Reversibility of Chronic Disease and Hypersensitivity

Clinical Environmental Manifestations of the Neurocardiovascular Systems

VOLUME 3

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REVERSIBILITY OF CHRONIC DEGENERATIVE DISEASE AND HYPERSENSITIVITY

Reversibility of Chronic Degenerative Disease and Hypersensitivity, Volume 1: Regulating Mechanisms of Chemical Sensitivity

Reversibility of Chronic Disease and Hypersensitivity, Volume 2: The Effects of Environmental Pollutants on the Organ System

Reversibility of Chronic Disease and Hypersensitivity, Volume 3: Clinical Environmental Manifestations of the Neurocardiovascular Systems

Reversibility of Chronic Disease and Hypersensitivity, Volume 4: The Environmental Aspects of Chemical Sensitivity

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Clinical Environmental Manifestations of the Neurocardiovascular Systems

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Preface

The clinical aspects of the diagnosis and treatment of chemical sensitivity and chronic degenerative disease presented in this book are now complete. This book is for people interested in the origin of the clinical aspects of chemical sensitivity and chronic degenerative disease. The clinical aspects of chemical sensitivity are growing in leaps and bounds and need to be known and considered in every case of chronic degenerative disease.

In treating chronic degenerative disease, health-care providers must consider every aspect of chemical sensitivity. In this way, they will be able to help more patients obtain health and prevent advanced disease. Also, considering the aspects of chemical sensitivity will help each clinician to direct research for the prevention of advanced irreversible end stage disease. Modern technology has contributed to the advancement of chemical sensitivity, and it should be brought to bear on the solution of the problem.

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Kalpana D. Patel, MD, FAAP, FAAEM

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Authors

William J. Rea, MD, is a thoracic, cardiovascular, and general surgeon with an added interest in the environmental aspects of health and disease. He founded the Environmental Health Center–Dallas (EHC–D) in 1974 and currently serves as the director of this highly specialized Dallas-based medical facility.

Dr. Rea was awarded the Jonathan Forman Gold Medal Award in 1987 for outstanding research in environmental medicine, the Herbert J. Rinkle Award in 1993 for outstanding teaching, and the 1998 Service Award, all by the American Academy of Environmental Medicine. He was named Outstanding Alumnus by Otterbein College in 1991. Other awards include the Mountain Valley Water Hall of Fame in 1987 for research in water and health; the Special Achievement Award by Otterbein College in 1991; the Distinguished Pioneers in Alternative Medicine Award by the Foundation for the Advancement of Innovative Medicine Education Fund in 1994; the Gold Star Award by the International Biographical Center in 1997; Five Hundred Leaders of Influence Award in 1997; The Twentieth Century Award for Achievement in 1997; the Dor W. Brown, Jr., M.D. Lectureship Award by the Pan American Allergy Society; and the O. Spurgeon English Humanitarian Award by Temple University in 2002. He was also named in *Who's Who in the South and Southwest* in 1997. He is the author of five medical textbooks, *Chemical Sensitivity (Volumes 1–4)* and *Reversibility of Chronic Degenerative Disease and Hypersensitivity, Volume 1: Regulating Mechanisms of Chemical Sensitivity* and coauthor of *Your Home, Your Health and Well-Being*. He also published the popular *how to* book on building less polluted homes, *Optimum Environments for Optimum Health and Creativity.* He has published more than 150 peer-reviewed research papers related to the topic of thoracic and cardiovascular surgery as well as that of environmental medicine.

Dr. Rea currently serves on the board and is president of the American Environmental Health Foundation. He is vice president of the American Board of Environmental Medicine and previously served on the board of the American Academy of Environmental Medicine. He previously held the position of chief of surgery at Brookhaven Medical Center and chief of cardiovascular surgery at Dallas Veteran's Hospital. He is also a past president of the American Academy of Environmental Medicine and the Pan American Allergy Society. Dr. Rea has served on the Science Advisory Board for the US Environmental Protection Agency, on the Research Committee for the American Academy of Otolaryngic Allergy, and on the Committee on Aspects of Cardiovascular, Endocrine and Autoimmune Diseases of the American College of Allergists, Committee on Immunotoxicology for the Office of Technology Assessment, and on the panel on Chemical Sensitivity of the National Academy of Sciences. He was previously adjunct professor with the University of Oklahoma Health Science Center College of Public Health. Dr. Rea is a fellow of the American College of Surgeons, the American Academy of Environmental Medicine, the American College of Allergists, the American College of Preventive Medicine, the American College of Nutrition, and the Royal Society of Medicine.

Dr. Rea graduated from Otterbein College in Westerville, Ohio, and Ohio State University College of Medicine in Columbus, Ohio. He then completed a rotating internship at Parkland Memorial Hospital in Dallas, Texas. He held a general surgery residency from 1963 to 1967 and a cardiovascular surgery fellowship and residency from 1967 to 1969 with The University of Texas Southwestern Medical School System, which includes Parkland Memorial Hospital, Baylor Medical Center, Veteran's Hospital, and Children's Medical Center. He was also part of the team that treated Governor Connelly when President Kennedy was assassinated.

From 1969 to 1972, Dr. Rea was assistant professor of cardiovascular surgery at The University of Texas Southwestern Medical School. He held the position of adjunct professor of environmental

sciences and mathematics at the University of Texas from 1984 to 1985 and acted as clinical associate professor of thoracic surgery at The University of Texas Southwestern Medical School from 1972 to 1982. Dr. Rea held the First World Professorial Chair of Environmental Medicine at the University of Surrey, Guildford, England, from 1988 to 1998. He also served as adjunct professor of psychology and guest lecturer at North Texas State University.

Kalpana D. Patel, MD, is a pediatrician with an added interest in the environmental aspects of health and disease. She is a founder of the Environmental Health Center–Buffalo (EHC–Buffalo) in 1985, a specialized Buffalo-based medical facility. She was awarded the Jonathan Forman Gold Medal Award in 2006 for outstanding research in environmental medicine and the Herbert J. Rinkle Award in 2008 for outstanding teaching by the American Academy of Environmental Medicine. She was a recipient of the prestigious Hind Ratna Award by the NRI organization in India. She is a coauthor of the medical textbook, *Reversibility of Chronic Degenerative Disease and Hypersensitivity, Volume 1: Regulating Mechanisms of Chemical Sensitivity.* Dr. Patel has published many peer-reviewed research papers related to the topic of environmental medicine. She currently serves on the board and is president of the Environmental Health Foundation of New York. She was a president of the American Board of Environmental Medicine and previously served on the board of the American Academy of Environmental Medicine. She also held the position of director of child health in the Erie County Department of Health and chief of pediatrics at Deaconess Hospital, Buffalo, New York. She is also a fellow of the American Academy of Environmental Medicine.

Dr. Patel graduated with honors from St Xavier's College, Gujarat, India, and also with honors from B. J. Medical College, Gujarat University, Ahmadabad, India. She then completed a rotating internship at Bexar County Hospital in San Antonio, Texas. She held a pediatric residency from 1969 to 1972. Dr. Patel has served as an assistant professor of pediatrics at the State University of New York, Buffalo, since 1973.

Section I

Integration of the Musculoskeletal and Neurological Systems

1 Introduction

The neuromuscular system will be discussed in this section since much of the pathology after the entry of pollutants is found in these two systems. Many pollutants are sequestered in the neuromuscular system. It is hoped that once the clinician understands the signs, symptoms, and principles of the dynamics of local, regional, and generalized clinical homeostasis and the early signs and principles of dyshomeostasis, chemical sensitivity and chronic degenerative disease can be prevented or that early disease can be reversed if caught promptly and acted upon therapeutically.

Our studies show that 85% of chemical sensitivity and chronic degenerative disease can be arrested or reversed at this early stage. Early recognition results in using fewer complex medical resources (such as costly technical procedures) with a greater savings to the patient in the long-term treatment. For patient care, the clinician requires much less effort and fewer medical resources when simple environmental and dietary manipulations are carried out early. Definition and elimination of as many triggering agents as possible is essential for the reversal of early chemically originating diseases and maintenance of optimum health. These agents include toxic chemicals such as pesticides, solvents, and car exhaust and other chemicals, bacteria, parasites, viruses, mold, particulates, and EMF. Each particulate has its own range: ultrafine <0.1 μm, fine <2.5 μm, and large <10 μm. Local exposure to environmental incitants usually initially causes localized reactions such as rhinitis, cough, foggy thinking, heartburn, and dysphagia. However, regional effects of muscle aches and spasms and signs of early neuropathy (numbness, tingling, itching, pain) are the harbingers of early neuromuscular sensitivity.

The clinical picture of local disordered neuromuscular homeostasis may be periodic, aperiodic, or both. *Periodic homeostatic disturbance* (hypersensitivity) may manifest early in chemical sensitivity or chronic degenerative disease as isolated muscle spasm or fatigue or localized intermittent nerve numbness, itching, tingling, or pain. Other early symptoms may be localized to various organs and include rhinorrhea, sinus irritation, bronchial irritation and cough, localized vascular dysfunction (spasm, flushing from vascular dilatation), and bladder irritation. *Aperiodic homeostasis* (or chronic degenerative disease) may manifest in deteriorating disturbance fields, for example, spondylosis, scleroderma, arteriosclerosis, and benign and malignant tumors. Both hypersensitivity (periodic homeostasis) and chronic degenerative disease (aperiodic homeostasis) are characterized by symptoms and signs of the organs, regions of, or systems of the body involved and are either locally specific, regional, or generalized. For example, the neuromusculoskeletal, vascular, respiratory, gastrointestinal, immunological, and genitourinary systems will present with their own unique local symptoms of that particular organ, especially if the hypersensitivity limb of the dysfunction is involved. However, local symptoms (i.e., fleeting numbness, tingling, pain, fatigue, itching) can occur if episodic degenerative disease is perceived early in the diagnosis.

At times, the hypersensitivity stage is masked, and these patients will only experience local fatigue, pain, numbness, tingling, spasm, and itching. On the other hand, chronic degenerative disease may manifest initially with generalized symptoms of fatigue, pain, itching, or diminished senses (as seen in Alzheimer's, diabetes mellitus, arthritis, myocardial dysfunction, heart failure, age-related macular degeneration, hearing loss, or motor dysfunction).

