PRESENTED TO CANADA PENSION PLAN PHYSICIANS
SEPTEMBER 30, 1992

There has been an increasing number of applications to Canada Pension Plan from people claiming to suffer from Environmental Sensitivity Disorder or Multiple Chemical Sensitivity. In the past twelve years I have seen over 4,000 patients because of multiple system complaints. Ninety-five percent of these people have complaints involving at least two systems of the body, and they have been ill an average of just under six years' duration. Most of the patients are adults in the 30's and 40's, and the females outnumber males about 7 to 1. The chief complaint involves the central nervous system in 63% of these patients; the gastrointestinal system in 25%, and the respiratory system in 10%. When one looks at all the complaints, the central nervous system is involved in 92% of these patients; gastrointestinal system 88%; musculoskeletal system 83%; ear, nose and throat 67%; skin 67%;, respiratory system 50%; and genitourinary system 17%. The central nervous system seems to be the most involved system. The patients complain of fatigue, mood swings, irritability, anxiety, depression, decreased sex drive, poor concentration, poor memory, distractability, and disturbed sleep patterns. Other complaints include symptoms of irritable bowel syndrome, myalgia, arthralgia, headache, rhinitis, nasal congestion, post-nasal drip, shortness of breath, asthma, eczema, psoriasis, seborrheic dermatitis, and vaginitis. In my practice, 40% of these patients admit on initial interview, to have come from a dysfunctional home in which there was alcoholism, emotional, physical or sexual abuse.

The differential diagnosis of these patients includes: psychiatric illness (anxiety states, depression, somatization disorders), endocrinological disorders (hyper/hypothyroidism), nutritional disorders (e.g. B12 deficiency, copper toxicity, aluminum toxicity), chronic fatigue syndrome, myfibrositis, auto-immune diseases (e.g. lupus, sarcoidosis), and environmental sensitivity disorder (food sensitivities, allergies, sick building syndrome, multiple chemical sensitivity).

While environmental sensitivity disorder may not be a new phenomenon, our awareness of it has increased and quite likely the number of people suffering from this illness has increased markedly in the last 20 years. One hundred thousand new man-made chemicals have been introduced into the environment since 1940 (Molot, 1989). Being at the top of the food chain, every person tested so far in the United States has been found to have measurable levels of

chemicals stored in their fat which could be measured in parts per million or parts per billion in blood (Kutz, 1979). The clinical significance of this xenobiotic load is not known. Our greatest source of pollution contact on a day to day basis, is indoor air. The level of volatile organic compounds in indoor air is 4 to 10 times the levels measured outdoors (Wallace, 1985). The source of this increased pollution is due to a combination of inadequate ventilation standards together with increasing chemicals gassing-off from cleaning fluids, perfumes, deodorizers, new carpets, paints, machines (especially photocopy machines), particle board, chipboard and plywood.

The ventilation standard in 1936 was based on detectable human odour limits. The standard was lowered in the 1970's in response to the energy crisis. Chronic exposure safety levels derived from known toxic levels. Chronic CNS changes were never suspected. Multiple chemical exposures (which is normal in indoor air) were never studied.

An early description of patients with sensitivity to environmental chemicals was given by Randolph (Randolph, 1962). He described five characteristics:

1. acquired - often after chronic, insidious or acute high-dose exposure to a petrochemical.

2. chemical exposures trigger physical or mental symptoms.

3. specific adaptation syndrome - adaptation to specific chemicals with chronic exposure is followed by maladaptation and chronic illness, withdrawal symptoms when removed from the chemical environment, and shock reactions on re-exposure.

4. spreading phenomenon - as an individual becomes maladapted to the chemical environment, intolerance to increasing numbers of environmental chemicals develops.

5. avoidance - by avoiding the chemical environment, chronic illness may resolve.

The chemicals that Randolph discussed as triggering this illness, are indoor air contaminants such as perfume, tobacco smoke, and outdoor air contaminants including car exhaust, chemical additives, and contaminants of food and water, synthetic drugs and cosmetics. Studies have verified that our population's greatest exposure to organic inhalants comes from indoor air contaminants, rather than industrial or other sources (Wallace, 1985, Wallace, 1987).

