

Toxic times – exposure to multiple chemicals

Recognition of multiple chemical sensitivity (MCS) as an illness with a biological basis is still controversial in the UK. Professor Malcolm Hooper examines the role of pesticides in the development of MCS and evidence supporting its recognition.

Multiple chemical sensitivity (MCS) is a multiple symptom, multi-system and multi-organ illness triggered by acute large or chronic low doses of chemicals. It results in subsequent responses to very small exposures to often structurally diverse chemicals. MCS affects some 5-16% of people in western communities (some studies report up to 33%) and is a subject of considerable debate, within legal, medical, chemical, political and patient domains. A variety of names have been used that give rise to confusion with proponents and advocates taking contradictory positions accompanied with polemical claims.

MCS is increasingly recognized by legal and medical systems. It was first officially recognised in Germany and described using the World Health Organisation's (WHO) International Classification of Diseases as ICD-10-SGB-V, November 2000, under the code T 78.4, 'allergy, otherwise not specified'. Reports from Australia and Denmark have recently been published^{1,2}. The Australian report includes a literature assessment, evidence from 22 witnesses, and 167 written submissions from Australia and overseas. It makes a recommendation for classification of MCS under its own modification of the WHO codes as ICD-10-AM. The Danish report is more limited drawing largely on a published review³.

In North America MCS is widely recognized. In the US in 1998 it was listed by 25 federal and 28 state authorities and summaries of medical and legal/compensation papers and cases provided. Canada has recognized MCS in 10 state authorities⁴.

In contrast, official sources in the UK have been resistant to any recognition of chemical sensitivity. The British Society for Allergy, Environmental and Nutritional Medicine, BSAENM (now the British Society for Ecological Medicine, BSEM) has published substantial evidence in recognition of MCS as an organic illness that can be diagnosed and treated effectively^{5,6}. Whilst MCS does not fit comfortably into current views on allergy the recent Royal College of Physicians' report 'Allergy: the Unmet Need'⁷ records a huge increase in allergy in the UK. Currently one person in three suffers some form of allergy, a total of 18 million people, and of this number some three million suffer from severe allergies. The Royal Commission on Environmental Pollution, 2003, identified the need for a proper understanding of the health effects of novel chemicals widely used and distributed ubiquitously in the environ-

ment⁸. The Research Advisory Committee on Gulf War Illnesses from the US summarised epidemiological studies that indicate that 28-32% of veterans from the first Gulf War are now ill with symptoms of MCS⁹ (Table 1).

Overlapping syndromes

Recently physical effects from electro-magnetic sensitivity have sometimes been included with MCS¹⁰. Some biological agents, viruses and some bacteria^{11,12,13} can provoke the same underlying disturbances as chemicals, including components of vaccines (thiomersal, aluminium salts)^{14,15} (Table 1). Multiple sclerosis (MS) and AIDS/HIV sufferers also share many of the symptoms pointing to a common disturbance of both the immune and nervous systems.

The neuroendocrine-immune (NEI) paradigm provides a basis for understanding these overlapping syndromes and the mechanisms underlying their shared constellation of symptoms and organic damage to the body's major systems and organs. The network of communications involving transmitter molecules has

been comprehensively described¹⁶.

Some well-defined clinical conditions have also been identified in excess among chemically injured Gulf War veterans and among sheep dippers. These include osteoporosis^{17,18} and motor neurone disease^{19,20}, and there is anecdotal evidence of increased incidence of Parkinson's disease, and MS^{21,22,23}.

Recognition of chemical injury

The recognition of MCS as a complex multi-system and multi-organ illness requires a comprehensive clinical approach so numerous biochemical and clinical tests are part of any assessment. Useful guides to diagnosis, assessment and treatment are available^{24,25,26}. Heuser provides a helpful clinical overview²⁷. Studies on Gulf War veterans have identified unequivocal damage to major brain areas, the basal ganglia, brain stem, hippocampus and thalamus. The major chemical exposure suffered by these veterans is now recognized to be low dose exposure to the nerve agent sarin together with chlorpyrifos (an organophosphate) and pyridostigmine bromide²⁸ which act at the same sites. These studies are of great significance to those suffering such exposures in agriculture, homes and aeroplanes.

Challenges in toxicology

Current toxicological understandings of dose, synergism, timing of exposure, delayed responses, mechanisms of action, and genetics are all being challenged by contemporary science.

