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A volunteer community organisation providing support for people with allergy, food and chemical sensitivity

A participating organisation of National Toxics Network

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## **Response to the NICNAS/OCS Scientific Review of Multiple Chemical Sensitivity Addendum**

Thank you for allowing us an extension of time to revisit the review. This is an addendum to the document provided by ASEHA on 28 Oct 2008 to submit further scientific information on the issues of

- 1. Evidence of harm from low levels of chemicals, and complex mixtures of chemicals.**
- 2. Chemical testing: sensitisers/irritants; low levels; problems with current/past toxicological testing procedures**
- 3. Important MCS articles and reviews in addition to those cited in the OCS MCS review .**
- 4. Impact of MCS**
- 5. Health care facilities and treatment of MCS .**
- 6. Evidence supporting neurological/ psychological symptoms as a result of chemical toxicity &/or the stress of living with a chronic illness - negating a psychological etiology**
- 7. Testing/ diagnosis of MCS. While a specific test for MCS has not been developed, there are tests for specific chemicals, allergy, newer procedures for oxidative stress, detoxification and animal models**
- 8. Odours**
- 9. Evidence that chemicals in the environment cause adverse health effects such as asthma and allergy. These health effects overlap some of those seen in MCS. The abstracts provided relate to both specific chemicals and mixtures of chemicals.**
- 10. Concluding information on Australian Worksafe standards**

**The information provided in this addendum is mainly in the form of summary information from abstracts. Articles strongly recommended \*\*\*, of special interest \*\***

## **1. EVIDENCE OF HARM FROM LOW LEVELS OF CHEMICALS, AND COMPLEX MIXTURES OF CHEMICALS.**

### **SYMPTOMS OF LOW DOSE SOLVENT EXPOSURE AND NEUROTOXICITY**

**\*\* Kishi R Harabuchi I Katakura Y Ikeda T Miyake H 1993.** Neurobehavioral effects of chronic occupational exposure to organic solvents among Japanese industrial painters. *Environ Res* (1993 Aug) 62(2):303-13

- Subjects with chronic exposure to low levels of organic solvents had symptoms such as dry and scaly skin, being easily depressed without reason, coldness of hands and legs, being easily irritated without

- reason, loss of appetite, dizziness, and unsteadiness significantly more often than among the referents.
- Results indicated that inquires into symptoms and some behavioural tests would assist in detecting effects of exposure to low levels of organic solvents.
- The effects of organic solvent exposure did not show a consistent pattern of effect on neurobehavioural function which paralleled the type I toxic central nervous system disorder classified by the World Health Organization.

#### LOW LEVELS, AIR POLLUTANTS, EVIDENCE OF HARM

\*\*\***Cizao Ren<sup>1,2</sup> and Shilu Tong<sup>1</sup>** .2008 Health effects of ambient air pollution – recent research development and contemporary methodological challenges. *Environmental Health* 2008, 7:56

- As many recent epidemiological studies have consistently shown positive associations between low-level exposure to air pollution and health outcomes, the authors of this paper overviewed recent research and identified the direction of future air pollution epidemiological studies.

#### AIR POLLUTION; MULTIPLE CHEMICALS SYNERGISTIC EFFECTS

\*\*\* **Joe L. Mauderly<sup>1</sup> and Jonathan M. Samet<sup>2</sup>**. 2009. Is There Evidence for Synergy Among Air Pollutants in Causing Health Effects? *Environ Health Perspect* 117:1–6 (2009)

- Air pollutants are complex mixtures of individual chemicals
- Research has only focused on studying the effects of individual chemicals
- The authors reviewed the literature and found studies that demonstrated synergism amongst these pollutants, although different effects were sometimes observed at different times after exposure
- The authors conclude that synergism amongst environmental pollutants is plausible but there are only limited comparable studies at levels higher than that expected in environmental pollution.

**Michael Shapira<sup>1</sup>, Ilan Tur-Kaspa<sup>2</sup>, Leonard Bosgraaf<sup>1</sup>, Nadav Livni<sup>1</sup>, Alastair D. Grant<sup>1</sup>, Dan Grisaru<sup>1,3</sup>, Mira Korner<sup>1</sup>, Richard P. Ebstein<sup>4</sup> and Hermona Soreq<sup>1</sup>**, 2000 A transcription-activating polymorphism in the ACHE promoter associated with acute sensitivity to anti-acetylcholinesterases *Human Molecular Genetics*, 2000, Vol. 9, No. 9 1273-1281

- Hypersensitivity to acetylcholinesterase inhibitors (anti-AChEs) causes severe nervous system symptoms under low dose exposure.
- The authors investigated regions of the ACHE gene in individuals with adverse reactions to anti-AChE
- This study found polymorphisms in the ACHE gene may be the susceptibility factor responsible for the adverse responses to exposure or treatment with anti-AChEs

#### ALDEHYDE MIXTURES; ANIMAL MODEL

**Cassee FR; Arts JH; Groten JP; Feron VJ.** 1996. Sensory irritation to mixtures of formaldehyde, acrolein, and acetaldehyde in rats. *Arch Toxicol* 1996;70(6):329-37

- Study of sensory irritation of formaldehyde (FRM), acrolein (ACR) and acetaldehyde (ACE) in rats after inhalation by measuring the decrease in breathing frequency (DBF)
- The results found that sensory irritation in rats exposed to irritant aldehyde mixtures is greater than that found for the aldehydes separately, similar to those found for ACE alone, and might have been caused by effects on the upper respiratory tract
- The combined effect of the aldehydes was postulated to be a result of competition for a common receptor (Trigeminal nerve)

## **2. CHEMICAL TESTING: SENSITISERS/IRRITANTS; LOW LEVELS; PROBLEMS WITH CURRENT/PAST TOXICOLOGICAL TESTING PROCEDURES**

## UNDISCLOSED INGREDIENTS

\*\*\***Steinemann AC**, 2008. *Fragranced consumer products and undisclosed ingredients*, *Environ Impact Asses Rev* (2008), doi:10.1016/j.eiar.2008.05.002

- Fragranced consumer products—such as air fresheners, laundry supplies, personal care products, and cleaners—are widely used in homes, businesses, institutions, and public places and these products can contain chemicals that are not disclosed to the public through product labels or material safety data sheets (MSDSs)
- The author investigated the chemical analysis of 6 products' and the limits to product disclosure and found that
  - US law does not require disclosure of all chemicals in consumer products or in fragrances
  - in the 6 products investigated nearly 100 VOCs were identified that were not listed in the product ingredients
  - of the identified VOCs, 10 were found to be regulated as toxic or hazardous pollutants (HAPs)
- The authors point out the need for improved understanding of product chemicals and the mechanisms between exposure and effect

## PROBLEMS WITH CURRENT TOXICOLOGICAL METHODS:

\*\*\* **Alexander Suvorov and Larissa Takser**. 2008 *Facing the Challenge of Data Transfer from Animal Models to Humans: the Case of Persistent Organohalogenes*. *Environmental Health* 2008, 7:58

- Appropriate regulation of PCBs was delayed for up to 50 years, today similar delays are occurring with polybrominated diphenyl ethers (PBDEs) another compound of concern for public health.
- The delays could be attributed to the low coherence between experimental studies of toxic effects in animal models and human studies.
- The authors explored this by reviewing studies of the toxic effects of PCB and PBDE in animal models and found that human epidemiological studies of PBDE stand to gain little from animal studies due to several reasons which they explore.
- Their review showed that there are a number of shortfalls in current toxicological methods including a lack of communication between various branches of toxicology

\*\* **Keith A. Houck, a, and Robert J. Kavlocka**. 2008. *Understanding mechanisms of toxicity: Insights from drug discovery research* *Toxicology and Applied Pharmacology* Volume 227, Issue 2, 1 March 2008, Pages 163-178.

- Toxicology relies heavily on use of animal testing for predicting potential toxicity of chemicals in humans
- This paper reviews the application of high-throughput screening assay as a method of screening chemicals for toxicity and the underlying mechanism.
- Highlights the need for integration of successful approaches that will contribute to understanding of the effects of chemicals on biological systems and aid in rationale risk assessments.