In 1985, the Ontario Ministry of Health published a report of the Ad Hoc Committee on Environmental Sensitivity Disorders. It defined environmental sensitivity disorder as a chronic, multi-system disorder usually involving symptoms of the central nervous system and at least one other system. Affected persons are frequently intolerant to some foods and they react adversely to some chemicals and to environmental agents, singly or in combination, at levels generally tolerated by the majority. Affected

persons have varying degrees of morbidity, from mild discomfort to total disability. Upon physical examination the patient is normally free from any abnormal objective findings. There is no single laboratory test which is consistently altered. Improvement is associated with avoidance of suspected agents, and symptoms recur with re-exposure (Thomson, 1985). In 1987, Cullen gave a case definition of the illness based on his observations at the Occupational Medicine Clinic at Yale, together with other physicians from other occupational health clinics around the United States (Cullen, 1989). His case definition includes:

1. the illness is acquired as a result of some environmental exposure, insult or illness that can be documented.

2. symptoms involve more than one organ.

3. symptoms recur and abate in response to some predictable stimuli.

4. symptoms are elicited by exposures to chemicals of diverse structural classes and toxicological modes of action.

5. symptoms are elicited by demonstrable exposures.

6. exposures that elicit symptoms must be low - many standard deviations below the "average" exposures known to cause adverse human responses.

7. no single, widely available test of organ system function can explain the symptoms.

While these working definitions are useful in a clinical practice, they are not strict enough to define the illness accurately enough to do good quality research. We are presently involved in a study with Johns Hopkins University to try and determine a very exact definition of M.C.S.

The National Academy of sciences in the United States (NAS 91) has stated that the gold standard for diagnosis of Multiple Chemical Sensitivity is through inhalation challenge, double-blind, in a de-adapted state, in an environmental control unit. An environmental control unit is a section of a hospital where patients are admitted in which the environment is strictly monitored and controlled, so that the indoor air is as free of chemicals and particulate inhalants, as is technologically possible. (Edgar, 1979).

The central nervous system seems to be the main organ system involved with this disorder. Symptomatic patients with chronic exposure to volatile organic compounds, below threshold limit values, have shown a variety of CNS changes when compared to control groups. There are disturbances in psychological function which can be demonstrated in behavioural changes and neuropsychological testing (addendum #1). Fatigueability, mood swings and memory problems have been reported in subjective evaluation. Psychological testing has shown changes in simple reaction time, manual dexterity, perceptual speed, short term memory, concen-

tration/attention, and abstract function. Neuropsychological testing has also shown changes in Minnesota Multiphasic Personality Inventory (MMPI) scales (somatization, depression, and hypochondriasis), and with Bender Gestalt testing (Morrow, 1989).

There have also been changes reported in immune function. These tests are not diagnostic but changes have been recorded in patients diagnosed with multiple chemical sensitivity when compared to control groups. These changes include: low total WBC, increases or decreases in CD4, increases or decreases in CD8, increases or decreases in CD4:CD8 ratios, increased CD26, decreased CON A mitogen response, lymphocyte infiltrates in sub-epithelial connective tissue of nose, decreases in complement (C3, C4), increase in numbers of autoantibodies, and alterations in immunoglobulin levels (addendum #2).

In order to try and understand the phenomenon of environmental disorder, it seems necessary that we develop a physiological explanation or theoretical model. An argument can be made that this disease process is due to immune dysfunction. There is the specificity of triggering agents, the acquired nature following an initial exposure, the spreading phenomena, the above-mentioned immune findings in these patients compared to control groups, and the observation made by a variety of clinicians that 90% of these patients suffer from allergies and food sensitivities. Ninety-percent of these patients have an immediate hypersensitivity reaction to candida albicans or T.O.E. (trichophyton, oidiomycetes, epidermophyton). However, it also appears that the central nervous system is involved. There are abnormalities reported in mood, behaviour, cognitive functioning, sleep and fatigue-ability. Most of the symptoms seem to be due to autonomic nervous system dysfunction. It appears that neither the CNS or immune system can be held entirely responsible for the phenomena being observed. To reconcile this duality, one must look at the interplay of these two systems which is known as psychoneuroimmunology (Ader, 1981).

