

What really causes multiple sclerosis

HAROLD D. FOSTER

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and “What really causes Alzheimer’s disease”
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Dedicated to Beautiful Jim Key

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*The era of procrastination, of half-measures,
of soothing and baffling expedients, of delays,
is coming to its close. In its place we are entering
a period of consequence.*

Winston Churchill (1936)

WHAT REALLY CAUSES MULTIPLE SCLEROSIS: AN EXECUTIVE SUMMARY

In young adults, in temperate Western climates, multiple sclerosis is the most common disease of the nervous system.¹ Globally, some 2.5 million people suffer from this illness.² Multiple sclerosis is a progressive disease for which there is no recognized conventional cure. It is associated with inflammation and ultimately the loss of myelin from the surface of nerves. This process of demyelination causes disruption to nerve transmission that can affect many body functions. It eventually leads to the patches of nerve scarring, known as ‘sclerosis,’ that give multiple sclerosis its name.³

Multiple sclerosis occurs more often in some families than chance alone would dictate. The average person living in the United States, for example, has roughly a 1 in 750 chance of developing multiple sclerosis.⁴ However, the children, brothers, sisters, or non-identical twins of somebody who already suffers from the disorder have a risk of getting it that ranges from about 1 in 100 to 1 in 40. In the case of identical twins, this risk increases to 1 in 3.⁵ Of course, if genetics were the only causal variable, the sibling of an identical twin with multiple sclerosis would always get the disorder. More specifically, in a large Canadian study of 5,463 multiple sclerosis patients, attending 10 different clinics, the disorder was found in 7 pairs of 27 monozygotic (identical) twins, that is in 25.9 percent of them, and in 1 of 43 dizygotic (fraternal) twins, or 2.3 percent.⁶ The risk of a first-degree relative of a multiple sclerosis patient developing the disorder was between 5 and 15 times higher than that of the general population.⁷ Indeed, in Vancouver, British Columbia,⁸ first-degree relatives of multiple sclerosis patients were found to have a risk of developing the disorder that was 30 to 50 times greater than that of the general population.

What do these figures really mean? Well in schizophrenia, the lifetime risk of developing the disease for relatives of a victim of the illness are roughly as follows:⁹ grandchildren (5 percent); uncles and aunts (2 percent); half siblings (6 percent); siblings (8 percent); siblings with one schizophrenic parent (17 percent); children (13 percent); fraternal twins (18 percent); identical twins (48 percent), and the offspring of two schizophrenics (47 percent). Clearly, genetics play a much stronger role in deciding who becomes schizophrenic than they do in controlling who develops multiple sclerosis. Even so, there appear to be not one, but four or perhaps more genetic aberrations involved in schizophrenia.¹⁰

There can be no single genetic key to multiple sclerosis. Incidence and mortality for the disorder have highly non-random distribution patterns, typified by well developed global zones. The incidence and mortality rates for multiple sclerosis are not constant, but fluctuate markedly. They are probably falling, for example, in North America and Western Europe, but rising in many Mediterranean countries. Beyond that, migration is likely to increase or decrease the risk of developing multiple sclerosis. Every one of these characteristics is inconsistent with a dominant role for genetics in the etiology of this disease.

Similarly, virologists, neurologists, and numerous other researchers have spent a century or more searching for a causal pathogen in multiple sclerosis.¹¹ However, it is apparent that no such pathogen exists. If it did exist, it would have to infect women roughly twice as often as men, except where the disorder was rare. In these latter regions, it would cause illness in females at a rate of about six times that seen in males. It would also be much more infectious in certain families. This pathogen would pose more of a threat to adolescents than to young children, but it would almost never infect Lapps or Inuits.

Nevertheless, it would cause multiple sclerosis in predictable global belts of infection in which prevalence declined both toward the equator and westward into Asia. In short, the genetic, epidemiological, and geographical evidence makes it very likely that virologists and neurologists will spend the next century looking for this elusive pathogen, with no more success than that accompanying their work in the last one hundred years.

Taken as a whole, the available scientific and alternative evidence suggests that multiple sclerosis patients suffer from chronic inflammation caused by diets that contain inadequate antioxidants, omega-3 deficiencies, excess sugar, and foods that fail to significantly reduce oxidative stress. In addition, gluten, cow's milk, or some other allergen further promotes autoimmune disease. The coup de grâce, however, is a thyroid hormone deficiency that causes an abnormal need for dopamine.¹² Dopamine is very susceptible to oxidative stress and can break down to form toxins such as dopachrome and other chrome indoles. These, in turn, kill oligodendrocytes,¹³ the cells needed to repair the damage to myelin caused by chronic inflammation. Beyond this, a shortage of triiodothyronine in multiple sclerosis patients appears to reduce their ability to produce new oligodendrocytes.¹⁴ Therefore, myelin deteriorates and the symptoms of multiple sclerosis worsen. Wilcoxon and Redei have shown that such associated thyroid malfunctions in adults may be triggered by environmental challenges early in life.¹⁵ This process is termed fetal programming.

If the three step hypothesis presented in this book is correct, then it is possible to prevent and reverse multiple sclerosis. However, to achieve such goals requires societal and individual commitment. This volume concludes with an outline of the strategies that are needed. These include promoting anti-inflammatory diets¹⁶ and methods for avoiding the allergens that trigger inflammatory cascades and associated chronic

autoimmune disease.¹⁷ Also discussed are orthomolecular techniques for mitigating the negative impacts of the neurotoxins associated with the oxidation of excess dopamine and for stimulating the body to produce higher levels of antioxidant enzymes, such as glutathione peroxidase.¹⁸ In summary, this book provides new evidence on the causes of multiple sclerosis and offers approaches for reversing its impacts.

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There are causes for all human suffering, and there is a way by which they may be ended, because everything in the world is the result of a vast concurrence of causes and conditions and everything disappears as these causes and conditions change and pass away.

The teachings of Buddha by Bukkyo Dendo Kyokai,
112th revised edition

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Independence is my happiness, and I view things as they are, without regard for place or person; my country is the world, and my religion is to do good.

Thomas Paine, *The Rights of Man*, 1791

MULTIPLE SCLEROSIS: THE CONVENTIONAL WISDOM

1

Truth arrives in microscopic increments, and when enough has accumulated, in a moment of recognition, you just know. You know because the truth fits.

Jane Pauley, *Skywriting: A Life Out of the Blue*¹

THE DISEASE

In young adults, in temperate Western climates, multiple sclerosis is the most common disease of the nervous system.² Globally, some 2.5 million people suffer from this illness.³ Multiple sclerosis is a progressive disease for which there is no recognized conventional cure. It is associated with inflammation and ultimately the loss of myelin from the surface of nerves. This process of demyelination causes disruption to nerve transmission that can affect many bodily functions. It eventually leads to patches of nerve scarring, known as ‘sclerosis,’ which give multiple sclerosis its name.⁴

These lesions may be numerous and very disseminated throughout the brain, spinal cord, and/or the nerves that serve the eyes. Their number and locations can vary over time. Clinical symptoms that occur because of the lesions range from muscle weakness and the loss of coordination to difficulties with speech and sight. Attacks or relapses, known as exacerbations, are suffered intermittently. Their onset may be sudden, with the development of new symptoms in a few minutes, or may occur slowly over days, weeks, or even months. A characteristic feature of such exacerbations is the subsequent remissions that take place, either completely or partially,⁵ after a variable

time period. In the early stages of multiple sclerosis such recoveries tend to be almost total, but as the disorder progresses they are generally less complete.

Multiple sclerosis may have a highly variable course. In some cases there is only one attack, while in others there are a few relapses spread over a lifetime and the patient recovers with no permanent disabilities. Unfortunately, in many cases patients experience a slow progression of disability that continues for 10 to 25 years, by the end of which they are helpless.⁶ As a result of such variation in symptoms, multiple sclerosis is often subdivided into four types: relapsing-remitting (25 percent); benign (20 percent); secondary progressive (40 percent); and primary progressive (15 percent).⁷

While the *Multiple Sclerosis International Federation*⁸ claims that lifespan is not significantly affected by multiple sclerosis, this seems questionable. Colville,⁹ for example, recently analysed the mortality statistics of 350 multiple sclerosis patients from Victoria, Australia, concluding that their life expectancy from onset had been approximately halved.

Multiple sclerosis also displays a gender preference. Not only does it tend to become manifest clinically at an earlier age in White women, but they are attacked substantially more frequently than White men. McAlpine, Lumsden, and Acheson¹⁰ suggest that the crude incidence rates show a female to male ratio of about 1.9:1. That is, White women suffer from the disease almost twice as often as White men. This preponderance of female over male cases reaches its peak when the disease is relatively rare, that is, in regions where men tend not to get multiple sclerosis, women still do. To illustrate, in the Canton of Berne, Switzerland,¹¹ where the prevalence rate is 110 per 100,000, the female to male multiple sclerosis ratio is 1.8:1. However, in Istria¹² in the former Yugoslavia (now

Croatia and Slovenia), where prevalence is only 25.0 per 100,000, the female to male ratio is 2.13:1. Indeed, although multiple sclerosis is very uncommon among the Chinese, this female preference appears even more marked. In Hong Kong,¹³ where disease prevalence is only 0.77 per 100,000, the female to male multiple sclerosis ratio is 9.6:1. Elsewhere in South-East Asia,¹⁴ the disorder appears to be between 3.2 and 6.6 times as common in women as in men.

Multiple sclerosis is acquired in childhood or adolescence, long before symptoms occur. Migration between regions of high or low prevalence after this age does not substantially affect the probability of development.¹⁵ However, risk is not defined at birth, and migration during childhood or adolescence can increase, or decrease, the risk of developing the disorder. It has been shown, for example, that White males moving from the north of the United States (where multiple sclerosis is more common) to the south, between their birth and entry into military service, clearly decreased the risk of suffering from multiple sclerosis. The reverse is true if the move was in the opposite direction, that is from south to north.¹⁶ Similar migratory effects have been established in many other countries.¹⁷ This evidence seems to indicate that there is an “incubation” or “latency” period before clinical symptoms appear, but after the disease process has been triggered.

This latency period in multiple sclerosis means that it tends to be diagnosed most frequently among individuals in their early thirties. McAlpine and co-workers,¹⁸ for example, describe 12 studies that indicate that the risk of first developing the symptoms of multiple sclerosis increases steeply with age until it peaks at about 30. After that, it declines quite sharply until risk of diagnosis becomes trivial in the sixth decade of life. The curves of age-specific incidence rates for Boston, New Orleans, Winnipeg, Iceland, Northern Ireland, South Africa, and

Wellington all show such symmetry and illustrate a peak of clinical diagnosis occurring at about age 30. Colville¹⁹ recently provided similar data from Victoria, Australia which suggests a slightly late onset peak, at about 42 years of age.

CONVENTIONAL PARADIGMS

According to the *Multiple Sclerosis International Federation*,²⁰ the cause of multiple sclerosis is still unknown:

...though it is generally believed to be a combination of genetic, immunological and environmental factors. However, because it often takes many years for someone to be diagnosed, and because there are so many variables, it has so far been impossible to determine a specific cause or trigger.

It is not surprising that, since conventional medicine does not know what causes multiple sclerosis, its ability to prevent or treat the disease is less than impressive. A number of drugs, however, appear to have some effect on the frequency and severity of exacerbations, but there is no evidence that they slow the overall progression of the disability. Such drugs, designed to modify disease progression, include glatiramer acetate, interferon beta-1a and beta-1b, and mitoxantrone.²¹ Acute exacerbations can also be treated with prednisone and dexamethasone. A wide variety of other drugs are prescribed for multiple sclerosis patients to mitigate symptoms such as spasticity, fatigue, and bowel and bladder dysfunction.²²

ALTERNATIVE PARADIGMS

Marrie and co-workers²³ have questioned 20,778 people enrolled in the North American Research Consortium on Multiple

Sclerosis (NARCOMS) Patient Registry about their use of alternative medicine. Lifetime use of any alternative medicine was reported by 54 percent of this sample. Chiropractors (51 percent), massage therapists (34 percent), and nutritionists (24 percent) were the most frequently visited. A recent paper by Hussain-Gambles and Tovey²⁴ on the experience of complementary alternative medicine use by patients with multiple sclerosis suggests that this is increasing for a wide variety of reasons. These may include a loss of confidence in orthodox medicine²⁵ caused by its inability to adequately treat chronic diseases, combined with its perceived obsession with technology and an associated lack of compassion.²⁶ Hussain-Gambles and Tovey²⁷ found homeopathy, acupuncture, and dietary supplements to be the most widely used treatments by their small sample of multiple sclerosis patients.

According to Barrett,²⁸ on his *Quackwatch* webpage, the *Therapeutic Claims Committee of the International Federation of Multiple Sclerosis Societies* has analysed more than 100 alternative treatments for the disease. Their results have been published in *Therapeutic Claims in Multiple Sclerosis*. This committee argues that no nutritional deficiency is known to be a factor in multiple sclerosis, and that no special diet or the addition of vitamins or minerals have been proved to alter its course. Barrett²⁹ also claims that, while polyunsaturated fatty acids have slight immunosuppressive properties, studies involving sunflower seed, evening primrose, and fish oils have produced only conflicting results. In short, Barrett and conventional medicine in general believe that there is no evidence of any dietary change affecting the progression of multiple sclerosis.

Bee venom therapy, the regular administering of honey bee stings, usually three times a week, is widely used to treat both rheumatoid arthritis and multiple sclerosis. The New England Skeptical Society's³⁰ *Encyclopedia of Skepticism and*

the Paranormal argues strongly against the use of bee venom therapy on the grounds that it can be associated with a very real risk of severe, even fatal, allergic reaction. It is also pointed out that those seeking bee venom therapy to treat such serious disease might neglect more effective mainstream treatments. Given the recent disclosure that mainstream drug treatments have killed tens of thousands of arthritis patients,³¹ bee venom therapy must at least be the lesser of two evils!

SUMMARY

Conventional medicine has not identified the causes of multiple sclerosis and is still unable to rank potential disease triggers. This illness, however, has certain unusual characteristics. It is most common in young White female adults in temperate Western climates, and is rarer in Orientals, especially those living in Asia. While symptoms vary, the disease most often follows a slow progression into disability. It also displays a latency period, suggesting the trigger(s) is active long before symptoms first appear.

Conventional treatment includes use of a wide range of drugs designed to mitigate the frequency and severity of attacks, but there is no evidence that these slow disease progression. There are more than one hundred alternative medicine treatments for multiple sclerosis, although very few have been adequately tested.

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IT'S ALL MY PARENTS' FAULT: THE MENDEL EXCUSE

2

If everything has to be double-blinded, randomised, and evidence-based, where does that leave new ideas?

John Wu¹

I begin this chapter with a little plagiarism from *What Really Causes Alzheimer's Disease*² because the situation in multiple sclerosis research seems to closely mirror that in Alzheimer's disease. A series of risk factors have been identified for both disorders but, despite years of hype, none have provided much progress in the prevention or treatment of either disease. I've learned from sad experience that it is not easy to accurately predict the outcome of a horse race. If you consider only how fast each horse has run previously and bet on the one with the best times, you will probably identify the favourite, which wins only one race in three. Concentrating on class, the quality of the horses competed against in earlier races, will probably provide you with a fairly similar winning percentage. Running styles, track condition, jockey ability and nerve, legal and illegal drug use, equipment differences and failures, trainer skills, owner instructions (both good and bad), weather, the distance run, and horse health and mood all combine to affect the outcome of every race. That is why handicapping is so difficult, yet so much fun. Horse racing is a system that is influenced by a very large group of variables. As a result, even the most sophisticated computer programs have great difficulty in predicting winners with any reliable frequency. Perhaps multiple sclerosis is like that. Maybe many of the risk factors play small, but significant, roles in determining who will, and who will not, get the disorder.

In contrast, some systems have outcomes that are easy to predict from a few, or even one, key inputs. An atomic bomb is dropped and explodes. If you are at ground zero, or nearby, you will die. This is true for people within many miles of this location, whose injuries at greater distances may be affected by the type of building they are in at the time and the way the wind is blowing. There is no doubt, however, that the key input is the explosion of the weapon. Maybe multiple sclerosis is similar. There may be one key, overriding variable that determines who does and doesn't get this disorder.

ARE GENETICS DOMINANT?

In his interesting and well-written book, *Multiple Sclerosis: The History of a Disease*, Dr. T. Jock Murray³ describes the history of research into the role of genetics in this illness. In summary, multiple sclerosis occurs more often in some families than chance alone would dictate. For example, the average person living in the United States has roughly a 1 in 750 chance of developing multiple sclerosis,⁴ but the children, brothers, and sisters, or non-identical twins of somebody who already suffers from the disorder have a risk of getting it that ranges from about 1 in 100 to 1 in 40. In the case of identical twins, this risk increases to 1 in 3.⁵ Of course, if genetics were the only causal variable, the sibling of an identical twin with multiple sclerosis would always get the disorder. More specifically, in a large Canadian study of 5,463 multiple sclerosis patients attending 10 different clinics, the disorder was found in 7 of 27 pairs of monozygotic (identical) twins, that is in 25.9 percent of them, and in 1 of 43 pairs of dizygotic (fraternal) twins.⁶ The risk of a first-degree relative of a multiple sclerosis patient developing the disorder was 5 to 15 times higher than that of the general population.⁷ Indeed, in Vancouver, British Columbia,⁸ first-degree relatives of multiple sclerosis patients were found to

have a risk of developing the disorder that was 30 to 50 times greater than that of the general population.