## TOXICOLOGICAL TESTING METHODS; CONTACT AND RESPIRATORY SENSITISERS

**Michèle Goutet, Elsa Pépin, Isabelle Langonné, Nelly Huguet, Masarin Ban**. 2005. *Identification of contact and respiratory sensitizers using flow cytometry*. *Toxicology and Applied Pharmacology*, Volume 205, Issue 3, 15 June 2005, Pages 259-270

- The aim was to develop a method of identification of chemicals responsible for respiratory and contact allergies in the occupational setting
- Their study successfully used flow cytometry as a tool to discriminate between contact and respiratory sensitizers by identifying differences in expression of immune responses in mice

## CHEMICAL ALLERGENS/SENSITISERS

**Dearman RJ; Moussavi A; Kemeny DM; Kimber I.** 1996. *Immunology* 1996 Dec;89(4):502-10 and **Dearman RJ; Smith S; Basketter DA; Kimber I.** 1997. Classification of chemical allergens according to cytokine secretion profiles of murine lymph node cells. *J Appl Toxicol* 1997 Jan-Feb;17(1):53-62

- Studies in mice that demonstrated that differences in cytokine secretion profiles characterize immune responses to different classes of chemical allergen and suggest that it may be possible, in a single integrated assay, to identify and classify chemical allergens as a function of induced cytokine production patterns.

ANIMAL MODEL; LOW LEVELS; NON IgE ALLERGY; IMMUNE BIOMARKER

**\*\*\* Fukuyama T, Ueda H, Hayashi K, Tajima Y, Shuto Y, Saito TR, Harada T, Kosaka T.** 2008. Detection of low-level environmental chemical allergy by a long-term sensitization method. *Toxicol Lett.* 2008 Jul 30;180(1):1-8.

- Animal model to study the allergenicity of MCS and the detection of low-level chemical-related hypersensitivity
- Using long-term sensitization followed by low-dose challenge to evaluate sensitization they found that all chemicals tested induced significant increases in number of lymphocytes and surface antigen expression of B cells.
- The authors propose that this long-term sensitization method would be useful for detecting environmental chemical-related hypersensitivity

ANIMAL MODEL; CHEMICAL SENSITISERS; IMMUNE CHANGES IN RESPIRATORY SYSTEM

**Jeroen A.J. Vanoirbeek, Maciej Tarkowski, Hadewijch M. Vanhooren, Vanessa De Vooght, Benoit Nemery, Peter H.M. Hoet.** 2006. Validation of a mouse model of chemical-induced asthma using trimellitic anhydride, a respiratory sensitizer, and dinitrochlorobenzene, a dermal sensitizer. *Journal of Allergy and Clinical Immunology*, Volume 117, Issue 5, May 2006, Pages 1090-1097

- Using a mouse model of occupational asthma caused by chemicals they concluded that avoiding skin contact with chemical sensitizers in the workplace could be used as a way of preventing occupationally chemical-induced asthma.

ANIMAL MODEL; NON IgE ALLERGY MECHANISMS

**Josje H. E. Arts, Sonja C. M. Dröge, Steven Spanhaak, Nanne Bloksma, AndréH. Penninks, C. Frieke Kuper.** Local lymph node activation and IgE responses in Brown Norway and Wistar rats after dermal application of sensitizing and non-sensitizing chemicals. *Toxicology*, Volume 117, Issues 2-3, 28 February 1997, Pages 229-237

- Using rats a proposed models for predictive recognition of low molecular weight chemicals causing IgE-mediated allergic airway reactions in man was tested
- The results with formaldehyde indicated the need for further studies of chemicals that have both irritant and sensitizing properties at about similar concentrations or may act through non-IgE-mediated immune mechanisms.

OTHER ISSUES AFFECTING CHEMICAL REGULATION

**VALERIO GENNARO, MD, LORENZO TOMATIS, MD** 2005. Business Bias: How Epidemiologic Studies May Underestimate or Fail to Detect Increased Risks of Cancer and Other Diseases *INT J OCCUP ENVIRON HEALTH* 2005;11:356–359

- In spite of claiming primary prevention as their aim, studies of potential occupational and environmental health hazards that are funded either directly or indirectly by industry are likely to have negative results.

The authors present three common scenarios in which faulty design of epidemiologic studies skews results, and list 15 study design flaws that lead to results that are dangerously misleading with regard to both the evaluation and the improvement of public health.

**SUSANNA RANKIN BOHME, AM, JOHN ZORABEDIAN, DAVID S. EGILMAN, MD, MPH.** 2005. Maximizing Profit and Endangering Health: Corporate Strategies to Avoid Litigation and Regulation. *INT J OCCUP ENVIRON HEALTH* 2005;11:338–348

- Reviews the problem associated with corporation and industry using various tactics to hide information that may suggest their product is toxic at the expense of public health.

**DAVID S. EGILMAN, MD, MPH, SUSANNA RANKIN BOHME, AM.** 2005. OVER A BARREL: Corporate Corruption of Science and Its Effects Workers and the Environment *INT J OCCUP ENVIRON HEALTH* 2005;11:331–337

- Reviews how corporations can influence science and how that has an influence on environmental and occupational health
- Provides evidence of a systemic problem.

### **3. IMPORTANT MCS ARTICLES AND REVIEWS IN ADDITION TO THOSE CITED IN THE OCS MCS REVIEW**

#### MCS REVIEW

\*\*\* **Spencer, T R and Schur, P M.** 2008. The challenge of multiple chemical sensitivity. *Journal of Environmental Health* 70(10): 24-27

- Review of the current literature of MCS and discusses the difficulties in resolving health complaints
- Aimed at encouraging an understanding of MCS among environmental health and medical professionals

\*\*\* **Davidoff AL, Keyl PM.** 1996. Symptoms and health status in individuals with multiple chemical sensitivities syndrome from four reported sensitizing exposures and a general population comparison group. *Arch Environ Health* 1996 May-Jun 51:3 201-13

- The study collected information by telephone interview and found that diverse samples of patients with multiple chemical sensitivities syndrome had very similar characteristic features. This was despite whether they had or had not received treatment by clinical ecologists.
- Members of the general population reported mild sensitivity to chemicals, and even those with more sensitivity differed from the multiple chemical sensitivities syndrome groups with respect to number and types of symptoms reported, duration and frequency of response, and associated features.
- Multiple chemical sensitivities syndrome was associated consistently with only one psychiatric variable, elevated negative affect scores, which were correlated significantly with the presence of illness.

#### CO-EXISTING DISEASES IN MCS

##### ASTHMA

\*\*\* **Caress SM and Steinman AC.** 2005. National Prevalence of Asthma and Chemical Sensitivity: An examination of potential overload. *J Occup Env Med* 47:518-522

- A study of the link between asthma and chemical hypersensitivity found that
- 14.1% of the respondents were diagnosed with asthma and 11.2% reported a hypersensitivity to chemicals.
- Of those with asthma, 27.2% also reported being hypersensitive to chemicals and 7.4% reported being diagnosed with chemical sensitivities (MCS).
- Of those diagnosed with MCS, 42% reported being diagnosed with asthma. Additionally, 29.7% of those with asthma said air fresheners caused breathing difficulties, and 37.2% found scented products

irritating.

- The authors concluded that their study indicates that there is a significant overlap between some forms of asthma and MCS.

#### ALLERGIC CONTACT DERMATITIS

**\*\* Stitt WZ, Scott GA, Martin RE, Gaspari AA.** 1996. Multiple chemical sensitivities, including iatrogenic allergic contact dermatitis, in a patient with chronic actinic dermatitis: implications for management. *Am J Contact Dermat* 1996 Sep 7:3 166-70

- Significance of identification and avoidance of allergens/chemicals to achieve significant improvement of allergy (chronic dermatitis).

