidence.

Bell IR et al. *Toxicol Ind Health* 1999;15(3-4):295-304

*“This paper summarises...evidence for a neural sensitisation model of hyperresponsivity to low-level chemical exposures in MCS. MCS is a chronic polysymptomatic condition in which patients report illness from low levels of many different, structurally unrelated environmental chemicals....Findings implicate, in part, dopamine mesolimbic pathways and limbic structures....The neural sensitisation model provides direction for further systematic human and animal research on the physiological bases of MCS”.*

Presentation by Jonathan Brostoff at the International Conference Fatigue 2000 arranged by The National ME Centre, Harold Wood, Essex, in conjunction with Essex Neurosciences Unit, 23-24 April 1999. At the time, Jonathan Brostoff was Professor of Allergy and Environmental Health at University College, London and was Director of the Centre for Allergy Research.

*“A number of these associated symptoms are often accepted as part and parcel of the total CFS symptomatology....These symptoms consist of chemical sensitivity”.*

A Review of multiple chemical sensitivity. RA Graveling, A Pilkington et al. *Occup Environ Med* 1999;56:73-85 (Journal of The Faculty of Occupational Medicine of The Royal College of Physicians of London). This Report was commissioned by the UK Health & Safety Executive.

Multiple Chemical Sensitivity: A 1999 Consensus. *Archives of Environmental Health* May/June 1999;54:3:147-149

The Environmental Exposure and Sensitivity Inventory (EESI): a standardised approach for measuring chemical intolerances for research and clinical applications. Claudia S Miller and Thomas J Prihoda. *Toxicology and Industrial Health* 1999;15:370-385

A controlled comparison of symptoms and chemical intolerances reported by Gulf War Veterans, implant recipients and persons with multiple chemical sensitivity. Claudia S Miller and Thomas Prihoda. *Toxicology & Industrial Health*, 1999;15:386-397

Interferon-induced proteins are elevated in blood samples of patients with chemically or virally induced chronic fatigue syndrome. Vojdani A; Lapp CW. Immunopharmacol Immunotoxicol 1999;21(2):175-202

*“Overlapping symptomatologies between Chronic Fatigue Syndrome (CFS) and Chemical Sensitivity have been observed by different investigators. Therefore, it is of great importance to develop biomarker(s) for possible differentiation between viral induced CFS (without sensitivity to chemicals) versus chemically induced CFS....To elucidate mechanisms involved in viral versus chemical induction of 2-5A Synthetase and PKR, MDBK cell lines were cultured either in the presence or absence of HHV6, MTBE, or benzene, heat shock proteins and interferon-beta....When MDBK cells were incubated either with MTBE + benzene or HHV6 in the presence or absence of anti-IFN-beta or anti-HSP70, the activities of both 2-5 A and PKR in HHV6 infected cells were inhibited by more than 90%....This variation in the induction of 2-5A and PKR by anti-HSP70 or IFN beta indicates involvement of IFN-beta in viral induction 2-5A and PKR, and HSP involvement in chemical induction of these enzymes”.*

## **2000**

Symptom patterns in long-duration chronic fatigue syndrome. F Friedberg et al. J Psychosom Res 2000;48:59-68

*“The pattern of comorbid disorders in the chronic fatigue syndrome groups was consistent with hypersensitivity and viral reactivation. Evidence for hypersensitivity in CFS was found. A related finding suggests the presence of drug hypersensitivity as well. Hypersensitivity reactions may influence CFS symptoms generation. A hypersensitivity mechanism and viral infection may contribute to illness persistence in CFS”.*

Multiple Chemical Sensitivity – Recognition and Management. Third Scientific Report of the British Society for Allergy, Environmental and Nutritional Medicine. Ed: KK Eaton and HM Anthony. Pub. BSAENM, Knighton, UK 2000.

Multiple Chemical Sensitivity and Management. Keith Eaton. J Nutr Environ Med 2000;10:39-84

Self-reported sensitivity to chemical exposures in five clinical populations and healthy controls.