Metabolic overuse of nutrients by the adjustment reactions or by the detoxification and repair mechanisms or by malabsorption or by peripheral vascular spasm (which results in hypoxia of the specific area involved anywhere in the body) can cause nutrient deficiency. Nutrient deficiency can then result in tissue malfunction due to degenerative changes in the cervical and lumbar disks, joints, neuromuscular, gastrointestinal tract, bronchopulmonary tract, brain, etc.

In addition to trophic changes (color change [blue to red], numbness, prickly, burning hyperesthesia, anesthesia, vascular spasm, cold or hot sensation, edema, degenerative pain of neuropathy), inflammation, and degeneration, this malfunction may manifest as benign and malignant tumors. These early malfunctions cause weakness, fatigue, and pain. Although pain, fatigue, itching, and muscle spasm as well as individual end-organ symptoms may seem to occur in a repetitive pattern in early chronic degenerative disease and in the masked hypersensitive states, these are the symptoms of early homeostatic dysfunction and nutritional deficiency. Recognizing and acting upon these symptoms with the identification and elimination of triggering agents for treatment at this early stage can precisely prevent disease and restore the body to optimum function.

The problem with prevention lies with the individual as well as with the primary physician in defining and eliminating the proper triggering agent(s), correcting the homeostatic reaction and the correction of specific organ nutrient deficiency(ies). When the observer sees only symptoms of generalized pain, itching, numbness, tingling, and fatigue, the triggering agents often are imperceptible due to the masking phenomena in relation to the reproduction of specific end-organ symptoms and signs. In addition, understanding the kinetics of the offending agent(s) or their combination and how the body responds to them over time is crucial for understanding the clinical functions of homeostasis and dyshomeostasis (see Chapters 1[1] and 2[2] of *Reversibility of Chronic Disease and Hypersensitivity: Regulating Mechanisms of Chemical Sensitivity*). Many neuromuscular problems can be rationalized as psychosomatic when, in fact, they are early end-organ responses to toxicity and hypersensitivity.

The most common symptom of periodic (hypersensitive) state is odor sensitivity to minute doses of both noxious substances (e.g., formaldehyde, phenol, mycotoxins, pesticides, chlorine, natural gas) and substances generally accepted as nonnoxious (e.g., perfume, newsprint, fabrics), followed by pain, itching, and fatigue. Muscle spasm and fatigue are prime symptoms and signs of early pollutant overload in the neuromuscular system (Figure 1.1).

In both early chronic degenerative disease and in chemical sensitivity, if the patient is not in the deadapted state, the generalized clinical response is often not related to any specific area of the body except the entry phenomenon, making it difficult to relate cause (triggering) and effect (the body's response). However, the entrance of pollutants occurs directly in the nasal cavity, bronchial tubes, alveolar areas of the lungs, gastrointestinal tract, skin, bladder, and vagina. Pollutant entry into the rest of the organs is secondary. This relationship is made difficult because in this masked (adaptive) state, the clinical cause and effect are not necessarily related to organ specificity but is generalized. Early in their disease process, both types of illnesses manifest as transient chronic fatigue, headache, itching, flu-like symptoms, brain fog, loss of concentration, and/or mild pain (especially in the muscles and fascia of the neck and lumbar region). These *transient* symptoms are the result of dyshomeostasis from noxious stimuli entry, pollutant sequestration and subsequent mobilization, and nonspecific local nutrient deficiency.

Many early cases of chronic degenerative disease are initially asymptomatic, for example, spondylosis, arteriosclerosis, and degenerative joint disease. In these states, the patient is in the adaptation stage and is no longer in the alarm stage (where cause and effect can easily be clinically ascertained by a challenge with an incitant, e.g., biological inhalants, foods, chemicals, bacteria, virus, toxics, and electromagnetic frequencies [EMFs]) unless deadaptation occurs. Specific etiology of triggering agents cannot usually be found. If symptoms occur, chronic degenerative disease is characterized by generalized pain, itching, and fatigue. In fact, introduction of toxic and nontoxic inhalants or oral substances and their subsequent homeostatic or dyshomeostatic reactions are often impossible to define when the patient is in the masked or adaptive stage. Most studies of patients in the masked state give false information when looking for etiologies. Yet the masked state is how most patients who are chronically ill present to the clinician. Here, the stimulatory phase of the body's compensatory processes has been partially neutralized by the adjustment mechanism of homeostasis. This state results in a clinical appearance of normalcy, where cause and effect are difficult or impossible to isolate

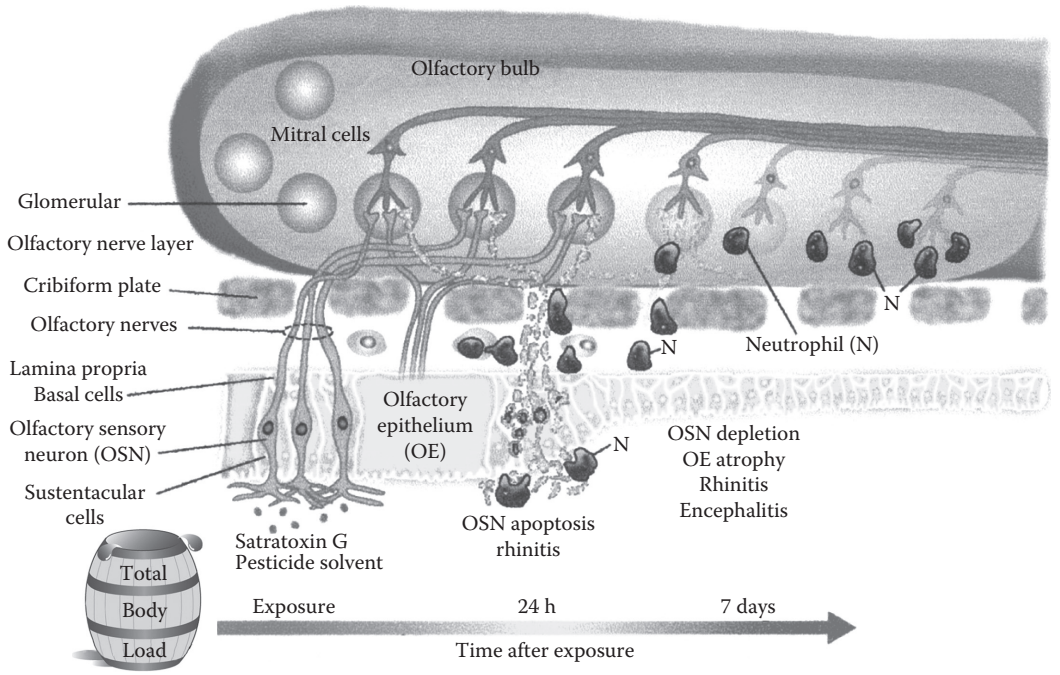

FIGURE 1.1 Effect of toxic substances on the olfactory bulb and olfactory epithelium. This diagram represents toxic induced pathology in olfactory epithelium and olfactory bulb with time after exposure. One can see the olfactory epithelium, normal olfactory sensory neurons, and neutrophils phagocytosing apoptotic olfactory sensory neurons. (Modified from Vojdani, A., Immunosciences Lab., Inc., Los Angeles, CA, 2006. Personal communication. With permission.)

and where pain, itching, and fatigue occur intermittently (i.e., from natural gas, formaldehyde, phenol, alcohol, pesticide) and randomly until the patient is deadapted.

Clinically, the causes of dyshomeostasis, which are usually multifactorial (car exhaust, jet fuel, mycotoxins, solvents, etc.), are initially not readily apparent when the patient presents in the masked (adapted) state for diagnosis and treatment. A precise diagnosis, however, may rule out many causes when the patient is unmasked. Because of this masking, the usual causes that result in a clear clinical picture of early disease and altered biochemical parameters are difficult to find, measure, and eliminate. Initially, the clinical situation may dictate that there is no reference point to obtain a specific etiologic diagnosis for a specific therapy and treatment, unless one studies the patient under environmentally controlled conditions, where the deadapted state can be obtained and where cause and effect can be proven by individual oral, inhaled, or intradermal challenge tests once the unmasked state is obtained.

This phenomenon explains why the onset of chronic disease is often misdiagnosed by many clinicians who want to attribute early symptoms (i.e., fleeting muscle pains, itching, fibromyalgia, chronic fatigue, arthralgia, anxiety, depression, bloating, gas, constipation, diarrhea, heart palpitations, and a host of other symptoms) to unprovable psychosomatic function or somatization disorder. These patients at this stage are then placed on symptom-suppressing medication, which allows the hypersensitivity or the degenerative disease to progress since the triggering agent(s) are not eliminated and the nutrients are not replaced. This trap should not be fallen into, since the early symptoms and signs of the dyshomeostasis of chronic disease must be recognized in order to prevent a debilitating and eventually fatal outcome.

Early diagnosis and elimination of the triggering agents at this time may be the only time that the illness is reversible. For example, many soldiers from the Gulf War were misdiagnosed by their

military physicians with somatization disorder because of the stresses of combat. Many of these soldiers, in fact, were exhibiting early symptoms and signs of myoneurotoxicity due to environmental triggering agents, such as sarin nerve gas, insecticides, phenols, and formaldehyde, which caused symptoms of pain, itching, and fatigue. Since the definitive causes were not investigated, found, and eliminated or neutralized, proper treatment was not instituted, and these soldiers went on to develop a clinically recognizable fixed-named debilitating and often-fatal neurological or musculoskeletal disease (i.e., amyotrophic lateral sclerosis, multiple sclerosis, degenerative neuropathy, and myopathy). These diseases might have been prevented or reversed if the early symptoms and signs had been definitively interpreted and the primary and secondary triggering agents had been found, eliminated, and/or neutralized. Symptoms of neurotoxicity and myopathy are already being suppressed in the soldiers deployed to Iraq by the widespread prescription of symptom-suppressing drugs.

The study of dyshomeostasis of the neuromuscular system in the controlled environment is the most important technique that one can use when attempting to restore normal homeostatic function and find the basic triggering agents of the dysfunction. Once the total body pollutant load is reduced in the controlled environment, the patient becomes deadapted, and cause and effect can be proven by oral, inhaled, or intradermal challenge. However, the failure to find the etiologic factors that alter the proper diagnosis of homeostatic dysfunction often leads to failure of therapy with the resultant fixed, autonomous, and fatal end-organ failure (named disease) eventually occurring. These diseases would include fatal and/or debilitating neuropathy and myopathy in which chemical sensitivity is a part.