Over the last ten years, a wealth of scientific information has been discovered. It strongly supports the fact that there is a two-way axis between the brain and the immune system. This bidirectional communication is both neuronal and humoral. The central nervous system can stimulate the immune system by direct nerve stimulation of the thymus, bone marrow, spleen, lymph glands and lymphocytes. There is also suppression of lymphocytes as well as the above-mentioned organs from corticosteroids released via the hypothalamus-pituitary-adrenal axis. There is stimulation of lymphocytes with hormones secreted from the pituitary such as TSH, growth hormone, estrogen, LH, FSH, and endorphins. There are also many studies of chronic stress and depression which demonstrate both stimulatory and suppressing effects on various components of the immune system. For example, patients with autoimmune disease or allergies can trigger or exacerbate their disease process when stressed. It should be noted too, that this stress does not have to be psychological but could be heat, cold, or trauma. While these phenomena are well known and well publicized, the effects of the immune system on brain function are not. Stimulation of the

immune system with the release of IgG antibodies has been well documented to cause stress responses in the hypothalamus mainly in the locus coerulus, ventromedial nucleus, and supraoptic nucleus. The classical changes of the stress response including release of norepinephrine and neuron firing have been reported (Besedovsky, 1983). Patients with immune function diseases such as asthma and eczema have been shown to have abnormalities in MMPI testing. The release of IgG antibodies causing these changes in central nervous system functioning are at first difficult to understand because IgG antibodies do not cross the blood brain barrier. It appears that the release of neurotransmitters from basophils are responsible for these changes occurring. There are very abundant numbers of receptor sites for the neurotransmitters released by the immune system in the limbic system of the brain which appears to be the area which may be responsible for the central nervous system symptoms observed. For example, interleukin 1 (Obal, 1990) and interleukin 2 (DeSarro, 1990) have been shown to cause CNS changes.

Patients suffering from environmental sensitivity disorder have been told by many physicians that their symptoms are due to "stress", while doctors practising environmental medicine are telling these patients that they have not adapted to the changes in their physical environment. Stress is not listed in the DSM III because it is a physiological phenomenon rather than a diagnostic label. Understanding this physiological phenomenon is beneficial in understanding patients with environmental illness and maladaptation to the environment. When measurements are taken in the brain of animals, the acute stress response has been shown to cause a decrease in measurable levels of neurotransmitters such as norepinephrine (see graph #1). If these stresses are repeated, and they are not too strong, the animal will adapt to the stress; it will show no signs of maladapted behaviour and the neurotransmitter levels in the brain will remain constant. However, if this chronic low grade repeated stress is continued, the animal will eventually show maladaptive behaviour. At this time the neurotransmitter level in the brain increases above normal levels, and when the animal is stressed again, the neurotransmitter level actually rises in the brain rather than falls. If the stressor is discontinued, the neurotransmitter level will fall back to baseline, and the animal will once again show normal behaviour. However, if that same stress is then repeated within a short period of time, the neurotransmitter level, rather than fall, will rise quickly to the same levels as seen in the maladapted state. This appears to be a conditioned response which will discontinue only after a prolonged period of avoidance of the stressor. This phenomenon is explained by adaptation to the chronic stress followed by maladaptation, and when the stressor is removed, the animal is said to be in the de-adapted state, and is therefore primed to have an exaggerated conditioned stress response which can be measured as well physiologically.

Many people look at the immune system as a sensory organ of the central nervous system. Through its communication with the brain, it keeps us informed regarding molecular contact with the outside world and attempts to invade our body by organisms. It also screens the inside of the body for abnormal molecular structures.

It is interesting to note that the immune system functions very similarly to the central nervous system, e.g., there are many functions of the immune system which can also be conditioned such as phagocytosis, antibody responses, histamine release, lymphocyte suppression and anaphylaxis. Lymphocytes can also secrete and have receptor sites for immunostimulants (thyroid hormone, endorphins, growth hormone, lymphokines, estrogen) and immunosuppressors (ACTH, glucocorticoids and insulin). The interplay of hormones on these two systems should not be forgotten. It is a known phenomenon that immunological disease processes are more likely to occur in women, and it has also been observed that women are much more likely to get environmental sensitivity disorder than men. Perhaps estrogen may be playing a role. While large doses of estrogen have been shown to suppress thymus function, small doses stimulate immune responses (e.g. sheep RBC antibody responses in rats) (Ader, 1981).

Understanding psychoneuroimmunology and adaptation/maladaptation is essential in understanding the phenomenon of environmental sensitivity disorder. It is for this reason that the National Academy of Sciences in United States has recommended that the gold standard for research is an environmental control unit where the patients can be put in an environment which removes all physical and environmental stressors and puts them in a de-adapted state where they can then be tested with double-blind inhalation challenge to low doses of chemical pollutants in order to make clear and precise observations (NAS, 1991).