Dose

It can no longer be assumed lower doses will

Table 1. Symptoms of overlapping syndromes

Symptoms	OPs	GWS/I	MCS	FMS	CFIDS	MS	HIV/AIDS
Joint pain	+	+	+	around joint area	+	+	+
Fatigue	+	+	+	+	+	+	+
Headache	+	+	+	+	+	+	+
Memory problems	+	+	+	+	+	+	+
Sleep disturbed	+	+	+	+	+	?? due to medicines	+
Concentration problems	+	+	+	+	+	+	+
Skin problems	+	+	+	+	+	burning skin	+
Depression	+	+	+	+	+	+	+
Muscle pain	+	+	+	+	+	+	+
Dizziness	+	+	+	+	+	+	+
Irritable bowel	+	+	+	+	+	+	+
Peripheral paresthesia/tingling	+	+	+	+	+	+	+
Chemical/environmental sensitivity	+	+	+	+	+	reported	-
Eye problems	+	+	+	+	+	+	+
Anxiety	+	+	+	+	+	+	+
Tachy and/or chest pain	+	+	+	+	+	+	+
Breathing problems	+	+	+	reported	+	+	+
Light sensitivity	+/-	+	+	reported	+	+	-

OP = Organophosphate poisoning; GWS/I = Gulf War Syndrome/Illness; MCS = Multiple Chemical Sensitivity; FMS = Fibromyalgia Syndrome; CFIDS = Chronic Fatigue Immune Dysregulation Syndrome, also called ME/CFS = myalgic encephalomyelitis/chronic fatigue syndrome; MS = Multiple Sclerosis; HIV/AIDS = Human Immunovirus/Acquired Immune Deficiency Syndrome.

elicit smaller responses. Toxic responses have now been identified at doses orders of magnitude below the extrapolated zero risk from classical studies. Such responses have been found with radiation²⁹, oestrogen-like compounds³⁰, and drugs used to treat autism spectrum disorders³¹ (Figure 1).

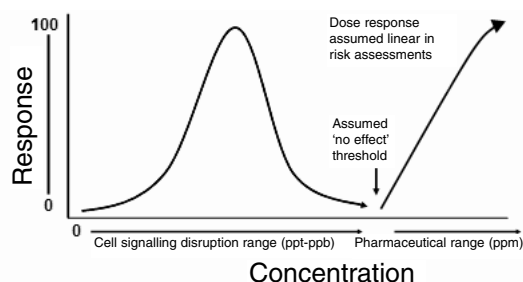
Synergism

Toxic effects of some chemicals can be multiplied by orders of magnitude in the presence of structurally different compounds, for example, pyrethroids, organophosphates and DEET (an insect repellent)^{32,33,34}. It has been established that malathion and permethrin act synergistically making their use as a combined treatment for head lice in children particularly unwise. Many pesticide formulations contain more than one active ingredient. Furthermore, compounds used as solvents, dispersants and wetting agents in pesticide formulations that are generally regarded as inert may also be toxic in their own right, trigger MCS, and/or act synergistically, for example phenols in organophosphate pesticide³⁵ and in some herbicide³⁶ formulations. It is unusual for pesticides to be applied alone therefore mixtures of active compounds and 'inerts' must be fully tested.

Timing

It is becoming clear that the timing of any exposures can be critical in their potential for damage. The foetus is especially vulnerable and can suffer extensive injury with permanent loss, for example, of the eyes^{37,38}. Children and babies can receive a toxic load of persistent bioaccumulative and other xenobiotics through the food chain and breast milk³⁹⁻⁴³. Concern about mental disability in children has been linked to the widespread use of large numbers of xenobiotics in contemporary society⁴⁴. The impact on fertility in young people, particularly men, is also a matter for concern⁴⁵. The increased prevalence of chronic degenerative diseases in the elderly has also been linked with the rapidly escalating use of untested novel chemicals⁴⁶. Some clinicians are drawing attention to 21st century environmental illnesses affecting growing numbers of people⁴⁷.

Figure 1. Inverted-U dose-response curve for cell signalling disruptors



On the right the graph shows the expected linear dose response: the higher the dose the greater the response. On the left the graph shows that some chemicals can also elicit a response at much lower doses.

Mechanisms

Novel mechanisms that offer meaningful explanations of MCS and related disorders are emerging including intraneuronal transport, triggering and kindling, involving the limbic system⁴⁸, opening of the blood-brain barrier⁴⁹, neurogenic inflammation^{50,51}, intracellular messenger disruption⁵².