#### RESPIRATORY DISEASE AND MCS

**\*\*\* Ross, G H.** 1997. Clinical Characteristics of Chemical Sensitivity: An Illustrative Case History of Asthma and MCS. *Environ Health Perspect* 105(Suppl 2):437-441 (1997)

- Provides clinical characteristics of the development of MCS (onset and spreading intolerance)
- Idiosyncratic medication reactions (especially to preservative chemicals) are common in MCS patients
- A body burden of xenobiotic chemicals is frequently found in these patients when they are tested.
- Reactive airways dysfunction syndrome is a recently identified condition that exhibits features of both asthma and chemical sensitivity.
- MCS patients frequently have patterns of neurotoxic brain metabolism that can be confirmed on single photo emission computed tomography imaging

**\*\*\* Meggs WJ.** 1995. Multiple chemical sensitivities--chemical sensitivity as a symptom of airway inflammation [editorial] *J Toxicol Clin Toxicol* 1995 33:2 107-10

- Discusses the problems associated with confusing etiology with diagnosis
- Chemical sensitivity is a symptom of acute exposure as is asthma reactive airway dysfunction syndrome or rhinitis following a single acute exposure, (reactive upper airway dysfunction syndrome) reported by a majority of patients

#### TRIGGERS OF MCS

**\*\* Naoko Inomata, Hiroyuki Osuna, Hiroyuki Fujita, Toru Ogawa and Zenro Ikezawa.** 2005. Multiple Chemical Sensitivities Following Intolerance to Azo Dye in Sweets in a 5-year-old Girl *Allergology International* 2006; 55: 203-205doi:10.2332/allergolint.55.203

- Reports on case of MCS in a 5 year old female where various treatments for recurrent urticaria exacerbated her condition
- Triggers found were azo dyes (used in foods) and NSAIDs

**\*\*\* Tomlinson, K. 2009.** Toxic chemicals in hangar made B.C. aviation workers sick., *ES&T Online*, January 12, 2009

- Recognition of harm to aviation technicians by exposure to paint chemicals
- Suspected that chemicals used were the trigger for chronic or permanent damage
- Problems associated with obtaining work cover

#### MCS MODELS

For a comprehensive model of MCS we would like to direct the reviewers to the work of Prof. Martin Pall. The

department of OCS has received a response from Prof Pall to the review, as well as a scientifically detailed report on his work (Annex 2) to ASEHA response. This model is based on the process of oxidative stress and its potential to cause pathological changes that can account for the multi organ symptomology of MCS. Oxidative stress is a disturbance of the equilibrium status of prooxidant and antioxidant systems in favour of the prooxidant state. The term oxidative stress describes the number of chemical reactions involved in the production of free radicals and other reactive molecules that can potentially induce cellular injury.

In 2005, Kennedy et al investigated oxidative stress levels in CFS, by measuring oxidative by-products in the blood of individuals with CFS and compared the results to those of healthy volunteers. The results of this testing was then compared to CFS symptom severity. Elevated levels of isoprostanes (marker of oxidative stress) were found to be associated with CFS and their symptoms. (Kennedy et al, 2005). Complementary to Pall's work where his model points to a common mechanism for the unexplained diseases CFS, MCS, fibromyalgia, this work is potentially significant to the elucidation of testing for MCS.

A recent article by Bessac and Jordt, 2008 addresses the TRP channels (TRPA1 and TRPV1) in airway chemosensation and reflex control, the same receptors discussed by M Pall (TRPV1). TRPA1 is activated by chlorine, reactive oxygen species and noxious products of smog and cigarette smoke causing irritation and airway reflex responses. They postulate that the TRPV1 (capsaicin receptor) and TRPA1 together contribute to chemical hypersensitivity, chronic cough, and airway inflammation in asthma, COPD, and reactive airway dysfunction syndrome. Their review of many studies demonstrated that almost all major neuronal inflammatory signalling pathways converge on TRPV1 and TRPA1 to increase C-fiber excitability during airway inflammation. Inflammatory oxidants, lipid products and protons further promote activity of these ion channels through direct interactions or covalent modification. The mechanism of activation of TRPA1 by covalent modification due to reactive irritants implies dose response and activation kinetics do not conform to standard pharmacological measures.

Ali M in a 2000(a) article proposed that redox dysregulation was the basis of change in patients with environmental illness and demonstrated evidence of advanced oxidative injury to all elements of circulating blood in patients with chronic environmental illness. In this model a common theme of environmental toxins is that they are oxidising in nature. Of the proposed damages from oxidative damage, oxidative cell membrane injury. this potential of membrane damage is further explored in a research article by Luckenbach and Epel in 2005 where they demonstrate indirect effects of environmental chemicals as efflux transporter chemo sensitizers and that their effects may continue long after the exposure event .

A number of xenobiotics, particularly aromatic amine containing compounds are capable of inducing oxidative injury in erythrocytes. These agents seem to potentiate the normal redox reactions and are capable of overwhelming the usual protective mechanisms. The interaction between these xenobiotics and hemoglobin leads to formation of free radicals that denature critical proteins, including hemoglobin, thiol dependent enzymes and components of the erythrocyte membrane. (Klaassen 2008)

Klaassen C. 2008. Toxicology The Basic Science of Poisons. 7<sup>th</sup> Edition Ed. Cassert & Doull. McGraw Hill. p463

Luckenbach T and Epel D. 2005. Nitromusk and polycyclic musk compounds as long-term inhibitors of cellular xenobiotic defense system mediated by multidrug transporters. EHP. 113(1): 17-24.

#### OXIDATIVE STRESS; CHEMOSENSORY DIFFERENCES; LOW LEVELS; VARIABLE RESPONSES TO CHEMICALS

\*\*\* **Bret F. Bessac and Sven-Eric Jordt.** 2008. Breathtaking TRP Channels: TRPA1 and TRPV1 in Airway Chemosensation and Reflex Control Physiology, Vol. 23, No. 6, 360-370, December 2008

- Presents new information on that reveals the essential role of receptor (TRPA1) in airway chemosensation and inflammation
- TRPA1 is activated by chlorine, reactive oxygen species, and noxious constituents of smoke and smog, initiating irritation and airway reflex responses
- Postulates that both the TRPA1 and the capsaicin receptor TRPV1, may contribute to chemical hypersensitivity, chronic cough, and airway inflammation in asthma, COPD, and reactive airway

dysfunction syndrome.

#### OXIDATIVE STRESS; BIOMARKER; DIAGNOSTIC MARKER ENVIRONMENTAL ILLNESS

\*\*\* **Majid Ali**. 2000. Oxidative coagulopathy A proposed pathogenetic mechanism for environmental illness *Environmental Management and Health*. 11(2); 175-191.

- The author, using peripheral blood smears, was able to demonstrate evidence of advanced oxidative damage to all elements of circulating blood in patients with chronic environmental illness
- The author proposes that oxidative coagulopathy represents one of the core pathogenetic mechanisms of homeostatic dysregulation seen in environmental illness and leads to oxidative injury to intracellular matrix, cell membranes, and intracellular organelles such as mitochondria

#### OXIDATIVE STRESS; ALLERGY AND ENVIRONMENTAL ILLNESS MODEL

\*\* **Ali, Majid MD**. 2000. Recent advances in integrative allergy care. *Current Opinion in Otolaryngology & Head and Neck Surgery*: Volume 8(3)June 2000pp 260-266

- Presents an integrated model for clinical allergy and chemical hypersensitivity where oxidative processes may be the primary mechanism for perpetuating oxidative molecular injury
- In this article, the classical studies of atopy and the core clinical concepts of environmental medicine are briefly reviewed to provide a framework for presenting the integrative oxidative-dysoxygenative model of clinical allergy.

#### 4. IMPACT OF MCS

##### DISABILITY

\*\*\* **Gibson PR and Vogel VM**. 2009. Sickness-related dysfunction in persons with self-reported multiple chemical sensitivity at four levels of severity. *J Clin Nurs*. 2009 Jan;18(1):72-81.

- The article examines the quality of life for people with self-reported chemical sensitivity
- Triggers/incitants included pesticide, formaldehyde, fresh paint, new carpet, diesel exhaust, perfume and air fresheners.
- The 5 highest reported symptoms were tiredness/lethargy, difficulty concentrating, muscle aches, memory difficulties and long-term fatigue
- Overall mean Sickness Impact Profile score was 25.25%, showing serious impairment, with the most serious dysfunction in the categories of work (55.36%), alertness behaviour (53.45%) and recreation and pastimes (45.20%).
- It was found that chemical sensitivity is poorly understood by providers and results in extensive financial and treatment obstacles for those who experience it.
- Understanding the impact of the health condition is crucial to communicate with and treat persons who experience the sensitivities

\*\*\* **Gibson PR, Placek E, Lane J, Ostroff Brohimer S, Earehart Lovelace, A C**. 2005. Disability-Induced Identity Changes in Persons With Multiple Chemical Sensitivity. *Qualitative Health Research*, 15(4):1-23

- The author found that people with MCS suffered loss of a stable family life, familiar personality, loss of self positioning, emotional suppression to meet others' expectations, redesigning the planned life, forced growth, struggling with support, discovering the spiritual self, and identity reconsolidation
- These findings were in line with that in people with chronic illness and other delegitimized illnesses

#### SOCIOECONOMIC COSTS OF MULTIPLE CHEMICAL SENSITIVITY/ENVIRONMENTAL SENSITIVITIES

\*\* **Dalal A, et al** "Economic impact of allergic rhinitis to managed care: a retrospective claims analysis," ACAA Meeting 2007; P234.