Further understanding the disease process can come from looking at the limbic system. The hypothalamus which is in close association with the limbic system, has attracted considerable attention because it is the focal point in the brain where the immune, nervous and endocrine systems interact (Bell, 1982). The olfactory system has known links to the hypothalamus and other parts of the limbic system (Kare, 1968, Maller et al 1967). Substances placed in the oropharynx in rats migrated to the brain in minutes by a pathway other than the bloodstream and in higher concentrations than if administered by the gastrointestinal tract, suggesting a direct route from mouth to brain. Inhaled substances that contact the nasal epithelium may cross into the brain and be distributed widely by a transneuronal transport (Shipley, 1985). Thus molecules that are inhaled in contact with olfactory apparatus could conceivably influence functions in other parts of the brain. It appears that strong odours and even mild ones can provoke increased electrical activity in the amygdala and hippocampal areas of the limbic system (Munro, 1986). Subsequent re-exposure to chemicals can cause protracted if not permanent alterations in electrical activity of the brain beginning first with the most sensitive structures particularly that portion of the amygdala that analyzes odours (Bokina, 1976). It has therefore been postulated that the responses observed in patients with chemical sensitivity are conditioned responses to odours. It is also a well known phenomenon that it is easier to condition responses if one is already stressed. However, patients experience reproducable symptoms to specific chemical exposures:

1. often before the odour is perceived (Ziem, 1989).

2. with their noses clamped during provocative testing.

3. when anosmia is present (Shim, 1986).

Furthermore, patients with multiple chemical sensitivities were compared to healthy control subjects to see whether or not they were more sensitive to smells. They were subjected to very low levels of phenyl ethyl alcohol, and methyl ethyl ketone at less than 1% of permissible occupational levels. No difference in ability to detect odours was found between the two groups but nasal resistance was 2 to 3 times higher in the chemically sensitive group than in the controls (Doty, 1988). This has also been noted in patients claiming sensitivity to tobacco smoke (Bascom, 1990).

Another concept which may help understand the phenomenon of hypersensitivity is "kindling". In other words, a small signal would more readily trigger firing of nerve cells in brain regions where kindling was present. Kindling might be enhanced by genetic endowment, prior environmental exposures, psychological stress, hormonal variations or other factors. Kindling is a kind of stimulatory lesion (Girgis, 1986). Stimulation of the amygdala with electrodes may elicit rage or loss of control of emotions, a phenomenon frequently reported by patients with multiple chemical sensitivities. The amygdala is particularly susceptible to electrical discharge following either electrical (Girgis, 1986) or chemical provocation (Bokina, 1976) and is subject to long-lasting alteration given repeated stimuli. Very potent or repeated stimuli, whether electrical or chemical, may permanently augment a tendency for neurons to fire in the presence of future stimuli, even when challenged with much lower levels than those originally involved. It has also been reported that there is a decrease in acetylcholinesterase, an enzyme that breaks down the neurotransmitter acetycholine in junctions between nerve cells that parallels the increase in supersensitivity to stimuli. The limbic system is especially rich in acetylcholine (Girgis, 1986). Bokina (1976) found impaired speed of execution and coordination of complex motor processes in humans repeatedly exposed to carbon disulfide for 10-15 minute intervals at subsensory levels. Animals primed by high concentrations of various chemicals such as formaldehyde and ozone, and subsequently re-exposed to low concentrations of the same chemicals, showed an increased tendency towards paroxysmal electrical discharge in the amygdala. Thus it can be seen that kindling could help to explain the apparent loss of adaptive capacity in multiple chemical sensitivity. Formerly well tolerated low level exposures to tobacco smoke or perfume for example, might trigger symptoms in individuals whose limbic areas have been kindled by a prior exposure. Likewise, spreading of sensitivities to chemically unrelated substances might be understood on this basis. A possible role for the enzyme systems for detoxification has also been postulated. It has been reported that enzyme systems such as cytochrome P450 which are used to break down chemicals, are faulty in patients with multiple chemical sensitivity (Mustafa, 1977).

Summary - Observations on MCS (Miller, 1991)

A. Induction (priming or sensitization)

1. Unset following a major chemical exposure

In many cases MCS appears to follow a major exposure to any of a wide range of environmental chemicals. The exposure may occur briefly at high levels, or repeatedly or continuously at a lower level. Commonly reported inducing exposures include pesticides, solvents or complex mixtures such as combustion products or indoor air pollutants. However, onset of illness has been attributed to various other events, e.g. surgery, pregnancy, extreme stress or courses of various drugs. A disproportionate number seems to involve organophosphate pesticides.

2. Demographic diversity

MCS-like illnesses have been reported by industrial workers, individuals exposed in contaminated communities, tight building occupants, and individuals with personal and unique exposure histories (e.g. exposure to pesticides in the home). These groups differed greatly in terms of age, sex, social group, and the kinds of medical specialist that they consult.

