

**ALLERGIES AND MULTIPLE CHEMICAL SENSITIVITY  
IN MYALGIC ENCEPHALOMYELITIS / CHRONIC FATIGUE SYNDROME**

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At this auspicious time of celebration of 25 years of Bart's Fatigue Service for those suffering from chronic fatigue -- interchangeably referred to by Wessely School members as fatigue, chronic fatigue syndrome, CFS, CFS/ME, ME, MUS (medically unexplained symptoms), MUPS (medically unexplained physical symptoms) and as a functional somatic syndrome -- it is perhaps worth recalling that as part of the "service" provided over the last 25 years, the Head of the Unit, psychiatrist Professor Peter White (who is also Principal Investigator of the MRC PACE Trial) seems to have been so busy providing this remarkable "service" that he has been unable to keep abreast of the emerging medical science relating to the chronic inflammatory neuroimmune disorder known internationally as ME/CFS.

There are many examples of Professor White's apparent lacunae. A particularly notable one concerns the incidence of allergies and multiple chemical sensitivity in ME/CFS which, curiously, given the sheer amount of published evidence, Professor White denies.

The draft NICE Guideline on CFS/ME that was sent out for consultation included a section on multiple chemical sensitivity (MCS) as a component of CFS/ME and called for "*proper training*" about it to be given to "*those caring for an individual with severe CFS/ME professionally*". Professor White sprang into action over this, stating starkly: "*A patient with increased sensitivity to the smell of various chemicals may be suffering from multiple chemical sensitivity, but you would be making a dubious assumption to state that this is part of or even characteristic of severely disabling CFS/ME. MCS is a potentially remediable condition through a graded exposure programme on the basis that the underlying pathophysiology is a conditioned response. **It should not be considered as a part of CFS/ME***" (Stakeholder comments on Full Guideline: 92: 261 3). NICE's response was to remove this section on MCS and it did not appear in the final Guideline.

It is worth recalling that Multiple Chemical Sensitivity (MCS) may be classified in ICD-10 at T78.4 (Allergy, Unspecified) and that "Allergy Unspecified" is coded in the UK Read Codes at SN53.

The following examples were published during the 25 years of the "fatigue service" of which Professor White is so proud.

**Allergies, hypersensitivities and intolerances**

Multiple allergies are frequently a component of ME/CFS. Throughout the ME/CFS literature from at least the 1970s there is increasing reference to the existence of allergies and hypersensitivities to foods, normal household chemicals, gas, petrol, perfumes, prescription drugs, agricultural chemicals and even to seminal fluid; there is also reference to adverse reactions to tap water, an early such reference being in 1982 (Hypersensitivity to Mains Tap Water in Adults: its Clinical Features and Treatment. CWM Wilson. Nutrition and Health 1982:1:85-91). **Up to 60% of patients with ME/CFS appear to be allergic.**

Multiple Chemical Sensitivity (MCS) is a well-documented component of ME/CFS due to the significant immune system disruption and dysregulation that since the 1980s has been documented in the disorder in peer-reviewed international journals (there are over 3,000 pages on MCS on the internet using one search engine alone).

In 1983 it was recognized that such patients fare badly, not least because of the obstacles allergy sufferers have to overcome in coping with their allergies on a day-to-day basis: apart from the frightening nature of the symptoms themselves, their worrisome unpredictability and the limitations in diet and lifestyle they impose, many difficulties are attributable to the ignorance of other people, including medical professionals, who are often the worst offenders. The instability of the condition and its liability to deteriorate is a source of much additional distress to sufferers and the cruel and mindless attitudes they encounter add insult to injury (The Allergy Problem: Why People Suffer and What Should Be Done. Vicky Rippere MA; PhD; BSc; M Phil. Thorsons, 1983).

Given the evidence of a disrupted immune system, it was known in 1989 that raised interleukin levels could ultimately lead to raised IgE by stimulating the B cells (in other words, if not dealt with by the immune system, an on-going virus may result in allergies – Int Arch Allergy Appl Immunol 1989:89:90-97).

Normal body cells cannot be attacked by the immune system unless they have been persuaded to display on their surfaces complex glycoprotein molecules known as class II MHC antigens (which they do not normally display). They can be induced to do this by gamma interferon, an anti-viral chemical produced by the immune system when under virus attack, which make cells susceptible to this on-going attack by the immune system, thus doing further damage to the very system upon which the body depends for its defence.