Nawab SS, Miller Claudia S, Straus SE et al. Psychiatry Res 2000;95(1):67-74

*“Patients with CFS...self-reported more sensitivity to chemical exposures than normal controls....A possible relationship between reported chemical sensitivity and hypothalamic-pituitary-adrenal (HPA) axis functioning is discussed”.*

Chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities in a community-based sample of persons with chronic fatigue syndrome-like symptoms. Jason LA et al. Psychosom Med 2000:Sept-Oct: 62(5):655-663

*“The aim of this study was to determine illness comorbidity rates for individuals with CFS, FM and MCS....Individuals with MCS or more than one diagnosis reported more physical fatigue.....People with CFS, MCS or FM endure significant disability in terms of physical, occupational and social functioning, and those with more than one of these diagnoses also report greater severity of physical and mental fatigue”.*

Book / Faces of CFS: Case Histories of Chronic Fatigue Syndrome. David S Bell. Lyndonville Publications, New York 2000. ISBN 0-970770-0-0

## **2001**

The compelling anomaly of chemical intolerance. Miller CS. Ann NY Acad Sci 2001:933:1-23

*“In science, anomalies expose the limitations of existing paradigms and drive the search for new ones....Today we are witnessing another medical anomaly – a unique pattern of illness involving chemically exposed groups in more than a dozen countries, who subsequently report multisystem symptoms and new onset chemical, food and drug intolerances....observations...suggest that multiple neurotransmitter pathways may be involved”.*

Controlled exposure to volatile organic compounds in sensitive groups. Fiedler N, Kippen HM. Ann N Y Accad Sci 2001:933:24-37

*“Sensitivities to chemicals are characterized by symptoms in multiple organ systems in response to low level chemical exposure...Sensitive subgroups include subjects who met Cullen’s 1987 criteria for multiple chemical sensitivity (MCS)....Controlled...exposure studies reveal that significant responses can be observed in chemically sensitive subjects even when de-adaptation has not occurred”.*

Delayed-type hypersensitivity and chronic fatigue syndrome: the usefulness of assessing T-cell activation by flow cytometry. Brunel JL et al. J Allerg Immunol (Paris), April 2001: 33(4):166-192

*“This article describes the detection of delayed-type hypersensitivity responses to certain common environmental antigens in almost 50% of patients with this syndrome. This work is in the spirit of a multifactorial approach to the group of conditions referred to as ‘chronic fatigue syndrome’ ”.*

First International Environmental Illness Conference, 18 -19 May 2001, Ottawa, Canada

This Conference examined Environmental Illness (EI) from the perspective of the medical management of the EI patient, including how to meet patients' needs for accommodation and a healthy environment. Environmental illness includes multiple chemical sensitivity (MCS), Chronic Fatigue Syndrome (CFS), Fibromyalgia (FM) and Gulf War Syndrome (GWS). Speakers included Dr Gerald Ross, Professor Tang Lee, Dr Gunnar Heusar and Professor Nicholas Ashford.

Chronic Fatigue Syndrome following a toxic exposure. D Racciatti et al. Sci Total Environ, 10 April 2001:270:1-3:27-31

*"All subjects were investigated by clinical examination, neurophysiological and immunologic studies and neuroendocrine tests. Patients exposed to toxic factors had disturbances of hypothalamic function (and) showed more severe dysfunction of the immune system with an abnormal CD4 / CD8 ratio (and) decreased levels of NK cells (CD56+)"*.

2002

Symptomatology and etiology of multiple chemical sensitivities in the southeastern United States.

Caress SM, Steinemann AC, Waddick C. Arch Environ Health 2002: Sept-Oct: 57(5):429-436

Exquisite Chemical Sensitivity Mechanism in MCS (the full title being "NMDA Sensitization and Stimulation by Peroxynitrite, Nitric Oxide and Organic Solvents as the Mechanism of Chemical Sensitivity in Multiple Chemical Sensitivity"). Martin L Pall. The FASEB Journal, September 2002: 16: 1407-1417.