3. Temporal cohesiveness

The temporal cohesiveness of MCS-like illness occurring within a group of individuals sharing a recognized major chemical exposure, helps point to the problem as real in those circumstances.

4. Total load

An apparent threshold effect referred to by some as the patient's "total load" has been noted and cited by some practitioners of environmental medicine to help explain why an individual develops this syndrome at a particular time. Illness is said to occur when the total load of biological, chemical, physical and psychological stressors exceed some threshold for the patient. This concept has emerged from clinical observations and likely causes a breakdown in the homeostasis of the brain immune system axis. While no direct experiments have been done to test its validity in humans, Selye's work, demonstrating the general adaptation syndrome in animals exposed to various stressors, lends support to this idea (Selye, 1946).

B. Triggering

5. Triggering by extremely low levels of chemicals

Following induction of the illness, patients report subsequent triggering by extremely low levels of exposure to common chemicals, levels that are tolerated by most of the

population.

6. Spreading

Spreading of sensitivities to other often chemically dissimilar substances with each substance triggering a different but reproducable constellation of symptoms, is commonly reported.

7. Characteristic constellation

For a given patient with a given exposure, a characteristic constellation of symptoms results. Even when no odour is present, MCS patients may be able to identify the nature of the exposure based solely upon the pattern of symptoms they experience.

8. Dose dependence

The severity of symptoms is proportional to "dose" (duration and magnitude) of the exposure in the sensitized individual.

9. Pronounced stimulatory and withdrawal symptoms

MCS patients sometimes report that when they are exposed to environmental excitants, either foods or chemicals, they initially may experience a stimulated feeling that is either pleasant or unpleasant, followed by withdrawal symptoms such as headache, irritability, depression and fatigue.

10. Inter-individual variability

Different MCS patients exposed to the same substances may experience different symptoms and symptom severity.

11. Intra-individual reproducability

Individual MCS patients report similar symptoms occurring each time a specific exposure is encountered.

12. Multiple exposure routes trigger symptoms

Patients' symptoms may be triggered by inhalation, ingestion, mucosal contact or injection, eyedrops, dental material, suppositories, I.V.'s and other exposures have have been reported to elicit symptoms. Exposures to a given substance in a given patient, but by a different route, has been reported to result in similar symptoms.

13. Subsensory triggering

Onset of symptoms with exposure to subolfactory threshold concentrations of chemicals may occur.

14. Rapid onset of symptoms

MCS patients frequently report onset of symptoms within a few seconds of being exposed. Such responses might suggest rapid shifts of ions across cell membranes, a neurological or immunological mechanism, or possibly conditioning.

15. Variable threshold for triggering

Following development of MCS, major exposures may result a general decrease in tolerance for chemical substances, even those for which tolerance may have been gained. Following such exposures gradual improvement usually occurs but may take days, weeks, or even months, depending upon the patient and the severity of the exposure. This variability and responsiveness in some ways resembles the increased bronchial reactivity that occurs in asthma, and increased basophil releaseability in atopic dermatitis following a major exposure to incriminated inhalants or foods respectively.

16. Decrease in symptoms with oral vs nasal inhalation

Some MCS patients have noticed that faced with an unavoidable exposure (e.g. traffic fumes or perfume), inhaling via their mouths instead of their noses, mitigates symptoms.

17. Limited voluntary control

Certain patients report that biofeedback, hypnosis or variations on these techniques, improved their ability to cope during their exposures and lessen symptom severity. Such techniques seem to be less helpful for more severe exposures and symptoms.

18. Adaptation

With frequent or continuous exposure, adaptation occurs and acute symptoms may become chronic and no longer appear related to particular exposures.

C. Other intolerances

19. Food and alcohol intolerance

These are estimated to occur in a sizeable percentage, perhaps 80% (Rea 1988), of individuals with MCS. Most of these patients complain of food intolerances and many MCS patients first become aware of an intolerance for ingestions when they consume an alcoholic beverage such as red wine or beer. Many of these patients are mould sensitive.

20. Drug intolerances

MCS patients often respond poorly to usual doses of medications and may even report difficulties with excipients, binders, colouring and flavouring agents.

21. Hyper-responsiveness to physical stimuli

Physical stimuli such as touch, sound and light may be perceived as greatly magnified by some MCS patients.

D. Symptoms/Signs

22. Multisystem symptoms

Symptoms involving virtually any system in the body and often several systems simultaneously which do not coincide with other known multisystem disorders, are common in this patient group.