Delayed effects

A very worrying aspect of some toxic exposures is the delayed appearance of symptoms many years after an initial low dose exposure with no identifiable immediate effects. Survivors of sarin exposure in Toyko and Matsumoto were found to have a chronic delayed neuropathy some three years after an initial exposure that provoked no overt symptoms. In animals this effect has been widely studied⁵³. Similar effects have been identified with organophosphates and would be expected with other acetylcholinesterase inhibitors. Compounds should be tested for their capacity to exert such delayed effects.

Genetics

Studies of changes in gene regulation in carefully selected myalgic encephalomyelitis / chronic fatigue syndrome (ME-CFS) patients showed significant up-regulation of genes associated with the immune response, mitochondrial function, and nerve function (including NTE gene associated with pesticide poisoning)⁵⁴. Organophosphates that reduce PON1 (paraoxonase 1) activity modify the expression of multiple genes^{55,56,57}. Genetic aspects of xenobiotic metabolism have been correlated with susceptibility to various toxins^{58,59}.

Psychiatric lobbies

A major divide exists between those who see MCS and related syndromes deriving from biological disruption and dysfunction and advocates of various psychiatric theories of what they describe as 'unexplained' multi-symptom syndromes. There are a multiplicity of terms used to describe these psychiatric theories: somatisation, functional somatic, psychosomatic, biopsychosocial syndromes/disorders. However, the use of the term 'unexplained' is no longer tenable in the light of newly identified biological processes. An example is the use of functional somatic disorder to describe Gulf War Syndrome (GWS), MCS and related overlapping syndromes in 1999⁶⁰. The chief exponent of this term, Professor Wessely, in a recent lecture at Gresham College declined to use this term preferring to label GWS as depression⁶¹.

Chemicals and pesticides

Not all chemicals are pesticides but the distinction between these terms is far from simple in relation to MCS and other chemically induced illnesses. All the above comments apply equally to pesticides. The organochlorine, DDT, is

still used in some developing countries. It is one of the major persistent bioaccumulative chemicals commonly stored in fat and can be detected in most people. It is also oestrogenic and one of many endocrine disrupters⁶². Recent studies have found xenobiotic contamination on a large scale, with up to 57 different chemicals identified in a single person⁶³⁻⁶⁸. We currently have no way of knowing what this means in terms of immediate and delayed health effects, synergism, dose limits, and gene regulation. Dioxins are now recognised as major human toxins with current exposure limited to parts per trillion. They can give rise to a wide range of toxic effects, including cancers, that occur long after the initial exposure. Seveso and the Vietnam war⁶⁹ gave rise to populations suffering from the consequences of exposure to herbicides containing only trace amounts of dioxin. These effects are now recognised but only after long and painful political rather than scientific battles. Organophosphates cause significant changes in the immune system^{70,71} as well as to the nervous system. Studies initiated as a result of research into GWS show how defence against atherosclerosis and diabetes^{72,73} has been compromised by exposures to these agents along with nerve agents liberated during bombing of Iraqi locations⁷⁴.

Science, medicine and politics

A disturbing feature of many of these issues is the suppression of information or the deliberate avoidance of major biological effects by official government committees asked to look into them. For example, the Department of Health advisory body, the Committee on Toxicity (COT) refused to consider the effects of organophosphates on the immune system despite being sent evidence^{75,76}. Official studies have excluded severely ill sufferers from sheep dip poisoning and GWS⁷⁷. These attitudes must be exposed for science to be set free from political control. Official bodies have given assurances too readily, misleading the public and workers about possible harm from pesticides⁷⁸. All committees established to advise government and the public must be truly independent of all vested interest particularly from corporate concerns.

A regrettable feature of the debates about MCS and other overlapping syndromes is the political intrusion of policy demands, often coupled with denigration of some scientists and patients, in attempts to control funding and direct biological research away from these complex illnesses. Currently there is an independent parliamentary inquiry, headed by Dr Ian Gibson, which is looking at the research into ME-CFS. One of the great fears of those with this illness is that current legislation aimed at getting people back to work will be used to withhold benefits when the psychiatric explanation of their illness is being promoted by government departments^{79,80}. Similar experiences are reported by those with MCS, GWS, sheep dippers' flu and aerotoxic syndrome^{81,82,83}.

A major aspect of all these considerations is the almost total lack of information about

the impact of modern chemicals including pesticides, herbicides, fungicides, other chemicals and radiation, on communities within the developing world⁸⁴. In the name of science, good government and humanity things must change now.