What do these figures really mean? Well, the lifetime risk of developing schizophrenia, for relatives of a victim of the illness, are roughly as follows:⁹ grandchildren (5 percent), uncles and aunts (2 percent); half siblings (6 percent); siblings (8 percent); siblings with one schizophrenic parent (17 percent); children (13 percent); fraternal twins (18 percent); identical twins (48 percent); and the offspring of two schizophrenics (47 percent). Clearly, genetics play a much stronger role in deciding who becomes schizophrenic than they do in determining who develops multiple sclerosis. Even so, there appear to be not one, but four, or perhaps more, genetic aberrations involved in schizophrenia.¹⁰

Interestingly, the chromosome 19q13 region surrounding the apolipoprotein E (APOE) gene has shown consistent evidence of involvement in multiple sclerosis.¹¹ Indeed the APOE-4 allele may be associated with more severe disease and rapid progression of symptoms. This is extremely interesting because the APOE-4 allele plays a key role in another disorder involving demyelination, Alzheimer's disease.¹²

In 2001, members of the *Transatlantic Multiple Sclerosis Genetics Cooperative*¹³ combined data from three large multiple sclerosis genome screens and performed a global meta-analysis to establish what was then known about the genetics of multiple sclerosis. Their results are summarized below:

The highest non-parametric linkage (NPL) score in the meta-analysis was observed on chromosome 17q11 (NPL score 2.58), although this score falls short of genome-wide significance. A total of eight regions had NPL scores greater than 2.0. One of the regions with an NPL score greater than 2.0 was the HLA region on

chromosome 6p21 (NPL=2.2). This region is known, from association studies, to be involved in MS susceptibility, but the modest linkage result observed here suggests the encoded susceptibility effect is not large compared with the high familial recurrence in MS (λ approximately 20). Overall, our linkage results suggest that MS is likely to be multigenic in its genetic susceptibility.

This overview suggested that there was no dominant genetic aberration involved in multiple sclerosis, and that a number of them played relatively minor, but significant, roles in determining susceptibility to the disorder.

Despite all the evidence to the contrary, some geneticists¹⁴ still continue to argue that “compelling epidemiologic and molecular data indicate that genes play a primary role in determining who is at risk for developing multiple sclerosis.” This may be true at the very local scale, but not regionally, nationally, or globally. The remainder of this chapter is devoted to demonstrating that geography is more important than genetics in the etiology of multiple sclerosis, as it is in almost all other chronic degenerative diseases.¹⁵

WHY MULTIPLE SCLEROSIS CANNOT BE PRIMARILY GENETIC

If chronic degenerative diseases develop largely because of genetic inheritance, three corollaries follow.¹⁶ Firstly, the genetic aberrations responsible for such common diseases must be widely distributed throughout the human population. If this is the case, each degenerative disease ought to display a relatively uniform but random pattern of age-adjusted mortality. Incidence and prevalence, in contrast, would vary with global differences in age structure and life expectancy. Secondly, genetic diseases are constrained by the slow pace of human

reproduction. There can be no rapid changes in their incidence or mortality rates without large scale immigration and emigration, and even then such fluctuations would be due to changes in the age structure of the population. There can be no epidemics or pandemics of genetic diseases. Thirdly, if a disease is preeminently caused by a widely dispersed genetic aberration, there can be no significant change in its incidence or mortality because of migration because the dominant risk factor would be internal.

These three corollaries make it possible to examine the widely held belief that major risk factors in chronic degenerative diseases, such as multiple sclerosis, are genetic. This objective can be achieved by comparing the existent spatial and temporal patterns of incidence and mortality with those that ought to occur if a particular disease were of genetic origin. It follows, of course, that the more closely the global pattern of the disease matches that implied by the genetic hypothesis, the greater the likelihood that it is the correct one. Conversely, the reverse holds true. If the actual and implied geographies are very different, it is impossible for the key causal variable of the disease/disorder to be genetic.

GENETIC COROLLARY ONE: SPATIAL DISTRIBUTIONS

There are three global zones of multiple sclerosis. It is most common in a belt which includes northern and central Europe into the former USSR, southern Canada, and the northern United States. A similar high risk belt occurs in the Southern Hemisphere encompassing New Zealand and south-eastern Australia. In all these areas, prevalence rates are usually 30 or higher per 100,000 inhabitants.¹⁷ Such regions of elevated prevalence are adjacent to a second more moderate zone with multiple sclerosis rates of 5 to 29 per 100,000. Rates here are

typically in the order of 10 to 20 per 100,000. This moderate zone includes the southern United States, south-western Norway and northern Sweden, the entire Mediterranean basin from Spain to Israel, and that part of the former USSR that stretches from the Urals into Siberia and the Ukraine. In the Southern Hemisphere, this intermediate risk zone includes the Whites in South Africa and perhaps central South America and Australia, excluding the south-east. Elsewhere, multiple sclerosis prevalence rates appear to be low, that is less than 5 per 100,000 population. Definitely included in this third belt of minimum risk are China, Japan, Korea, Africa, and the Caribbean and Mexico. At the international level, therefore, multiple sclerosis prevalence varies by at least a factor of 10.

In addition to these major global zones, there is strong regional variation. In the Orkney and Shetland Islands of Scotland, prevalence rates are 152 per 100,000, while in Trail, British Columbia rates as high as 200 per 100,000 have been recorded.¹⁸ Other clusters include that of Key West¹⁹ and the Zoroastrian, largely Parsi communities in the adjacent Indian communities of Bombay and Poona.²⁰ Such clustering occurs in many other countries, including Norway, Denmark, and Switzerland, where there is a six-fold difference in risk between certain areas. These clusters appear fairly permanent because resurveys, a generation apart, display strong positive correlations between early and later multiple sclerosis prevalence rates.²¹

If multiple sclerosis was preeminently linked to the presence of an aberration on chromosome 17q11, or to the APOE-4 allele, or to some other genetic characteristic that was widely dispersed in the human population, age-adjusted incidence and mortality from this disorder should have a relatively uniform, but random distribution pattern. However, as has just been demonstrated, there are three very distinct global zones of multiple sclerosis, combined with a bias toward Whites,

especially women. In addition, clusters of cases are known to occur in Scotland, Canada, United States, Norway, Denmark, Switzerland, and India. It is obvious, therefore, that from the international to the local scale, multiple sclerosis incidence and mortality is non-random. This geographical reality is the opposite of what would occur if one or more genetic aberrations controlled the spatial distribution of this disorder.

GENETIC COROLLARY TWO: VARIATIONS OVER TIME

If multiple sclerosis has predominant common genetic risk factors then, in any stable population, the age-adjusted incidence and mortality rates would not vary much over time. This is because evolution occurs slowly—genetic pandemics are impossible. In contrast, the global multiple sclerosis prevalence zones are not static and there is plenty of evidence of ongoing changes. Lai and colleagues,²² for example, analysed multiple sclerosis mortality statistics from 35 countries for the period 1965 to 1984. They concluded that the disorder had declined steadily in North America and most of Western Europe, as well as in countries with a Western culture, but had remained stable or increased in Eastern and Northern Europe. Incidence has also increased in many Mediterranean countries, with prevalence rising to 69 per 100,000 in Sardinia.²³ The disorder also appears to be increasing in Kenya²⁴ and Saudi Arabia.²⁵

If multiple sclerosis was preeminently due to the presence of an aberration on chromosome 17q11, or to the APOE-4 allele or some other genetic characteristic, incidence and age-adjusted mortality rates for this disorder would tend to remain relatively constant. As has just been demonstrated, they are rapidly fluctuating in many countries. Such trends are totally inconsistent with a dominant genetic “trigger” for the disease.

GENETIC COROLLARY THREE: MIGRATION AND DISEASE STABILITY

If the major “trigger” for multiple sclerosis was genetic, the migration of a specific group should not cause any significant change in either the incidence or the age-adjusted death rate for the disease. This is because the preeminent risk factor would be internal and, therefore, carried within the migrant. Migration, however, does have a significant impact on whether or not an individual develops multiple sclerosis. The north of the United States lies in the high prevalence zone, while the south is located in the zone of moderate multiple sclerosis prevalence. The risk that helps determine this disorder appears to be acquired in childhood or adolescence, long before the clinical onset of symptoms. However, migration from north to south, or vice versa, during childhood or adolescence, in the United States, clearly reduces or increases the probability of subsequently developing multiple sclerosis, depending on the direction of migration.²⁶ Similar migratory effects have been established in other countries.²⁷

Dean and Kurtze,²⁸ for example, found that the risk of developing multiple sclerosis in north European immigrants to South Africa varied with the age at which they migrated. For those aged less than 15 years old when they arrived in South Africa, there was a prevalence rate of multiple sclerosis of about 13 per 100,000. Interestingly, for those north Europeans who had migrated to South Africa aged from 15 to 19 years, the disease prevalence rate was more than 60 per 100,000. The multiple sclerosis rate for those older than 19 at immigration was about 50 per 100,000. In South Africa, those older than 15 at immigration, therefore, retained the multiple sclerosis risk of their birthplace, while those who left at an earlier age apparently acquired the risk of their new, adopted homeland. Alter and colleagues²⁹ reported the same phenomenon in Israel. These three studies, conducted in the United States, South Africa,

and Israel, shows that the “trigger” that determines whether or not an individual develops multiple sclerosis seems to be most active in adolescence. Migration greatly influences incidence of multiple sclerosis, a characteristic that is inconsistent with a preeminent genetic risk factor for the disorder.

SUMMARY

The key to multiple sclerosis is not genetic. Incidence and mortality for the disorder have very non-random distribution patterns, typified by well developed global zones. The incidence and mortality rates for multiple sclerosis are not constant, but fluctuate markedly. They are probably falling, for example, in North America and Western Europe, but rising in many Mediterranean countries. Beyond that, migration is likely to increase or decrease the risk of developing multiple sclerosis only if it occurs in those younger than 15 years of age. All of these characteristics are inconsistent with a major role for genetics in the etiology of this disease.

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For the ordinary man is passive. Within a narrow circle (home life, and perhaps the trade unions or local politics) he feels himself master of his fate, but against major events he is helpless as against the elements. So far from endeavouring to influence the future, he simply lies down and lets things happen to him.

George Orwell, *Inside the Whale* (1940)

JUST ANOTHER PATHOGEN?

It is impossible for anyone to begin to learn what he thinks he already knows.

Epicetetus¹

According to Michael Crichton,² “Historically, the claim of consensus has been the first refuge of scoundrels; it is a way to avoid debate by claiming that the matter is already settled.” Nobody reasonably can argue that there is consensus over the role, if any, of infectious disease in the etiology of multiple sclerosis. Debate over whether or not a pathogen plays a key role in this disorder began in the 19th century in the time of Pasteur and still continues unabated to this day.³ In 1917, for example, it was suggested by Kuhn and Steiner⁴ that multiple sclerosis was caused by a spirochete (*Spirocheta myelophthora*), a motile bacteria, and that the injection of cerebrospinal fluid from a patient could be used to produce the disorder in rabbits and guinea pigs.⁵ Seventy years later, Gay and Dick⁶ argued that multiple sclerosis might be due to the spirochete *Treponema denticola*. In addition, there were newspaper reports in the 1990s of a spirochete found in multiple sclerosis patients in a European clinic.⁷ Sackett,⁸ not a big supporter of the idea that spirochetes cause multiple sclerosis, referred to such ideas as “zombies”—just when such hypotheses seem dead and buried, they again arise from their graves.

SUPPORTIVE EVIDENCE OF A PATHOGEN

Rare “epidemics” of multiple sclerosis have occurred in several locations. In the Faeroe Islands, 24 cases occurred that had their clinical onset during the period 1943 to 1960. It was

suggested by Kurtzke⁹ that these were the result of infection spread by British troops who occupied the islands in large numbers during World War II. Multiple sclerosis was unknown in the Faeroe Islands in 1939 prior to troop deployment. By 1950, the prevalence rate of this disease had risen from zero in 1939 to 41 per 100,000 population, climbing to 64 by 1961. By 1972, prevalence of the disorder had fallen to 38 and by 1977 the rate was down to 34 per 100,000.

Iceland, which shared much of its ethnic history with the Faeroes, was occupied by Canadian, British, and American troops during World War II. Here, it appears there was a two stepwise increase in the incidence of multiple sclerosis, with plateaus following each increment.¹⁰ To illustrate, the annual incidence rate for multiple sclerosis in Iceland was 302 per 100,000 for the period 1945 to 1954. This was double that of the prewar time period 1923 to 1944. Incidence has since returned to its earlier lower level. More recently, a multiple sclerosis “epidemic” occurred in Key West, Florida, where an unusual cluster of 37 cases was identified among 26,000 residents. This represented a prevalence close to 140 per 100,000.

Of course, these disease clusters were not necessarily caused by a pathogen and might represent, for example, the impact of a toxin or some abnormal aspect of diet. Indeed, whether these multiple sclerosis clusters represented “epidemics” in the usual sense of the term has been a point of considerable disagreement, and still remains unclear.

THE CASE AGAINST

In 1972, McAlpine, Lumsden, and Acheson¹³ reviewed the evidence that had been put forward to suggest multiple sclerosis was a communicable disease, caused by a pathogen. They

pointed out that, on many occasions, laboratory workers that had claimed to have found microorganisms, such as rickettsia, spirochetes, and a virus or provirus in tissue or fluids taken from multiple sclerosis patients. As Murray¹⁴ pointed out, viruses that have been suspected of causing multiple sclerosis include measles, Epstein-Barr virus, rubella, mumps, HSV, HZV, HHV-6, canine distemper virus, Marek's virus SV5, JC, animal retroviruses, human retroviruses, HTLV-1, and new retroviruses. Recently, a number of organisms have been added to this list, including *Clostridium pneumonia* and *Chlamydia pneumoniae*.¹⁵ It has been suggested, for example, that multiple sclerosis might be caused by a slow virus infection like visna, a transmissible encephalomyelitis in sheep. It is known that, in special circumstances, infection by a common virus, like herpes simplex, can result in a serious neurological illness. In subacute sclerosing panencephalitis, the disease process in the brain may become manifest many years after the original measles virus infection. It is thought by some that multiple sclerosis might be related, in a similar manner, to a common illness.

Antibodies to various viruses have been compared in multiple sclerosis patients and controls, including those for measles, mumps, polio, herpes, influenza, and many others. Kurland¹⁶ considers only the measles differences ambiguous enough to warrant further studies. Similarly, comparisons of the frequency of acute viral diseases in the childhoods of subsequent multiple sclerosis patients and controls have proved negative in many countries, including Switzerland and Scandinavia.

McAlpine and co-workers¹⁷ have argued that it is statistically impossible for any disease, including multiple sclerosis, with a maximum prevalence of some 1 per 1,000 to be perpetuated by direct person-to-person transmission. However, there are two possible explanations that avoid this statistical difficulty.

Firstly, there might be a pool of subclinical human infection. That is, many more people might carry the pathogen but show no symptoms. In this case, multiple sclerosis could be an occasional variant or sequela of this much more frequent infection. Secondly, it is possible for a pathogen to exist in an animal pool, in which case multiple sclerosis might be a rare or accidental human infection from this source. Dogs have been suggested as such hosts, especially if they are suffering from canine distemper.¹⁸ However, McAlpine and colleagues concluded that neither of these options can be supported by the epidemiologic evidence.

KOCH'S POSTULATES

Soon after Pasteur discovered the vaccination process that enormously reduced the human death rate from rabies, the German bacteriologist and physician Robert Koch proved that tuberculosis also was caused by specific bacteria.²⁰ His first step was to establish that every tuberculosis patient was infected with this suspected bacteria. While this was suggestive, it was not totally convincing since infection by such bacteria might have been a secondary result of a greater susceptibility to infection in tuberculosis. To disprove this, Koch demonstrated that a condition very closely resembling tuberculosis could be induced in suitable animals by inoculating them with the suspected causal bacteria. A third step, isolating bacteria from these animals and using them to cause tuberculosis in a second generation of infected animals, provided absolutely convincing proof of a specific bacterial cause for the disease.²¹

These steps became known as Koch's²² postulates and are generally accepted as the classical method of establishing whether or not a specific pathogen is the cause of a particular disease. Despite virtually endless attempts to apply Koch's postulates

to pathogens suspected of causing multiple sclerosis, these three major steps have never been successfully demonstrated. Probably the least ethical, yet very significant attempt to apply Koch's postulates to multiple sclerosis occurred during World War II. In 1940, Shaltenbrand,²³ an internationally known German neurologist, injected monkeys with cerebrospinal fluid taken from multiple sclerosis patients. Claiming that these animals had developed disease-like symptoms, he then tried to induce multiple sclerosis in six mentally ill patients using monkey cerebrospinal fluid. Although none of the six patients showed any signs of multiple sclerosis, attempts were made to infect 39 more. Highly unethical though this research was, it seemed to provide convincing proof that there is unlikely to be a specific key causal pathogen involved in multiple sclerosis.

SUMMARY

As shown in the two preceding chapters, any pathogen playing a key, causal role in multiple sclerosis would have to infect women roughly twice as often as men, except where the disorder was rare. In these latter regions, it would cause illness in females at a rate of about six times that seen in males. It would also be much more infectious in certain families, especially those with identical twins. This pathogen would pose more of a threat to adolescents than to young children, but it would almost never infect Lapps or Inuits. Nevertheless, it would cause multiple sclerosis in predictable global belts of infection in which prevalence declined both towards the equator and westward into Asia. In short, the genetic, epidemiological, and geographical evidence makes it very likely that virologists and neurologists will spend the next century looking for this elusive pathogen, with no more success than that accompanying their work in the last one hundred years.

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The bigger the investment the stronger the denial.

Phil Rickman, *The Lamp of the Wicked* (2003)

A PLACE FOR EVERYTHING

Science became an educated cadaver of thought, above which congregate expert players. If the encyclopedia of the ignorance of the acknowledged authorities in the history were to be published, it would number many fat volumes. Nothing will interest scientists anymore. They are like oxen which feed off fenced-off pasture.

Professor Wlodzimierz Sedlak¹

MEDICAL GEOGRAPHY

For millennia, it has been recognized that disease patterns often reflect human behaviour and environments. If multiple sclerosis is not primarily the result of genetic or infectious factors, then there is a strong possibility that its dominant cause is geographical. This would hardly be surprising since, in his book *On Airs, Waters and Places*, the Greek physician Hippocrates² wrote:

Whoever wishes to investigate medicine properly should proceed thus: in the first place to consider the seasons of the year, and what effects each of them produces. Then the winds the hot and cold, especially such as are common to all countries, and then such as are peculiar to each locality... One should consider most attentively the waters which the inhabitants use...the mode in which the inhabitants live, and what are their pursuits, whether they are fond of drinking and eating to excess, given to indolence, or are fond of exercise and labour.