23. Frequent central nervous system complaints

Fatigue, mood, memory and concentration difficulties are among the CNS symptoms most frequently reported by these patients.

24. Rhinitis

The majority of MCS patients appear to have nasal inflammation or rhinitis. As previously mentioned, it has been reported that patients with MCS have greater nasal airway resistance than normal controls.

E. Personal/predisposing characteristics

25. Apparent female preponderance

A greater number of females than males appear to be affected. Females are more likely to encounter immunological diseases. In a Soviet experiment, females were shown to be more susceptible to the effects of low level organophosphate exposure than their male counterparts (Karsovskii et al, cited in Calabrese 1985). The incidence of cutaneous drug reactions in females is 35% greater than among males (Bigby 1986).

26. Food cravings and addiction

Patients often report having carbohydrate or other food cravings especially sugar and chocolate.

27. Premorbid history of ill-defined medical condition

Diagnoses such as hypothyroidism, chronic fatigue, tempromandibular joint dysfunction and fibrositis seem to be more prevalent among MCS patients. Simon et al (1990) reported an average of 6.2 unexplained physical symptoms among workers who developed "environmental illness" prior to the workplace exposure vs 2.9 for controls.

28. Premorbid history of depression

Anxiety or depression has been reported prior to the workplace exposure in 54% of workers who developed chemical sensitivity vs 4% of controls. However, the sources of these patients' depression and anxiety, whether endogenous or chemically related, have yet to be demonstrated.

29. Target organs vary over time

Patients may report lifelong medical problems but affecting different organ systems over time, e.g. colic as a baby, asthma in grade school, stomach problems in high school, headaches in college, and finally chronic fatigue and memory and mood difficulties following a major exposure event in their 30's and 40's.

30. Family history of chemical intolerance

The fact that similarly exposed co-workers or family members of patients often do not develop MCS suggest possible genetic, nutritional, psychological or other predisposition, or an accumulation of effects of prior exposures in MCS patients. Many patients report a family history of chemical intolerance as well as an addiction.

F. Laboratory findings

31. Lack of a consistent immunological abnormality

A variety of immunological tests have been conducted in these patients including measures of both cellular immunity (T & B lymphocyte counts and ratios), and humoral immunity (immunoglobulin and complement levels).

32. Increased frequency of autoimmune antibodies

There appears to be an increased frequency of low titres of various autoimmune antibodies (ANA, antismooth antibody, thyroid antibodies, etc.) especially among individuals who report becoming ill after identifiable exposure to pesticides and solvents. The physiological significance of low titres of auto-antibodies is unknown, and the importance of this finding is compromised by the fact that 20% of healthy controls had similar findings (Broughton 1990, Connachie 1991).

33. Increased frequency of activated T-lymphocytes

The same researchers mentioned above reported an increased frequency of activated T-lymphocytes. This suggests an inappropriate or persistent immune response that fails to clear chemicals from the tissues. Activated T-cells have been reported and associated with multiple sclerosis, infections and various other inflammatory states. Once again the clinical significance of this finding is unknown.

34. EEG abnormality

A recent study compared EEG's from 58 "universal reactors", 55 healthy controls, and 89 patients from a psychology practice (Staudenmaer 1990). They found that the EEG's of the universal reactors more closely resembled the EEG's of psychological patients, rather than those of controls. Similar EEG changes with increased beta and decreased alpha activity have been reported among organophosphate exposed workers (Duffy 1979).

G. Diagnosis

There is no simple way to make a diagnosis of environmental sensitivity disorder without double-blind testing in an environmental control unit which is not available in Canada. One therefore relies on a detailed history. Physical examination is usually not contributory. Supportive evidence can be obtained through Serial Dilution Titration provocative testing. Intradermal testing provides more objective evidence of reaction than does sublingual challenge. Most patients found to have multiple chemical sensitivity in double-blind testing in an environmental control unit, have positive intradermal whealing responses to chemicals when compared to control groups. The above-mentioned immune system abnormalities with abnormalities in neuropsychological testing lends further support to the diagnosis.

H. Treatment

As further research helps us to understand this illness, more treatment modalities may become apparent. However, at this time, the only known treatment is environmental control with avoidance of incitrants or triggers.