2 Entry of Environmental Pollutants

External and Internal Mechanisms of the Total Body Pollutant Load

Many external pollutants like car and factory exhaust, pesticides, natural gas, formaldehyde, and phenols and internal pollutants like glutamic acid, D-methylaspartate, and approximately 70 other toxics incitants can cause environmental hypersensitivity and chronic degenerative disease. Each will be discussed.

I. EXTERNAL POLLUTANTS

The causative external noxious stimuli (i.e., pesticides, solvents, formaldehyde, phenols, ethanols, factory and car exhausts, mycotoxins, heavy metals, natural gas, particulates) continue to enter and assault the body. At this stage, as the hypersensitivity occurs and progresses, the local area of the specific organ or the end organ per se becomes hyperactive and hypersensitive. Then even nonnoxious stimuli (perfumes, newsprint, detergents, etc.) appear to become the triggers for homeostatic dysfunction. As shown in *Reversibility of Chronic Disease and Hypersensitivity: Regulating Mechanisms of Chemical Sensitivity*, the total body pollutant load is also as important as are the specific triggering agents in causing the increasing hypersensitivity as well as causing chronic degenerative disease. These external triggers eventually cause dyshomeostasis and end-organ failure as overuse of the repair nutrients depletes body's healing capacity. Then dyshomeostasis usually occurs through the internal excitotoxin mechanism using glutamate (Glu) and aspartate and various other internal excitotoxins of which there are over seventy.[3,4]

Much evidence shows the relation of environmental pollutants and neuromusculoskeletal abnormalities. Our patients and communities are exposed to pesticides through air, food, and water or through dermal absorption. Thousands of pesticide products exist for many uses. In addition to insect, rodent, and landscape management, pesticides are also used in antimicrobial hand soaps, cosmetics, and cleaning products. Yet the impact of cumulative pesticide exposure and the synergistic effects of exposure to multiple pesticides and other chemicals are rarely considered. Typically, only the risks of acute exposure to an individual pesticide are assessed. Initial research indicates that neuromusculoskeletal, endocrine, immune, vascular, or developmental and degenerative effects increase when combined exposures are studied. The full health impact of multiple exposures to any one pesticide, or to multiple pesticides over an extended time, remains unknown.[5] However, some studies and logic tell the clinician that multiple exposures could be debilitating and eventually lethal. Examples of the chronic effects of these exposures are shown in the following studies.

Rauh et al.[6] showed the proportion of delayed development in children in the high-exposure group to prenatal and the first 3 years of life when chlorpyrifos was five times greater for psychomotor development index and 2.4 times greater for the mental development index. Ascherio et al.[7] showed that pesticide exposure gave an increased risk of Parkinson's disease similar to exposure to asbestos, chemicals, acids, and solvents; coal and stone dust; or eight other occupational exposures. Morahan et al.[8] showed that in ALS the Pon1 enzyme was impaired by organophosphates.

Caress and Steinemann[9] found that of their patients who were hypersensitive to chemicals, 27% were initially exposed to pesticide. Fernández-Solà et al.[10] found that exposure to insecticides in 26 patients was associated with their neuromuscular symptoms. Richardson et al.[11] found that developmental exposure to dieldrin alters the dopamine system and increases the neurotoxicity in an animal model of Parkinson's disease. Kamel et al.[12] showed that neurologic symptoms were accumulative in pesticide applicators. Beseler et al.[13] found that there was a high incidence of depression in the wives of pesticide applicators. Kofman et al.[14] found motor inhibition and learning impairment in school-age children following their exposure to organophosphate pesticides. Dahlgren et al.[15] reported memory loss, decreased concentration, irritability, and personality changes in the family exposed to diazinon. London et al.[16] reported that exposure to organophosphate pesticides posed a risk of suicide to the general population. Chatzi et al.[17] showed an association for allergic rhinitis with paraquat, dithiocarbamate pesticide, and bipyridyl herbicides. Puerta et al.[18] showed that prenatal exposure to mirex impairs neurodevelopment at the age of 4 years. Exposures to aerial emissions of nanocomposite materials resulted in cholinesterase inhibition in patients with chemical sensitivity, according to Staninger.[19] Fonnum and Mariussen[20] showed that polychlorinated biphenyls and brominated flame retardants affect learning, memory, and fine motor movements. Approximately 1.2 million metric tons of PCB has been produced, and 30% has been discharged into the environment. Approximately 200,000 metric tons of brominated flame retardants is produced annually. These are spread globally. Natural gas used for home cooking and heating is tied with pesticides as the number one pollutant offender in the home.

Zinc in denture adhesives has been blamed for cases of nerve damage, according to Avery.[21] DeVader and Barker[22] suggest that fragrance in the workplace is the new secondhand smoke. The industrial cleaner trichloroethylene was found to be associated with Parkinson's disease in twins.[23] Autoimmunity and neurological symptoms were found in slaughterhouse workers who inhaled pig blood and brain tissue.[24,25] Environmental chemicals such as 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and rotenone produce symptoms in the mouse similar to Parkinson's disease, as does paraquat.[26] From these copious studies, it is clear that a myriad of environmental incitants, especially pesticides and natural gas and its products, can trigger neuromuscular dysfunction.

As shown in Chapters 1[1] and 2[2] of *Reversibility of Chronic Disease and Hypersensitivity: Regulating Mechanisms of Chemical Sensitivity*, pollutant entry causes local acidosis. This occurs in two ways: first, by the local injury phenomena, in which acetates and sulfates are changed to their acid forms, and, second, by the neural vascular response, which causes vascular spasm and thus local tissue hypoxia followed by acidosis. Acidosis and room heat or cold can trigger the vanilloid and other associated neuroreceptors in the peripheral sensory, spinal sensory, and afferent autonomic nerves, which innervate peripheral voluntary and involuntary muscles to produce the internal excitotoxins, primarily Glu and *N*-methyl-D-aspartate (NMDA). As the receptors on these sensory nerves are assaulted by chronic pollutant exposure and entry, the nerves can be augmented, increasing their sensitivity sometimes up to 1000 times, thus rendering the patient mildly to extremely hypersensitive. This process of acquiring hypersensitivity occurs by protein kinase phosphorylation on the sensory nerve.[27] Other endogenous chemicals produce hypersensitivity by including an increase in prostaglandin (PG) E-2, TNFα, leukotriene (LT) 1B, and cAMP on the cell membrane.[28]

II. INTERNAL EXCITOTOXINS

Some stimuli other than environmental are already present in the body, and the endogenous (nonenvironmental) excitotoxins like Glu, NMDA, and approximately 70 others[3,28,29] are waiting to be triggered by various means. These substances are part of normal physiologic function generated in the body, but when they are augmented by external environmental pollutants and occur in excess, they become toxic. Therefore, internal toxins must be included along with the external environmental pollutants as part of the problem that causes chemical sensitivity and chronic degenerative disease and in this case neural and muscular sensitivity.

Glutamic acid ("Glu") and NMDA are the chief excitatory neurotransmitters (NTs) in the human and mammalian brain.[4,30,31] Glu-producing neurons make up an extensive network throughout the cortex, hippocampus, striatum, thalamus, hypothalamus, cerebellum, and visual/auditory system[32] as well as peripheral sensory and spinal sensory nerves and muscles. Glu output is stimulated by various neural receptors, including the vanilloid, GABA, sodium, potassium, magnesium, and muscarinic. Normally, Glu stimulates brain and peripheral nerve function. As a consequence, Glu neurotransmission is essential for normal cognition, memory, movement, and sensation (especially taste, sight, hearing).[31] Glu and its biochemical "cousin," aspartic acid or aspartate, are the two most plentiful amino acids in the brain.[33] Aspartate is also a major excitatory NT, and aspartate can activate neurons in place of Glu.[4,30] According to Pall,[29] Glu can stimulate the NMDA receptor, which at times can stimulate the nitric oxide/peroxynitrite receptors, causing brain dysfunction.

Glu and aspartate can be synthesized by cells from each other and their toxic stimuli: Glu can also be made from various other amino acids.[33] Glu and aspartate are also both common in foods. Wheat gluten is 43% Glu, the milk protein casein is 23% Glu, and gelatin protein is 12% Glu.[33] Wheat, beef, and milk are three of the most potent food sensitizers seen in chemical sensitivity and chronic degenerative disease.

According to Blaylock,[4] one of the most common food additives in the developed world is monosodium glutamate (MSG), a flavor enhancer. By 1972, 576 million pounds of MSG was added to foods yearly, and MSG use has doubled every decade since 1948.[4] We have found that most patients with chemical sensitivity cannot tolerate excess MSG. Patients who ingest these chemicals often get brain dysfunction. Often postprandial fatigue and/or muscle aches or hand and feet tingling occur. Aspartate is one-half of the now ubiquitous sweetener aspartame (NutraSweet®), which is the basis of diet desserts, low-calorie drinks, chewing gum, etc.[4,34] The patient with chemical sensitivity usually cannot tolerate aspartame or Glu. Glu and aspartame are in the brain chemistry of foods and food additive technology, indicating a major role for them in patients with chemical sensitivity and chronic degenerative disease. According to Blaylock, without normal Glu/aspartate neurotransmission, we would be deaf, blind, mental and behavioral vegetables. However, when in excess, these NTs will act as excess pollutants causing hypersensitivity of the nerves involved. Yet Glu and aspartame are the two major excitotoxins out of 70 so far discovered.[4,30,31,34] Examples of some of the other internal excitotoxins include the following: kainic acid,[35] 1-methyl-4-phenyl,-1,2,3,6-tetra-hydro pyridine (MPTA),[35] quinolinic acid,[36] beta-*N*-methylamino-1-alanine (BMAA),[37] complement factor C5a,[38] domoic acid (DOM),[39] and alpha-amino-3-hydroxy-5methyl-4-isoxazote propionic acid (AMPA).[40] Most of these can be so toxic that they can induce cell death by both necrosis and apoptosis but also often cause neuromuscular dysfunction.