Subsequently, many Roman physicians also accepted that the environment was the chief determinant of many disease patterns. However, after the Roman Empire's collapse in the 5th century AD, the Christian West began to see disease as a punishment by God for past sins and as a signal for more repentance.³ As a consequence, interest in diseases' links to the local environment did not receive much recognition until the 1790s, when Fink published his three volume study of the geography of diseases.⁴ The practical significance of these spatial relationships was established in 1848 by Snow,⁵ who mapped cholera mortality in the Soho district of London, showing that such deaths were linked to polluted drinking water. Medical geography is now an established subdiscipline in many countries, including the United Kingdom, France, Germany, the Benelux countries, Canada, the United States, India, and especially in the People's Republic of China.⁶⁻⁷

The aim of the great majority of medical geographical studies, with which I have been involved, is to establish whether or not particular variables, such as the selenium content of human toenails or animal fodder crops, have distribution patterns that are very similar to, or very different from, those of specific diseases. Simply put, we try to establish whether maps of the distribution of a disease are very like, or very different from, those of maps of suspected causes.⁸ This is done because, if a disease, such as dental fluorosis, is being caused by elevated levels of a particular environmental element, such as fluoride, it is likely to be most common where levels of the suspected causal variable are very high. That is, fluorosis would be expected to occur most often in regions where fluoride levels in water, soils, and foods were elevated. A disease and its causal variable(s) will have very similar distribution patterns, especially if the population affected is not mobile. Conversely, if a disorder, for example goitre, is due to a deficiency of some variable, such as iodine, it will tend to be most common in

regions where the substance is rare.⁹ Consequently, the disorder and the deficient substance will have extremely different distributions. It can also be expected that if two disorders or diseases, such as SIDS (Sudden Infant Death Syndrome) and goitre, have a similar cause, for example thyroid malfunction due to deficiencies of iodine and selenium, they will also have similar distribution patterns.¹⁰⁻¹¹ The reverse is true if what causes one disorder prevents another.¹² Geographers utilize a wide variety of medical data to look for strong positive and negative spatial relationships between diseases and disorders and environmental variables.¹³ Health information ranges from morbidity (illness) and mortality (death) data, often collected by vital statistics agencies and stored in government databases, to those collected by researchers using interview surveys or detailed questionnaires.¹⁴

A variety of correlation techniques can be applied in efforts to compare health information data with that collected about physical and social environments. The statistical methods used to analyse these data will vary, depending on the type of information and whether it is normally distributed. It must be stressed, however, that correlation, however strong, does not, in itself, prove cause and effect. Nevertheless, such studies stimulate many new hypotheses that may or may not be correct, but which all deserve further study. Correlation cannot prove that one variable causes another because it is usually beset by one or more of three key problems: specification, multicollinearity, and the ecological fallacy.¹⁵ The first of these problems, specification, occurs because no matter how strong an obtained correlation between a disease and its suspected cause, researchers can never be sure that they have not failed to collect data on an even more important variable. One of the key assumptions of most statistical techniques is that the potential causal variables being analysed are not highly inter-related, that is they are not multicollinear. Unfortunately, in

the real world this is very rarely true. Climate, for example, is very strongly linked to rainfall, sunlight, temperature, soil type, plant species, human activities, and many more groups of variables. Similarly, minerals often occur together in the same rock types, while class and race are strongly correlated to numerous social variables. In addition, as the geographical scale of analyses varies, usually so too does the strength of correlation between disease and the suspected environmental causal variables. As previously pointed out, the main value of medical geography correlation studies, then, is the generation of new hypotheses that can be tested further against the existing literature, laboratory experiments, or clinical and field studies.

It is very important to know if a strong correlation between an illness and a particular geographical variable(s) is real or merely an artifact of the technique. To address this issue, a set of nine principles, often referred to as the Bradford-Hill criteria¹⁶ after their originator, can be used to establish further whether a relationship is actually one of cause and effect. These criteria, for example, have been utilized to examine possible links between SIDS and selenium and iodine deficiency,¹⁷ aluminum and Alzheimer's disease,¹⁸ and schizophrenia and inadequate selenium intake.¹⁹ These nine Bradford-Hill criteria are listed in Table 1. They include coherence, biological plausibility, temporal relationship, experimental support, and specificity. They are applied later in this book to establish how probable it is that a suspected link between multiple sclerosis and a shortage of a specific trace element is likely to be one of cause and effect.

Table 1: The Bradford-Hill Criteria Used to Establish Cause and Effect Relationships

<i>Criterion</i>	<i>Key Question</i>
COHERENCE	Does this association agree with known facts, or with the established scientific truth?
BIOLOGICAL PLAUSIBILITY	Can biological and biochemical links be elaborated between the suspected causal variable(s) and the disease?
TEMPORAL RELATIONSHIP	Does the suspected cause precede the effect, or at a minimum, is it simultaneous with it?
DOSE-RESPONSE CURVE	As exposure to the suspected causal agent increases, do its deleterious effects become more extreme?
EXPERIMENTAL SUPPORT	Has the cause and effect relationship been demonstrated by human or animal experiments?
CONSISTENCY	Has the suspected relationship been observed in different populations, places, circumstances, and times?
STRENGTH	Is the magnitude of the relationship, that is the relative risk between suspected cause and effect, high?
SPECIFICITY	Does the exposure to the suspected causal variable result in only one disease? (This criterion has been abandoned as unreliable)
ANALOGY	Can the relationship be established by reasoning from analogy? (Reasoning from analogy can never produce conclusive supportive evidence, but can generate, at best, novel hypotheses)

After Foster²⁰

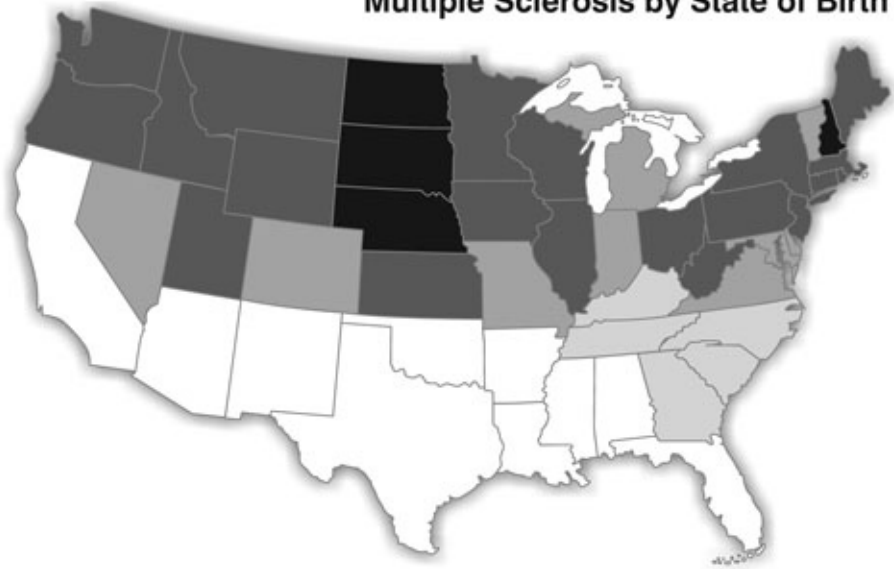
MULTIPLE SCLEROSIS IN THE UNITED STATES

Medical Data

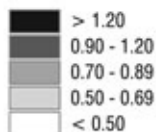
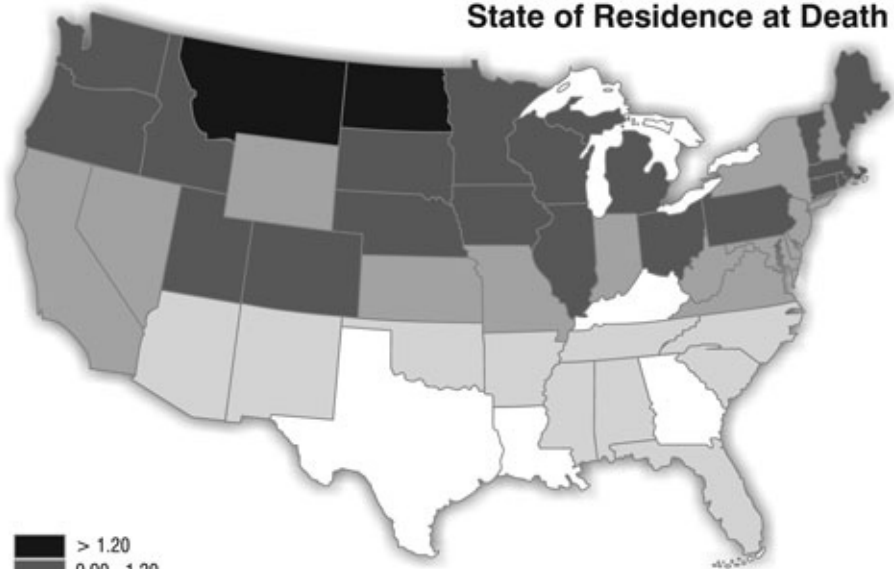
To study the medical geography of multiple sclerosis in any region, two types of data are obviously needed, medical and geographical. Fortunately, high quality data of both types is readily available for the United States. To illustrate, the American Public Health Association sponsored a series of monographs that were based on mortality during the period from 1959 to 1961. One of these reviews focused on neurological diseases, including multiple sclerosis. This report, by Kurland and colleagues,²¹ contained a map indicating average age adjusted death rates for multiple sclerosis per 100,000 population, by state of residence, at death. I used these data for analysis.²² In addition, this monograph provided a table that showed average annual death rates per 100,000 population for multiple sclerosis among native born Americans by the state of their birth. This data, provided for both Whites and non-Whites, was also included in the analyses upon which much of the geographical component of this book is based. It is clear from the resulting maps (Figure 1) that it is virtually impossible for the key trigger for multiple sclerosis to be genetic.

There is also a third valuable source of medical information on multiple sclerosis in the United States. During World War II, about 16.5 million Americans saw military service, and another 5 million served in the Korean conflict. Legislation established multiple sclerosis as a “service-connected” illness if its symptoms were diagnosed either during military service or within 7 years after discharge. From the resulting claims for medical benefits, Kurtzke and co-workers²⁵ identified 5,305 veteran service-connected multiple sclerosis cases. Each was matched, on the basis of age, date of entry, branch of service, and war survival, with a military peer who did not have the disorder. This

Multiple Sclerosis by State of Birth



Multiple Sclerosis by State of Residence at Death



Average annual age-adjusted death rate per 100,000 population

Figure 1: United States Mortality from Multiple Sclerosis by State of Birth and by State of Residence at Death, 1959-1961 (data from Kurland et al., 1973²¹)

provided an unbiased, pre-illness case control series of national scope and unprecedented size. As a result, Kurtzke²⁶ was able to publish a map of the contiguous United States showing the distribution of multiple sclerosis in White male veterans of World War II, according to their state of residence at entry into military service, expressed as case control ratio percentages. These data were also abstracted and analysed by this author.²⁷

Fortunately, when conducting research needed to write *Reducing Cancer Mortality: A Geographical Perspective*, I developed a data base²⁸ consisting of geographical distribution of mortality from 66 cancers and groups of cancers in the United States, at the state level. Beyond this, many subsequent articles led to the eventual expansion of this data base to include mortality, incidence, or prevalence data for 124 diseases, or disease time periods, beyond those for multiple sclerosis. This allowed the statistical comparison of spatial distribution of this disorder, in the United States, with those of 84 other specific diseases.²⁹

Environmental Data Sources

The analyses that preceded the publication of *Reducing Cancer Mortality: A Geographical Perspective*³⁰ had also necessitated the development of a data base, at the state level, that contained information on 219 environmental variables. This data base has been described in detail elsewhere³¹ and will be discussed only briefly here. One excellent source from which environmental data was extracted was the *Water Atlas of the United States*.³² This book includes 122 maps ranging from average annual precipitation, through hardness and sodium content of finished public water supplies, to the presence of dieldrin, lindane, cadmium, chromium, and arsenic in surface waters.

However, the most comprehensive source of environmental data was publications by the United States Geological Survey.³³⁻³⁵

In 1961, the Geological Survey began a soil and regolith sampling program designed to establish the natural range of element abundance in surface materials that were as unaltered as possible by human activity and so represented the natural geochemical environment of the entire conterminous United States. Samples were taken at a depth of some 20 centimetres below the surface from sites about 80 kilometres apart. This process resulted in 863 sample sites at which the levels of 35 elements were analysed. These elements ranged from aluminium and arsenic through fluorine and gallium to selenium, sodium, and zinc. A more detailed description of this geological data is provided in *Health, Disease and the Environment*.³⁶

In summary, this author had developed an environmental data base at the state level that included information on a wide range of natural geographical variables, such as rainfall and sunlight, together with air and water pollutants and a variety of industrial, commercial and agricultural activities. In addition, geological information which appeared to reflect, as closely as was possible, the natural chemical environment of the United States was utilized. Most of this data had originally been collected between 1950 and 1970, so it was quite compatible with the multiple sclerosis mortality and morbidity data which also was from this general time period.

ANALYTICAL RESULTS

Correlation With Other Diseases/Disorders

In the initial stage of analysis, the three measures of the spatial distribution of multiple sclerosis in the United States, which have been described previously, were compared statistically with mortality, incidence, or prevalence data for 124 other diseases or disease time periods. The idea, of course, was to

identify which other diseases had very different or very similar distribution patterns. Several interesting and thought provoking relationships were revealed by this correlation process. Since all three measures of multiple sclerosis frequency in the United States produced similar groups of correlations, and because place of birth seems particularly important in the etiology of this disorder, death by state of origin is emphasized in the following discussion. As can be seen from Table 2, three groups of diseases appear to have either extremely similar or very different distribution patterns to that of multiple sclerosis in native born Whites.

The most obvious of these is the group comprised of the two measures of Parkinson's disease. Multiple sclerosis mortality, for example, displayed marked positive correlations with both death from Parkinson's disease at any age ($r=0.77555$, $p=0.0001$) and in individuals aged 65 years or older ($r=0.71663$, $p=0.0001$).

Table 2: Most Statistically Significant Associations Between Multiple Sclerosis Mortality, by State of Birth (1959-1961), and Other Disease Distributions, in the United States

<i>Disease</i>	<i>Time Period</i>	<i>Pearson Correlation Coefficient</i>	<i>Significance Level</i>
Parkinson's Disease (mortality at any age)	1959-1961	0.77555	0.0001
Parkinson's Disease (mortality 65+)	1959-1961	0.71663	0.0001
All cancer of the integument	1950-1967	-0.63258	0.0001
Skin cancer	1950-1967	-0.61864	0.0001
Melanoma	1950-1967	-0.60121	0.0001
Goitre	World War I	0.53513	0.0001

What this means is that multiple sclerosis and Parkinson's disease have very similar mortality patterns in the United States. In regions where people are commonly dying of Parkinson's disease, others also are losing their lives to elevated levels of multiple sclerosis. Conversely, both diseases are relatively uncommon in some other states. This is very interesting, since Berne-Fromell and colleagues³⁷ have shown that levodopa is beneficial in reducing the symptoms not just of Parkinson's disease, but also multiple sclerosis. This drug has been used for many years as the treatment of choice for Parkinson's disease, but not for multiple sclerosis.

It can be seen also from Table 2 that multiple sclerosis mortality, by state of birth, correlates very negatively with various skin cancers, including melanoma. The association between the distributions of multiple sclerosis and of cancer of the integument, for example, is -0.63258 , $p=0.0001$. These negative links appear consistent with the repeated suggestion of a protective effect for sunlight (and probably vitamin D) in the etiology of multiple sclerosis.³⁸⁻³⁹

The strong positive correlation between multiple sclerosis mortality, by state of birth, and the prevalence of goitre in World War I troops ($r=0.53513$, $p=0.0001$) also seems noteworthy. Goitre is indicative of a thyroid malfunction that is often related to a dietary iodine deficiency. Perhaps there is also a lack of iodine intake involved in the early stages of multiple sclerosis?

Environmental Correlations

The second stage in the United States analysis involved correlating mortalities from this disorder with the spatial distribution of the 219 geographical variables in the state data bank.

The most noteworthy associations revealed by this process are shown in Table 3. Interestingly, virtually all the most significant correlations between the milieu and multiple sclerosis in Whites were with very low concentrations of specific soil elements and this disorder. With one important exception, every one of these correlations was negative. In the United States, therefore, mortality from multiple sclerosis, by state of birth, appears negatively correlated with very low levels of soil sodium (-0.68588), strontium (-0.64865), potassium (-0.63490), gallium (-0.60001), and phosphorus (-0.59230).

Table 3: Most Statistically Significant Associations Between Mortality from Multiple Sclerosis (1959-1961), in the United States, in Whites, by State of Birth and Environmental Variables

<i>Independent Variable</i>	<i>Pearson Correlation Coefficient</i>	<i>Significance Level</i>
Very low soil sodium	-0.68588	0.0001
Very low soil strontium	-0.64865	0.0001
Very low soil potassium	-0.63490	0.0001
Sunlight (langleys)	-0.60456	0.0001
Very low soil gallium	-0.60001	0.0001
Very low soil phosphorus	-0.59230	0.0001

Interestingly, only iodine deficient soils displayed any marked positive correlation between an element and multiple sclerosis (0.47944, p=.000.6). It should also be pointed out that there was a significant negative correlation between mortality from multiple sclerosis (1959-1961) by state of birth and sunlight (0.60456). In all cases, except where stated, p=0.0001.