There have been many published papers demonstrating the association of numerous viruses in ME/CFS patients, most notably the enterovirus Coxsackie B (CBV), but in 2009, emerging evidence demonstrated the involvement of a gamma retrovirus in ME/CFS (XMRV, which is only the third human retrovirus known, the other two being HIV/AIDS and HTLV, the Human T-cell lymphotropic virus that causes leukaemia and lymphoma). A retrovirus inserts itself into the host's DNA by using RNA and once there, it stays for life. Viruses such as XMRV can cause blood vessels around the body to leak, a common symptom of ME/CFS. XMRV is thought to disrupt the immune system which, once

dysregulated, cannot control the reactivation of multiple latent viruses (including enteroviruses) and microbial agents, nor the cascade of allergic reactions that, once triggered, cannot be switched off, as there is no feed-back loop in the immune system.

**The following pages provide information about MCS and about allergies in ME/CFS**

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).

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 peroxyxynitrite (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.

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. 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 UK Reports on allergies / sensitivities / effects of chemicals**

1. The National Task Force on ME/CFS/PVFS 1994, published by Westcare, Bristol, which was supported by the Department of Health.

2. 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.

3. “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*”.

3. 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)*”.

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

5. 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 1997. In particular, the US Department of Housing specifically recognises MCS as a disability granting those afflicted with full protection of federal housing laws for the disabled
- US Information for Physicians (1996) (for more information, see below)
- The Australasian Medical Association Guidelines for Physicians (1997)
- 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
- 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.

### **Books which specifically refer to allergies/sensitivities as being part of ME/CFS**

As well as published medical reference papers, there are a number of published textbooks and books on ME/CFS which refer to allergies as being part of the disorder (resulting from the immune system dysfunction that is recognised as the key reproducible laboratory finding in ME/CFS).

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

### **Major Textbooks on ME/CFS which refer to allergies/hypersensitivities**

1. Myalgic Encephalomyelitis and Postviral Fatigue States: A Melvin Ramsay (second edition); Gower Medical Publishing, 1988 (the first edition, Postviral Fatigue Syndrome: The Saga of The Royal Free Disease, was published in 1986)
2. Allergies are referred to in the 724-page textbook on ME: "The Clinical and Scientific Basis of Myalgic Encephalomyelitis Chronic Fatigue Syndrome". Ed: BM Hyde et al; Nightingale Research Foundation, Ottawa 1992, which is the published proceedings of the International Symposium on ME held at the University of Cambridge, UK in 1990).
3. Allergies are mentioned as a component of ME/CFS in the textbook on ME: "Postviral Fatigue Syndrome". Ed. Professors James Mowbray and Rachel Jenkins. John Wiley & Sons, Chichester, 1991.
4. Betrayal by the Brain: The Neurologic Basis of Chronic Fatigue Syndrome, Fibromyalgia Syndrome and Related Neural Network Disorders Jay A Goldstein The Haworth Medical Press, New York, 1996
5. The existence of allergies in ME/CFS is referred to in a comprehensive over-view: Chronic Fatigue Syndrome: A Biological Approach Ed: Patrick Englebienne & Kenny De Meirleir. CRC Press 2002.

### **Non-medical and self-help books**

An illustrative-only selection of books includes the following:

### **1982**

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

### **1985**

Better Recovery from Viral Illness. Darrel Ho-Yen. Dodona Books, Inverness, 1985 ISBN 0 9511090 1 4

### **1986**

Myalgic Encephalomyelitis. Celia Wookey. Croom Helm, 1986. ISBN 0-7099-3672-9

### **1988**

The Body at War. John Dwyer. Unwin Hyman, 1988 ISBN0-04-320225-X

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).

### **1989**

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

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

Why M.E.? Belinda Dawes & Damien Downing. Grafton 1989 ISBN0-586-20666-3

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

Understanding ME David Smith. Robinson Publishing, London 1989 ISBN 1 85487 019 X

Overload: beating ME, the Chronic Fatigue Syndrome. Jacqueline Steincamp (originally published in 1988 by Cape Catley Ltd, New Zealand). Fontana/Collins, 1989 ISBN 0-00-637478-6

**1990**

Chronic Fatigue Syndrome Jay A Goldstein. Published by The CFS Institute, Beverly Hills, CA.1990  
ISBN 0-9625654-0-7

**1991**

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

Many more such books exist, but these earlier books demonstrate that allergies as a component of ME/CFS have been known about for decades.