According to Blaylock,[4] these excitotoxins are biochemical substances (usually amino acids, amino acid analogs, or amino acid derivatives) that can react with specialized neuronal receptors (Glu receptors) in the brain or spinal cord and can cause injury or death from a wide variety of chemical triggers.[4,30,31,41–43] There is a fine line between normal function, which the normal individual has, and excess function that causes hypersensitivity and toxicity in both patients and animals. Hypersensitivity, hyperalgesia, and itching frequently occur when the Glu and NMDA are increased. Sensitivity of the nerve can increase up to 1000 times[28] if it is injured and overstimulated. This hypersensitivity will allow other less or nontoxic substances to trigger the homeostatic mechanism resulting in neuromuscular dysfunction.

When the levels of Glu and aspartate are chronically in excess, fixed-named disease occurs. A broad range of chronic neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, Huntington's chorea, stroke (multi-infarct) dementia, amyotrophic lateral sclerosis, and AIDS dementia, are now believed to be caused, at least in part, by the excitotoxic action of excess Glu, aspartate, or other excitotoxins.[3,4,30,31,41–43] The other parts of the triggering agents for neural stimulation or inhibition are external environmental toxins.

Even the typical memory loss, confusion, and mild intellectual deterioration that frequently occur in late middle age and old age can be induced by chemical sensitivity, according to Pall.[29] According to Blaylock,[4,34] these symptoms may be caused by Glu or some other 70 excitotoxins and

aspartate excitotoxicity. Acute diseases and medical conditions such as brain damage due to stroke, ischemic (reduced blood flow) brain damage, alcohol withdrawal syndrome, headaches, prolonged epileptic seizures, hypoglycemic brain damage, head trauma brain damage, and hypoxic/anoxic brain damage (e.g., from carbon monoxide or cyanide poisoning, near drowning) are also believed to be caused, at least in part, by Glu and aspartate excitotoxicity.[4,30,31]

Glu and aspartate are NTs, which serve either to excite neurons into action or to inhibit them. According to Pall[29] and Szallasi and Blumberg,[28] Glu and aspartate can exacerbate or even help induce chemical sensitivity and chronic degenerative disease. These NTs are normally stored inside neurons in "vesicles" because of their toxicity. These NTs must be contained so that they do not spread their toxic effects. They must be released at synapses only when needed for function. When an electric current "fires" across the surface of a neuron, it causes some of the vesicles to migrate to the synapses and release their NT contents into the synaptic gap. See Figure 2.1.

The NTs then diffuse across the gap and "plug in" to receptors on the receiving neuron. When enough receptors are simultaneously activated by the NTs, two reactions are possible: (1) If the transmitter/receptors are excitatory, the neuron will fire an electric current all over its surface membrane, and (2) if the NTs/receptors are inhibitory, the neuron will be inhibited from electrically discharging. All of the neural circuitry of the brain works through this interacting "relay race" of NTs inducing electrical activation or causing inhibition of function.

If in excess, Glu and aspartate can damage the myoneural junction, causing hypersensitivity, hyperalgesia, and pruritus in patients with chemical sensitivity and chronic degenerative disease. In addition, muscle weakness resulting in chronic fatigue, spasm, and fibromyalgia may occur.

When Glu receptors are excitatory, they literally excite the neurons containing them into electrical and cellular activity. When chemically or electromagnetically triggered, their production and release by substances such as pesticides, solvents, formaldehyde, and a myriad of other toxics occurs.

The four main classes of Glu receptors are the NMDA receptor, the quisqualate/AMPA receptor, the kainite receptor, and the AMPA metabotropic receptor. Each of these receptors has a different structure and has somewhat different effects on the neurons they excite. The NMDA is the most common Glu receptor in the brain.[3] The NMDA, kainite, and quisqualate receptors all serve to open ion channels. The NMDA receptor is the most complex and has more diverse and potentially devastating effects on receiving excess neuron impulses than the others. When Glu or aspartate attaches to the NMDA receptor, it triggers a flow of sodium (Na^+) and calcium (Ca^{++}) ions into the neuron and an outflow of potassium (K^+). Because of this event, edema and weakness may occur clinically, followed by itching and pain. Sensitivity can increase up to 1000 times.

Pyrethroid pesticides have been shown to trigger the sodium–calcium channels to stay open.[29] This event increases Glu and triggers NMDA receptors in the cell. This ion exchange triggers the neuron to "fire" an electric current across its membrane surface, in turn triggering an NT release to whatever other neurons the just-fired neuron synaptically contacts. Here, the NMDA receptors that have excess Glu will fire. The kainite and AMPA ion channels primarily permit the exchange of Na and K ions and generally cause briefer and weaker electric currents than NMDA receptors. Thus, when Glu/aspartate acts through kainite/AMPA receptors, it is weakly excitatory, but when Glu/aspartate acts through NMDA receptors, they are strongly excitatory.[44] NMDA receptor activation is the basis of long-term potentiation (LTP), which in turn is the basis for memory consolidation and long-term memory formation.[44] The increased action of these receptors is often seen in chemical sensitivity and chronic degenerative disease. At least 55% of our patients with chemical sensitivity and chronic degenerative disease have pyrethroid pesticide in their breath analysis, suggesting a triggering of these changes in the neuromuscular system. Most of the rest of the triggers are petroleum-derived triggering agents that can also alter nerve conduction.

Short-term memory is often disturbed in patients with chemical sensitivity and chronic degenerative disease, and its pattern can be observed in the triple-camera SPECT scans made by Simon and Hickey at the EHC–Dallas.[45] These scans usually show temporal lobe asymmetry, blurring of boundaries, and hot and cold areas in the cerebrum and a halo effect around the cerebrum.

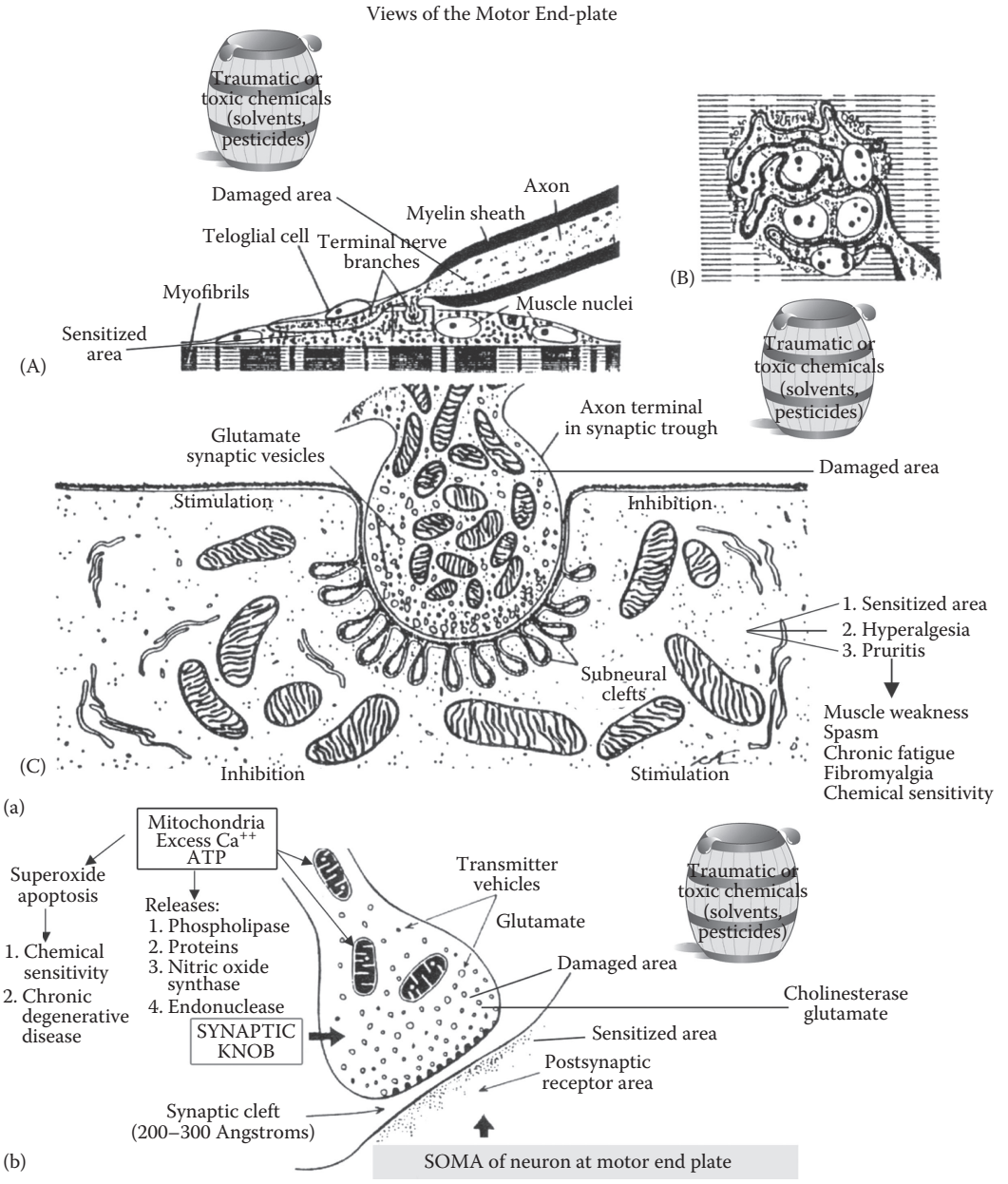

FIGURE 2.1 (a) Different views of the motor end plate, (A) longitudinal section through the end plate, (B) surface view of the end plate, and (C) electron micrographic appearance of the contact point between one of the axon terminals and the muscle fiber membrane, representing the rectangular area shown in A. (b) Physiologic anatomy of the synapse. Damage to the nerve will cause sensitized muscle. (Modified from Guyton, A.C., *Textbook of Medical Physiology*, 6th edn., W.B. Saunders, Co., Philadelphia, PA, 1981, pp. 138, 565.)

Neurons in a resting state prefer to keep Ca^{++} inside the cell at a level only 1/10,000 of the outside, with Na levels 1/10 as high as outside the neuron.[46] These mineral pumps require ATP energy to function, and if neuronal energy production is low for any reason (hypoglycemia, low oxygen, damaged mitochondrial enzymes, serious B vitamin or CoQ10 deficiency, etc.), the pumps may gradually fail, allowing excessive Ca^{++} and Na^{+} buildup inside the cell. Excess Glu or increased

aspartate binds to the NMDA receptors and increases calcium flow into the neurons. This condition can be disastrous[3,29,30] since it can cause both severe chronic fatigue and chemical sensitivity.