I. Prognosis

The prognosis for these patients is quite varied. Severity of symptoms, number of known triggers and psychological illness, are inversely related to healing. Patients suffering from a more simple form of the disorder such as sick building syndrome, may recover after a few weeks of avoidance. However, patients with fullblown multiple chemical sensitivity are severely disabled because of their inability to control their symptoms without very strict environmental control, and they usually take many years before they develop any degree of tolerance at all. These patients become disabled because of exposure to chemical pollutants in the workplace, in all public areas such as shopping centres, movie theatres, restaurants, automobiles, buses, airplanes, hospitals, libraries and schools. Their social lives become restricted because of difficulty in visiting other peoples' homes and of the need to avoid contact with friends and relatives who smoke, wear perfumes or colognes, hairsprays, and even dry cleaned clothing. Patients who are very sensitive will also react to physical stressors and will frequently report exacerbation of their symptoms with excessive heat, excessive cold, fluorescent lighting, humidity, and low barometric pressures. They also have exaggerated responses to psychological stresses. The lack of understanding by their peers, professional colleagues, and health professionals adds to their burden of stress, and the difficulties that they have in fighting third party insurances such as Workers' Compensation Board or Canada Pension Plan, seems to add to the degree of misery felt by these patients.

I hope that this information will be of significant value to you in understanding the disease process and disability that these patients are suffering so that the processing of claims of disability for patients with environmental sensitivity disorder can go more smoothly in the future.

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Vice President
Chairman of Education
Canadian Society for
Environmental Medicine

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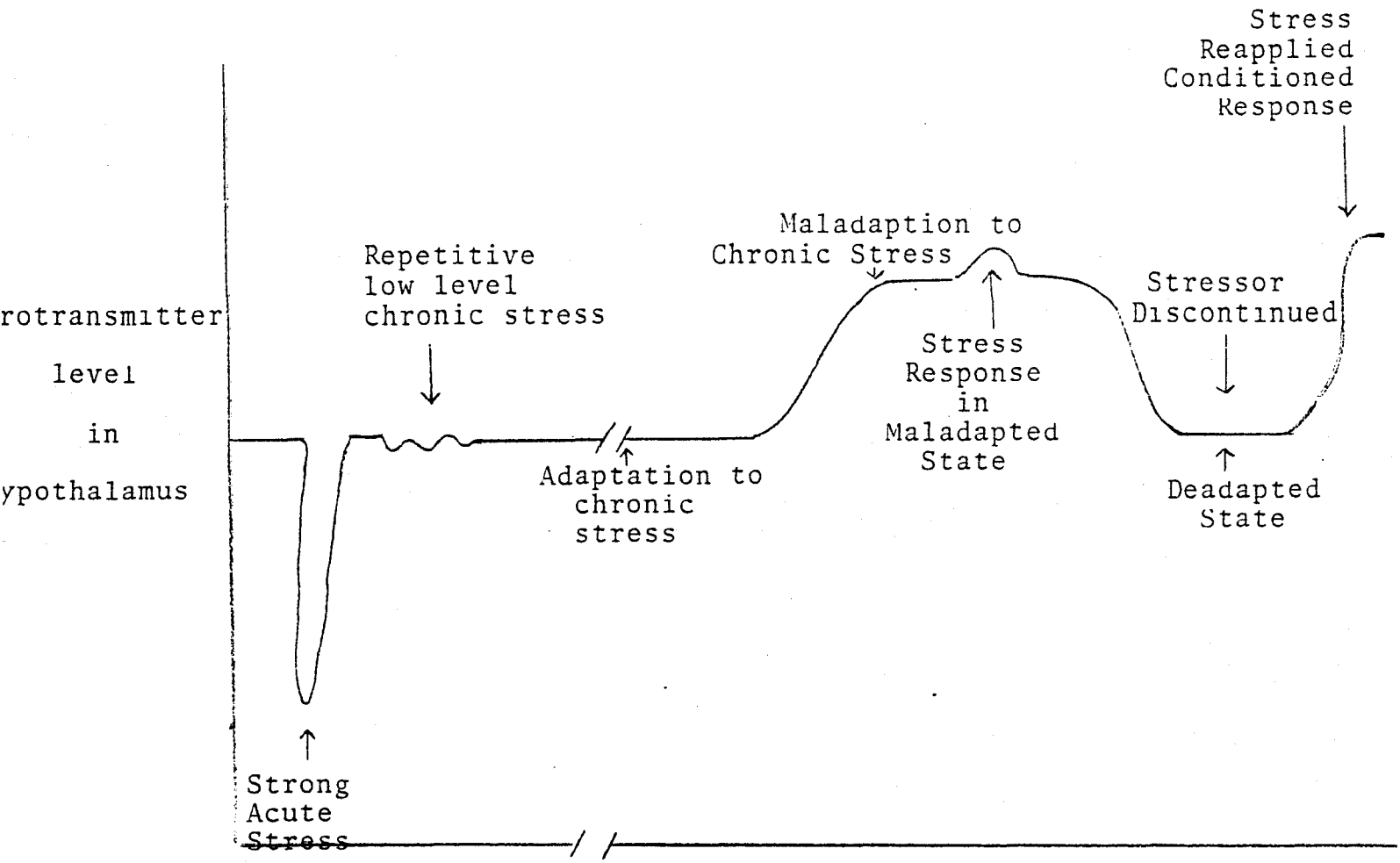
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GRAPH #1