These correlations seem to be consistent with the previously described hypotheses, generated by comparing the death rates from multiple sclerosis in the United States with other disease patterns. That is, they tend to support a protective effect for sunlight (and probably vitamin D),⁴⁰ together with some role for thyroid malfunction, possibly linked to iodine deficiency. Anyone who wishes to examine these correlations in more detail can do so in the author's book *Health, Disease and the Environment*.⁴¹

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*The history of medicine is a history of conflict.
We should be making awards for infamy, but the
list would be too long and thus no one would
stand out.*

Abram Hoffer, Speech at the 2nd Annual
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IODINE: THE SALT OF THE EARTH?

Health is not valued til sickness comes.

Thomas Fuller, *Gnomologia*, 1732

The geographical analysis, described in the preceding chapter, is very suggestive of a link between multiple sclerosis and iodine deficiency. Geographers are widely aware, however, that such correlations in themselves do not prove cause and effect. As discussed previously, a set of principles, usually referred to as the Bradford-Hill criteria after their author,¹⁻² are used to explore whether such relationships are likely to be causal. These principles are similar to those used by the Surgeon General's Expert Committee³ to evaluate potential links between lung cancer and smoking. This chapter applies the Bradford-Hill criteria to the possible iodine deficiency-multiple sclerosis relationship to see if it is likely that the lack of this trace element has a causal role in this disorder.

COHERENCE

Hill⁴ argued that an association, that is a strong correlation, is more likely to be causal if it agrees with the "known facts," or with the "established scientific truth," of a particular discipline. This is a rather confusing criterion to apply to a new idea as it ignores the reality that some novel concepts cause paradigm shifts that invalidate the current conventional wisdom. As Jones and Moon⁵ point out, if coherence was insisted upon "we would never discover anything new; coherence supports existing theory while incoherence potentially generates new theory."

However, I am not claiming that the hypothesis that those who develop multiple sclerosis have at some time in their lives been iodine deficient requires a paradigm shift. Rather, it is argued that the existing literature supports the view that iodine deficiency may well occur in multiple sclerosis. To illustrate, the conventional view of multiple sclerosis is that it is a disorder that ultimately results from the loss of myelin from the nerves.⁶ Is there any evidence, therefore, that such a process could be triggered or accelerated by iodine deficiency? The answer to this question is certainly yes.

In 1881, the Clinical Society of London produced a survey highlighting the influence of normal thyroid function in brain development. In the following 125 years, many studies of rats, sheep, and humans have supported this relationship, usually by studying the effects of fetal and/or maternal thyroid deficiencies.⁷ This body of research has shown that thyroid hormones, which cannot be produced without iodine, seem to have their greatest impacts on the terminal stages of brain differentiation, including synaptogenesis, growth of axons and dendrites, neuronal migration, and myelination.⁸⁻⁹ Simply put, in humans and other mammals, iodine is essential for the production of thyroid hormones, which in turn are necessary for normal myelination.¹⁰ So, clearly, the idea that iodine deficiency, capable of resulting in the development of goitre, could cause abnormal myelination is consistent with the “known facts” or “established scientific truth.” That is, this hypothesis meets the coherence criterion.

BIOLOGICAL PLAUSIBILITY

Biological plausibility is also a useful criterion for determining cause and effect relationships. For example, it is necessary to know whether a postulated relationship makes biological sense; that is, whether it is possible to elaborate the biological and

biochemical links between the suspected causal variable(s) and the disease.¹¹ In this case, the question to be asked must be “is it possible to sketch biological mechanisms by which a lack of iodine might interfere with the normal development and/or repair of myelin, eventually leading to demyelination and the patches of nerve scarring that give multiple sclerosis its name?” An attempt will now be made to show that this seems to be so.

It is clear that iodine deficiency can cause hypothyroidism during fetal or early life.¹² When it does, the results may be extreme as thyroid hormones are needed for the proper development of the central nervous system, especially its myelination.¹³ Individuals who were hypothyroid at this critical time often suffer permanent mental retardation that cannot be corrected by later administration of thyroid hormone or iodine. This process has been duplicated in animals. Ramos and Ruiz-Marcos,¹⁴ for example, added methimazole, a substance that causes thyroid hormone depression, to the drinking water of pregnant rats. Their offspring also had methimazole added to their water. These researchers were able to show that depressed thyroid hormone levels significantly reduced development of the myelin sheaths of the axons that cross the rat caudate nucleus. That is, this goitrogen reduced the myelination of nerves in the rat brain by some 32 percent. It seems biologically plausible, therefore, that iodine deficiency, through inadequate levels of associated thyroid hormones, may reduce human myelin production, increasing its susceptibility to the gradual demyelination seen in the nervous systems of multiple sclerosis patients.

THE TEMPORAL RELATIONSHIP OF THE ASSOCIATION

Obviously, if you are trying to establish cause and effect, the suspected cause must precede, or at least be simultaneous with, its suspected effect(s). This is called the principle of

temporality. It implies that if a thyroid hormone deficiency plays a significant role in multiple sclerosis, it must occur before the illness develops, not after. That is, thyroid deficiency must occur before multiple sclerosis, not be caused by it.

As stated in Chapter 4, multiple sclerosis seems to be acquired in childhood or adolescence, long before symptoms occur.¹⁵ Risk, however, is not defined at birth. White males moving from the low iodine north of the United States to the higher iodine south between birth and entry into military service clearly decrease their risk of developing multiple sclerosis. The reverse is true if the move is in the opposite direction, from south to north.¹⁶ Similar migratory relationships have been seen in other countries.¹⁷ This “incubation” or “latency” period occurs before clinical symptoms of multiple sclerosis appear, showing that exposure to low dietary iodine and/or to depressed thyroid hormones is much more likely to be a cause, rather than a consequence, of multiple sclerosis. This does not mean that thyroid depression cannot be a continuing symptom of multiple sclerosis, merely that it precedes the disorder’s initial diagnosis.

DOSE-RESPONSE CURVE

Those who smoke three packets of cigarettes a day generally become sicker more rapidly than those who smoke only one.¹⁸ This is called a dose-response relationship and is a criteria used by Bradford-Hill to establish cause and effect. Such relationships imply that as exposure to any suspected causal agent increases, so too must its harmful effects.

Fluoride is a goitrogen known to interfere with the operation of the thyroid.¹⁹ For this reason, it was used traditionally to treat hyperthyroidism. It might be expected, then, if goitrogens promote multiple sclerosis, that this disorder would be most

common in regions where fluoride levels are elevated. One such area lies around Trail, British Columbia, Canada. In this valley town, a lead-zinc smelter has been polluting the environment with sulphur dioxide and fluoride since 1896. This smelter has been an issue between the Canadian and United States governments for many years as these pollutants often blow southwards, across the international border, into Washington State.²⁰ It is interesting, therefore, to note that the highest prevalence rate for multiple sclerosis on Earth appears to be the 200 per 100,000 recorded in the smelter town of Trail, British Columbia.²¹

Beyond this, Washington State has its own major polluters, one of which has been the United States Department of Energy's Hanford Site. This plant was used, during the Cold War, to produce plutonium for nuclear weapons. One of the worst effects of this process was the release of enormous quantities of radioactive I-131 to the atmosphere. Inevitably, this goitrogen, known to seriously damage the thyroid gland, seems to have been responsible for a significant increase in thyroid cancer in people living downwind of Hanford.²² These unfortunate people are known as the "Downwinders," and have been involved in litigation against DuPont and General Electric, which operated the plant for the United States government from 1943 to 1965. Interestingly, the Downwinders also seem to be suffering from very high levels of multiple sclerosis that some believe is also due to the thyroid damage they suffered from Hanford's radioactive pollutants. Downwinders in Idaho, for example, suffer from a multiple sclerosis prevalence rate that is higher than the highest state rate in the United States.²³

Taken as a whole, the evidence suggests that in North America, where levels of goitrogens like fluoride and radioactive I-131 have been unusually elevated, so has multiple sclerosis in exposed local populations. This suggests a thyroid hormone dose-

response relationship in this disorder; the lower the thyroid hormone levels, the higher the prevalence of multiple sclerosis.

EXPERIMENTAL SUPPORT

It is rarely possible, for ethical reasons, to perform strictly controlled experiments on humans in an effort to see whether a deficiency or excess of a nutrient causes a particular disease. Normally, one must rely on animal models or quasi-experimental or simply observational studies.²⁴

There are, for example, numerous studies attempting to discover the impact of iodine deficiency on myelination of animal nerves. Matthieu and co-workers,²⁵ for example, have shown that hypothyroidism in rats, during the first 30 days after birth, caused a very serious decline in brain myelin. Production of myelin in hypothyroid rats was only 60 percent of that in controls given a normal diet. Similarly, Ramos and Ruiz-Marcos²⁶ showed that thyroxine deficiency during pregnancy produced offspring with a significant reduction (32 percent) in density of myelinated brain axons. Experimentally, therefore, it has been proven that a malfunctioning thyroid, caused by either iodine deficiency or goitrogens, can result in abnormally thin myelin sheaths around nerves. Whether this process promotes multiple sclerosis in humans is unclear, but it seems consistent with the geographical evidence from the United States that it may.

One obvious criticism of the hypothesis that multiple sclerosis is, in part, related to iodine deficiency, would appear to be that this disorder's incidence did not fall with the introduction of the United States' iodization of table salt. In only 4 years, from 1924 to 1928, the use of iodized salt, for example, reduced the incidence of goitre in Michigan from 38.6 to 9 percent.²⁷ We did not see any later associated decline in multiple sclerosis.

There appear to be at least two possible explanations for this. Warren,²⁸ for example, demonstrated that a lack of iodine in soil deprives cattle of the ability to produce the thyroid hormone, thyroxin. This hormone is essential for the conversion of carotene to vitamin A. As a result, newborn infants and very young children fed with milk from cows raised on iodine deficient fodder may suffer from a vitamin A deficiency long before they are likely to be exposed to iodized salt. Warren²⁹ has suggested that such a vitamin A deficiency may be the root cause of multiple sclerosis. It is also possible that infants breast fed by iodine deficient mothers may receive iodine deficient milk. Whether or not this is the cause, it is of interest to note that Dip³⁰ identified a marked correlation between the incidence of multiple sclerosis and the dairy industry. In addition, Field claimed that diets low in saturated fats (i.e., a significant reduction in dairy products) help patients with multiple sclerosis.

It also has been demonstrated experimentally that thyroxine deficiency in the rat fetus results in a serious decline in brain myelin thickness.³¹⁻³² It is possible, therefore, that iodine deficient milk depresses myelin production in the human infant, encouraging the later development of multiple sclerosis. This suggested thinning of the myelin sheath may not be remedied by more adequate dietary intake subsequently.

CONSISTENCY OF THE ASSOCIATION

The consistency principle emphasizes the need for repetition, arguing that a link between a suspected cause and its effect(s) is more likely to be true if it occurs in different populations, places, circumstances, and times.³³ If the iodine deficiency-multiple sclerosis hypothesis is correct, there ought to be evidence of such a relationship in countries other than the United States.

In my book "Health, Disease and the Environment," I published a table that showed the relationship between international multiple sclerosis prevalence rates and latitude.³⁴ This table was based on the work of various authors, in particular, Sutherland,³⁵ Mayer,³⁶ and Palo and co-workers.³⁷ It included data from 39 countries and/or regions. From the data in this table, it is clear that above latitude 60°, the mean multiple sclerosis prevalence rate is 60 per 100,000; between latitudes 50° and 60° it is 56.3 and between latitudes 40° and 50° it is 60.3 per 100,000. This suggests the prevalence of the disorder is more or less the same north and possibly south of latitude 40°. In contrast, the prevalence falls to 15.6 per 100,000 from latitudes 30° to 39° and 3.0 per 100,000 in latitudes 20° to 29° and 10° to 19° respectively. In the 10 degrees nearest the equator, there appears to be virtually no multiple sclerosis.

This distribution pattern is interesting as it suggests an abrupt decrease in the prevalence of multiple sclerosis below latitude 40°. The global distribution of iodine also varies markedly with latitude. Iodine originates in molten rock beneath the Earth's crust and reaches the surface as a component of igneous rock. The average iodine content of such rocks is roughly 0.3 ppm.³⁸ Weathering releases much of this iodine, most of which is transported to the oceans in river water. In this way, the oceans have become great iodine reservoirs, containing one-fourth of the Earth's total supply of this trace element. For this reason, many marine sedentary rocks, such as clays and shales, may be very iodine enriched, levels of up to 380 ppm being recorded.³⁹

Not all iodine remains locked in marine sediment, however, as it appears also to be lost from the oceans into the atmosphere, where it is returned to the continents through precipitation. Its deposition, however, is very uneven. It has been calculated that 22 to 50 micrograms per acre falls each year on areas such as the Atlantic Coastal Plain that are near to the ocean, while

only 0.7 micrograms per acre per year is deposited in continental interiors, like the Great Lakes regions.⁴⁰ Therefore, iodine levels in soils seem to reflect three factors: the nature of the parent bedrock, the distance from the sea, and probably above all, the age of the deposit. Typically, as Goldschmidt⁴¹ pointed out, areas covered by Pleistocene glaciers, especially the most recent Wisconsin ice sheet, are very deficient in iodine. This is because old soils that had accumulated iodine from the atmosphere for many hundreds of thousands of years were eroded or buried by glaciers. Present-day young soils, developing on till and glaciofluvial sediments, have had insufficient time to accumulate large amounts of atmospheric iodine. The point to be made here is that the highest risk zone for multiple sclerosis, above latitude 40°N, lies almost entirely in the low iodine areas of Pleistocene glacial erosion and deposition. Nearer the Equator than this, where glaciation was rarer and much more restricted to high mountain ranges,⁴² the prevalence of multiple sclerosis is significantly lower. In short, globally there appears to be a consistency of association between iodine deficiency caused by glacial erosion and deposition and the prevalence of multiple sclerosis, at least in Caucasians.

As has been stated previously, however, multiple sclerosis is much rarer in persons of Oriental descent. The lack of multiple sclerosis in Japan, despite its northerly latitude, is easy to explain if the hypothesis is correct. It can be seen from the review of the geochemistry of iodine, published by the *Chilean Iodine Educational Bureau*,⁴³ that Japanese soils have some of the world's highest known iodine levels. This is probably due to the historical use of iodine-enriched seaweeds as a fertilizer. Seaweeds have an unusual capacity to absorb iodine from the environment in large quantities. Shacklette and Cuthbert,⁴⁴ for example, analysed the iodine content in a variety of plants. The typical garden vegetable contained some 6.9 ppm iodine. In contrast, the mean iodine content of marine brown and

marine red algae is 2,488.7 ppm and 382.5 ppm respectively. In short, by using seaweeds as fertilizers and including them regularly in their diets, the Japanese generally avoid all iodine deficiency diseases, apparently including multiple sclerosis.

This still does not explain why the Chinese rarely develop this disorder, despite the fact that goitre and cretinism, due to iodine deficiency, are quite common in Mainland China.⁴⁵ Interestingly, Swank and Pullen⁴⁶ noted that in Europe:

...two parallel and little mixed cultures based on food have evolved. These are the “beer-butter” and “wine-oil” cultures. The first extends across northern Europe (Scandinavia, Germany, Holland, Belgium, northern France, northern Switzerland and the British Isles) and has become the mode of life in the United States and Canada. The second predominates in the Mediterranean area (Spain, Italy, southern France, southern Switzerland and Greece) and stretches to the Middle East and North Africa. The beer-butter culture corresponds geographically to the area of high incidence of multiple sclerosis and vascular disease; the wine-oil culture corresponds to the area where these conditions have a low incidence.

If multiple sclerosis is linked, not to a simple iodine deficiency, but to consumption of dairy products from iodine deficient cows,⁴⁷ then the low levels of multiple sclerosis in Orientals are easy to explain. Dairy products make up a far larger part of the Caucasian diet than either those of the Japanese or Chinese.

STRENGTH OF ASSOCIATION

A variable is more likely to be involved in causing an illness if the magnitude of the association between the suspected cause and effect is high. A very large relative risk of, say, 10:1 suggests any association is almost certain not to be entirely due to chance.⁴⁸ The screening of some 2.5 million potential military

recruits during World War I established that the national United States male prevalence rate for simple goitre was 4.4 per 1,000. However, goitre prevalence varied from a high of 26.91 per 1,000 in Idaho to a low of 0.25 per 1,000 in Florida.⁴⁹ In addition to Idaho, goitre was discovered to be most common in potential recruits from Oregon, Washington, Montana, Utah, Wyoming, and Wisconsin. In contrast, the disorder's prevalence was lowest in Florida, Texas, Massachusetts, Arkansas, New Jersey, Georgia, and Rhode Island. In the seven states that had the highest male goitre prevalence rates in 1917-1918, the average annual death rate for multiple sclerosis among native born Americans, in 1959-61, was 1.07 per 100,000 population. This contrasts with a multiple sclerosis death rate of 0.64 per 100,000 in the seven states that used to experience the lowest goitre rates.⁵⁰ These comparisons yield a relative risk of 1.67:1. This suggests that for every two deaths from multiple sclerosis in the states with low goitre prevalence rates there were more than three in those with previously high goitre prevalence. Obviously, much had happened to the racial and ethnic mix and to dietary habits in these 14 states between the two periods 1917-1918 and 1959-61. This difference in relative multiple sclerosis risk among formerly high and low goitre prevalence states is supportive of the hypothesis that iodine deficiency and/or thyroid malfunction may have been more common in multiple sclerosis patients than in the general population. This strength of association is moderate, however, implying that, if iodine deficiency plays a role in multiple sclerosis, it is not the only causal variable involved.

SPECIFICITY OF THE ASSOCIATION

Hill⁵¹ originally argued for specificity of association—that a particular type of exposure should result in one specific disease, and perhaps even to its development at a unique site.