- The study found that the economic burden of allergic rhinitis is high, per patient cost for treating the condition accounted for more than 10% of total medical spending for a year

#### SOCIAL ISSUES AND PUBLIC HEALTH

**JAMES HUFF, PHD. 2007.** Industry Influence on Occupational and Environmental Public Health. *INT J OCCUP ENVIRON HEALTH* 2007;13:107–117

- Explores the problems associated with industry influence on occupational and environmental health (OEH) policies

**SKIP SPITZER, MA 2005.** A Systemic Approach to Occupational and Environmental Health *INT J OCCUP ENVIRON HEALTH* 2005;11:444–455

- Explores the problems associated with corporate influence on environmental health and social problems and the need for a more integrated approach

#### 5. HEALTH CARE FACILITIES AND TREATMENT OF MCS

\*\*\* **Charles C. Engel Jr., Joyce A. Adkins and David N. Cowan** 2002. Caring for Medically Unexplained Physical Symptoms after Toxic Environmental Exposures: Effects of Contested Causation. *Environ Health Perspect* 110(suppl 4):641-647 (2002). <http://ehpnet1.niehs.nih.gov/docs/2002/suppl-4/641-647engel/abstract.html>

- Explores the Medically unexplained physical symptoms (MUPS) in syndromes such as chronic fatigue syndrome, fibromyalgia syndrome, and multiple chemical sensitivities.
- Common to all is the possible occurrence of "contested causation" – disagreement on the cause being an environmental exposure or injury
- Patient-provider disagreement over causation may have serious negative effects on healthcare for individuals with MUPS
- These issues may distract patients and providers from therapeutic goals

#### CHRONIC CARE MODEL

**Coleman K, et al. 2009.** Evidence on the chronic care model in the new millennium *Health Aff* 2009; 28: 75-85.

- Provides a set of 6 interventions aimed at improving patient care and health outcomes

#### HOSPITAL ENVIRONMENT

\*\* **Weinhold, B. 2001.** Making Health Care Healthier. *Environmental Health Perspectives* 109(8):A370-377.

- In the hospital setting health problems in both patients and staff can be triggered by exposure to indoor air pollutants, mercury, latex, polyvinyl chloride (PVC), disinfectants, laboratory chemicals, and hundreds of other substances integral to medical care.
- The US EPA's list of potential culprits includes tightly sealed buildings, reduced ventilation rates, mold contamination, synthetic building materials and furnishings, and chemically formulated personal care products, pesticides, and cleaning supplies
- For some people, exposure to contaminated indoor air can lead to short-term health problems such as headaches, dizziness, difficulty thinking, fatigue, and irritation of the eyes, nose, and throat. Longer term problems may include respiratory disease, heart disease, and potentially even cancer.
- The authors found that while there is mounting evidence on problems associated with exposure to indoor air pollutants, there are only a handful of criteria that deal directly with indoor air quality in hospital accreditation processes.

\*\*\* **Pershall, K E.** 2003. Contact and chemical sensitivities in the hospital environment. *Otolaryngol.Clin.N.Med* 36(2003):1021-1034.

- Surgeons, health care workers, and patients all come into contact with a variety of chemicals in the hospital setting and all are risk for injury or reaction.
- The author included information on some specific chemicals in order to raise clinicians awareness of the problem.

\*\* **Fox L, Luce S, Keiko N.** 2003. Health Status of former Brigham and Women's Hospital (BWH) Nurses. Massachusetts Nursing Association.

- Explores chemical sensitivity in nurses exposed to indoor air pollutant substances such as vapours from sterilising agents, particulate matter from latex gloves and aerosolised disinfectants used in the hospital environment
- The health and disability problems most frequently reported were, MCS 72 %, diagnosed with MCS 61 % worked up for thyroid dysfunction 28%, diagnosed with thyroid dysfunction 6%, worked up for Chronic Fatigue Immune Dysfunction System (CFIDS) 22%, diagnosed with CFIDS 14%, worked up for lupus 19%, diagnosed with lupus 0, worked up for fibromyalgia 19%, diagnosed with fibromyalgia 17%, worked up for rheumatoid arthritis 19%, and diagnosed with rheumatoid arthritis 3%.
- The most prevalent immune system conditions are: diagnosed with MCS 53%, diagnosed with CFIDS 14%, and diagnosed with Fibromyalgia 11%.

#### TREATMENT/MANAGEMENT OF CHEMICAL TOXICITY AND ASSOCIATED DISEASES

\*\*\* **Bernhard Hennig,1 Adrienne S. Ettinger,2 Ronald J. Jandacek,3 Sung Koo,4 Craig McClain,5 Harold Seifried,6 Allen Silverstone,7 Bruce Watkins,8 and William A. Suk9.** 2007. Using Nutrition for Intervention and Prevention against Environmental Chemical Toxicity and Associated Diseases. *Environ Health Perspect.* 2007 April; 115(4): 493–495.

- Discusses the importance of diet and lifestyle in the management of chronic diseases
- Modulation of nutritional status may have positive effects on biological processes and the ability to handle/detoxify environmental toxicants

#### TREATMENTS FOR CFS/RELEVANCE TO MCS

\*\* **Gordon, B R.** 2000. Chronic Fatigue Syndrome: An allergic entity. *Curr Opin Otolaryngol Head Neck Surg* 2000, 8:253–259

- CFS once thought a psychological condition is now being viewed as a biochemical derangement of the functioning of the neuroimmune and neuroendocrine systems
- Treatment emphasis is also shifting from primarily psychiatric treatment to attempts to intervene on a molecular level
- This review discusses the history, diagnosis, pathophysiology, and treatment of CFS, with emphasis on the still unexplained strong association of CFS with allergy

#### CHEMICAL AVOIDANCE AS A PRIMARY PREVENTION STRATEGY

**US Centers for Disease Control and Prevention (CDC).** n-Hexane--Related Peripheral Neuropathy Among Automotive Technicians --- California, 1999–2000. *MMWR* 50(45):1011-1013, 2001.

- Solvents, glues, spray paints, coatings, silicones are some of the products that contain n-hexane (petroleum distillate and simple aliphatic hydrocarbon)
- N-hexane is a peripheral neurotoxin, this article describes n-hexane- associated peripheral neuropathy in an automotive technician
- The findings suggest that solvent manufacturers should avoid using hexane when producing automotive

degreasing products, and automotive technicians should avoid regular contact with hexane-based cleaning solvents

## **6. EVIDENCE SUPPORTING NEUROLOGICAL/ PSYCHOLOGICAL SYMPTOMS AS A RESULT OF CHEMICAL TOXICITY &/OR THE STRESS OF LIVING WITH A CHRONIC ILLNESS - NEGATING A PSYCHOLOGICAL ETIOLOGY**

### **FALSE PSYCHOGENIC DIAGNOSIS**

The MCS Working Draft is biased and the emphasis throughout the document weighs heavily on a psychogenic aetiology. Many with MCS can be isolated and suffer from deprivation, loneliness and worsening ill health because they are unable to avoid substances that contribute to their disability, pain state or other suffering. They are unable to attend hospital because of chemical exposures related to hospital air quality, medications, medical equipment and fragranced products worn by hospital staff. They are also unable to access supported accommodation and home care services again, because of fragrances and other substances used by home help staff. Many lack visitors and the only contact they can have with other humans is via telephone or email, or when other MCS sufferers are able to visit. Clinicians often associate this deprivation with depression and want to prescribe anti-depressants which can be detrimental to someone who has already been poisoned by neurotoxins or has sensitivities to multiple medications. However, such a problem cannot be medicalised – it is a social issue that requires a social response. Observing the basic human rights of individuals with MCS is essential to ensure that their issues of access are addressed and that they have the same access to goods and services as those who do not have MCS.