Review by Margaret Williams (August 2002): This paper presents an explanation for the biological basis of the specific symptom pattern found in MCS (including the "spreading phenomenon") associated with chemical exposure and injury. When the elevated nitric oxide / peroxynitrite theory, together with the neural sensitization theory, are put together, the four mechanisms (nitric oxide-mediated stimulating of neural transmitter release; peroxynitrite-mediated stimulation of post-synaptic NMDA sensitization; peroxynitrite-mediated blood brain barrier permeabilization and nitric oxide inhibition of cytochrome P450 metabolism) would all be expected to act synergistically in line with the well-determined properties of LTP and the NMDA receptor system, thus producing the exquisite sensitivity found in MCS. All four mechanisms are individually well-documented and provide explanations for the most puzzling aspects of MCS, notably (i) how people with MCS can be so exquisitely sensitive to chemical exposure (ii) why hydrophobic organic solvents and organophosphate pesticides are implicated in MCS (iii) why MCS is chronic and (iv) how previous chemical exposure can lead to the induction of chemical sensitivity. The hypersensitivity is apparently two orders of

magnitude greater than that of ordinary individuals, and sufferers often report being sensitive to perfumes worn by people seated several seats away or even walking past them. MCS results in greatly reduced quality of life for sufferers. More symptoms of MCS may be attributed to central nervous system (CNS) dysfunction than to dysfunction of any other organ or organ system; however, there are MCS symptoms which are not attributed to a CNS origin, such as cardiovascular, respiratory, gastro-intestinal, genito-urinary, musculoskeletal and dermatologic origin. Thus whilst many of the symptoms seen in MCS appear to be of neurologic origin, various other organs appear to be impacted also. Other mechanisms of spread beyond the CNS include autonomic dysfunction, neurogenic inflammation and neuroendocrine dysfunction. Sceptics have been wont to scoff at MCS sufferers, claiming that 'there is no known mechanism whereby low levels of chemicals of widely varied chemical structure can interact adversely with numerous organ systems'; thanks to Pall, such disbelief and dismissal will no longer be tenable.

Role of pathological delayed-type hypersensitivity in chronic fatigue syndrome: importance of the evaluation of lymphocyte activation by flow cytometry and the measurement of urinary neopterin [Article in French]. Brunet JL, Fatoohi F, Liaudet AP, Cozon GJ. *Allerg Immunol (Paris)* 2002 Feb;34(2):38-44.

*"This article describes the detection of delayed-type hypersensitive responses to certain common environmental antigens in almost fifty per cent of patients with this syndrome....The results showed that the intensity of the DTH (delayed type hypersensitivity) response correlated with the number of T-cells activated in vitro".*

## 2003

Elevated nitric oxide/peroxynitrite theory of multiple chemical sensitivity: central role of N-methyl-D-aspartate receptors in the sensitivity mechanism. Pall ML. *Environ Health Perspect* 2003: Sept: 111(12):1461-1464

Engaging with Multiple Chemical Sensitivity. Malcolm Hooper. Presentation and Conference Proceedings; MCS International Conference, London, 2<sup>nd</sup>-3<sup>rd</sup> September 2003

## 2004

The vanilloid receptor as a putative target of diverse chemicals in multiple chemical sensitivity.  
Pall ML, Anderson JH. *Arch Environ Health.* 2004 Jul;59(7):363-75.

A national population study of the prevalence of multiple chemical sensitivity.

Caress SM, Steinemann AC. Arch Environ Health. 2004 Jun;59(6):300-5.

Case-control study of genotypes in multiple chemicals sensitivity: CYP2D6, NAT1, NAT2, PON1, PON2 and MTHFR. Gail McKeown-Eyssen et al; International Journal of Epidemiology 2004;33:971- 979

Illness and disability in Danish Chronic Fatigue Syndrome patients at diagnosis and 5-year follow-up. Andersen MM, Permin H, Albrecht F. J Psychosom Res. 2004 Feb;56(2):217-29.

*“Work disability was very high and increased further, social isolation remained high, emotional adjustment improved. There were increased problems with reading and with allergies..... CONCLUSION: CFS patients exhibit severe, long-term functional impairment. Substantial improvement is uncommon, less than 6%. Allergies and aspects of cognition may worsen, emotional adjustment often improves”.*

2005

Multiple-chemical sensitivity. Glinton GJ. Medsurg Nurs. 2005 Dec;14(6):365-9.

Clinical aspects of patients with MCS - from the standpoint of allergy. Hasegawa M, Ohtomo M, Mita H, Akiyama K. Arerugi. 2005 May;54(5):478-84.

Symptom profile of multiple chemical sensitivity in actual life. Saito M et al. Psychosom Med. 2005 Mar-Apr;67(2):318-25.