Normal levels of calcium inside the neuron allow normal functioning, but when excessive Ca^{++} builds up inside neurons, this activates a series of enzymes, including phospholipases, proteases, nitric oxide synthases, and endonucleases, which can further damage the neuron.[28,30] Excessive intraneuronal calcium can also make it impossible for the neuron to return to its resting state and instead cause the neuron to "fire" uncontrollably.[28,30] This phenomenon is seen in the tetanic muscle spasms in a subset of patients with chemical sensitivity (discussed later in this chapter). Anxiety, depression, and isolated muscle spasm often occur in a subset of patients with chemical sensitivity, which suggests that this intracellular buildup of Ca^{++} accompanied by Mg^{++} loss has occurred.

Phospholipase A2 breaks down a portion of the cell membrane. This breakdown not only releases arachidonic acid (AA), a fatty acid, but also will release toxic xenobiotics stored in the cell membrane. Other enzymes then convert AA to trophic changes and eventually into inflammatory PGs, thromboxanes (TXs), and LTs, which then damage the cell[30,31] as do the toxic solvents, methane, ethane, propane, butane, benzene, toluene, xylene, organophosphate pesticide. The clinician sees many patients with chemical sensitivity who have trophic and then eventually chronic mild-to-severe inflammation, most likely through this process, which makes their illness more difficult to treat. Phospholipase A2 also promotes the generation of platelet-activating factor, which also increases cell Ca^{++} influx by stimulating release of more Glu.[31]

Whenever AA is converted to PGs, TXs, LTs, and free radicals, including superoxide, peroxide, and hydroxyl, all are automatically generated as part of the reaction.[4,30,31,47] These free radicals then trigger a vicious downhill cycle depleting the body of nutrients to counteract the free radicals and overutilize the repair mechanisms. Eventually, fixed-named end-organ disease occurs because of the constant triggering and overuse of the adjustment and repair mechanisms, resulting in degenerative conditions, that is, degenerative disk, chronic muscle spasm, tremors, and chronic fatigue.

Excessive intracellular calcium can further the degeneration by activating various proteases (protein-digesting enzymes), which can digest various cell proteins, including tubulin, microtubule proteins, and spectrin.[30,31] Intracellular calcium can also activate nuclear enzymes (endonucleases) that result in chromatin condensation, DNA fragmentation, and nuclear breakdown, that is, apoptosis, or "cell suicide."[31]

Excessive intracellular Ca^{++} also activates nitric oxide synthase, which produces nitric oxide (NO). When this NO reacts with a superoxide radical produced during inflammatory PG and LT formation, the supertoxic peroxynitrite radical is formed.[31,48] Chemical sensitivity is then exacerbated. Peroxynitrite oxidizes membrane fats, inhibits mitochondrial ATP-producing enzymes, and triggers apoptosis.[48] These are just some of the ways Glu–NMDA-stimulated intracellular Ca^{++} excess can damage or kill neurons! According to Pall,[29] nitric oxide/peroxynitrite stimulates the production of chemical sensitivity.

Excitatory neurons using Glu as their NT normally contain a high level of Glu (10 mmol/L) bound in storage vesicles.[31] The ambient or background level of Glu outside the cell is normally only about 0.6 μmol/L, that is, about 1/17,000 as much as inside the neuron.[31] Excitotoxic damage may occur to the cortex or hippocampus neurons at levels around 2–5 μmol/L[31] when the containment vesicles are released. Therefore, the brain works hard to keep extracellular (synaptic) levels of Glu low.

Glu pumps are used to rapidly return Glu secreted into synapses back into the secreting neuron, to be restored in vesicles, or to pump the overflow of Glu into astrocytes and glial cells, which are nonneural cells that surround, position, protect, and nitrify neurons.[4,31] These Glu pumps also require ATP to function so that any lack of neuronal ATP for any reason can cause the Glu pumps to fail. As shown previously, a myriad of environmental incitants can sap the body of ATP causing weakness and fatigue.

As we have shown throughout this book, toxics such as pesticides, solvents, and natural gas can directly damage ATP and/or ATP production or release. This decrease in the load of neural ATP then allows extracellular Glu levels to rise dangerously.[4,31] If a Glu neuron dies and dumps its Glu stores into the extracellular fluid, this can also present a serious Glu-excess hazard to nearby

neurons, especially if remaining active Glu pumps are unable to remove the spilled Glu quickly.[31] This process can itself trigger the spreading phenomenon that is seen in severe degenerating chemical sensitivity. Here, the patient becomes sensitive to more and more foods, molds, and chemicals. This heightened sensitivity then disturbs the neutralization–desensitization mechanism. When Glu is pumped into astrocytes, which is a major mechanism for terminating its excitatory action, the Glu is converted into glutamine. Glutamine is then released by the astrocytes, picked up by Glu neurons, stored in vesicles, and converted back to Glu as needed.[31]

This Glu–glutamine conversion also requires ATP energy; however, this antiexcitotoxic mechanism is at risk if cellular energy production is compromised for any reason.[31] Chronic fatigue will be seen in patients with chemical sensitivity. In addition, excessive free radicals can prevent Glu uptake by astrocytes, thereby significantly (and dangerously) raising extracellular Glu levels.[49]

It has also been discovered that there are Glu receptors on the blood–brain barrier (BBB).[3] Glu appears to be an important regulator of brain capillary transport and stability, but it can also overstimulate the BBB. If the BBB, including the vascular supply, is disturbed by environmental factors, then there may be difficulty with local O_2 extraction resulting in local tissue hypoxia. (See Chapter 1,[1] vascular, and the respiratory chapter.) This phenomenon will also destabilize the intradermal provocation–neutralization (desensitization) process leading to an inability to get precise desensitization endpoints. Local intermittent hypoxia will lead to transient short-term memory loss, confusion, weakness, pain, and itching, all of which are seen in the early stages of chemical sensitivity.

NMDA receptors are influenced through dietary MSG/aspartate. This change in the receptors lessens exclusion of Glu and aspartate[3] and other environmental stressors by the BBB, resulting in further toxic incitants going to the brain tissue. Food, food additive, and water contaminant sensitivity may then trigger not only the "leaky gut syndrome" (see Chapter 4 of *Reversibility of Chronic Disease and Hypersensitivity: The Effects of Environmental Pollutants on the Organ System*) but also leaky peripheral and central neural membrane syndrome. A number of conditions may impair the integrity of these barriers, including the BBB, which then allows seepage from MSG/aspartate and external stressors. The results of MSG/aspartate entry into the brain cells include severe hypertension, diabetes, stroke, head and peripheral muscle malfunction, multiple sclerosis, brain infection, brain tumor, AIDS, Alzheimer's disease, and aging.[3,4]

In certain areas of the brain, the "circumventricular organs," which appear to regulate homeostasis, are not shielded as well by the BBB because of their cellular anatomy (4-cell versus 6-cell layers—see *Reversibility of Chronic Disease and Hypersensitivity: Regulating Mechanisms of Chemical Sensitivity*[1]). These include the hypothalamus, the subfornical organ, the organum vasculosum, the pineal gland, the area postrema of the fourth ventricle, the reticular activating system, the limbic system, the subcommisural organ, and the posterior pituitary gland.[4] The research of Inouye,[4] using radioactively labeled MSG, indicates that MSG may gradually seep into other brain areas following initial brain entry through the circumventricular organs, causing disturbed function and exacerbating or triggering chemical sensitivity. The same appears to occur at the myoneural junction and peripheral and spinal sensory and autonomic nerves.

Another issue that makes the BBB defense of Glu–NMDA axis less important is brain glucose transport. Glucose is the primary fuel the brain uses to generate its ATP energy. Continual adequate brain ATP levels are needed, as noted earlier, to prevent Glu/aspartate from shifting from NTs to excitotoxins. This condition apparently occurs in patients with chemical sensitivity and chronic degenerative disease who have episodes, and at times long episodes, of chronic fatigue with brain dysfunction. This fatigue is accentuated by various laboratory findings. For example, Creasey and Malawista[50] found that feeding high doses of Glu to mice could decrease the amount of glucose entering the brain by 35%, with even higher Glu doses leading to a 64% reduction in brain glucose content. This finding was associated with weakness in these animals. Since the brain is unable to store glucose, this glucose–Glu effect alone could be a major basis for promoting excitotoxicity and thus the "hypoglycemic" symptoms and fatigue seen in many patients with chemical sensitivity.

To summarize, inadequate neuronal ATP levels (whatever the cause by external environmental pollutants and internal excitotoxins) become an energy problem resulting in chemical sensitivity, chronic fatigue, and fibromyalgia. Inadequate neuronal levels of magnesium, the natural, nondrug calcium channel blocker, result in muscle spasm and hyperexcitability of the nerves and myoneural function. High inflammatory PG/LT levels can be caused by excessive Glu–NMDA-stimulated calcium invasion into the cell. Excessive free radical formation (caused by PG/LT formation and/or insufficient intracellular antioxidants/free radical scavengers) is present in patients with chemical sensitivity and chronic degenerative disease. Inadequate removal of Glu from the extracellular (synaptic) space back into neuron spheres or into astrocytes causes toxicity. Addressing each of these conditions will provide appropriate environmental nutritional/life extension strategies to minimize excitotoxicity.

The same principle of adaptation and deadaptation holds true for the treatment of chronic degenerative disease and hypersensitivity, which usually does not respond to acute injury treatment, except when acute exacerbations of the chronic process occur. In other words, one must find the multiple triggering agents and eliminate or neutralize as many as possible in order to diagnose and manage chronic disease, especially chemical sensitivity.

In addition, nutrient replacement for the nutrient deficiency acquired by the inefficiency of homeostasis and excess use of this process is essential in the management of either hypersensitive or chronic degenerative disease. In the author's experience, from studying over 40,000 patients with chronic disease, early dyshomeostasis that usually occurs with the chronic degenerative disease is intermingled with the hypersensitivity type. (See Chapter 1[1] of *Reversibility of Chronic Disease and Hypersensitivity: Regulating Mechanisms of Chemical Sensitivity.*) Usually, the clinician can positively influence this degenerative process by eliminating the external and sometimes internal triggering agents to which the patient has become hypersensitive. In other words, decreasing the total body pollutant load is essential for proper functioning. By finding and eliminating the multiple triggering agents, the nutrient deficits can be corrected and the basic physiology of the dynamics of homeostasis can be restored. If this is not done, it is like giving an antibiotic without first cleaning the wound. If triggers are not eliminated, a nutrient drain will always occur, resulting in an injured area that is then too large to stop the sensitivity. Because environmental control is so crucial in the understanding of homeostasis and dyshomeostasis, the next section will contain detailed facts to aid in the initial diagnosis, prevention, and early treatment of chemical sensitivity and chronic degenerative disease.