\*\*\* **Bloch, R M and Meggs, W J. 2007.** Comorbidity patterns of self-reported chemical sensitivity, allergy, and other medical illnesses with anxiety and depression. *Journal of Nutritional & Environmental Medicine*, 16(2): 136 - 148, May 2007 ,

- The authors concluded that the relationship between anxiety and chemical sensitivity is not unique and does not support the contention that chemical sensitivity is somatized anxiety.

\*\*\* **Mariko Saito, MD, Hiroaki Kumano, MD, PhD, Kazuhiro Yoshiuchi, MD, PhD, Naomi Kokubo, Kyoko Ohashi, PhD, Yoshiharu Yamamoto, PhD, Naohide Shinohara, PhD, Yukio Yanagisawa, PhD, Kou Sakabe, MD, PhD, Mikio Miyata, MD, PhD, Satoshi Ishikawa, MD, PhD and Tomifusa Kuboki, MD, PhD. 2005.** Symptom Profile of Multiple Chemical Sensitivity in Actual Life. *Psychosomatic Medicine* 67:318-325 (2005)

- The authors concluded that MCS patients do not have either somatic or psychologic symptoms under chemical-free conditions, and symptoms may be provoked only when exposed to chemicals.

### **NEUROTOXIC EFFECTS OF SOLVENTS**

**Kyrklund T. 1992.** The use of experimental studies to reveal suspected neurotoxic chemicals as occupational hazards: acute and chronic exposures to organic solvents. *Am J Ind Med (1992) 21(1):15-24*

- Experimental studies using specified exposure conditions have shown that different organic solvents have very diverse neurotoxic effects.
- The toxic mechanism may differ between acute and chronic exposure.
- No specific method used to describe a neurotoxic effect or single toxic response can be used for the overall occupational risk assessment of all organic solvents. Each solvent has to be considered as having its own unique toxic effects

**Roto P; Sala E. 1996.** Occupational laryngitis caused by formaldehyde: a case report. *Am J Ind Med 1996 Mar;29(3):275-77*

- Case of occupational laryngitis from exposure to formaldehyde fumes in the dairy industry
- A laryngeal provocation test with formaldehyde was positive, and the patients' reaction to formaldehyde worsened over time

## NEUROTOXIC EXPOSURE RELATED TO MULTIPLE CHEMICAL SENSITIVITIES

**\*\* Lohmann K Prohl A Schwarz E. 1996.** Vielfache Chemikalienunverträglichkeit (Multiple Chemical Sensitivity Disorder) bei Patienten mit neurotoxischen Gesundheitsstörungen. [Multiple chemical sensitivity disorder in patients with neurotoxic illnesses] *Gesundheitswesen* (1996 Jun) 58(6):322-31 (Published in German)

- Neurotoxic substances used as indoor wood preservatives (mainly Pentachlorophenol and/or Lindane) were found to be the causative agents in 63% of the cases with neurotoxic health impairments and MCS.
- Other important neurotoxic substances to which the patients were mainly exposed were organic solvents (25%), formaldehyde (15%), dental materials (15%), pyrethroides (13%), and other biocides (19%) (multiple exposures were possible).

## NEUROBEHAVIOURAL EFFECTS OF LOW DOSES OF SOLVENTS – ACUTE AND CHRONIC EXPOSURES

**White RF Proctor SP Echeverria D Schweikert J Feldman RG. 1995.** Neurobehavioral effects of acute and chronic mixed-solvent exposure in the screen printing industry. *Am J Ind Med* (1995 Aug) 28(2):221-31

- Workers with higher chronic exposure demonstrated significantly poorer performance on visual memory tasks and mood.
- The authors suggest that results show that the mixed solvents used in the screen printing industry have an effect on central nervous system functioning in the absence of obvious clinical disease.
- Exposure levels were below the recommended threshold limit

## NEUROLOGICAL DEFICIT FOLLOWING LOW DOSE SOLVENT EXPOSURE IN WORKERS

**Foo SC Lwin S Chia SE Jeyaratnam J 1994.** Chronic neurobehavioural effects in paint formulators exposed to solvents and noise. *Ann Acad Med Singapore* (1994 Sep) 23(5):650-4

- Study found that paint formulators, in all the neurobehavioural tests, performances were observed to be poorer than the controls'

## NEUROLOGICAL DEFICIT FOLLOWING LOW DOSE SOLVENT EXPOSURE IN WORKERS

**Colvin M Myers J Nell V Rees D Cronje R 1993.** A cross-sectional survey of neurobehavioral effects of chronic solvent exposure on workers in a paint manufacturing plant. *Environ Res* (1993 Oct) 63(1):122-32

- Neurological impairment was found in workers with long-term exposure to organic solvents in a paint manufacturing plant

## BIOCHEMICAL AND NEUROLOGICAL ABNORMALITIES FOLLOWING TCDD EXPOSURE

**Peclova, D et al. 2001.** Biochemical, neuropsychological and neurological abnormalities following 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) exposure. *Archives of Environmental Health* 56(6):493-500.

- Dose-related signs were observed indicating that 2,3,7,8-TCDD exposure is capable of inducing chronic central and peripheral system impairment which can last as long as 30 years after exposure has ceased
- They found other chronic disorders related to 2,3,7,8-TCDD exposure, indicating that chloracne is not the only chronic disease related to 2,3,7,8-TCDD exposure, other problems include irritability, emotional instability, sleep disturbances, headache and neuralgia.

**7. TESTING/ DIAGNOSIS OF MCS. WHILE A SPECIFIC TEST FOR MCS HAS NOT BEEN DEVELOPED, THERE ARE TESTS FOR SPECIFIC CHEMICALS, ALLERGY, NEWER PROCEDURES FOR OXIDATIVE STRESS, DETOXIFICATION AND ANIMAL MODELS**

\*\*\* **US National Institutes of Environmental Health Sciences.** 2006. New Technology For Detecting Biological Responses to Environmental Factors (leaflet) <http://www.niehs.nih.gov/>

- Discusses the development of methods to measure the biological responses of individuals to environmental exposures
- Measures of chemicals in samples of air, water, soil and food do not provide accurate measures of exposure in individuals.
- It is suggested that the biological response to an exposure rather than just the exposure is most likely to relate to the impact on human health.
- To understand how both genes and environmental exposures affect human health, new methods to precisely measure the **biological response** of individuals to environmental exposures are needed.

**McFadden SA. 1996.** Phenotypic variation in xenobiotic metabolism and adverse environmental response: focus on sulfur-dependent detoxification pathways. *Toxicology* 1996 Jul 17 **111:1-3** 43-65

- Investigates the link between phenotypic variations in xenobiotic detoxification pathways and adverse responses to chemicals in the environment by measuring polymorphisms in the gene for enzymes for sulfation of phenolic xenobiotics .
- Impaired sulfation has been found in many conditions including degenerative neurological and immunological conditions and drug intolerances, including Alzheimer's disease, Parkinson's disease, motor neuron disease, rheumatoid arthritis, and delayed food sensitivity. It may also be relevant to intolerance of phenol, tyramine, and phenolic food constituents.
- Preliminary data suggests that it may be important in multiple chemical sensitivities and diet responsive autism..
- The authors conclude that these studies indicate the need for the development of genetic and functional tests of xenobiotic metabolism as tools for further research in epidemiology and risk assessment.

\*\* **Nakamura, Yoichi.** 2006. Clinical and experimental research on definition of sick building syndrome. Comparison of healthy individuals and patients with chemical sensitivity: related study at cooperating institutions. Shikkuhausu Shokogun no Shikkan Gainen ni kansuru Rinshoteki, Kiso Igakuteki Kenkyu Heisei 17 Nendo Sokatsu, Buntan Kenkyu Hokokusho.

- The author developed a simple tolerance testing system for volatile chemicals
- Examination of the air quality in a newly built hospital revealed a high concentration of TVOC in some areas.
- The tolerance testing system was found useful for pathological analysis of and development of a new therapy for chemical sensitivity.

**Nater UM, et al.** 2008. Attenuated morning salivary cortisol concentrations in a population-based study of persons with chronic fatigue syndrome and well controls" *J Clin Endocrin Metab*:

- Women with symptoms of chronic fatigue syndrome have a muted morning cortisol response that may represent an underlying mechanism of the condition, according to investigators.
- The spike in cortisol levels that occurs during the first hour after awakening was significantly lower in women with chronic fatigue symptoms compared with well women.