The value of this criterion in establishing causality has been criticized by a variety of authors⁵¹⁻⁵³ for several reasons. It has been shown repeatedly, for example, that most disease-producing factors cause more than one observable effect. This is certainly true of both iodine and selenium imbalances in humans. Hetzel,⁵⁴ for example, identified 22 iodine deficiency disorders, of which 12 occur in the fetus and 2 more in the neonate. They vary from spontaneous abortion to dwarfism. Iodine excess also has been implicated in several disorders, including goitre⁵⁵⁻⁵⁶ and melanoma.⁵⁷ Similarly, selenium deficiency is a significant risk factor in Keshan and Kaschin-Beck diseases⁵⁸ and is thought to play a major role in many cancers⁵⁹ and in heart disease.⁶⁰ Beyond this, selenium deficiency may be involved in some forms of dementia,⁶¹ schizophrenia,⁶² and even infertility in males.⁶³ Selenium excess, in contrast, is known to result in loss of hair and nails, skin lesions, abnormalities of the nervous system, disturbance of the digestive tract, and possibly tooth decay.⁶⁴

Houeland⁶⁵ considered specificity of association to be an invalid criterion for establishing causality, and argued that it was a relic from the early days of modern disease theory. Similarly, Rothman⁶⁶ considered it useless and misleading. The current author agrees with these researchers. Indeed, it seems logical to argue that the lack of specificity of association makes it more, rather than less, likely that iodine deficiency is involved in multiple sclerosis.

ANALOGY

Analogy is the last criterion discussed by Hill⁶⁷ for establishing causality. Reasoning from analogy, however, can never produce conclusive supportive evidence; at best it helps generate hypotheses that must then be tested further. This is exactly how the current author first became interested in the

possibility that iodine imbalances may be involved in the etiology of multiple sclerosis. My interest was awakened by the realization that, in the United States, multiple sclerosis had a spatial distribution that was extremely similar to that of goitre, prior to the introduction of iodine supplementation.

SUMMARY

The hypothesis that, at some time during their gestation or childhood, multiple sclerosis patients suffered from inadequate levels of thyroid hormones appears to meet all but one of Bradford-Hill's criteria.⁶⁸ The exception is specificity of association. However, this particular criterion itself has been criticized widely and is considered invalid by many authors.⁶⁹⁻⁷⁰ The evidence seems to suggest that iodine deficiency plays a role in the etiology of multiple sclerosis but that it is indirect. That is, it seems more likely to exert its influence, at least in part, through dairy products from iodine deficient cows.

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Longevity is only desirable if it increases the duration of youth, and not that of old age. The lengthening of the senescent period would be a calamity.

Alexis Carrel (1935)

TWO PEAS IN A POD

*You see things; and you say, "Why?"
But I dream things that never were; and I say,
"Why not?"*

George Bernard Shaw¹

HISTORICAL BACKGROUND

The geographical analysis discussed previously also shows that, in the United States, the death rates from multiple sclerosis and Parkinson's disease tend to rise and fall together. Where mortality from multiple sclerosis is common, so too is that from Parkinson's disease. Where either is uncommon, so too is the other. A key question that must be asked, then, is whether this disease relationship is merely a statistical quirk, or do both disorders have similar environmental or social trigger(s), and as a result, spatial distributions.

Parkinson's disease was the first illness for which specific neurochemical deficits were identified in particular regions of the brain.² In the early 1960s, Birkmayer and Hornykiewicz in Vienna, and Barbeau and Sourkes in Montreal, discovered that affected sections of Parkinson's disease patients' brains were receiving insufficient quantities of the neurotransmitter dopamine.³ Dopamine cannot access the brain directly, so its natural precursor, laevodihydroxyphenylalanine (L-DOPA), was used in clinical trials. By 1967, Cotzias and colleagues⁴ had shown that, in large oral doses, L-DOPA caused dramatic improvements in the symptoms of Parkinson's disease patients. This discovery encouraged a chemical therapy for the illness and so began the era of clinical neurochemistry.

Naturally, the success in the treatment of Parkinson's disease gave rise to a frantic search for other neurological diseases that might involve dopamine deficiencies. Barbeau,⁵ who was then the Director of the Department of Neurobiology at the Clinical Research Institute of Montreal, published an article that summarized the progress of the search for other neurological illnesses that responded to L-DOPA. His paper described the effects of this precursor of dopamine in the treatment of a wide range of disorders that included Parkinson's disease, amyotrophic lateral sclerosis, Steele-Richardson-Olszewski Syndrome, mania, Wilson's disease, Pick's and Jakob-Creutzfeldt diseases, and depression. It does not seem to have been until the mid-1980s that high doses of L-DOPA were used to treat multiple sclerosis. In 1987, Berne-Fromell and colleagues,⁶ for example, described the results of a clinical trial, conducted in Linköping, Sweden, in which 300 multiple sclerosis patients were treated with L-DOPA and tri- and tetracyclic antidepressants. The results were very impressive—after only 1 or 2 months, three quarters of these patients had experienced substantial sensory, motor, and autonomic symptom improvements. Many also saw the return of functions that had been lost for several years. Clearly, multiple sclerosis patients were dopamine deficient.

The health improvements that followed after the oral correction of dopamine deficiencies in Parkinson's disease, multiple sclerosis, and some other disorders appeared almost too good to be true. They were. Then came the bad news. It became obvious that, although the initial results achieved by treating Parkinson's disease patients with L-DOPA were dramatically beneficial, a tolerance developed to the drug. This resulted in an increase in dosages over time. Before long, side effects of taking the drug, such as dyskinesias (abnormal movements), insomnia, gastrointestinal problems, hallucinations, and even psychosis began to outweigh its benefits.

A comparable picture became obvious in Encephalitis lethargica (sleepy sickness, sleeping sickness) patients. As described in his book *Awakenings* and in a film of the same name,⁷⁻⁸ Oliver Sacks began treating patients suffering from this illness with an initial daily dose of 500 mg of L-DOPA. If required, the amount given was increased gradually to 6 grams. Many patients initially dramatically improved, but then began to experience decline. Sacks' book *Awakenings* was first published in 1973. By the time the revised 1982 edition appeared, 17 of his 20 Encephalitis lethargica patients had died and the other 3 had relapsed. The main cause of these deaths was Parkinsonism.

Sacks⁹ describes the experiences of such sleeping sickness patients receiving high dose L-DOPA as follows:

For the first time, then, the patient on L-DOPA enjoys a perfection of being, an ease of movement and feeling and thought, a harmony of relation within and without. Then his happy state—his world—starts to crack, slip, break down, and crumble; he lapses from his happy state and moves toward perversion and decay.

Despite the dramatic improvements that occurred with the use of L-DOPA, in high doses, to treat Swedish multiple sclerosis patients,¹⁰ this drug was never used as a medication for the disorder. This strongly suggests that there were negative side effects, similar to those observed in Parkinson's disease and Encephalitis lethargica, in the multiple sclerosis patients that were given L-DOPA. Nevertheless, the obvious initial benefits, described by Berne-Fromell and co-workers,¹¹ seem very consistent with the evidence, presented in Chapter 4, that suggests that Parkinson's disease and multiple sclerosis involve some of the same causal variables and so have similar geographical distributions.

Two key questions are triggered by this Parkinson's disease-multiple sclerosis association. The first is, "What causes the collapse in health in Encephalitis lethargica, Parkinson's disease, and probably multiple sclerosis after the experience of the initial benefits of taking L-DOPA?" This question has been addressed in detail by Dr. Abram Hoffer and myself¹² and is discussed at length later in this book. The second key question is as follows: "Is there any causal relationship between the abnormal need for dopamine in Parkinson's disease and multiple sclerosis patients and the deficiency of iodine that both groups of patients appear to have experienced early in life?"

The answer to this second question appears to be yes. In two articles published in the mid 1980s, Overstreet and his colleagues¹³⁻¹⁴ showed that rats who were made hypothyroid by either the radioactive isotope iodine-131, or by an iodine-deficient diet, developed an abnormally high number of dopamine receptors in the striatum (a subcortical part of the brain). This shows that interfering with thyroid hormone levels, at least in rats, causes considerable behavioural and physiological alterations, including an increased concentration of dopamine receptors in parts of the brain.

Gilbert¹⁵ has argued that long exposure to a lack of iodine, seen for example in many Africans and Chinese, results in a crucial dopamine-thyroid action that slows cell timing mechanisms. Certainly, dopamine D1 and D2 receptors are consistently elevated in Parkinson's diseased striata from patients who have not been medicated pre-mortem with levodopa.¹⁶ This shows that there is an abnormal need for dopamine that is associated with the disorder and not its treatment. Interestingly, in women suffering from multiple sclerosis, the rate of relapse declines during pregnancy as dopamine levels increase.¹⁷ In contrast, pregnancy often is associated with a depressed thyroid function, which in some cases culminates in goiter.¹⁸⁻¹⁹

While, as yet, the evidence is not conclusive, it suggests that early iodine deficiency may cause abnormalities in the dopaminergic system²⁰ and so increase susceptibility, later in life, to some dopamine-related disorders, such as Parkinson's disease and multiple sclerosis. Certainly there is a link between dopamine and the thyroid since Kaptein and colleagues²¹ have shown that dopamine reduces serum Thyroid Stimulating Hormone (TSH) and aggravates low thyroxine levels in patients for whom it is prescribed.

SUMMARY

In the United States, multiple sclerosis and Parkinson's disease have very similar geographical distributions. Both diseases also seem to involve a thyroid hormone deficiency that occurred either during gestation or childhood and which appears likely to have caused neurological dopamine receptor anomalies. As a consequence, both disorders initially respond well to treatment with L-DOPA. This improvement, however, is temporary.

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*If you can look into the seeds of time,
And say which grain will grow and which will not,
Speak then to me, who neither beg nor fear
your favours nor your hate.*

Banquo. Macbeth Act 1, Scene III
William Shakespeare (1564-1616)¹

I am lucky enough to count Dr. Abram Hoffer, who introduced Dr. Linus Pauling to the health benefits of vitamin C, as a close friend. We have written articles and a book together and frequently meet for lunch or dinner. Not long ago, over an evening meal, Abram reminisced about one of his patients who had displayed muscle weakness and loss of coordination. She was depressed because a neurologist had just diagnosed her as having multiple sclerosis and predicted she would be in a wheelchair within 3 months.²⁻³ This patient was not impressed by either the neurologist's diagnostic skills or his bedside manner, so she visited Abram for a second opinion. This was quickly given. The patient was suffering from vitamin D deficiency and, after taking supplements for a few weeks, completely recovered. Interestingly, this misdiagnosis by the neurologist may be indicative of links between inadequate exposure to sunlight, vitamin D deficiency, and multiple sclerosis. It was pointed out, in Chapter 4, that in the United States, there was a strong negative correlation between skin cancer ($r=-0.61864$, $p=0.0001$) and melanoma ($r=-0.60121$, $p=0.0001$) deaths and mortality for multiple sclerosis. It is well known that skin cancer and melanoma are linked to overexposure to the sun. It seems possible, therefore, that multiple sclerosis reflects inadequate

exposure to sunlight. If this is the case, it is likely that vitamin D deficiency plays a role in the etiology of this disorder. The Bradford-Hill criteria⁴ are now applied in an attempt to see whether such a link appears scientifically feasible.

COHERENCE

The first question Hill⁵ asked of any suggested cause and effect relationship was “Does this association agree with known factors, or with the established scientific truth?” He termed this criterion coherence. The geographical analyses described in Chapter 4 suggest a strong negative correlation between mortality from multiple sclerosis and exposure to sunlight ($r=-0.60456$, $p=0.0001$) in the United States. That is, the more sunlight a state receives, the lower multiple sclerosis mortality.

Obviously, the major factor controlling sunlight is distance from the equator, that is latitude. The latitudinal variation of multiple sclerosis has been known since 1922 when first commented on by Davenport.⁶ As Grant⁷ has demonstrated, the latitudinal dependence of multiple sclerosis prevalence in the United States, in veterans of World War II and the Korean conflict, has an adjusted r^2 of 0.72. This implies that 72 percent of the variation in multiple sclerosis in such United States troops could be explained by latitude. Similarly, an ecologic Australian analysis established an r^2 value of 0.83, an even stronger link, between solar ultraviolet radiation and multiple sclerosis prevalence.⁸

How logical is it that sunlight exposure, largely regulated by latitude, could play a very significant role in the etiology of multiple sclerosis? One of the major health implications of sunlight is that it is essential for the body’s production of vitamin D, which in turn is necessary for calcium utilization.

The process by which vitamin D is formed and exerts its biological effects is complex and involves several vitamin D-related molecules.⁹ Initially, UVB light produces a change in a cholesterol-related molecule in the membranes of skin cells. The vitamin D that is created passes from the skin into the circulatory system and on to the liver. Here it is transformed into 25-hydroxyvitamin D. This precursor is then converted in the kidney and certain other tissues into the most active vitamin D metabolite called calcitrol (1,25-hydroxyvitamin D₃).¹⁰ Calcitrol is a hormone that, together with parathyroid hormone, is responsible for regulating blood calcium levels and, as a result, bone density. In this role, it is active in the intestine where it encourages the absorption of calcium, and in the bone where it catalyzes the release of calcium to restore depleted levels of this bulk element in the blood. Recent studies, however, have shown that calcitrol has other key functions, exerting numerous biological effects on diverse tissues. This implies that this sunlight-generated hormone is necessary for maintaining health throughout the body.¹¹ It would not be surprising, then, if inadequate exposure to sunlight, resulting in a deficiency of vitamin D, was involved in the etiology of multiple sclerosis. This seems even more likely since significant deficiencies of vitamin D produce symptoms that mimic, and indeed can be mistaken for, multiple sclerosis.¹²

BIOLOGICAL PLAUSIBILITY

As Hill¹³ pointed out, in trying to prove cause and effect it is also necessary to know whether a postulated relationship makes biological sense; that is, whether it is possible to elaborate the biological and biochemical links between the suspected causal variable(s) and the disease. In the present case, the question that must be asked appears to be “is it possible to sketch biological mechanisms by which a lack of adequate sunlight might

ultimately interfere with myelin production or protection?” Obviously, since sunlight deficiency reduces vitamin D levels in the body and so may interfere with calcium metabolism, it is possible that a lack of sunlight’s impact may occur through inadequacies of either, or both, of these nutrients.

Peterlik and Cross,¹⁴ for example, have pointed out one probable way in which vitamin D and calcium deficiencies may cause a malfunction of the immune system:

...the efficiency of vitamin D receptor-mediated intracellular signaling is limited by the negative effects of hypovitaminosis D on extrarenal 25-hydroxyvitamin D-1alpha-hydroxylase activity and thus on the production of 1,25-dihydroxyvitamin D(3). Calcium malnutrition eventually causes a decrease in calcium concentration in extracellular fluid compartments, resulting in organ-specific modulation of calcium-sensing receptor activity. Hence, attenuation of signal transduction from the ligand-activated vitamin D receptor and calcium-sensing receptor seems to be the prime mechanism by which calcium and vitamin D insufficiencies cause perturbation of cellular functions in bone, kidney, intestine, mammary and prostate glands, endocrine pancreas, vascular endothelium, and, importantly, in the immune system.

It will be recalled that multiple sclerosis is widely recognized as an autoimmune disease. Cantorna and Mahon¹⁵ have provided more detail on how vitamin D availability can increase or decrease the severity of such diseases.

Experimentally, vitamin D deficiency results in the increased incidence of autoimmune disease. Mechanistically, the data point to a role for vitamin D in the development of self-tolerance. The vitamin D hormone (1,25-dihydroxy vitamin D(3)) regulates T helper cell (Th1) and dendritic cell function while inducing regulatory T-cell function. The net result is a decrease in the Th1-driven autoimmune response and decreased severity of symptoms.

The literature suggests, therefore, feasible biological and biochemical links between inadequate exposure to sunlight and an associated vitamin D deficiency and autoimmune diseases, including multiple sclerosis.

THE TEMPORAL RELATIONSHIP OF THE ASSOCIATION

The principle of temporality implies that a suggested cause must occur before, or at least be simultaneous with, its effects.¹⁶ Otherwise, of course, it may simply be a symptom of the disease, rather than one of its primary triggers. In the current context, this means that if a deficit of sunlight plays any causal role in multiple sclerosis, it must occur before the disorder's symptoms appear.

There is some evidence that sunlight-related vitamin D deficiency is present at the fetal stage in those who later develop multiple sclerosis. To illustrate, a recent study¹⁷ of the birthdates of 29,000 multiple sclerosis patients in Europe and Canada, for example, concluded that children born in May had the highest risk of developing this disorder, while those with birthdays in November had the lowest risk. These researchers concluded that a mother's exposure to sunlight during pregnancy may be a significant factor in whether or not her offspring eventually develops multiple sclerosis.

Interestingly, in Finland, Soilu-Hanninen and co-workers¹⁸ measured the serum concentrations of 25-hydroxyvitamin D in 40 patients at the time they were first diagnosed with multiple sclerosis and compared them with those of 40 controls. It was found there was no difference in the serum levels of 25-hydroxyvitamin D between multiple sclerosis patients and controls when all samples, or samples obtained during winter months, were compared, but new multiple sclerosis patients had significantly

lower serum 25-hydroxyvitamin D concentrations in June to September than controls. Whether this seasonal difference is due to avoidance of the summer sun by undiagnosed multiple sclerosis patients, or an impaired ability to produce 25-hydroxyvitamin D, is unclear. Certainly, multiple sclerosis patients first diagnosed in the summer have abnormally low serum vitamin D levels. It is also clear that vitamin D deficiency is characteristic of long-term multiple sclerosis patients, where it is usually associated with low bone density.¹⁹⁻²⁰

It appears, therefore, that the available evidence tends to indicate that the low sunlight-depressed vitamin D hypothesis for multiple sclerosis meets Hill's principle of temporality.²¹

DOSE-RESPONSE CURVE

As exposure to any suspected causal agent increases, its deleterious impacts should become more extreme. If a vitamin D deficiency (due to inadequate exposure to sunlight) is involved in the etiology of multiple sclerosis, it is to be expected that this disorder would be more common in environments where latitudes are higher and sunlight exposure lower.