References

1. Parliament of South Australia, *Inquiry into MCS*, 22nd Report of the Social Development Committee on MCS.
2. MCS Danish Environmental Protection Agency, 2005. download 22 April 2006
3. Graveling RA, Pilkington A, George JPK, Butler MP, Tannahill SN. A Review of multiple chemical sensitivity. *Occupational and Environmental Medicine* 1999;56:73-85.
4. Donnay A. www.mcsrr.org
5. MCS; Recognition and management. Eaton KK, Anthony HM (moderators). *British Society for Allergy, Environmental and Nutritional Medicine, BSAENM, Knighton*, 2000. See also www.bsaenm.org.uk
6. Anthony H, Birtwistle S, Eaton K, Maberly J. *Environmental Medicine Clinical Practice, BSAENM, Knighton*, 2000.
7. Royal College of Physicians, *Allergy the Unmet Need; A blueprint for better patient care*. Chairman Stephen Holgate, Royal College of Physicians, London, 2003.
8. Royal Commission on Environmental Pollution, 24th Report, *Chemicals in Products: safeguarding the environment and human health*. Chairman Sir Tom Blundell. HMSO Cm 5827. London, 2003.
9. Research Advisory Committee on Gulf War Veterans' Illnesses, *Scientific Progress in Understanding Gulf War Veterans' Illnesses. Report and Recommendations*, 2004.
10. *Electro-Sensitivity—UK information at www.electrosensitivity.org.uk/*
11. Richardson J. Four Cases of Pesticide Poisoning Presenting as 'ME', Treated with a Choline Ascorbic Acid Mixture. *Journal of Chronic Fatigue* 2000;6:11-21.
12. Richardson J. *Enteroviral and Toxin Mediated Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and other Organ Pathologies*. Haworth Medical Press, Binghampton NY, 2001.
13. Vojdani A, Lapp CW. Interferon-induced proteins are elevated in blood samples of patients with chemically or virally induced chronic fatigue syndrome. *Immunopharmacology and Immunotoxicology* 1999; 21:175-202.
14. Mutter J, Naumann J, Schneider R, Walach H, Haley B. Mercury and autism: accelerating evidence? *Neuroendocrinology Letters* 2005;26(5):439-46.
15. Gherardi PK, Coquet M, Cherin L, Moretto P, Drexhous PA, Pellissier J-F, Chariot P, Authier F-J. Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle. *Brain* 2001;124:1821-31.
16. Hooper M. Engaging with MCS. *Rowat et al. Environmental Health Perspectives* 1998;106(Suppl 1):85-109.
17. Compston JE, Vedi S, Stephen AB, Bord S, Lyons AR, Hodges SJ, Scammell BE. Reduced bone formation after exposure to organophosphates. *Lancet* 1999;354:1791-2.
18. Compston JE, Vedi S, Stephen AB, Bord S, Lyons AR, Hodges SJ, Scammell BE. Reduced bone formation in UK Gulf War veterans: a bone histomorphometric study. *J Clin Pathol* 2002;56:897-9.
19. Haley RW. Excess incidence of ALS in young Gulf War veterans. *Neurology* 2003;61(6):750-6.
20. Horner RD, Kamins KG, Feussner JR, Grambow SC, Hoff-Lindquist J, Harati Y, Mitsumoto H, Pascuzzi R, Spencer PS, Tim R, Howard D, Smith TC, Ryan MA, Coffman CJ, Kasarskis EJ. *Neurology* 2003;61:742-9.
21. Todd Ackerman Houston Chronicle, undated download 26 April 2006 www.gulfwarvets.com/brain.htm
22. Coghlan A. Exposure to pesticides can cause Parkinson's disease. *New Scientist* 25 May 2005.
23. Gherardi RK. [Lessons from macrophagic myofasciitis: towards definition of a vaccine adjuvant-related syndrome] *Reviews in Neurology (Paris)*. 2003;159(2):162-4.
24. Rea WJ. *Chemical Sensitivity Volumes 1-4*, CRC Press-Lewis Publishers, New York 1992,1994,1996, and 1998.
25. Op cit 5.
26. Op cit 6.
27. Heuser G, Axelrod P, Heuser S. Defining chemical injury: a diagnostic protocol and profile of chemically injured civilians, industrial workers and Gulf war veterans. *International Perspectives in Public Health* 2002;13:1-16.
28. Op cit 10.
29. Busy C. *Wings of Death: Nuclear Pollution and Human Health*, Green Audit Books, Green Audit (Wales) Ltd. 1995.