#### MRI IMAGING IDENTIFIES BRAIN TISSUE CHANGES IN SOLVENT EXPOSED INDIVIDUALS

**Thuomas KA, Moller C, Odkvist LM, Flodin U, Dige N.** 1996. MR imaging in solvent-induced chronic toxic encephalopathy. *Acta Radiol (1996 Mar)* 37(2):177-9

- Workers occupationally exposed to solvents showed were found to have changes in brains structures by MRI

## RAST TESTING - FORMALDEHYDE SENSITISATION

**F. WANTKE , C. M. DEMMER , P. TAPPLER , M. GÖTZ and R. JARISCH.** 1996. Exposure to gaseous formaldehyde induces IgE mediated sensitization to formaldehyde in schoolchildren. *Clinical & Experimental Allergy* 26(3): 276- 280;

- Study to evaluate whether IgE-mediated sensitization as well as symptoms in children was associated with formaldehyde exposure at school
- Headache, nose bleeding, rhinitis, fatigue, cough, dry nasal mucosa and burning eyes were found in the affected children. There was a correlation between symptoms and the formaldehyde concentrations in the classrooms. However, the elevated IgE levels to formaldehyde did not correlate with symptoms.
- After transferral to a new classroom the incidence of symptoms decreased

The authors concluded that Gaseous formaldehyde, besides its irritant action, leads to IgE-mediated sensitization. As children are more sensitive to toxic substances than adults, threshold levels for indoor formaldehyde should be reduced for children.

## DETOXIFICATION MARKERS

### BIOMARKERS OF DETOXIFICATION; URINARY ORGANIC ACIDS

**\*\* Lord RS, Bralley JA.** 2008. Clinical applications of urinary organic acids. Part I: Detoxification markers. *Altern Med Rev.* 2008 Sep;13(3):205-15.

- Investigation of measurement of organic acids in the urine that can serve as markers for specific toxicant exposure or detoxification challenges.
- Patterns of these organic acid compounds measured in an overnight urine specimen help to identify focal areas of clinical concern and monitor patient responses to detoxification interventions.

### OXIDATIVE STRESS BIOMARKERS; LOW LEVELS

**\*\* Hong YC, Park EY, Park MS, Ko JA, Oh SY, Kim H, Lee KH, Leem JH, Ha EH.** 2009. Community level exposure to chemicals and oxidative stress in adult population. *Toxicol Lett.* 2009 Jan 30;184(2):139-44.

- Study to investigate the role of oxidative stress in exposure to chemicals in the environment
- The oxidative stress biomarkers measured significantly affected the indicators of insulin resistance, particularly glucose level.
- This study indicates that environmental chemical exposure is associated with oxidative stress in urban adult populations and suggests that exposure to certain environmental chemicals might contribute to insulin resistance.

### OXIDATIVE STRESS BIOMARKERS

**\*\* Gwen Kennedy, Vance A., Spence, Margaret McLaren, Alexander Hill, Christine Underwood, Jill J.F. Belch.** 2005. Oxidative stress levels are raised in chronic fatigue syndrome and are associated with clinical symptoms. *Free Radicals Biology & Medicine.* 39(2005) 584–589

- This study investigated levels of plasma markers of oxidative stress (8-iso-prostaglandin-F2a-isoprostanes) alongside other plasma markers of oxidative stress in CFS patients and control subjects
- CFS patients had higher levels of plasma markers compared to controls
- Levels of the marker isoprostane correlated with CFS symptoms

### OXIDATIVE STRESS CHEMICALLY INDUCED; BIOMARKER – DNA EXPRESSION

**Ivan Rusyn<sup>1,2</sup>, Shoji Asakura<sup>2</sup>, Brian Pachkowski<sup>2</sup>, Blair U. Bradford<sup>1</sup>, Mikhail F. Denissenko<sup>3</sup>, Jeffrey M. Peters<sup>4</sup>, Steven M. Holland<sup>5</sup>, Janardan K. Reddy<sup>6</sup>, Michael L. Cunningham<sup>7</sup> and James A. Swenberg<sup>2</sup>.** 2004 Expression of Base Excision DNA Repair Genes Is a Sensitive Biomarker for in Vivo Detection of Chemical-induced Chronic Oxidative Stress Identification of the Molecular Source of Radicals Responsible for DNA Damage by Peroxisome Proliferators Cancer Research 64, 1050-1057, February 1, 2004.

- The authors found that expression of base excision DNA repair genes is a sensitive in vivo biomarker for chemically induced oxidative stress to DNA that can be successfully used for the identification of the molecular source of radicals responsible for DNA damage in vivo.

## 8. ODOURS

ODOURS ARE NOT NECESSARILY DETECTABLE

**Gaffney, S H and Paustenbach, D J.** Ann. A proposed model for setting occupational exposure levels (OELs) for sensory irritants based on chemosensory models. *Occup. Hyg., Vol. 51, No. 4, pp. 345–356, 2007*

- Reports on the problems of setting occupational exposure limits (OELs)
- There are a substantial number of odorous or irritating chemicals that are in need of OELs. Of the >600 substances for which an OEL has already been established, > 66% are sensory irritants

OLFACTORY AND IMMUNE SYSTEM INTERRELATIONSHIP

**\*\* Moscavitch SD, Szyper-Kravitz M, Shoenfeld Y. 2008.** Autoimmune pathology accounts for common manifestations in a wide range of neuro-psychiatric disorders: The olfactory and immune system interrelationship. *Clin Immunol. 2008 Dec 17.*

- Data from animal models and human studies currently imply numerous and complex effects of smell on behavior, mood, and on the immune response.
- This review discusses a possible inter-relationship between olfactory impairment, autoimmunity and neurological/psychiatric symptoms in several diseases affecting the central nervous system (CNS) such as Parkinson, Alzheimer's disease, autism, schizophrenia, multiple sclerosis and neuropsychiatric lupus erythematosus.
- Pathological manifestations were proposed as a novel approach to the understanding of the interactions between the CNS, the smell and the immune system

**9. EVIDENCE THAT CHEMICALS IN THE ENVIRONMENT CAUSE ADVERSE HEALTH EFFECTS SUCH AS ASTHMA AND ALLERGY. THESE HEALTH EFFECTS OVERLAP SOME OF THOSE SEEN IN MCS. THE ABSTRACTS PROVIDED RELATE TO BOTH SPECIFIC CHEMICALS AND MIXTURES OF CHEMICALS.**

FORMALDEHYDE SENSITISATION

**Wilhelmsson B; Holmstrom M.** 1992. Possible mechanisms of formaldehyde-induced discomfort in the upper airways. *Scand J Work Environ Health 1992 Dec;18(6):403-7*

- Investigated the mechanism of nasal irritation following chronic exposure to formaldehyde
- They found that about 50% of the studied population of workers occupationally exposed to formaldehyde during formaldehyde production experienced nasal discomfort through hyperreactivity. Atopics were not significantly overrepresented among the persons with occupational nasal symptoms.
- They concluded that exposure to formaldehyde should be minimized as much as possible for all

AVOIDANCE EARLY CAN HALT PROGRESSION; CO-EXISTING ALLERGY CAN EXACERBATE CHEMICAL IRRITATION.

**Kriebel D; Sama SR; Cocanour B.** 1993. Reversible pulmonary responses to formaldehyde. A study of clinical anatomy students. *Am Rev Respir Dis 1993 Dec;148(6 Pt 1):1509-15*

- Irritant symptoms in students exposed to formaldehyde during a clinical anatomy laboratory course increased strongly over the course of the average laboratory period, but this effect was stronger at the beginning than at the end of the semester
- After 14 weeks away from the laboratory peak expiratory flow (PEF) and reported symptoms returned to pre-exposure levels

#### CO-EXISTING CHRONIC DISEASES EXACERBATE EFFECTS OF CHEMICALS

**Liu KS; Huang FY; Hayward SB; Wesolowski J; Sexton K.** 1991. Irritant effects of formaldehyde exposure in mobile homes. *Environ Health Perspect* 1991 Aug;94:91-4

- Irritant effects were found to be associated with formaldehyde exposure in a mobile home after controlling for age, sex, smoking status, and chronic illnesses.
- They found there were synergistic effects between formaldehyde exposure and chronic health problems.