3 Environmental Control for Reducing Total Body Load

The dominant principle in the diagnosis and treatment of the early aperiodic (chronic degenerative disease) and/or for the periodic chronic disease (chemical sensitivity) is that the patient usually must be returned to the basal deadapted state (the alarm stage of Selye)[51] by decreasing the total environmental pollutant load and thus the total body pollutant load, depurating the patient of toxics[52] and thus reducing early trophic (neuropathic) changes[53] as well as inflammation.[54] Here, the body's compensation mechanisms can be more precisely defined and the kinetics of the incitant can be crisply elaborated.

By using environmental control procedures, with time spent in the environmentally controlled unit (ECU), or ECU-like conditions, usually for 4–7 days, the total environmental pollutant load is decreased, and, thus, the total body load reduction is achieved and the patient is deadapted.[55] This near-normal basal state will allow physiology to then return to normal, but for a while, the patient is often hypersensitive to challenge when exposed to some noxious and even nontoxic stimuli. This load reduction keeps the patient symptom-free without medications or at least allows him or her to obtain a steady condition of low intensity of symptoms. Therefore, cause and effect can be determined by challenge.

Challenge tests can be performed, which allow definition of a single triggering agent and a view of its kinetics in that particular chemical in the individual. With this technique, definition of multiple triggers can be defined (if each single test is meticulously performed).

Once this basal state has been achieved, the challenge, which can be oral, intradermal, or inhaled, can prove cause and effect with reproduction of observable and measurable signs and symptoms. In our studies of thousands of chronically ill patients, trophic (neuropathic) changes (increase in receptor sensitivity) and/or inflammation with release of its precursors (i.e., cytokines, leukotrienes, and prostaglandins) has been observed (see *Reversibility of Chronic Disease and Hypersensitivity: The Clinical Environmental Manifestation of the Neurocardiovascular Systems*, for more information). These conditions and effects are markedly reduced, localized, or eliminated once the switch for the trophic changes and/or inflammatory process, that is, free radical generation or muscle spasm, is turned off. Once the toxic load reduction has been obtained, the patient reverts to the physiological basal state of the acute alarm phase where cause and effect reactions can be easily observed upon challenge. This sequence of clearing of symptoms and signs, stabilization of physiology, and response to challenges is easy to see in the hypersensitive state (i.e., chemical sensitivity), but more difficult with the neuropathic degenerative trophic changes (i.e., relief of lumbar disc pain and surrounding muscle spasm) of chronic degenerative disease. It must be emphasized that the hypersensitive and chronic degenerative disease signs and symptoms are usually mixed. Therefore, it may take time to isolate and dissect the triggering agents of these entities.

To provide the clinician with the precise tools in order to separate and plot the etiology and the course of hypersensitivity and chronic degenerative disease, the environmental unit will be discussed in detail.

I. ECU CONSTRUCTION AND MAINTENANCE

The concepts of the ECU were developed by Randolph.[57] Dickey[58] constructed the first functional environmental unit adhering to Randolph's[57] guidelines. In 1974 (a few years after Dickey's[58] unit closed), Rea elaborated and refined Randolph's and Dickey's model by creating more sophisticated and less chemical and particulate emanating contaminated units.[59–61] The ECU is a specially designed and constructed controlled interior environment, which operates with at least five times less particulate matter than other indoor and outdoor environments.

It functions free of pesticides, formaldehyde, phenol, perfume, cigarette smoke, and other toxic substances. It has minimal to no outgassing of odors or shedding of particulates (Table 3.1). These units were and continue to be very successful, as evidenced by the thousands of patients placed in them who were able to clear their symptoms and return to normal homeostasis and clinical health without medications.

The ECU principle and the facts derived from its construction and use are now used as a benchmark for the construction of all less polluted outpatient clinics, homes, and public buildings. Understanding the details of the less polluted construction, including how to evaluate a polluted building successfully, is of paramount importance to the clinician for exercising the proper diagnosis and treatment of the environmental aspects of disease, while reversing early periodic and aperiodic homeostatic dysfunction (see *Reversibility of Chronic Disease and Hypersensitivity: The Effects of Environmental Pollutants on the Organ System*[62,63]).

The materials used to construct the unit are inert, with little or no outgassing or particulate shedding and are mold-free. These materials include hardwood, glass, stone, ceramic, plaster, porcelain, and aluminum (especially anodized). No glues and little synthetics are used. Examples of the different types of materials are shown in Figures 3.1 through 3.9 and Tables 3.1 and 3.2, which site the

TABLE 3.1
Pollutant Measurement Data Comparison in the ECU, Regular Hospital, and Outdoors

Pollutant	ECU	Hospital	Outdoors
Inorganics			
(e.g., ozone, CO, NO_2)	0.2	0.4	0.6
Organics			
(e.g., toluene, tetrachloroethylene)	0.5	3.1	1.6
Pesticide	0.0	+	+
Formaldehyde	0.0	+	+
Particulates	0.49[a]	1.25[b]	2.88[b]
Mold			
Old unit (1976–1982)	15	300	400
Porcelain (1982–1986)	0.0	11	11
Bacteria	0.0	300	400

Sources: EHC-Dallas (1985); Rea, W.J., *Chemical Sensitivity*, Vol. 4: *Tools of Diagnosis and Methods of Treatment*, CRC Publishers, Boca Raton, FL, 1997, p. 2218. With permission.

Notes: All in parts per million (ppm). Hospital/outdoors contain mostly large and small particles full of toxic volatile hydrocarbons. These were environmental units #1 and #2 created by the EHC-D. All figures are August averages for the different years of the units.

+, positive but not quantitated.

[a] ECU contains mainly cotton and charcoal.

[b] Petroleum products, phenols, anesthetics, plastics.

analytic analysis of these areas. Heating is all-electric or hot water is used with no gas and no oil or coal in the building. No toxic cleaning solutions, floor wash, deodorants, perfumes, etc., are used in these areas.

The technology of building these inpatient and outpatient centers has now progressed to the point where practical knowledge is readily available to the clinician and builder.[63–66] Several thousand

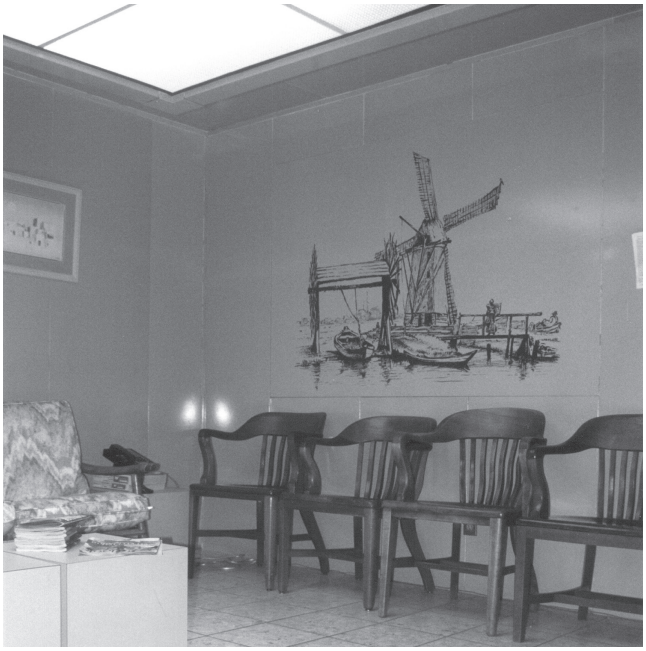

FIGURE 3.1 Porcelainized room. (From ECU-Dallas, 1996; Rpt. from Rea, W.J., *Chemical Sensitivity*, Vol. 4: *Tools of Diagnosis and Methods of Treatment of Chemical Sensitivity*, Lewis Publishers, Boca Raton, FL, 1997, p. 2196. With permission.)

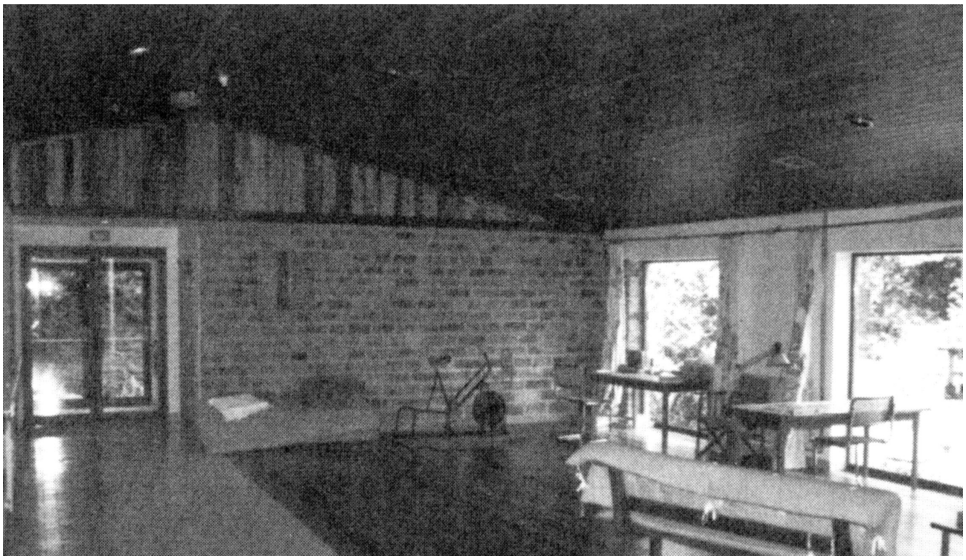

FIGURE 3.2 Ceramic tile and hardwood ECU. (Courtesy of J. Maberly, Keathly, Yorkshire, England, Personal communication. With permission.)

FIGURE 3.3 First porcelain unit. Carrollton Community Hospital, Carrollton, Texas. (From EHC-Dallas, 2002.)