30. Palanza P, Howdeshell KL, Parmigiani S, vom Saal FS. Exposure to a low dose of bisphenol A during fetal life or in adulthood alters maternal behaviour in mice. *Environmental Health Perspectives*, 2002;110 (Suppl 3):415-422.
31. Busse J. *Autismus und Autoaggression: theorie und Kaustik einer Rezeptoren-Regulations-Theorie phasischer Storungen durch intervalbehandlung mit low-dose Sulpirid*, 3rd Autism-Europe Congress Hamburg, 1988.
32. Op cit 10.
33. Abou-Donia MB. Stress and Combined Exposure to Low Daily Doses of Pyridostigmine Bromide, DEET, and Permethrin in Adult Rats Causes Blood Brain Barrier Disruption and Neurochemical and Neuropathological Alterations in the Brain. *AHMF Conference Proceedings*, Sydney, 2001.
34. Abou-Donia MB, Wilmarth KR, Jensen K, Oehme FW, Kurt TL. Neurotoxicity Resulting from coexposure to pyridostigmine Bromide, DEET, and Permethrin: Implications of Gulf War Chemical Exposures. *Journal of Toxicology and Environmental Health* 1996;48:35-56.
35. Professor Abou-Donia has published extensively in this field and these are just two key papers.
36. COT Reports. *Organophosphates. Committee on the Toxicity of Chemicals in food, Consumer Products and the Environment*, Woods HF Chairman, Crown copyright, 1999.
37. Koyama K, Koyama K, Goto K. Cardiovascular effects of a herbicide containing glufosinate and a surfactant: in vitro and in vivo analyses in rats. *Toxicology and Applied Pharmacology* 1997;145:409-414.
38. US\$4 million for Benlate eye victim. *Pesticide News* 33 June 1996.
39. European Commission on Radiation Risk, Chernobyl: 20 years on. *Health Effects of the Chernobyl Accident*. Documents of the ECCR 2006 No 1 Green Audit.
40. *Compromising our children: chemical impacts on children's intelligence and behaviour*. A WWF-UK Chemicals and Health Campaign Briefing, June 2004.
41. Ten Tusscher GW. *Later childhood effects of perinatal exposure to background levels of dioxins in the Netherlands*. Professorial Thesis University of Amsterdam, 2002.
42. Gee D. *Children in their Environment: vulnerable, valuable, and at risk*. Background briefing paper children and environmental health. WHO Ministerial Conference Environment and Health, London, 16-18 June 1999.
43. *Children's Health and Environment: A review of Evidence*. Environmental issue report No. 29. A joint report from the European Environment Agency and the WHO Regional Office for Europe. Tamburlini G, Ehrenstein Oy, Bertolini R. (eds), 2002.
44. Eskenazi B, Bradman A, Castorina R. *Exposures of Children to Organophosphate Pesticides and Their Potential Adverse Health Effects*. *Environmental Health Perspectives* 1999;107,suppl 3:409-419.
45. *The American Association on Mental Retardation Pollution, Toxic Chemicals and Mental Retardation*. A National Summit Racine Wisconsin July 22-24, 2003.
46. Cadbury D. *The Feminisation of Nature*, Penguin Science, Hamish Hamilton, 1997, pp190-8.
47. Pritchard C, Baldwin D, Mayers A. Changing patterns of adult (45-74 years) neurological deaths in the major Western world countries 1979-1997. *Public Health* 2004;118:268-283.
48. Baillie-Hamilton P. *Stop the 21st Century Killing You*. Vermillion, London, 2005.
49. Ashford AN, Miller CS. *Chemical Exposures: Low Levels and High Stakes*, 2nd Edition, John Wiley, New York, 1998.
50. Vogel JS, Garrett A, Keating II, Buchholz BA. Protein Binding of isofluorophate: in Vivo after Coexposure to Multiple Chemicals. *Environmental Health Perspectives* 2002;110suppl 6:1-7.
51. Meggs WJ. *Gulf War Syndrome, Chronic Fatigue Syndrome, and the Multiple Chemical Sensitivity Syndrome: stirring the cauldron of confusion*. *Archives of Environmental Health* 1999, 54:309-11.
52. Meggs WJ. *Mechanisms of allergy and chemical sensitivity*. *Toxicology and Industrial Health*, 1999;15:331-8.