This certainly seems to be the case. In the 11 United States with the highest mean daily solar radiation, the average annual crude death rate from multiple sclerosis, per 100,000 population (among native born by state of birth), was 0.58 during the period 1959 to 1961.²² In contrast, in the 11 states with the lowest mean daily solar radiation, the mortality rate was 1.08. Simply put, data from the United States suggests that the death rate from multiple sclerosis is roughly 1.86 times higher in Americans born in low sunlight states, such as Washington and Vermont, than it is in those states receiving high exposure to sunlight, like Arizona and New Mexico.

A similar sunlight-multiple sclerosis gradient appears to occur in Australia. Queensland has a lower rate than do Perth or Newcastle, while Hobart, Tasmania, and South Australia have the highest prevalences, peaking at approximately 30 per 100,000 population.²³

Alter and co-workers²⁴ have demonstrated that Jewish immigrants to Israel born in central and north-east Europe have a subsequent chance of developing multiple sclerosis that is roughly six to seven times higher than those originally from Asia, North Africa, or south-west Arabia. Conversely, Hammond and co-workers²⁵ showed that British and Irish immigrants to Queensland, Australia had a 75 percent reduction in their expected risk of developing multiple sclerosis as compared with their native countrymen. Similar immigrants settling further south and exposed, therefore, to less sunlight had decreasing reductions of risk that paralleled increasing latitude. Risk reduction reached zero in the Hobart area of Tasmania. That is, settlers from the British Isles had the same risk of developing multiple sclerosis when living in Hobart as they had before they emigrated.

EXPERIMENTAL SUPPORT

For ethical reasons, one must usually rely on animal models or quasi-experimental or observational studies to examine any suspected disease causal relationships in humans. In the case of multiple sclerosis, this disorder is often modelled using autoimmune encephalomyelitis in mice.²⁶ This disorder is very similar to multiple sclerosis and can be caused in such rodents by immunizing them with myelin basic protein.²⁷ Interestingly, experimental autoimmune encephalomyelitis in mice can be completely prevented by the administration of 1,25-dihydroxy-vitamin D₃. This active form of vitamin D can also prevent the

progression of experimental autoimmune encephalomyelitis if administered when the initial symptoms appear. Withdrawal of vitamin D₃ results in a resumption of the disorder's progression. In short, 1-25-dihydroxyvitamin D₃ can prevent the development of the disorder that is normally used as an animal model of multiple sclerosis. This strongly suggests, therefore, that vitamin D deficiency, usually caused by a lack of adequate sunlight, plays a significant causal role in multiple sclerosis.²⁸

It is well known that female multiple sclerosis patients suffer from vitamin D deficiency and reduced bone mass, thus increasing their risk of developing multiple sclerosis.²⁹ By giving a group of young multiple sclerosis patients dietary supplements of calcium, magnesium, and vitamin D for 1 or 2 years, Goldberg and co-workers³⁰ showed that this combination slowed disease progression. Indeed, the number of exacerbations experienced by patients while taking the supplements was less than half that expected from their case histories. This, then, was an experimental study that successfully tested the value of not just vitamin D, but also calcium and magnesium, as a treatment for multiple sclerosis.

Munger and co-workers³¹ pooled data from the Nurses' Health Study I and II, collected from some 180,000 women. They found that the intake of vitamin D from supplements was inversely associated with multiple sclerosis risk. To illustrate, those nurses taking 400 or more International Units of vitamin D daily had a relative risk of developing multiple sclerosis of 0.59 ($p = 0.006$) when compared with nurses who did not take supplements of this vitamin. Interestingly, these researchers found no such association between vitamin D obtained from food and multiple sclerosis.

While it is clear that experimental evidence is accumulating rapidly that sunlight and, therefore, vitamin D plays a key role

in the etiology of multiple sclerosis, a large scale clinical trial to further establish these relationships would still be of value.

CONSISTENCY OF ASSOCIATION

A suspected cause should be linked to a disease in many different populations, places, circumstances, and times.³² Since exposure to the ultraviolet B light needed to create vitamin D in the skin varies with the seasons, latitude, and altitude, one would expect that multiple sclerosis risk should also fluctuate in a similar way. That is, if sunlight really plays a causal role in multiple sclerosis then this disorder should also show seasonal, latitudinal, and altitudinal variations.

There is considerable evidence to suggest that it does show these variations. Bharanidharan,³³ for example, has shown that in Budapest, Hungary, multiple sclerosis patients have birthdates that peak in April and October. A more recent, much larger study,³⁴ involving 42,045 individuals with multiple sclerosis from Sweden, Denmark, England, Scotland, and Canada, suggested that such patients were most likely to have been born in May and least likely to have a November birthdate. This, of course, is consistent with a mother's exposure to sunlight during pregnancy, having a significant impact on her infant's risk of subsequently developing multiple sclerosis.

As previously described, in Caucasians multiple sclerosis prevalence also rises with latitude and, therefore, exposure to sunlight. Kurland and co-workers,³⁵ for example, have shown that in North America this disorder is six times as common in the urban north than in cities of the south. Similarly, Hammond and colleagues³⁶ have established that in Australia multiple sclerosis risk increases with latitude. This latitudinal variation appears global,³⁷ with multiple sclerosis being commonest

in Caucasians in central north-east and north-west Europe, that is at latitudes of some 45 to 50°N. Conversely, it is least common in equatorial regions.

It seems that the apparent link between multiple sclerosis and exposure to sunlight also can explain two peculiar geographic anomalies.³⁸ In Switzerland, as might be expected, multiple sclerosis is more common at low altitudes than at higher elevations. This seems to be due to the fact that ultraviolet light intensity, because of the thinner atmosphere, is greater at higher altitudes. As a result, the vitamin D₃ synthetic rate is increased. People living at higher altitudes in Switzerland produce more vitamin D, therefore, than their lowland countrymen and so suffer less multiple sclerosis. Multiple sclerosis is less common, however, in Norwegian coastal settlements than in the interior.³⁹ This appears to be because fish consumption, and as a result, vitamin D intake, is much higher in communities situated along Norway's coasts.

STRENGTH OF ASSOCIATION

Causality is more likely if the relationship between the expected cause and health effect is high. In the case of sunlight and the prevalence of multiple sclerosis there is good evidence that the negative association between the two is quite strong. To illustrate, Kurland and co-workers⁴⁰ have shown that, in Canada and in the United States, northern cities, such as Rochester, Minnesota; Missoula, Montana; and Kingston, Ontario, have multiple sclerosis prevalence rates roughly six times as high as southern cities, such as Houston, Texas; New Orleans, Louisiana; and Charleston, South Carolina. It would seem, therefore, that sunlight exposure is quite strongly protective against multiple sclerosis, especially since similar relation risk has been shown by Alter and colleagues⁴¹ at the global scale.

SPECIFICITY OF THE ASSOCIATION

In his original publication, Hill⁴² argued that a particular type of exposure should only cause one specific disease, perhaps even at one unique site. This criterion had been in large part rejected⁴³ because it is already known that many disease-producing variables cause several different adverse health effects. This is true of iodine and selenium deficiencies⁴⁴⁻⁴⁵ and is obviously true of inadequate exposure to sunlight. Whether or not an inability to manufacture adequate vitamin D due to a lack of ultraviolet radiation exposure plays a significant role in multiple sclerosis, this inability certainly is very important in the etiologies of both the bone disorder rickets⁴⁶ and the seasonal depression known as SAD (Seasonal Affective Disorder).⁴⁷ Inadequate exposure to sunlight, therefore, cannot be linked to only one disorder.

ANALOGY

The last of Hill's⁴⁸ criterion for establishing cause and effect is analogy. This can never produce conclusive evidence, but can stimulate the generation of hypotheses that can subsequently be tested further. To illustrate, in the United States⁴⁹ there are strong negative correlations between mortality for multiple sclerosis and both skin cancer ($r = -0.60121$, $p = 0.0001$) (Figure 2) and melanoma ($r = 0.60121$, $p = 0.0001$). Interestingly, Goldacre and co-workers⁵⁰ have been able to demonstrate that, in the Oxford Region of the National Health Service, England, skin cancer occurred at only approximately half the rate in patients with multiple sclerosis as it did in a control group with other autoimmune or neurological diseases. This inverse relationship clearly suggests that multiple sclerosis patients tend to have reduced exposure to the sun, so avoiding skin cancer.

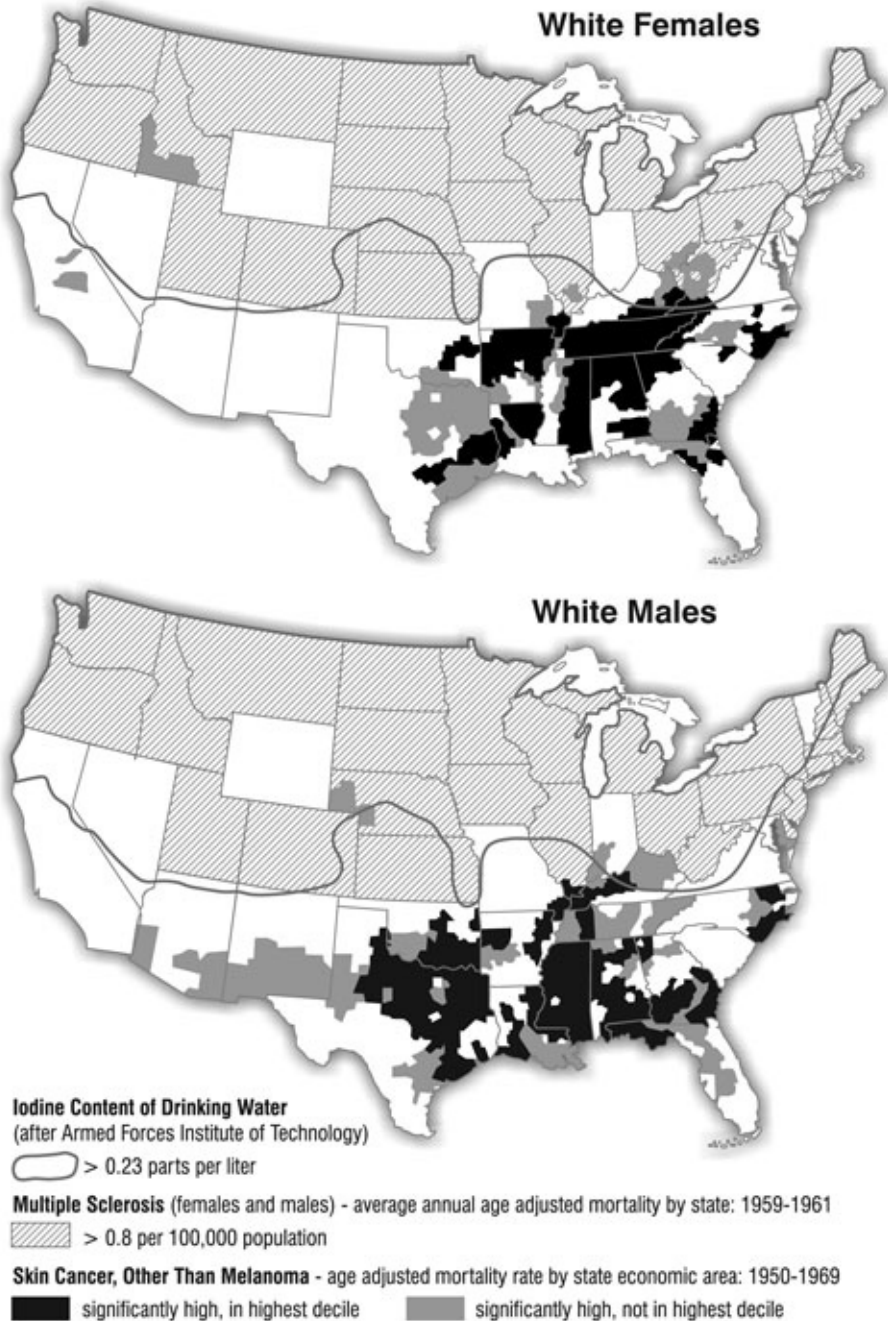


Figure 1: Relationships Between Multiple Sclerosis and Iodine Content of Drinking Water and Skin Cancer, Other Than Melanoma, in Both White Females and Males in the United States⁵¹

Further confirmation of this negative relationship between multiple sclerosis and non-melanoma skin cancer has been provided by Freedman and colleagues,⁵² who abstracted mortality data on these two illnesses from death certificates of 24 states of the United States, for the period 1984 and 1995. These researchers were able to show that those with the highest levels of both residential and occupational exposure to sunlight had the lowest risk of having died from multiple sclerosis (odds ratio = 0.24). Conversely, such people had an abnormally high risk of death from skin cancer (odds ratio = 1.38). Simply put, in the high sunlight states of the United States, those who work outdoors are unlikely to die of multiple sclerosis, but are at greater than normal risk of dying from non-melanoma skin cancer. Interestingly, Parkinson's disease patients, like those with multiple sclerosis, are at higher risk of both vitamin D deficiency and osteoporosis.⁵³

SUMMARY

There is convincing evidence that multiple sclerosis involves a vitamin D deficiency. The only Bradford-Hill criterion that is not met by this hypothesis is that of specificity of association. However, this particular criterion appears to be invalid and can be safely ignored.

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ANOMALIES - TERMITES IN THE FOUNDATION

He who does not know food, how can he understand the diseases of man?

Hippocrates (460-357 BC)

As I wrote in *What Really Causes AIDS*, scientific theories resemble architectural wonders.¹ They are interesting to visit and prestigious to be associated with. All too often, however, while they appear structurally sound to casual observation, termites are feasting deep within their foundations. Anomalies, facts that the ruling theory and its supporters cannot explain, are the termites of science. As they multiply, the infested theory weakens until eventually it collapses.

In the current book, I am not attempting to highlight anomalies in the conventional wisdom and so hasten the collapse of a current, erroneous hypothesis. Sadly, there is no hypothesis supported by conventional medicine that offers much hope to anyone afflicted by multiple sclerosis. Rather, the role I am attempting to play is that of a pioneering architect, sifting through potential building materials and trying to visualize what a new hypothesis, explaining the etiology of multiple sclerosis, should look like. Experience warns me that I must try to design an intellectual structure that is as termite free as possible, that is one not plagued by any obvious anomalies.

It will be recalled that there are three global zones of multiple sclerosis prevalence. The disorder is most common in a belt

that includes northern and central Europe into the former USSR, southern Canada, and the northern United States.² There is also a similar high risk belt in the Southern Hemisphere, encompassing southeast Australia and New Zealand. In these regions, multiple sclerosis prevalence rates are generally 30 or higher per 100,000. Below and adjacent to these belts are more moderate zones, with multiple sclerosis prevalence rates of between 5 and 29 per 100,000. These intermediate zones include the southern United States, the entire Mediterranean basin from Spain to Israel, and that part of the former USSR that stretches from the Urals into Siberia and the Ukraine. In the Southern Hemisphere, this intermediate risk zone includes the Whites in South Africa and, perhaps, central South America and Australia, excluding its southeast. Elsewhere, in places like China, Japan, Korea, Africa, the Caribbean, and Mexico, there is a third belt of minimum risk that has a multiple sclerosis prevalence rate below 5 per 100,000 population.

The evidence presented in the preceding four chapters suggests that multiple sclerosis occurs in those who, at some time during their gestation or childhood, suffered from thyroid hormone deficiencies, which in turn caused dopamine receptor anomalies and an abnormal need for dopamine. Beyond this, there is convincing evidence that multiple sclerosis involves an inadequate exposure to sunlight, with its associated deficiencies of both vitamin D and calcium.

It would appear relatively simple, therefore, to explain the major global belts of multiple sclerosis prevalence. They seem to reflect the availability of iodine and sunlight, the drivers that seem to control thyroid hormone and dopamine imbalances and vitamin D and calcium deficiencies. However, there is one serious weakness with this hypothesis. Why do iodine and vitamin D deficiencies only result in multiple sclerosis in

Caucasians, and not in those of Oriental or African descent? Logically, there must be one or more causal variable(s) missing from the preceding analysis that controls whether iodine and sunlight inadequacies result in subsequent multiple sclerosis. The key to identifying this variable appears to come from the work of Keen and Ekoe,³ who show that the global distribution of multiple sclerosis is very similar to that of another autoimmune disease, diabetes mellitus type 1, a form of diabetes that first occurs in childhood and requires the virtual lifelong use of insulin to survive.

Indeed, while multiple sclerosis and type 1 diabetes mellitus (juvenile) are completely different clinically, they are both autoimmune disorders that have almost identical geographical and ethnic distributions, show genetic similarities, and probably share one or more environmental triggers. Dosch and co-workers⁴ discovered that there is a high degree of similarity in the autoimmunity seen in diabetes mellitus and multiple sclerosis. Indeed, a widely used mouse model for diabetes can also develop a disease that is very similar to multiple sclerosis.⁵⁻⁶

To quote a *ScienceDaily* interview⁷ with Dosch:

Much to our surprise, we found that immunologically, type 1 diabetes and multiple sclerosis are almost the same – in a test tube you can barely tell the two diseases apart,” said Dr. Dosch, the study’s principal investigator, a senior scientist in the HSC Research Institute, and a professor of Paediatrics and Immunology at the University of Toronto (U of T). “We found that the autoimmunity was not specific to the organ system affected by the disease. Previously, it was thought that in MS autoimmunity would develop in the central nervous system, and in diabetes it would only be found in the pancreas. We found that both tissues are targeted in each disease.

DIABETES MELLITUS TYPE 1 AND COW'S MILK

Logically, if multiple sclerosis and diabetes mellitus type 1 have very similar global distribution patterns and are immunologically comparable, they are likely to have at least one significant causal variable in common. This common variable appears to have been established, in 1992, by Karjalainen and co-workers.⁸ These researchers collected blood samples from 79 healthy Finnish children and 142 who had developed insulin-dependent diabetes mellitus. Using immunoassays and Western blot analysis, they then measured blood antibody levels against an incompletely digested cow's milk protein known as bovin serum albumin. They found that the blood of every one of the diabetic children had elevated antibodies against bovin serum albumin, that is their levels were higher than 3.55. In contrast, every one of the 79 healthy children had blood levels below this figure.