**1992**

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

**1994**

The Canary and Chronic Fatigue Majid Ali. Life Span Press, New Jersey USA 1994  
ISBN 1-879131-04-8

**1996**

Surviving M.E. Joyce Fox. Vermillion (Random House UK Ltd) 1996 ISBN 0-09-181472-3

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

**2000**

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

**Important Textbooks on MCS**

1. Chemical Sensitivity, In: Clinical Ecology – the treatment of ill health caused by environmental factors.  
G. Lewith & J. Kenyon (University of Southampton), Thorsons, 1985



2. “Chemical Exposures: Low Levels and High Stakes”. Professors Nicholas Ashford & Claudia Miller, pub. van Nostrand Reinhold, New York, 1991. This book provides comprehensive coverage of chemical exposures, sensitive populations, key terms and concepts, origins and health effects, mechanisms, diagnosis, and how to respond to the problem.
3. The major international medical textbook on MCS is entitled “Chemical Sensitivity” (Professor William Rea; CRC Inc). Volume I: Principles and Mechanisms (1992); Volume II: Sources of Total Body Load (1994); Volume III: Clinical Manifestations of Pollutant Overload (1995); Volume IV: Tools of Diagnosis and Methods of Treatment (1997).
4. MCS is addressed in the standard medical textbook on environmental medicine: “Environmental Medicine in Clinical Practice”. H. Anthony et al. BSAEM 1997.

### **Notable (text)books which address the problem of allergies, hypersensitivities and intolerances**

As well as published medical reference papers, there are a large number of published books which refer to the problem of allergies, hypersensitivities and intolerances, including the following:

Food Allergy and Intolerance. Brostoff, J, Challacombe SJ (eds); Bailliere Tindall, London, Philadelphia, 1987

Food Intolerance. Ed: John Dobbing. Bailliere Tindall, 1987

The Complete Guide to Food Allergy and Intolerance. Brostoff J, Gamlin L. Bloomsbury Publications, London, 1989

Dietary Management of Food Allergies and Intolerances: A Complete Guide. Joneja JV; JA Halls Publishers Ltd; Vancouver, BC, Canada, second edition 1998 (pp 426).

### **Publications on ME/CFS, including allergies/sensitivities**

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.

### **Important papers on MCS**

MULTIPLE CHEMICAL SENSITIVITY: Chemical Injury Information Network: List of published reference papers on MCS (available online)

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

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

Ecological Illness Law Reports. June 1988

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

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

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

Winning Workplace Litigation: Chemicals in the Environment: MULTIPLE CHEMICAL SENSITIVITY. Earon S. Davis, Ecological Illness Law Report, October 1989

USA: Multiple Chemical Sensitivity. J.B. Sibbison, Lancet 1991: 337:1469-1470

Special report: Multiple Chemical Sensitivity. B. Hileman, Chemical & Engineering News, July 1991:26-42

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

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

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

Comparison of patients with Chronic Fatigue Syndrome, Fibromyalgia and MULTIPLE CHEMICAL SENSITIVITY. Dedra Buchwald & Deborah Garrity. Arch Int Med 1994;154:2049-2053

Psychogenic Origins of MULTIPLE CHEMICAL SENSITIVITY Syndrome: A Critical Review of the Research Literature. A.L. Davidoff, L. Foggarty. Arch Environ Health, 1994;49:5:316-325

Potential Animal Models of MULTIPLE CHEMICAL SENSITIVITY with Cholinergic Sensitivities. Overstreet D et al, Toxicology, 1996;111:1-3:119-134

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, 1996

Potential animal model of multiple chemical sensitivity with cholinergic sensitivities.  
Overstreet DH,  
Miller CS et al. Toxicology 1996;111:1-3

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

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

*"Substantial overlap between chemical sensitivity, fibromyalgia and chronic fatigue syndrome exists".*

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

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

Acceptance by Federal Agencies of MULTIPLE CHEMICAL SENSITIVITY. CFIDS Chronicle Spring 1997:49

Profile of Patients with Chemical Injury and Sensitivity. Grace Ziem and James McTamney. Environmental Health Perspectives 1997;101:2: pp 26

Prevalence and overlap of Chronic Fatigue Syndrome and Fibromyalgia Syndrome among 100 patients with MULTIPLE CHEMICAL SENSITIVITY, Albert Donnay: presentation at 4<sup>th</sup> International AACFS Research & Clinical Conference of CFIDS, Mass, USA, October 1998

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

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

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

A Review of Multiple Chemical Sensitivity. R A Graveling et al; Occup Environ Health: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 and Safety Executive

MULTIPLE CHEMICAL SENSITIVITY: A 1999 Consensus. Arch Env Health: 1999:54:3:147-149; signatories include 34 of the world's most eminent experts in MCS

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

Multiple Chemical Sensitivity and Management. Keith Eaton; J Nutr Env 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"*.