FIGURE 3.4 Portable porcelain steel unit. (Courtesy of Dr. Mike Lateri, 1994, Personal communication. With permission.)

FIGURE 3.5 Ceramic tile and plaster ECU. Tri-City Hospital, Mesquite, Texas. (From EHC-Dallas, 2002.)

FIGURE 3.6 Glass floor. (Courtesy of Lynn Carroll, Nederland, CO, 2002, Personal communication. With permission.)

homes, clinics, and public buildings have been constructed in a less polluted manner, allowing the occupants to live a healthier and more vigorous life.

II. USE OF THE ECU

Use of the ECU allows us to dissect varied complex immunological, metabolic, neurological, vascular, and other clinical responses. The use of this unit enables us to make concise observations about homeostasis and the etiology of dyshomeostasis that in the past were previously not possible. Etiology of the triggering agents can be found by using the facts and principles of the ECU;

FIGURE 3.7 Hardwood floors and glazed ceramic tile with nontoxic grout applied to walls and floor. (Courtesy of Mr. and Mrs. Mark Michalica, 2002, Personal communication. With permission.)

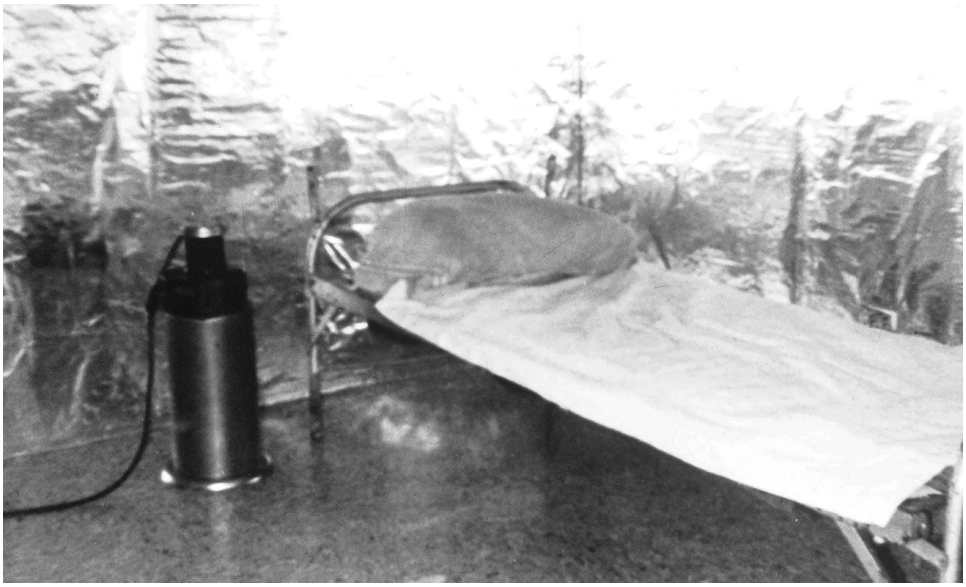

FIGURE 3.8 Simple aluminum room. (From EHC-Dallas, 2002.)

the clinician is freed from guesswork, allowing for precise diagnosis and treatment (Figure 3.10). Any dyshomeostatic or disease entity (if not too advanced) will have environmental triggers that, when eliminated, will aid in the management of the particular disease processes involved.

As shown in Chapter 1[1] of *Reversibility of Chronic Disease and Hypersensitivity: Regulating Mechanisms of Chemical Sensitivity*, physiologic adjustment reactions always result from the entry

(a) (b)

FIGURE 3.9 (a) Less polluted living room. (b) Less polluted room. (Anodized aluminum beds with ceramic floors, nontoxic paint, and organic cotton.) (From EHC-Dallas, 2006.)

TABLE 3.2
Inorganic Chemical Measurement in the ECU, Regular Hospital, and Outdoors

	Average Concentration (ppm) ECU #1		
Pollutants	**ECU**	**Regular Hospital**	**Outdoors**
CO	2.08	3.02	3.22
Ozone	0.007	0.013	0.042
N_2O_5	0.04	0.10	0.25
NO	<0.010	0.019	0.056
NO_2	0.001	0.014	0.036
Ammonia	<0.1	1.00	1.00
Bromine	<0.1		
Carbon dioxide	1000	800–1600	800–1600
Chlorine	<0.01	1.00	<0.01
Chlorine dioxide	<0.01		
Hydrogen cyanide	<0.04		
Hydrogen sulfide	<0.05		

Sources: EHC-Dallas (1984); Rpt. from Rea, W.J., *Chemical Sensitivity*, Vol. 4: *Tools of Diagnosis and Methods of Treatment*, CRC Press, Boca Raton, FL, 1997, p. 2218. With permission.

Note: All in parts per million (ppm). Hospital/outdoors contain mostly large and small particles full of toxic volatile hydrocarbons. These were environmental units #1 and #2 created by the EHC-D. All figures are August averages for the different years of the units.

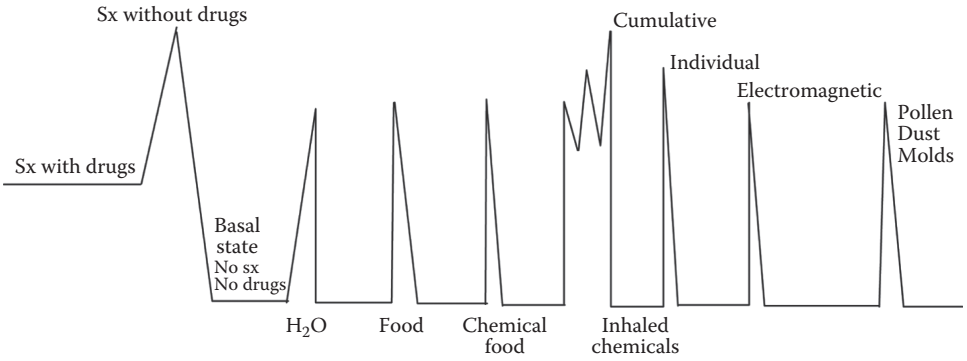

FIGURE 3.10 Flow chart assessing environmental incitants. Sample of a clinical course during a stay in the ECU. (From EHC-Dallas, 2002.)

of noxious environmental stimuli (toxic, bacterial, viral, or mechanical) in the normal dynamic homeostatic process. After being in the stable baseline deadapted state for a period of time, the individual aided by an aware clinician can perceive that a subtle and sometimes severe disruption of homeostasis is occurring. These homeostatic reactions to entry of a noxious substance can be monitored by the clinician using a variety of parameters, depending on the time he or she chooses to spend on the available tools and the timing that he or she uses to monitor and track a reaction. The tests for tracking a reaction can be serial measurements of a simple single blood test like a CBC, eosinophil count, or immune cell function (i.e., T and B cells) and/or direct blood and/or tissue measurements of toxics (i.e., benzene, hexane). Other tests include EKG, heart rate variability, pupillography for autonomic dysfunction, triple-headed SPECT brain scans for changes in neurotoxicity, a neurometer for testing for peripheral sensory neuropathy and denervation changes, and spirometry for testing pulmonary functions. Again, timing for the collection of data is all-important, or the clinician will miss the metabolic changes occurring after the introduction of a noxious stimulus (Figure 3.11).

Another point to emphasize is that if one performs individual challenges (i.e., oral, inhaled, or dermal exposure to phenol, formaldehyde, food, or mold) in a chemically sensitive or chronically ill degenerative diseased patient in the adapted state, a clinical reaction may not be apparent. The patient may become fatigued, develop itching, and/or develop *spontaneous* pain, but these symptoms may be interpreted as being caused by many different factors. Treating physicians, the patients themselves, and others may attempt to rationalize their occurrence and even suggest that they are *psychological* in origin. Regardless of the absence of empirical evidence to the contrary, however, many metabolic changes do occur after an adapted patient is exposed to noxious stimuli, and as a result, his or her nutrient fuels become depleted and he or she is then pushed toward sickness. If the challenge is performed on the patient who is in the deadapted state, the cause of the noxious or nonnoxious substance can be clearly defined.

Most physicians are unaware of the tools and principles used to clarify precisely a patient's challenge reactions. They do not know that the adaptive phenomena allow the patient to slip into symptoms of chronic fatigue, itching, and pain and that gradually, after initial treatment, the patient will become nonfunctional, with neither the patient nor the clinician perceiving the real problem.[67] Additionally, many physicians do not realize that cause and effect with repeated challenges can only rarely be observed if the patient being tested is in the adapted state, burdened by an increased toxic load.[68] The unaware physician, therefore, seldom uses objective challenge data to examine the causes of the adapted patient's fatigue or pain. By using the ECU and first placing the patient in the deadapted state, however, a physician can obtain objective data that would establish the direct cause of fatigue, itching, or pain.[67]