ADDENDUM I

IMMUNOLOGIC EFFECTS OF POLLUTANTS

(1) Antibodies

- antibody responses to pollutants

a) trimellitic anhydride (TMA)
b) toluene diiosocyanate (TD-1)
c) formaldehyde (HcHo)

Thrasher, J.D., "Building-Related Illness and Antibodies to Albumin Conjugates of Formaldehyde, Toluene, Diiosocyanate, and Trimellitic Anhydride". American Journal of Industrial Medicine, 15:187-195 (1989).

a) TMA - McGrath, F., et al, "Allergic Reactions to Industrial Chemicals", Clin Immunol Rev 2:1-58 (1983).

b) Isocyanate

(i) Bascom, R., "Specific bronchoalveolar lavage IgG antibody in hypersensitivity pneumonitis from diphenylmethane diisocyanate". American Review Respiratory Disease, 131:463-465 (1985).

(ii) Butcher, B.I., "Toluene diisocyanate pulmonary disease: immunologic and inhalation studies". Journal of Allergy and Clinical Immunology, 58:89-100,(1976).

(iii) Karol, M.H., "Respiratory Effects of Inhaled Isocyanates",

c) Formaldehyde

(i) Broughton, "Antibodies and Altered cell-mediated Immunity in Formaldehyde exposed Humans". Comments Toxicol. 2:155-174, (1988).

(ii) Thrasher, J.S., "Evidence for Formaldehyde Antibodies and Altered Cellular Immunity in Subjects Exposed to Formaldehyde in Mobile Homes". Archives of Environmental Health. 42:347-350, (1987).

(iii) Thrasher, J.D., "Antibodies and Immune Profiles of Six Individuals Occupationally Exposed to Formaldehyde: Six Case Reports". American Journal Industrial Medicine. 14:479-488, (1988).

(iv) Wilhelmsson, B., "Positive Formaldehyde-rast After Prolonged Formaldehyde Exposure by Inhalation". Lancet 11 (8551):164, (1987).

(2) Autoantibodies

(i) Thrasher, J.D., "Immune activation and autoantibodies in humans with long-term inhalation exposure to formaldehyde." Archives of Environmental Health 45(4):217-223, (1990).

(ii) Broughton, A.,"Immunological Effects of exposure to pesticides". Comments on Toxicology, 4:59-71, (1990).

(iii) McConnachie, P.,"Immune alterations following exposure to chlordane/heptachlor",1991. In press - Archives of Environmental Health.

(iv) Johnson, A., Review of 200 cases in the environmental control unit, Dallas. Presented at the seventh international symposium on man and his environment in Health and Disease, Feb. 25, 26, 1989, Dallas, Texas.

(3) Tal activation (i) see (2)(i) Thrasher (1990)

(ii) see (1)(c)(ii) Thrasher (1987).

(4) T-Cells

(i) Rea, W.T. "T & B lymphocyte parameters measured in chemically sensitive patients and controls." Clinical Ecology (1986) 4(1):11-14.

(ii) Levin, A., "Environmental Illness: A disorder of immune regulation" in:Cullen, M(ed),"Workers with multiple chemical sensitivities"(1987). Hanley and Belfus, Philadelphia. 2(4):669-682.

(iii) Moszczynxki, P.,"Organic solvents - T lymphocytes." Lancet (1982), 1:1464-1465.

(iv) Rea, W.J. "Lymphocytes in chemically sensitive patients with toxic volatile organic hydrocarbons in their blood." Clinical Ecology, 5(4)171-175, (1987/88).

(v) Schwartze, G.,"Behaviour of human lymphocytes under the influence of benzene in vitro-in vivo." Z. Gesamte HYG, IHRE Grenzegeb, 31:171-173 (1985).

(vi) Moszczynxki, P.,"Evaluation of the total immunity of workers exposed to organic solvents containing benzene and its homologues." Medycyna Pracy (Poland), 30:225-229 (1979).