As Campbell⁹ points out in *The China Study*, there was absolutely no overlap between levels of antibodies of healthy and diabetic children. This probably implies two things. Firstly, children with more antibodies consumed more milk from cows. Secondly, it seems likely that the antibodies against the incompletely digested protein bovin serum albumin had triggered diabetes mellitus type 1.

This study set off an avalanche of new and reinterpreted research that now suggests that infants, or very young children, with a particular genetic imbalance,¹⁰⁻¹¹ who were weaned from the breast at an early age¹² using cow's milk, and who were perhaps infected by a virus that damages the immune system of the gut,¹³ have a very high risk of developing diabetes mellitus type 1. Together with research conducted in France,¹⁴ evidence strongly suggests that genetically susceptible children, fed cow's milk as infants, are at a much greater risk of developing type 1

diabetes. What is important to the current discussion is that, regardless of genetics, exposure to cow's milk seems to be essential if a child is to subsequently develop diabetes mellitus type 1. Since, as Keen and Ekoe¹⁵ have pointed out, multiple sclerosis and diabetes mellitus type 1 have very similar global distribution patterns, it appears likely that cow's milk plays a key causal role in both disorders.

MULTIPLE SCLEROSIS AND COW'S MILK

Keen and Ekoe¹⁶ were by no means the first researchers to suggest that the etiology of multiple sclerosis involved the consumption of cow's milk. In 1979, for example, Agranoff and Goldberg¹⁷ pointed out that, at the state scale in the United States, the correlation between individual milk consumption and multiple sclerosis mortality was a highly significant 0.82. Similarly, in 1976, Dip¹⁸ emphasized a strong positive correlation between the global consumption of dairy products and the incidence of multiple sclerosis.

This relationship was reconfirmed, in 1992, by Malosse and co-workers,¹⁹ who demonstrated a striking positive correlation between multiple sclerosis prevalence and milk consumption in 26 populations in 24 countries.

Swank and Pullen,²⁰ in 1977, also pointed out that, in Europe, multiple sclerosis was much more common in the "beer-but-ter" cultures than those stressing "wine and olive oil." Even within individual countries, multiple sclerosis incidence seems to be elevated in dairying areas. In Norway, for example, Swank and colleagues,²¹ in 1952, established that multiple sclerosis was far less common in coastal fishing regions than in interior agricultural communities. This may, of course, be due in part to the high levels of vitamin D in fish. Interestingly, multiple

sclerosis and type 1 diabetes have been shown also to coexist in many of the same people, indicating similar risk factors.²²⁻²³

Warren²⁴ has suggested that the link between cow's milk consumption and multiple sclerosis may be limited to cattle raised on iodine deficient pastures. He argued that a lack of iodine in soil deprives such cattle of the ability to produce the thyroid hormone thyroxin, which is essential for the conversion of the carotene in their diet to vitamin A. As a consequence, newborn infants and very young children fed on milk from cattle raised on iodine deficient fodder may suffer from a vitamin A deficiency long before they are likely to be exposed to iodized salt. Warren²⁵ postulated that such a vitamin A deficiency may be the root cause of multiple sclerosis because it is linked to significant oxidative stress.

There might be other ways, of course, that cow's milk may help to trigger multiple sclerosis. Swank,²⁶ in 1950, argued that saturated fats (animal and butterfats) play a significant causal role in the disorder. This viewpoint has been recently supported by Campbell and coauthor²⁷ in their extremely informative book *The China Study*, an examination of the Chinese diet and health.

There can be no doubt that weaning infants on to cow's milk has an enormous number of implications. As described by Tierno²⁸ in *The Secret Life of Germs*, the feces of babies fed with cow's milk or formulas smell much stronger than those of breast-fed infants. This seems to be because cow's milk contains more than twice the protein of breast milk and is also more calcium enriched. These nutrients cause infants that are fed cow's milk to produce more feces than breast-fed infants, while growing bacteria in their intestinal tracts that are more adultlike. The result is a stronger smell and additional bacteria in their intestinal tracts, including *Bacteroids* and *Clostridium*, more

typically found in the normal adult flora. In contrast, the guts of breast-fed infants are more often colonized by *Bifidobacteria*, a beneficial anaerobic bacterial associated with a more pleasant odour. The health implications of altering the intestinal flora and fauna of infants that are fed cow's milk are unclear.

LACTOSE INTOLERANCE

Lactose intolerance seems to be one of the major reasons that many societies do not drink cow's milk. This health problem involves an inability to digest significant amounts of lactose, the dominant sugar in cow's milk.²⁹ This inability is caused by inadequate amounts of the enzyme lactase, which is produced normally by cells that line the small intestine walls. Lactase normally breaks down lactose into less complex, more easily absorbed substances. In those who cannot produce normal quantities of this enzyme, an intolerance to lactose occurs. As a result, about 30 minutes to 2 hours after eating dairy products rich in lactose, such people begin to suffer from symptoms such as nausea, cramps, bloating, gas, and diarrhea.

Peltonen and co-workers³⁰ studied nine extended Finnish families and Germans, Italians, and South Koreans who suffered from lactose intolerance. They discovered that this inability to digest the dominant sugar in cow's milk was linked to two genetic variations. One of these single nucleotide polymorphisms was seen in 236 of the lactose intolerant people who were studied, the other occurred in 229 of them. Both of these single nucleotide polymorphisms occur near the lactose encoding gene and are thought to affect proteins that regulate that gene's expression.³¹

The single nucleotide polymorphisms that result in lactose intolerance and the resulting inability to digest dairy products

are not randomly distributed.³² While only about 5 percent of Caucasians suffer from lactose intolerance, it occurs in as many as 75 percent of all African Americans and American Indians and 90 percent of Asian Americans. It is not surprising, therefore, that in Asia, Africa, and South America relatively little cow's milk is consumed and that many cultures have evolved that avoid dairy products.

SUMMARY

Cow's milk probably triggers at least two major autoimmune diseases, those being mellitus type 1 and multiple sclerosis. However, Asians, Africans, and many aboriginal societies suffer high rates of lactose intolerance and drink little cow's milk, thus avoiding lactose disorders. As a consequence, the global zones of high multiple sclerosis prevalence do not pass into Asia or Africa and are limited to countries where the population is predominantly Caucasian.

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We should be paying more attention to the exceptional patients, those who get well unexpectedly, instead of staring bleakly at all those who die in the usual pattern. In the words of René Dubos, “Sometimes the most measurable drives out the most important.”

B.S. Siegel (1986)

NOTHING SUCCEEDS LIKE SUCCESS

Nothing will benefit human health and increase the chances for survival of life on Earth as much as the evolution of a vegetarian diet.

Albert Einstein¹

If iodine, vitamin D, and calcium deficiencies and cow's milk play significant roles in the development of multiple sclerosis, then diet ought to be of prime importance in the treatment of this disorder. The United States National Multiple Sclerosis Society does not think so. Their website² points out that:

While many different diets have been proposed as a treatment, or even a cure, for the signs and symptoms of MS, evidence of effectiveness is very limited. There is some evidence that a diet low in saturated fats and supplemented by Omega-3 (from sunflower or safflower seed oil and possibly evening primrose oil) may have some benefit for people with MS. Most of the diets that have been touted as helping people with MS have not been subjected to rigorous, controlled studies, and the few that have been evaluated have produced mixed results. Most of the claims made for dietary treatments are based on personal accounts, and the reported benefits may have been spontaneous changes that would have happened without any treatment.

This official overview seems very questionable, so the following chapter reviews the alternative evidence for a significant role for the dietary treatment of multiple sclerosis.

GOLDBERT, FLEMING, AND PICARD: SUPPLEMENTS

In 1986, Goldberg and colleagues³ asked 16 young multiple sclerosis patients (6 males, 10 females) to take part in a 2 year nutritional supplement trial. Participants received calcium and magnesium in the form of dolomite tablets which provided 10 mg of magnesium and 16 mg of calcium per kilogram of body weight on a daily basis. Vitamin D, which encourages the absorption of these two minerals, was taken as cod liver oil, at a rate of 5,000 IU daily, roughly 20 grams of oil each day.

This trial was designed to involve self-pairing, that is the response of each patient to these nutrients was compared with his or her own previous case history. The number of exacerbations (declines in neurological abilities) seen in the period when the patients were taking calcium, magnesium, and vitamin D was less than half that expected from their case histories. There were no apparent supplement-related negative side effects. To quote the authors:

The dietary regiment may offer a new means of controlling the exacerbation rate in MS, at least for younger patients. The results tend to support a theory of MS which states that calcium and magnesium are important in the development, structure and stability of myelin.

There is a wealth of literature, reviewed in Chapter 7, indicating that shortages of vitamin D and calcium appear to promote the neurological decline seen in multiple sclerosis. It seems obvious, therefore, that high dose calcium, magnesium, and vitamin D should be given to patients diagnosed with this disorder.

H.T.R. MOUNT: DEMYELINATION REVERSAL

In 1943, Dr. H.T.R. Mount,⁴ a Canadian physician, began a small therapeutic trial that eventually involved 14 multiple sclerosis patients with a clear history of neurological deficits. Mount believed that the demyelination seen in such patients was of nutritional origin and that it occurred because of both a vitamin B₁ deficiency and a lack of one or more substances always present in liver extract. To test this hypothesis, the patients were initially given 150 mg of intravenous vitamin B₁ and 1 millilitre of intramuscularly injected liver extract. These treatments were administered 10 times, at intervals of 7 to 10 days, and were then continued as deemed necessary. Dr. Mount's patients were followed up for periods that varied from several months to 29 years. It was discovered that none of them had seen any progression of their illness while on the treatment. When multiple sclerosis symptoms recurred, because a patient's treatment had stopped, they were controlled by resumption of therapy. Interestingly, when one patient temporarily became allergic to liver extract and was given vitamin B₁₂ instead, her symptoms worsened. Following desensitization to liver extract, when normal treatment could resume, she again improved. Mount found that taking vitamin B₁ orally also did not work, suggesting that some people may not adequately absorb this vitamin through their gastrointestinal tracts.

Mount⁵ also found that recently diagnosed multiple sclerosis patients recovered much more quickly than those with more advanced symptoms of the disorder. In summary, between 1943 and 1973, Mount treated 14 multiple sclerosis patients for periods ranging from a few months to 30 years. Some of those were more conscientious than others in returning for their intravenous and intramuscular injections. Nevertheless,

patients' estimates of improvement were all positive, ranging from 98 to 40 percent, with a mean of 76 percent. It should be pointed out that most multiple sclerosis patients receiving conventional treatment for similar time periods would have experienced a decline in health.

Very reasonably, at the end of his 1973 *Canadian Medicine Association Journal* publication, Mount wrote"

My experience suggests that some factor or factors in liver extract, associated with vitamin B₁, can induce remyelination in patients suffering from multiple sclerosis and probably in other cases of demyelinating diseases. It is suggested that this clinical finding should now be subjected to detailed laboratory studies in order to enlarge its use or to circumscribe its limitations.

Unfortunately, this has never happened.

F.R. KLENNER'S PROTOCOL

Dr. F.R. Klenner,⁷ a physician from Reidsville, North Carolina, was another doctor who, in the 1940s, began giving multiple sclerosis patients high doses of vitamin B₁ and liver extract injections. While Mount⁸ considered paralysis was a contraindication for such therapy, Klenner⁹ began treating multiple sclerosis patients with paralysis intensively and successfully. His protocol involved very high doses of vitamins A, C, and E, together with all the B vitamins, choline, calcium, magnesium, and glycine, as well as high dose vitamin B₁ and liver extract injections. Even Abram Hoffer,¹⁰ an orthomolecular pioneer, considers that "It requires heroic dedication to take all the vitamins required [by the Klenner approach] orally and by injection, but some are able to do so and profit."

One of Klenner's greatest supporters, a recovered multiple sclerosis patient, Dale Humpherys¹¹ describes the therapy and his own results with it:

I have followed this protocol for over 25 years. Following two severe attacks of MS in 1973 I could walk only a short distance and was forced to discontinue working – my doctors said I would be in a wheelchair soon. After beginning treatment with Dr. Klenner I was able to return to work within 6 months, but it was 2 years before I became symptom-free. I have enjoyed excellent health since.

The protocol of Dr. Klenner's I have followed consists of: (1) a daily intramuscular injection of vitamin B₁ of 300 to 400 mg. The correct dosage can be determined by the level of fatigue the patient experiences. Some patients require 300 to 400 mg daily to experience relief of fatigue symptoms. The B₁ is available in a strength of 200 mg per ml. So a 200 mg injection would be 1cc. Twice weekly 1cc of liver extract is added to the B₁ injection so extra injections aren't needed. The B₁ injectable comes in a 30cc bottle and lasts for two to four weeks. The liver extract comes in a 10cc vial and lasts 5 weeks. The syringe is a 25 gauge by five-eighths inch 3cc syringe. Note: B₁ is not well absorbed in oral form – the daily injection is required for life for successful treatment and recovery.

Oral Vitamin Regimen. 1.5 grams daily in divided doses of Calcium Ascorbate (buffered Vitamin C) which is available in 500 mg tablets. This boosts the immune system and eliminates or shortens recovery time from colds and flu. (2) Vitamin E 400 to 1000 IU daily. (3) B-100 tablet. This tablet contains 100 mg of all of the B vitamins. (4) B₁₂ - One tablet (sublingual - dissolved under the tongue) daily. One to 2 mg strength. (5) Niacin. Once or twice weekly, 100 to 300 mg before breakfast. This is a vasodilator and opens the blood vessels allowing the nutrients to rebuild the myelin sheath damaged by MS. This will produce a flush and reddening of the skin for about 30 minutes, which most patients say they enjoy. It is advisable to lie down and cover up for the period of the flush.

Diet. A high protein diet is required to rebuild the myelin sheath. Examples: Breakfast - 1 or 2 eggs poached, with fruit and cereal. Lunch - fish and vegetables (steamed) and fruit. Supper - chicken or beef with vegetables and fruit. Soy, cheese and dairy products are a good source of protein if well tolerated. One 500 mg digestive enzyme tablet taken with each meal can often improve digestion and absorption.

The Victorian, Victoria, British Columbia, January 26, 1976 ran a story under the headline “Group of five beat multiple sclerosis.” These patients included a wheelchair-bound woman who, after following the Klenner protocol, could again dance.¹² Numerous other multiple sclerosis patients continue to use the Klenner approach.¹³

Interestingly, Klenner¹⁴ believed that multiple sclerosis had a viral cause, and that the virus in question damaged the cells of the central nervous system, rendering them incapable of retaining adequate vitamin B₁. As a consequence, the myelin sheath deteriorated, resulting in eventual paralysis. Regardless of whether this hypothesis is correct, it is interesting to note that Klenner’s protocol involves a combination of the mineral supplement provided by Goldberg and colleagues¹⁵ and the high vitamin B₁ and liver extract approach advocated by Mount.¹⁶

THE SWANK DIET

I stand in awe of Dr. Roy L. Swank’s¹⁷ conscientious scientific research into potential connections between diet and multiple sclerosis. In 1950, Swank¹⁸ decided that there might be a link between the increasing consumption of saturated animal fats and the rising incidence of multiple sclerosis. To test this hypothesis, 144 multiple sclerosis patients from the Montreal

Neurologic Hospital were selected for a nutritional trial. These patients had mildly impaired performance but could still walk, although when tired their ability to do so was impaired. They were largely still employed, but sometimes experienced fatigue, periodic exhaustion, and slight memory loss. Trial patients typically had been diagnosed with multiple sclerosis for 6 years and were between 30 and 42 years of age.

All 144 patients agreed to eat a low fat diet, designed by Swank and his colleagues. In 1950, their daily saturated fat intake was limited to 30 grams per patient. Late in 1951, saturated animal fat was further limited to no more than 10 to 15 grams daily, while fish and unsaturated vegetable oils were restricted to 20 to 40 grams. Patients also were given a multiple vitamin tablet and additional capsules of vitamin A and D.

Swank¹⁹ has been tracking the impact of this low fat diet on survivors of this group of 144 multiple sclerosis patients for some 50 years. His last published paper on the topic, that I am aware of, was co-authored with James Goodwin and appeared in *Nutrition* in 2003. Of course, some patients have been more conscientious in following this low fat diet than others. Swank divided them into two groups. The first group consisted of 70 patients who adhered strictly to the low fat diet and consumed less than 20 grams per day of saturated fat, who he termed the “good dieters.” The remaining 74 patients, called “poor dieters,” consumed an average of 38.0 ± 18.0 grams per day.

After attempting to follow this low fat diet for 34 years, there had been a total of 23 deaths among the 70 “good dieters,” with only 14 of these being due to multiple sclerosis. In contrast, 58 of the 74 “poor dieters” were dead, 45 from multiple sclerosis-related causes. Simply put, 67 percent of those who had strictly followed the low fat diet for 34 years were still alive, but this figure fell to 21 percent among “poor dieters.”

Swank²⁰ continued to follow the progress of the survivors, and in 2000 he was able to visit, observe, evaluate, and question 15 of them, who by then ranged in age from 72 to 84 years. Thirteen of the patients could still walk and were normal in all respects, being active, able to care for themselves, and mentally alert. The remaining two patients could still walk with assistance.

In the 2003 *Nutrition* article, Swank and Goodwin²¹ conclude that

This study indicated that, in all probability, MS is caused largely by consumption of saturated animal fat. This study also indicated that patients with MS, if they rigorously follow the extremely low-fat diet proposed by Swank, which contains no more than 10 to 15 g/d of saturated fat, can expect to survive and be ambulant and otherwise normal to an advanced age.