53. Palanza P, Howdeshell KL, Parmigiani S, vom Saal FS. Exposure to a low dose of bisphenol A during fetal life or in adulthood alters maternal behaviour in mice. *Environmental Health Perspectives*, 2002;110 (Suppl 3):415-422.
54. Kaushik N, Fear D, Richards SCM, McDermott CR, Nuwaysir EF, Kellam P, Harrison TJ, Wilkinson RJ, Tyrrell DAJ, Holgate ST, Ker JR. *Gene expression in peripheral blood mononuclear cells from patients with chronic fatigue syndrome*. *Journal of Clinical Pathology* 2005;58:826-832.
55. Op cit 10.
56. Furlong CE, Cole TB, Richter RJ, Yee NK, Costa LG, MacCoss MJ. *Biomarkers for exposure and sensitivity to organophosphorus (OP) compounds*. In *Proceedings of the Contaminated Air Protection Conference: Conference Proceedings*, Imperial College, London, 20-21 April 2005.
57. Abou-Donia MB. *Organophosphate Ester Induced Chronic Neuropathy(OPICN) idem p.59-90*.
58. McKeown-Eyssen G, Baines C, Cole DE, Riley N, Tyndale RF, Marshall L, Jaznavi V. *Case-control study of genotypes in multiple chemical sensitivity: CYP2D6, NAT1, NAT2, PON1, PON2 and MTHFR*. *Int J Epidemiol* 2004;33:971-8.
59. Sram RJ. *Effect of Glutathione S-transferase M1 Polymorphisms on Biomarkers of Exposure and Effects*. *Ehp* 1998;106(Suppl 1):231-239.
60. Wessely S, Nimnuan C, Sharpe M. *Functional somatic syndromes: one or many?* *Lancet* 1999;354:936-939.
61. Wessely S. *Something Old, Something New, Something Borrowed: the truth about Gulf War Syndrome*. Lecture Gresham College
62. Op cit 45.
63. Op cit 39.
64. Op cit 40.
65. Op cit 41.
66. Op cit 42.
67. Op cit 45.
68. *Chemical Check Up: an analysis of chemicals in the blood of Members of the European Parliament*. WWF Detox Campaign 2004.
69. Op cit 45.
70. Repetto R, Baliga S. *Pesticides and immunosuppression: The risks to public health*. *Health Policy and Planning* 1997;12:97-106.
71. Repetto R, and Baglia SS. *Pesticides and the Immune System*, World Resource Institute, WRI Publications, 1996.
72. Mackness B, Hunt R, Durrington PN, Mackness MI. *Increased Immunolocalization of Paraoxonase, Clusterin, and Apolipoprotein A-I in the Human Artery Wall With the Progression of Atherosclerosis*. *Arteriosclerosis thrombosis and Vascular Biology* 1997;17:1233-8.
73. Mackness B, Mackness MI, Arrol S, Turkie W, Julier K, Abuasha B, Miller JE, Boulton AJM, Durrington PN. *Serum paraoxonase (PON1) 55 and 192 polymorphism and paraoxonase activity and concentration in non-insulin dependent diabetes mellitus*. *Atherosclerosis* 1998;139:341-349.
74. *Gulf War Illnesses: DOD's Conclusions about U.S. Troops' Exposure Cannot be Adequately Supported*. General Accounting Office Report to Congressional Requesters, June 2004, GAO-04-159.
75. Op cit 35.
76. Panton I. *Unpublished correspondence*. Submission to Woods Committee [30].
77. Pilkington A, Buchanan D, Jamal GA, Gillham R, Hansen S, Kidd M, JHurler JF, Soutar CA. *An epidemiological study of the relations between exposure to organophosphate pesticides and indices of chronic peripheral neuropathy and neuropsychological abnormalities in sheep farmers and dippers*. *Occupational and Environmental Medicine* 2001;58:702-710.
78. Op cit 9.
79. *Gibson Inquiry First Day of Evidence, Report see www.meactionuk.org.uk*
80. Walker MJ. *Skewed: psychiatric hegemony and the manufacture of mental illness*, Slingshot Publications, London, 2003.
81. Op cit 79.
82. Op cit 80.
83. *Proceedings of the BALPA Air Safety and Cabin Air Quality International Aero Industry Conference*, Imperial College, London, 20-21 April, 2005. ISBN 0-7334-2282-9.
84. McConnell R, Pachecot F, Wahlberg K, Klein W, Malespin O, Magnotti R, Akerblom M Murray D. *Subclinical Health Effects of Environmental Pesticide Contamination in a Developing Country: Cholinesterase Depression in Children*. *Environmental Research* 1999;81:87-91.

Dr. Malcolm Hooper is Professor Emeritus of Medicinal Chemistry at Sunderland University; malcolm.hooper@virgin.net