#### VOCs ASSOCIATED WITH ASTHMA/COEXISTING MORBIDITY

**Rumchev, K et al.** 2004. Association of domestic exposure to volatile organic compounds with asthma in young children. *Thorax* 2004;59:746–751.

- Australian study investigating the association of domestic exposure to volatile organic compounds (VOCs) with asthma in young children
- Asthma cases were exposed to significantly higher VOC levels (mg/m<sup>3</sup>) than controls
- Most of the VOCs appeared to be significant risk factors for asthma with the highest odds ratios for benzene followed by ethylbenzene and toluene.
- The authors concluded that domestic exposure to VOCs at levels below currently accepted recommendations may increase the risk of childhood asthma. Measurement of total VOCs may underestimate the risks associated with individual compounds

#### AIR POLLUTANTS AND ASTHMA/COEXISTING MORBIDITY

**Wichmann FA, Müller A, Busi LE, Cianni N, Massolo L, Schlink U, Porta A, Sly PD.** 2008. Increased asthma and respiratory symptoms in children exposed to petrochemical pollution. *J Allergy Clin Immunol.* 2008 Dec 24.

- Authors studied the effects of exposure to petrochemical pollution on the respiratory health of children
- They concluded that exposure to particulate matter and volatile organic compounds arising from petrochemical plants was associated with worse respiratory health in children.

#### CHEMICAL INDUCED ALLERGY; CO-EXISTING DISEASES; SUSCEPTIBILITY

**Blömeke B, Brans R, Dickel H, Bruckner T, Erdmann S, Heesen M, Merk HF, Coenraads PJ.** 2008 Association between TNFA-308 G/A polymorphism and sensitization to para-phenylenediamine: a case-control study. *Allergy.* 2008 Mar 29.

- Common contact sensitizers, frequently causing allergic contact dermatitis (ACD). The cytokine tumor necrosis factor-alpha (TNF-alpha) plays a key role in contact sensitization
- They found that a genetic polymorphism may have a possible role as a susceptibility factor for chemically induced ACD

#### ASTHMA ONSET AND CHEMICAL EXPOSURE

**Kogevinas M, Zock JP, Jarvis D, Kromhout H, Lillienberg L, Plana E, Radon K, Torén K, Alliksoo A, Benke G, Blanc PD, Dahlman-Hoglund A, D'Errico A, Héry M, Kennedy S, Kunzli N, Leynaert B, Mirabelli MC,**

**Muniozguren N, Norbäck D, Olivieri M, Payo F, Villani S, van Sprundel M, Urrutia I, Wieslander G, Sunyer J, Antó JM. 2007.** Exposure to substances in the workplace and new-onset asthma: an international prospective population-based study (ECRHS-II). *Lancet*. 2007 Jul 28;370(9584):336-41.

- Study of the role of exposure to chemicals in the workplace in new-onset asthma
- A significant excess asthma risk was seen after exposure to substances known to cause occupational asthma..
- These risks were highest for asthma defined by bronchial hyper-reactivity in addition to symptoms
- Of common occupations, a significant excess risk of asthma was seen for nursing
- Asthma risk was also increased in participants who reported an acute symptomatic inhalation event such as fire, mixing cleaning products, or chemical spills
- They found that the population-attributable risk for adult asthma due to occupational exposures ranged from 10% to 25%, equivalent to an incidence of new-onset occupational asthma of 250-300 cases per million people per year

#### ALLERGY ONSET AND EXPOSURE TO ENVIRONMENTAL POLLUTANTS

**Karmaus, w et al. 2001.** Infections and atopic disorders in childhood and organochlorine exposure. *Archives of Environmental Health* 56(6): 485-492

- This study identified DDE as a risk factor in children for asthma and increased IgE blood levels

#### ALLERGIC CONDITIONS INCREASING IN AUSTRALIA

**Leanne M. Poulos, BMedSc (Hons),a Anne-Marie Waters, Grad Dip Pop Hlth, Patricia K. Correll, MPH,a Robert H. Loblay, PhD,b and Guy B. Marks, PhD. 2007** Trends in hospitalizations for anaphylaxis, angioedema, and urticaria in Australia, 1993-1994 to 2004-2005. *J Allergy Clin Immunol* 2007;120:878-84.)

- Reports an increase in hospitalization rates for allergic conditions and that the nature and causative factors differ between adults and children.
- Among older persons, angioedema is becoming an increasing problem. Among children, hospitalization because of food-induced anaphylaxis is a growing concern.

#### PHthalATES IN DUST ASSOCIATED WITH ALLERGIC SYMPTOMS/COEXISTING MORBIDITIES

**Bornehag, CG, J Sundrell, CJ Weschler, T Sigsgaard, Björn Lundgren, Mikael Hasselgren, Linda Hägerhed-Engman. 2004.** The Association between Asthma and Allergic Symptoms in Children and Phthalates in House Dust: A Nested Case-Control Study, *Environ Health Perspect* 112:1393-1397 (2004)

- In children those with persistent allergic symptoms there were higher levels of butyl benzyl phthalate (BBzP) in their house dust than controls
- This study shows that phthalates, within the range of what is normally found in indoor environments, are associated with allergic symptoms in children

#### CHEMICALS MODULATES THE IMMUNE SYSTEM

**Gavin W. ten Tusscher; Peter A. Steerenberg; Henk van Loveren; Joseph G. Vos; Albert E.G.K. von dem Borne; Matthijs Westra; Johannes W. van der Slikke; Kees Olie; Hendrik J. Pluim; and Janna G. Koppe. 2003.** *Environmental Health Perspectives* 111:1519–1523 (2003).

- This study provides indications of effects at the stem cell level of perinatal dioxin exposure, persisting until minimally 8 years after birth.

**Volker, D et al. 2002.** Associations of dichlorodiphenyltrichloroethane (DDT) 4.4 and dichlorodiphenyldichloroethylene (DDE) 4.4 blood levels with plasma IL-4. *Archives of Environmental Health*.

57(6): 541-547

- The authors found that frequent acute and chronic infections reported by many of the pesticide exposed individuals studied could be the result of these immunological abnormalities.

#### CHEMICALS ARE ASSOCIATED WITH OTHER ILLNESSES

#### HARMFUL CHEMICALS ACCUMULATE IN THE HUMAN BODY

**Kannan, K, S Corsolini, J Falandysz, G Fillmann, KS Kumar, BG Loganathan, MA Mohd, J Olivero, N Van Wouwe, JH Yang, KM Aldous.** 2004. Perfluorooctanesulfonate and Related Fluorochemicals in Human Blood from Several Countries. [Environmental Science and Technology, in press](#). DOI: 10.1021/es0493446.

- This study documents widespread human contamination by highly persistent chemicals involved in making Teflon, Scotchgard and related products

**Lin Tao; Kurunthachalam Kannan; Chung M. Wong; Kathleen F. Arcaro and John L. Butenhoff**

Perfluorinated Compounds in Human Milk from Massachusetts, U.S.A. *ASAP Environ. Sci. Technol., ASAP Article, 10.1021/es702789k*

- This study found Perfluorinated compounds (PFCs) in human milk from the U.S.A.

#### CHEMICALS CROSS THE PLACENTA

**Gilbert Schönfelder,<sup>1</sup> Werner Wittfoht,<sup>1</sup> Hartmut Hopp,<sup>2</sup> Chris E. Talsness,<sup>1</sup> Martin Paul,<sup>1</sup> and Ibrahim Chahoud** 2002. Parent Bisphenol A Accumulation in the Human Maternal-Fetal-Placental Unit *Environ Health Perspect* 110:A703-A707 (2002).

- . Exposure levels of Bisphenol A (BPA), an endocrine disruptor, were found within a range typical of those used in recent animal studies and were shown to be toxic to reproductive organs of male and female offspring.

#### CHEMICALS AND ENDOCRINE DISRUPTION

[Singleton DW, Feng Y, Yang J, Puga A, Lee AV, Khan SA.](#) 2005. Gene expression profiling reveals novel regulation by bisphenol-A in estrogen receptor-alpha-positive human cells. *Environ Res.* 2005 Jul 16;

- Bisphenol-A (BPA) has the potential to disrupt normal endocrine signaling through regulation of estrogen receptor (ER) target genes

#### BODY BURDEN, ADVERSE EFFECT OF CHEMICALS IN AGING

**Adler, T.** 2003. Aging research: the future face of environmental health. *Environmental Health Perspectives* 111(14):A761-A765 Focus.