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 2000.

Controlled exposure to volatile organic compounds in sensitive groups. Fiedler N, Kipen HM. Ann NY Acad 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”.*

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”.*

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

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

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%)”.*

Multiple chemical sensitivity: study of 52 cases [article in Spanish]. Nogue S et al. Med Clin (Barc) 2007:129(3):96-98

*“Multiple chemical sensitivity (MCS) is characterized by a loss of tolerance to various environmental chemicals....It is frequently triggered by exposure to chemical agents, especially insecticides. An association with chronic fatigue syndrome is common....the patients’ quality of life is seriously affected”.*

Multiple Chemical Sensitivity: Toxicological and Sensitivity Mechanisms. Martin L Pall, 2009

<http://www.thetenthparadigm.org>

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 Toxicology and Applied Pharmacology 2010: doi:10.1016/j.taap.2010.04.017

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

**That MCS is a recognised condition requiring home care is confirmed by the Brochure from Healthcare at Home Ltd, showing Total Allergy Syndrome as a condition for which they provide NHS Homecare. They are the UK’s leading providers 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 self-funding patients.**

### **Examples of published papers on allergies / ME/CFS**

There are over 5,000 papers showing that ME/CFS is a serious organic disorder and that the existence of allergies, hypersensitivities and intolerances in ME/CFS patients has long been recognised. Some extracts are included because they are illustrative.

**Please note:** for reasons of space (not to deflect from the meaning or intention of the papers), the sequential text has been separated by means of “...” or “....”.

### **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 by Viruses: 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. The Lancet Feb 1978:426-428

### **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

### **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 StC 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

## **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

## **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 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. 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

## **1986**

Food Intolerance. RH Loblay, AR Swain. In: *Recent Advances in Clinical Nutrition* Ed: Wahlquist M & Truswell A. pub. John Libby, London 1986:169-177

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 Epstein-Barr virus infections. GB Olson, MN Kanaan et al. J. Allergy Clin. Immunol. August 1986:315-320

*“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”.*

Correlation between allergy and persistent Epstein-Barr virus infections in chronic-active Epstein-Barr virus-infected patients. GB Olson, MN Kanaan. J. Allergy Clin. Immunol. August 1986:308-314

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

## **1987**

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

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

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

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

Allergy and the chronic fatigue syndrome. SE Straus, J Dale et al. J.Allergy Clin. Immunol May 1988:791-795

*“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”.*

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”.*

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”.*

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

## **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

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

## **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”.*

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 innoculated 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”.*

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

## **1992**

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”.*

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

### **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”.*

Immunologic, Psychological and Neuropsychological Factors in Multiple Chemical Sensitivity. GE Simon, W Daniell et al. Annals of Internal Medicine 1993;19:2:97-103

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

### **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”.*

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”.*

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”.*

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”.*

## **1995**

Clinical management of chronic fatigue syndrome - Physiology. DJ Clauw. J 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

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”.*



**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”.*

**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...”*

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.

*“Many patients with CFS have experienced atopic symptoms since childhood and the atopic symptoms often flare in CFS....People with CFS may have increased susceptibility to drug side effects”.*

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”.*

## **1998**

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 Edinb 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”.*

Allergology: Blimps versus nuts. H Anthony et al. The Lancet 1998:351:221-222

*“‘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 Choppa. Fourth International AACFS Research & Clinical Conference on CFIDS Oct 1998: Abstract page 100

Prevalence and Overlap of Chronic Fatigue Syndrome and Fibromyalgia Syndrome Among 100 Patients With Multiple Chemical Sensitivity. Fourth International AACFS Research & Clinical Conference on CFIDS Oct 1998 Abstract page 53

## **1999**

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 symptomatology 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 of 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 of 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”.*

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”.*

## **2001**

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”.*

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**

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”.*

## **2004**

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**

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...”.*

**2008**

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...”.*

**2010**

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...”.*

Idiopathic environmental intolerance (EI): from molecular epidemiology to molecular medicine. De Lucca C et al (Rome). Indian J Exp Biol 2010;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...”.*

**These examples serve to illustrate the long-recognised organic basis and the high incidence of allergies, hypersensitivities and intolerances that are often a component of ME/CFS.**

**In light of this corpus of empirical evidence it is notable that Professor White seems to have retained an inflexible belief -- a belief that has not changed in quarter of a century -- that simple graded exposure (analogous to his belief in the curative properties of incremental graded exercise) will reverse the documented organic pathophysiology illustrated above.**