Chronic fatigue syndrome and multiple chemical hypersensitivity after insecticide exposure. Fernandez-Sola J et al. Med Clin (Barc) 2005;124(12):451-453 [article in Spanish]

*“Chronic Fatigue Syndrome (CFS) and Multiple Chemical Sensitivity (MCS) are well-defined illnesses that may appear after some toxic exposures....We report a consecutive series of 26 patients who developed CFS after exposure to insecticide products. It was associated with MCS in a third of cases....The course of the disease was...disabling in 6 cases (23%)”.*

Are attention deficit hyperactivity disorder and chronic fatigue syndrome allergy related? Bellanti JA et al Allergy Asthma Proc 2005;26(1):19-28

*“...there are a group of diseases that the allergist-immunologist may be called up to manage...that appear to be initiated by allergic mechanisms....In patients with CFS, there*

*appears to be a fundamental dysfunction of the neuroendocrine-immunological system with deficiencies of immunological and neurological function which, together with chronic viral infection, may lead to a sequence of events responsible for the symptoms of this disorder....An understanding of the interactive responses involved in the neuroendocrine-immunological network is essential for a comprehension of the pathophysiology of...CFS...and the role of allergies appears to be an important triggering event...”.*

## 2007

Multiple chemical sensitivity: study of 52 cases. Nogué S, Fernández-Solá J, Rovira E, Montori E, Fernández-Huerta JM, Munné P. Med Clin (Barc). 2007 Jun 16;129(3):96-98

*“Chronic Fatigue Syndrome (CFS) and Multiple Chemical Sensitivity (MCS) are well-defined illnesses that may appear after some toxic exposures....We report a consecutive series of 26 patients who developed CFS after exposure to insecticide products. It was associated with MCS in a third of cases....The course of the disease was...disabling in 6 cases (23%)”.*

Multiple chemical sensitivity in the clinical setting. Cooper C. Am J Nurs. 2007 Mar;107(3):40-7

Odour processing in multiple chemical sensitivity Hillert L et al. Hum Brain Mapp 2007;28(3):172-182

Nitric oxide synthase partial uncoupling as a key switching mechanism for the NO/ONOO—cycle  
Martin L Pall. Med Hypoth 2007: doi:10.1016/j.mehy.2007.01.070

## 2008

The challenge of multiple chemical sensitivity. Spencer TR, Schur PM. J Environ Health. 2008 Jun;70(10):24-7.

Lower frequency of IL-17F sequence variant (His161Arg) in chronic fatigue syndrome.  
Metzger K, Fremont M, Roelant D, De Meirleir K. Biochem Biophys Res Commun  
2008;376(1):231-233

*“Chronic fatigue syndrome (CFS) is characterized by immune dysfunctions including chronic immune activation, inflammation, and alteration of cytokine profiles. T helper 17 (Th17) cells belong to a recently identified subset of T helper cells, with crucial regulatory function in inflammatory and autoimmune processes. Th17 cells are implicated in allergic inflammation, intestinal diseases, central nervous system inflammation, disorders that may all contribute to the pathophysiology of CFS.... We investigated the association between CFS and the frequency of rs763780, a C/T genetic polymorphism leading to His161Arg substitution in the IL-17F protein. The His161Arg variant (C allele) antagonizes the pro-inflammatory effects of the wild-type IL-17F. A significantly lower frequency of the C allele was observed in the CFS population, suggesting that the His161Arg variant may confer protection against the disease. These results suggest a role of Th17 cells in the pathogenesis of CFS”.*

Anaesthesia for patients with idiopathic environmental intolerance and chronic fatigue syndrome. Fisher MM, Rose M. Brit J Anaesth 2008;101(4):486-491

*“Idiopathic environmental intolerance syndrome (EI), formerly known as multiple chemical sensitivity syndrome (MCSS), and chronic fatigue syndrome (CFS) are controversial diseases and there is little information in the literature regarding the appropriate conduct of anaesthesia in such patients....The patients had a significant incidence of adverse events related to anaesthesia....Anaesthesia is likely to be associated with adverse effects in these patients...”.*

2009

Experiences of problems in individuals with hypersensitivity to odours and chemicals.  
Larsson C, Mårtensson L. J Clin Nurs. 2009 Mar;18(5):737-44.