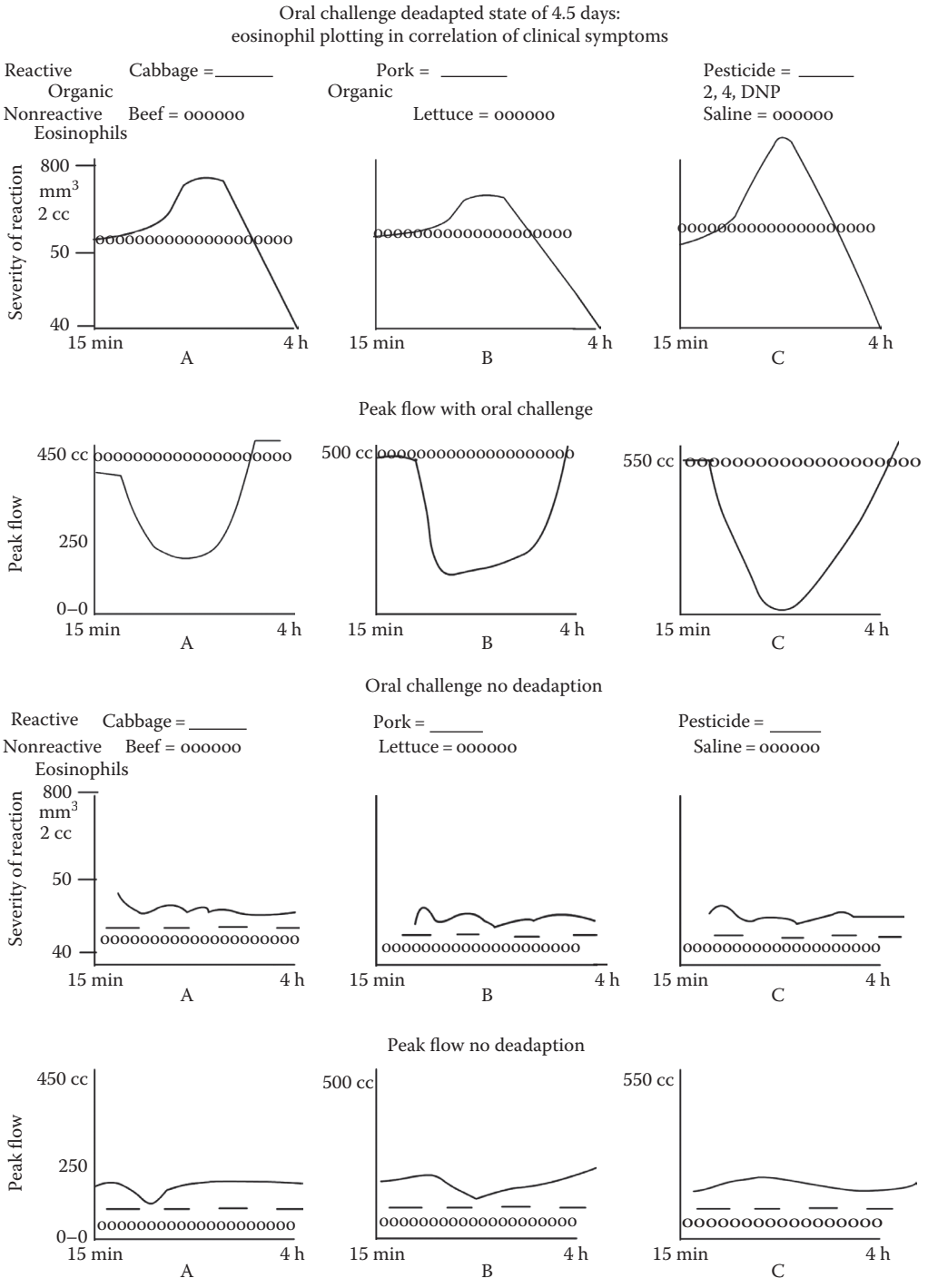

FIGURE 3.11 Eosinophil plotting in correlation of clinical symptoms after oral challenge in a deadapted state after 4.5 days in the ECU and fasting. Oral challenge with response measured by peak flow to discern symptoms and to detect minor subjective complaints like tight chest and audible wheezing can be heard by auscultation and documented by a change in peak flow. One cannot see changes in adapted state because eosinophils and peak flow have not returned to normal. Subjects in this adapted state are unaware of their triggering agents. (Adapted from the EHC-Dallas, 1999.)

The effective protocol for testing and treating the adapted patient is first to reduce his or her total environmental individual pollutant load for 4–7 days, by fasting and/or rotary diet and using the less polluted air of the ECU. This strategy results in deadaptation. Then, the patient gains energy, loses pain, and becomes aware of his or her environment with all of its potential triggers of the homeostatic mechanism. This environmental deadaptive procedure, which often throws the patient into the alarm phase of Selye,[51] can be used freely and cost effectively throughout the patient's life, allowing for easy identification of the causes and effects of inadvertent noxious stimuli exposures.

With this total load reduction and deadaptation occurring, both intentional challenge procedures and inadvertent exposures and the knowledge acquired from them allow for noxious stimuli elimination initially and then continuously throughout the individual's life. A state of good health can be obtained and maintained because patients and physicians are always aware of pollutant entry and its subsequent consequences. Thus, these patients can practice rigid avoidance with ease as they pass through life being well and vigorous. Entry of subtle and mild incitants can then be stopped before the patient relapses back into chronic illness. The aware clinician should constantly caution and remind those sensitive patients to deadapt by going on their rotary diet, fasting, or getting into their environmentally controlled home or room.

A. Local Stimulus Reaction Model

In order to understand homeostatic regulatory dysfunction clinically, one must learn to differentiate between the local stimulus reaction model (short-term stimuli like a needle puncture test reaction, intradermal provocative skin test challenge reaction, isolated oral food challenge, or isolated inhaled chemical challenge reaction that has short-term kinetics) and chronic repetitive long-term stimuli that lead to adaptation, maladaptation, and patient exhaustion (Table 3.3). Both of these conditions depend on local peripheral and spinal sensory nerve reflex reaction or the chronic, repetitive stimuli going to the dorsal root ganglia and/or the trigeminal ganglia up the spinal cord and/or the afferent autonomic nerves going to the brain acquiring sensitization.[69] The vanilloid,[70] GABA,[71] muscarinic,[72] sodium channel,[73] *N*-methyl-D-aspartic acid (NMDA),[74] nitric oxide/peroxynitrite (PRN) receptor sensitivity occurs.[75] The nonvanilloid, nonneuron cells like the leukocytes,[76] mast cells,[77] and glial cells[78] become overloaded and sensitized, and, at times, in addition to neural sensitization, an altered immune system response occurs.[79–81]

The local short-term stimulus reaction depends upon the kinetics (distribution, biotransformation, and one half-life) of the noxious stimulus and the dynamics of the homeostatic response (reception, adjustment, neutralization, and repair) in any patient. The first principle that one should understand when evaluating a noxious stimulus for hypersensitivity or even toxicity is that there can be a linear relationship or a hormetic effect (*J* or *U* effect) as shown in previous chapters. Linear dose cause and effect responses are easier to evaluate because the higher the dose of noxious stimuli, the more

TABLE 3.3
Homeostatic Regulatory Dysfunction

1. Short-term stimulus
   A. Needle puncture—acupuncture
   B. Intradermal provocative skin test—molds, foods, chemicals
   C. Isolated oral food challenge (i.e., beef, milk, yeast, soy, and wheat)
   D. Isolated inhaled chemical challenge (i.e., phenol, formaldehyde, and ethanol)
2. Chronic repetitive long-term stimuli—adaptation, maladaptation, patient exhaustion

Source: EHC-Dallas (2009).
Note: Both depend on local peripheral and spinal sensory nerve reflexes and/or afferent autonomic nerve involvement.

severe the response of the homeostatic reaction.[82] The principle of hormesis or (J/U) curves, which says that any substance (i.e., medication, foods, chemicals, electrical current) may cause a low-dose stimulating effect, and a high-dose inhibitory effect, is more difficult to ascertain.[82] The hormetic effect of a noxious stimuli is approximately 50% of the dose response reactions rather than a linear reaction. In addition, Rozman and Doull[83] also say that hormesis can be the opposite with a low-dose inhibition and a high dose causing stimulation at times further confusing the issue of dose response.[84]

Rozman and Doull[83–85] have now redefined *toxicity* as "the injury over short or long periods of time which renders an organism incapable of functioning within the limits of adaptation (overcompensation)." Their *toxicity* definition resulted from the many examples when a stimulatory effect is abolished by a kinetic effect thus missed clinically, rather than a dynamic mean (elimination of the causative agent), followed by a homeostatic overcompensation in the form of a depressing effect. This definition augments the definition given by Calabrese and Baldwin,[86] who defined the mechanism of *hormesis* as the overcompensation response to an inhibiting signal, without definition as to how the inhibitory signal is abolished and without regard to the beneficial or detrimental nature of an effect.

An example of the more expansive nature of the Rozman and Doull's[84] definition would be the case of amphetamine. Here, the stimulatory effect is abolished by rapid kinetics, but the homeostatic overcompensation, in the form of CNS depression, may last for days.[87] This phenomenon, though often misguided and misinterpreted, is used therapeutically in hyperactive children for its depressive effects. Therefore, in Rozman and Doull's view,[85] some low-dose effects are directly or indirectly stimulatory or inhibitory, and high-dose effects can be stimulatory or inhibitory. As long as the homeostatic capabilities of an organism are not exceeded, such signals, when abolished, will lead to homeostatic overcompensation and the response may have the shape of the B-curve or inverted B-curve (*U* or *J*) (see Chapter 1[1] of *Reversibility of Chronic Disease and Hypersensitivity: The Effects of Environmental Pollutants on the Organ System*).

In either case, triggering a specific system of a living organism disrupts the removal from equilibrium (steady state) that in turn leads to homeostatic overcompensation (hangover effect). High doses of the toxic push the system beyond the limits of kinetics (distribution, biotransformation, and elimination) or dynamic homeostatic (overcompensation, repair, or reversibility) recovery. The spectrum of potency of toxic agents ranges from negligible to extreme. The pharmacologic potency ranges from barely measurable to profound. Processes initiated by the inhibitory signal, followed by homeostatic overcompensation, may be viewed as the hallmark of hormetic responses. Whereas, those processes initiated by a stimulatory signal, followed by homeostatic overcompensation in the other direction, could be called hormoligosic (homeostatic) responses.[88] The transitional boundary between hormesis/hormoligosis and toxicity can be defined scientifically by determining the limits of recovery and overcompensation in terms of both dose and length of response.

Calebrese has now extensively reviewed the literature of low-dose effects of toxics and other substances and found the hormetic principle to be based on solid scientific facts.[82,89,90] Many scientists in several areas have published articles in their fields demonstrating this idea. For example, Schultz[91] showed that a motor neuron, stimulated by a peak electrical stimulus, undergoes the following sequence of events: contractory fibrillation (twitching), relaxation, and rest. High-dose current triggers the opposite: contraction, rest, relaxation, and fibrillation (twitching). Furthermore, Schultz[91] showed that chromate caused yeast to stimulate fermentation at 30 min and to inhibit fermentation at 3 h. Schultz[91] also decreased the concentration of the chromate and found that the time of peak stimulation of the fermentation process shifted toward a later time point, and eventually, no inhibition occurred. This was clearly a kinetic effect, in that the concentration of chromate reaching stimulatory levels occurred more rapidly at higher concentration than at lower concentration, but reached inhibitory levels only after equilibrium (uptake) or, at some point, approaching equilibrium. As a strong oxidizing agent without antiseptic and antifermentation properties, sodium chromate would not have been expected to stimulate fermentation.[59] Rinkel,[92] Lee et al.,[93] Miller,[94]