- Investigates the implications of environmental pollution in the health of older persons.
- Diseases can all be exacerbated by environmental contaminants on a body that may not have the energy reserves to deal with the environmental assaults
- The body burden of toxic substances is an issue with older people as high concentrations of certain toxic compounds can be the result of living for a long time
- Seniors are also likely to have been exposed to toxic chemicals that have now been banned for their persistence or were formerly not regulated by government
- . Research into aging is needed to protect people at all stages of life from environmental toxicants and reduce some diseases to allow seniors better quality of life in their advancing years.

## GENDER DIFFERENCES IN RESPONSES TO CHEMICALS

**E. NEIL Schachter , Eugenija Zuskin , Erin L. Moshier , James Godbold , Jadranka Mustajbegovic , Jasna Pucarín-Cvetkovic and Angelo Chiarelli.** 2009. Gender and respiratory findings in workers occupationally exposed to organic aerosols: A meta analysis of 12 cross-sectional studies. *Environmental Health* 2009, 8:1

- This study investigated gender related differences in respiratory findings by occupation.
- The results of this study suggest that in industries processing organic compounds there are gender differences in respiratory symptoms and lung function in exposed workers

### **10. CONCLUDING INFORMATION ON WORKSAFE STANDARDS**

**The existence of chemical injury/sensitivity is validated by Worksafe standards.**

ASEHA is concerned about the ability of the health care system to provide safe facilities and appropriate assistance to those injured by chemicals. The Worksafe Standard for air levels of contaminants in the occupational environment validates chemical injury as an organic disease state and contains sections devoted to sensitisers, solvents and odours.

#### **WORKSAFE STANDARDS**

***Some points of interest in the Worksafe Standard are as follows:***

Introduction p. 5

- ◆ 1.2 exposure standards are based only on current knowledge;
- ◆ 1.4 exposure standards do not guarantee protection for every worker because of individual susceptibility and biological variation, and it is inevitable that some workers will suffer adverse health impacts;
- ◆ 1.6 atmospheric exposure standards only consider absorption by inhalation and are only valid on the assumption that skin absorption cannot occur.

***Most substances used are untested/lack data***

Chapter 2. Unlisted substances p. 6

- ◆ 2.1 most substances used in industry have not been assigned exposure standards. This does not imply that the substances are safe or non-hazardous;
- ◆ 2.2 there is a lack of data on health effects of some substances to assign a standard.

***Lack of biological tests***

Chapter 8. Biological monitoring p. 13

- ◆ 8.3 there is limited knowledge of suitable and definitive biological tests for most substances.

***Odour and chemical interactions validated***

Chapter 9 Odour thresholds p.14

- ◆ 9.1 odours can serve as a useful warning signal as to the presence of a substance in the environment;
- ◆ 9.2 there may be interference from other substances;

***Avoidance validated***

Chapter 11 Effects on the skin p. 16

- ◆ 11.1 some substances can readily penetrate the skin and this method of exposure can pose a far greater danger than inhalation exposure;
- ◆ 11.3 some substances such as solvents can accelerate or alter the rate of skin absorption;
- ◆ 11.6 it is 'good practice' to avoid any unnecessary contact with all chemical substances.

***Sensitisation and low level exposures validated***

Chapter 12 Sensitisers p. 17

- ◆ 12.1 Some substances (TDI, Formaldehyde) can cause a specific immune response in some people. This is known as 'sensitisation';

- ◆ 12.2 Following sensitisation 'an affected individual may subsequently react to exposure to minute levels of that substance'. Although low values have been assigned the exposure standard may not be adequate to protect a hypersensitive individual and persons who are sensitised to a particular substance should not further be exposed to that substance. (NOHSC. 1995)

#### Chapter 15 Mixtures of substances p. 28

- ◆ 15.12 At present the understanding of interaction effects is incomplete. The knowledge that such effects occur is reason to maintain the concentrations of individual substances as low as is practicable under complex exposure conditions.

#### Part 2 Interpretation p. 70

'Exposure Standard' means an airborne concentration of a particular substance in the workers breathing zone, especially to which according to current knowledge, should no cause adverse health effects nor cause undue discomfort to **nearly all workers**.

Refs

NOHSC. 1995. Exposure standards for atmospheric contaminants in the occupational environment. AGPS, Canberra.

It is unethical to ignore the perceived small percentage to which these standards cannot be applied.

Why are we having so much trouble gaining recognition of the organic disease state induced by chemicals when Worksafe clearly acknowledges the problem exists and confirms the need for avoidance - even to low levels? The basis of chemical induced illness has always been in teaching toxicology texts such as Casarett & Doull's Toxicology: A basic science of poisons.

#### **SOLVENT SENSITIVITY**

Solvent sensitivity is acquired following exposure to a solvent or solvents that results in sensitisation or injury. While this is thought to occur only in an occupational setting following a single acute exposure, chronic exposure to solvents can cause the same spectrum of effects as a single acute exposure. (Amdur, MO et al. 1991). Because organic solvents have a special affinity for lipid-rich tissues, including brain tissue, they have been implicated in producing a wide range of CNS symptoms. These same solvents may be used as an ingredient in perfumes and perfumed products. AMDUR, M O et al. 1991 Casarett and Doull's Toxicology: the basic science of poisons. Fourth ed. Pergamon, NY. p.15

#### **SKIN AS A ROUTE OF CHEMICAL SENSITISATION**

Skin sensitisation was not covered in the MCS working draft. However, chapter 11 of the Guidance Note on the Interpretation of Exposure Standards for Atmospheric Contaminants in the Occupational Environment [NOHSC:3008(1995)] 3rd Edition states:

#### **11. EFFECTS ON THE SKIN**

##### SKIN ABSORPTION

11.1 For most substances in the occupational setting, the main route of entry into the body is via inhalation. However, certain chemical substances such as aniline, nitrobenzene, phenols and certain pesticides can readily penetrate the intact skin and thus become absorbed into the body. Frequently, there will be no accompanying skin damage. In some instances this dermal absorption can pose a far greater danger than inhalation exposure.

11.2 The adopted national exposure standards listed in the publication only consider absorption via inhalation, and are valid only on the condition that significant skin absorption cannot occur. In some instances, special measures may be required to prevent absorption through the skin. Chemical compounds requiring such precautions are specified by the notation 'Sk' in column 6 of the printed listing of the adopted national exposure standards, a skin absorption notation is provided in the database version of the exposure standards.

11.3 Skin absorption can result from local contamination, for example, from a splash onto the skin or clothing, or, in some rare cases, from exposure to very high atmospheric concentrations of vapour. In addition, some vehicles, such as solvents, can accelerate or alter the rate of skin absorption. Serious effects can result with little or no warning and it is necessary to take special precautions to prevent skin contact when handling these substances.

11.4 Where biological monitoring methods are available for such materials, it may be important to employ these

for personnel surveillance in addition to any air monitoring program. Biological monitoring is discussed in more detail in Chapter 8.

#### **OTHER EFFECTS ON THE SKIN**

11.5 Many substances can be injurious by their direct effect on the skin and mucous membranes, whether or not they are also absorbed in significant amounts. Solvents degrease the skin, thereby rendering the individual more vulnerable to the effects of the solvents and other substances. Some corrosive substances cause particularly serious injuries to the eyes and skin. Other substances, for example, derivatives of coal tar and certain dyes and drugs, by either coming into direct contact with the skin or reaching there by the systemic circulation, may react with selected wavelengths of natural or artificial light to cause dermatitis or other health effects.

11.6 Substances which may cause physical damage to the skin or eyes are not noted in this publication. However, it is good practice to avoid any unnecessary contact with all chemical substances.

11.7 **Note:** An initiative of the National Commission which addresses occupational skin disorders may lead to more detailed advice on this issue. 30

#### Reference

National Occupational Health and Safety Commission, National Strategy for the Prevention of Occupational Skin Disorders [NOHSC:4002(1989)], Australian Government Publishing Service, Canberra, 1989.

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