Multiple Chemical Sensitivity: Toxicological and Sensitivity Mechanisms. Martin L Pall. Wiley Online Library. Press Release: Epidemic of Multiple Chemical Sensitivity, A Disease Caused by Toxic Chemical Exposure. Martin L Pall 16<sup>th</sup> October 2009, announcing the publication of Pall’s contributed chapter entitled “Multiple Chemical Sensitivity: Toxicological Questions and Answers” in a prestigious textbook (“General and Applied Toxicology”, 3<sup>rd</sup> edition, pub. John Wiley & Sons). The press release said: (1) *“MCS is a stunningly common disease, even more common than diabetes.* (2) *MCS is caused by toxic chemical exposure. Cases of MCS are initiated by exposure to seven classes of chemicals.* (3) *The role of chemicals acting as toxicants in MCS has been confirmed by genetic studies.* (4) *We have a well-supported mechanism for MCS (which) explains both*

*the high level chemical sensitivity that is the most characteristic symptoms of MCS, as well as many other symptoms and signs of this disease. (5) For over 20 years, some have falsely argued that MCS is a psychogenic disease...this view is completely incompatible with the evidence”* <http://www.thetenthparadigm.org>

## 2010

### Idiopathic environmental intolerances (IEI): from molecular epidemiology to molecular medicine.

De Luca C, Scordo G, Cesareo E, Raskovic D, Genovesi G, Korkina L. Indian J Exp Biol. 2010 Jul;48(7):625-635.

*“Inherited or acquired impairment of xenobiotics metabolism is a postulated mechanism underlying environment-associated pathologies such as multiple chemical sensitivity, fibromyalgia, chronic fatigue syndrome...and others, also collectively names idiopathic environmental intolerances (EI)...These disabling conditions share the features of polysymptomatic multi-organ syndromes, considered by part of the medical community to be aberrant responses triggered by exposure to low-dose organic and inorganic chemicals and metals, in concentrations far below average reference levels admitted for environmental toxicants....Free radical/antioxidant homeostasis may also be heavily implicated...in the chronic damage of cells and tissues, which is in part correlated with clinical symptoms....More clinical studies of...the possible role of inflammatory mediators, promise a better understanding of this pathologically increased sensitivity to low-level chemical stimuli...”.*

### Biological definition of multiple chemical sensitivity from redox state and cytokine profiling and not from polymorphisms of xenobiotic-metabolising enzymes.

Chiara De Luca et al. Toxicol Allp Pharmacol 2010: doi:10.1016/j.taap.2010.04.017

Relationships among rhinitis, fibromyalgia, and chronic fatigue. Baraniuk JN, Zheng Y. Allergy Asthma Proc 2010:31(3):169-178

*“This article shows the relevance of CFS and allied disorders to allergy practice. CFS has significant overlap with...central nervous system maladaptations (central sensitization) recorded by functional magnetic resonance imaging (fMRI). Neurological dysfunction may account for the overlap of CFS with idiopathic nonallergic rhinopathy. Scientific advances are in fMRI...and, potentially, infection with xenotropic murine leukaemia-related virus provide additional insights to novel pathophysiological mechanisms....As allergists, we must accept the clinical challenges posed by these complex patients...”*

Book / Multiple Chemical Sensitivity. Malcolm Hooper; Chapter 50. In: Psychiatry – An evidence-based text. Ed: Basant K Puri & Ian Treaden; Hodder Arnold Publications 2010.

## 2011

Isolation and lack of access in multiple chemical sensitivity: A qualitative study. Gibson PR, Sledd LG, McEnroe WH, Vos AP. Nurs Health Sci. 2011 Sep;13(3):232-7. doi: 10.1111/j.14422018.2011.00606.x. Epub 2011 May 20.

Multiple chemical sensitivity is for real. Article in Finnish. Hannuksela M, Haahtela T. Duodecim 2011;127(7):706-711. Review.

*“Sometimes the symptom is manifested as flushing of the face”.*

The search for reliable biomarkers of disease in multiple chemical sensitivity and other environmental intolerances. De Luca C et al. Int J Environ Res Public Health 2011;8(7):2770-2797

*“The finding of relevant alterations of catalase, glutathione-transferase and peroxidase detoxifying activities significantly correlating with clinical manifestations of MCS has recently registered some progress towards the identification of reliable biomarkers of disease onset, progression, and treatment outcomes”.*

**This list is far from comprehensive and is merely illustrative.**