Although the United States National Multiple Sclerosis Society²² is unwilling to accept these conclusions, many patients now follow the Swank diet.²³ Known as Swankers,²⁴ they have their own Foundation and website. The latter provides dietary rules and recipes together with personal stories of recovery and hints for new multiple sclerosis patients wishing to begin the Swank protocol. Clearly, although the oldtimers are dying off, a new and probably far larger generation is replacing them.

Lipids form the majority of the myelin sheath and, as a consequence, many researchers have studied their potential roles in multiple sclerosis. Navarro and Segura,²⁵ for example, studied the plasma lipid profiles of 61 multiple sclerosis patients and a group of matched controls. They discovered that, in multiple sclerosis patients, levels of linoleic and arachidonic acids were depressed and saturated fats elevated. These plasma fatty acid

abnormalities correlated positively with the duration of the disease and the degree of disability. Beyond these polyunsaturated fat deficiencies, antioxidant inadequacies and decreased cellular antioxidant defence mechanisms have been recorded in multiple sclerosis.²⁶ It has also been shown that antioxidant and polyunsaturated fat supplements can reduce the clinical signs of allergic encephalomyelitis, the animal model of multiple sclerosis.²⁷ As a result, diets like Swank's that are low in saturated fats and elevated in polyunsaturated fats are gaining more widespread support.²⁸⁻²⁹

MACDOUGALL, SHATIN, AND GLUTEN-FREE DIETS

Professor Roger MacDougall,³⁰ a famous British playwright, was diagnosed with multiple sclerosis at the National Hospital for Nervous Diseases in London in 1953. Within a few years he was unable to use his legs, eyes, and fingers, and even his voice was affected. He could not stand erect for even a few seconds. Yet some 25 years later he could again run up and down stairs and lead a life as active as most men his age. MacDougall believed that he was in remission because of a diet that he had designed for himself which was based upon the food consumed by the hunter-gatherers, before mankind settled down in agricultural communities and grew cereals and tended cattle. Specifically, he believed that the dietary approach to degenerative conditions, like multiple sclerosis, should have a five-prong attack. MacDougall's³¹ diet contained no gluten or dairy, no foods to which he was allergic, low sugar, low animal fats but high unsaturated fats, and vitamin and mineral supplements. The latter included vitamins B₁, B₂, B₆, and B₁₂, vitamin C, vitamin E, calcium, magnesium, folic acid, nicotinamide, and lecithin from flax. MacDougall cut out gluten from his diet by avoiding the use of wheat, barley, oats, and rye and any processed foods containing these grains.

In 1965, Dr. R. Shatin³² published a short article in the *British Medical Journal* linking gluten to multiple sclerosis. He believed that there was an inherited susceptibility to multiple sclerosis that resulted in a primary lesion in the small intestine, and that demyelination was a secondary symptom of this process. Shatin felt that the Global Belts of multiple sclerosis reflected the consumption of wheat and other grains containing gluten.

There appears to be some evidence supporting MacDougall and Shatin's belief that gluten plays a role in multiple sclerosis. Many multiple sclerosis patients have structural and functional irregularities in their digestive tracts. Cook and co-workers,³³ for example, have reported the presence of measles virus protein and alteration of normal immunoglobulin ratios in the jejunum. These abnormalities seem linked to excess fat and undigested meat fibres in the stools of about 40 percent of multiple sclerosis patients. Gupta and colleagues³⁴ also established malabsorption of vitamin B₁₂ by 12 percent of the 55 multiple sclerosis patients that they had studied. Also relevant to the gluten hypothesis is the more recent work by Reichelt and Jensen,³⁵ who found that IgA antibodies against gluten occurred far more often than expected in the serum of people with multiple sclerosis. This is not surprising if Braly and Huggan³⁶ are correct, and 25 percent of multiple sclerosis patients have increased intestinal permeability that allows gluten proteins to leak into their bloodstreams.

DAVID DERRY'S THYROID PROTOCOL

It was noticed by Uthoff,³⁷ in 1890, that the symptoms of multiple sclerosis patients worsened after they had exercised. It was discovered later that this phenomenon was related to the rise of body temperature that accompanied such exertion.

These observations eventually led to the “hot bath test,” which began to be used as the principal diagnostic tool for multiple sclerosis in the 1950s. Uhthoff’s Phenomenon was the key to identifying multiple sclerosis until the 1980s, when safer and more accurate methods replaced it.

Despite its widespread use as a diagnostic tool, there has never been any consensus over the cause of Uhthoff’s Phenomenon.³⁸ Hypotheses attempting to explain why body heat temporarily worsens multiple sclerosis symptoms have included the direct impact of higher temperature, effects of serum calcium, circulatory changes, heat shock proteins, and the blockade of ion channels.

It is certainly true that heat plays a significant role in how those with multiple sclerosis feel, and that it can worsen their symptoms. As a result, some may wear cooling vests during the summer. Interestingly, given the apparent link between deficiencies in vitamin D and calcium and the progression of multiple sclerosis,³⁹ the avoidance of sunlight may trigger a positive-feedback system in the disorder. That is, patients with multiple sclerosis who avoid sunlight because higher body temperatures worsen the symptoms may unfortunately develop vitamin D deficiencies that exacerbate the progression of their disorder.

Body temperature is highly correlated with thyroid function⁴⁰ and it is at least possible that Uhthoff’s Phenomenon reflects an iodine imbalance in multiple sclerosis patients. One person who felt that this disorder involved such an iodine deficiency was Dr. David Derry, a physician from Victoria, British Columbia. Derry believed that the TSH test, used to monitor thyroid hormone levels in the body, was of little value since it showed no correlation with clinical presentation, that is with how people felt. Derry⁴¹ believed that many patients who were

within the normal TSH test range were still profoundly hypothyroid. As a result, he used levothyroxine and/or desiccated thyroid to treat a wide range of diseases, including breast cancer, chronic fatigue, fibromyalgia, and multiple sclerosis.

His willingness to speak out and criticize the medical establishment eventually resulted in serious repercussions for Dr. Derry.⁴² Although he developed an international reputation, and patients travelled from all over North America to see him, his medical license was suspended by the College of Physicians and Surgeons of British Columbia in June, 2002. In the debate that preceded this suspension, numerous patients, including some with multiple sclerosis, claimed to have been greatly helped by levothyroxine and/or desiccated thyroid prescribed by Dr. Derry.

SUMMARY

There is a considerable amount of evidence indicating that the course of multiple sclerosis can be greatly altered by personal dietary choice. As Goldberg and colleagues⁴³ demonstrated, supplements of vitamin D, calcium, and magnesium can reduce the number of exacerbations. Mount⁴⁴ and Klenner⁴⁵ also clearly demonstrated that intravenous vitamin B₁ and intramuscularly injected liver extract can reverse many multiple sclerosis symptoms. Beyond this, 50 years of evidence from patients following the Swank⁴⁶ diet, which is very low in saturated fats, shows that it can greatly prolong life and increase mobility in those who are willing to follow it. Avoiding gluten⁴⁷ also appears beneficial for some multiple sclerosis patients, as may be the use of desiccated thyroid.⁴⁸

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Natural laws have no pity.

Robert Heinlein

SO WHAT REALLY CAUSES MULTIPLE SCLEROSIS?

10

Ideals are like stars: you will not succeed in touching them with your hands, but like the seafaring man on the ocean desert of waters, you choose them as your guides, and following them, you reach your destiny.

Carl Schurz (1829-1906)¹

There appears to be no single dominant causal variable responsible for multiple sclerosis. This is not unusual.²⁻³ Most chronic degenerative diseases occur because of interaction between one or more genetic aberration(s) and physical or social environments that magnify their significance. This concept was described succinctly by Bishop and Waldholz⁴ in their book *Genome*. These authors point out that “aberrant genes do not, in and of themselves, cause disease. By and large their impact on an individual’s health is minimal until the person is plunged into a harmful environment.” In short, the genetic aberration is only a weakness under certain circumstances. The key to the prevention and treatment of multiple sclerosis, therefore, is not just the identification of the genetic variables involved, but also an appreciation of which environments magnify and which diminish their significance.

THE TWO FACES OF L-DOPA

It will be remembered that, in the United States, maps showing where people are dying from multiple sclerosis are very similar to those identifying deaths from Parkinson’s disease.

Beyond this, in 1987, Berne-Fromell and colleagues⁵ described a clinical trial conducted in Linköping, Sweden involving 300 multiple sclerosis patients who were treated with L-DOPA (a natural precursor of dopamine). The results were very impressive: after only 1 or 2 months, 75 percent of these patients had experienced significant sensory, motor, and autonomic symptom improvements. Many saw the return of functions that they had lost several years earlier. It would seem, therefore, that both Parkinson's disease and multiple sclerosis must involve important dopamine inadequacies.

Unfortunately, although patients with Parkinson's disease or Encephalitis lethargica who are treated with L-DOPA show dramatic initial improvements, a growing tolerance is developed. This results in a need to increase drug dosages over time. Eventually, side-effects of L-DOPA, such as dyskinesias (abnormal movements), gastrointestinal symptoms, insomnia, hallucinations, and eventually psychosis, become worse than its benefits.⁶ Despite the extremely impressive dramatic initial improvements seen in Swedish multiple sclerosis patients given L-DOPA, the drug is not used as a treatment. This suggests that there must have been significant subsequent negative side-effects, perhaps similar to those seen in Encephalitis lethargica⁷ and Parkinson's disease, that outweigh the benefits of L-DOPA use by multiple sclerosis patients.

As Abram Hoffer and I⁸ pointed out in an article in *Medical Hypotheses*:

The most logical interpretation of the L-DOPA experience is that patients with untreated Parkinson's disease, Encephalitis lethargica, multiple sclerosis, and amyotrophic lateral sclerosis all display two distinct types of symptoms. Some of these are due directly to a deficiency of dopamine and are quickly improved by L-DOPA. A second set of symptoms, however, are the

result of neurological damage caused by the metabolites of dopamine. The use of L-DOPA, therefore, increases the severity of these symptoms over time until they outweigh any improvement observed from the correction of dopamine deficiency. It is suggested that the damaging side-effects of L-DOPA's use stem not directly from the drug but from its oxidation products which include dopachrome and other chrome indoles which are hallucinogenic, toxic to neurons and have been seen to hasten death in Parkinsonism patients.^[9,10]

In short, multiple sclerosis patients have an abnormal need for dopamine, but when this requirement is met, dopamine's oxidation products can cause neurological damage. It may be recalled that, earlier in this book, I argued that the abnormal need for dopamine seen in both Parkinson's disease and multiple sclerosis patients probably stems from an earlier iodine deficiency. Overstreet and colleagues,¹¹⁻¹² for example, showed that rats rendered hypothyroid, by diet or the radioactive isotope iodine 131, developed an abnormally high number of dopamine receptors in parts of the brain. This suggests iodine deficiency probably increases the need for dopamine in humans, as argued earlier by Gilbert.¹³

COROLLARIES

If this hypothesis is correct, three corollaries obviously follow. Firstly, patients suffering from multiple sclerosis and Parkinson's disease should show evidence of excessive oxidative stress. Secondly, high doses of natural methyl acceptors, which are capable of decreasing the conversion of dopamine to dopachrome and other metabolites and so preventing the toxic impacts, should slow the development of these two disorders. Thirdly, elevated antioxidant supplementation, together with L-DOPA, ought to greatly prolong the period in which the benefits of the drug outweigh its adverse side effects.

Corollary one: Oxidative stress

Syburra and Passi¹⁴ studied signs of oxidative stress in the blood (plasma, erythrocytes, and lymphocytes) of 28 multiple sclerosis patients and compared them with those from 30 healthy controls of similar ages. The results showed that multiple sclerosis patients had significantly lower plasma levels of vitamin E and ubiquinone and depressed erythrocyte glutathione peroxidase. The authors concluded that multiple sclerosis patients experience significant levels of oxidative stress. This conclusion seems to confirm research conducted by Shukla and co-workers,¹⁵ who previously identified decreased glutathione peroxidase activity in the erythrocytes of 24 patients with multiple sclerosis. Similar conclusions were reached by Szeinberg and colleagues.¹⁶ Beyond this, abnormal catalase activity has been reported in the granulocytes and erythrocytes of multiple sclerosis patients, being depressed in the former and elevated in the latter, when compared with normal controls. In short, the levels of key enzymes used to protect the human body from oxidative stress are known to be depressed in the blood of multiple sclerosis patients.¹⁷ There is strong evidence that this is also true of Parkinson's disease.¹⁸⁻¹⁹ Corollary one, therefore, appears correct and both diseases must involve excessive oxidative stress.

Corollary two: High doses of natural methyl acceptors may delay development

If, as suggested here, the oxidation products of dopamine, such as dopachrome and other chrome indoles, play significant roles in multiple sclerosis and Parkinson's disease, it must follow that high doses of natural methyl acceptors, like thiamin (vitamin B₁), riboflavin (vitamin B₂), niacin (vitamin B₃), and ubiquinone (coenzyme Q₁₀), will delay disease progression. This is because methyl acceptors cause a decline in the rate of the conversion of dopamine to dopachrome and so help prevent the toxic effects of this and other chrome indoles.²⁰

The best evidence that this is certainly true for early Parkinson's disease comes from a double-blind clinical trial of the effects of coenzyme Q₁₀, conducted by Shults and co-workers.²¹ Eighty patients who were just beginning to show the early signs of Parkinson's disease, but who were not yet being prescribed L-DOPA, were assigned randomly to receive either a placebo or daily doses of 300, 600, or 1,200 mg of coenzyme Q₁₀. Less disability developed in patients given the natural methyl acceptor and the benefits rose with dosage. This strongly suggests that coenzyme Q₁₀ can slow the progressive deterioration of function that normally occurs in Parkinson's disease. This is exactly what would be expected if the neurological damage seen in Parkinson's disease was caused by the oxidation products of dopamine.

The author is unaware of any clinical trials of natural methyl acceptors in multiple sclerosis. However, Morini and co-workers²² have shown that the animal model of multiple sclerosis, relapsing experimental autoimmune encephalomyelitis, also can be suppressed and treated by high doses of alpha lipoic acid. Other workers²³ have confirmed that this natural methyl acceptor can prevent relapsing experimental autoimmune encephalomyelitis progression in mice. Alpha lipoic acid also greatly reduced demyelination and inflammation. As a result, Marracci and co-workers²⁴ strongly supported further studies of the use of alpha lipoic acid as a potential multiple sclerosis therapy.

Beyond this, two of the most effective alternative treatments for multiple sclerosis, those of Mount²⁵ and Klenner,²⁶ both involve the regular injection of the natural methyl acceptor, vitamin B₁. If the current hypothesis is correct, these injections could be expected to reduce the conversion of dopamine to dopachrome and so mitigate the resulting oxidative stress. In summary, it appears that corollary two is correct and that

natural methyl acceptors, such as coenzyme Q₁₀ and vitamin B₁, offer considerable potential as treatments for both multiple sclerosis and Parkinson's disease. Obviously, further clinical trials are urgently required to establish whether this is the case.

Corollary three: High dose antioxidant supplementation may mitigate the adverse side effects of L-DOPA

There is increasing evidence that antioxidants, taken in high doses, may help reduce the oxidative stress caused by dopachrome and other toxic indoles that appear to be produced by the metabolism of dopamine. The United States National MS Society, for example, reviews literature showing how oxidative stress may kill the cells that make nerve-insulating myelin and also disrupts the blood-brain barrier, weakening this protective lining and increasing the immune attack on the brain.²⁷

Interestingly, the Swank diet,²⁸ which is extremely elevated in the antioxidant vitamin A and low in saturated fats, has been used to delay the progression of symptoms normally seen in multiple sclerosis. High dose antioxidant supplementation is being recommended by some researchers²⁹ to help normalize the glutathione peroxidase activity of multiple sclerosis patients. Similarly, laboratory evidence is suggesting that oxidative stress also plays a significant role in Parkinson's disease. To illustrate, Kim-Han and Sun,³⁰ for example, examined the impact of L-DOPA on a line of PC12 cells overexpressing glutathione peroxidase. Their results suggested that L-DOPA causes neuronal cell death by an oxidative pathway and that glutathione peroxidase plays a key role in cellular defence against such oxidative stress. Similarly, Pedrosa and Soares-Da-Silva³¹ have demonstrated that the autoxidation of L-DOPA and of dopamine could be prevented by ascorbic acid, and other antioxidants such as glutathione and *N*-acetyl-L-cysteine, so reducing neuronal cell death.

THE DOPAMINE-DOPACHROME LINK

The evidence presented here seems to suggest that at least part of the neurological damage seen in multiple sclerosis and Parkinson's disease results from iodine related-dopamine abnormalities. These in turn appear to encourage the production of excessive dopamine metabolites, such as dopachrome and other toxic chrome indoles. The use of L-DOPA in Parkinson's disease and in a clinical trial by multiple sclerosis patients probably accelerated the creation of these neurotoxins. If this hypothesis is correct, it follows that combining L-DOPA with very high doses of natural methyl acceptors and antioxidants may permit the beneficial use of this drug in the treatment of multiple sclerosis. Beyond this, such a protocol ought to extend the time during which L-DOPA is valuable in Parkinson's disease.

DOPAMINE-GLUTAMATE RELATIONSHIPS

It is also possible that dopamine oxidation products have other negative biochemical impacts. To illustrate, glutamate is an excitatory amino acid neurotransmitter that is cytotoxic when over-expressed at synaptic terminals. As a result, elevated glutamate appears to play a role in several diseases, including ischemia and methamphetamine-induced toxicity. Berman and Hastings³² have shown that reactive oxygen species and dopamine oxidation products can modify glutamate transport function, resulting in the elevated levels implicated in such neuro-degeneration. It follows, therefore, that if multiple sclerosis involves the excessive oxidation of dopamine, it may involve associated high levels of cytotoxic glutamate. There is some evidence that it does. Glutamate abnormalities have been found also in multiple sclerosis where elevated levels are related to relapses. Increases in serum glutamate do not occur

sharply during relapses, rather they rise gradually for a month or two prior to the onset of a clinical relapse, peak during it, and then slowly decline.³³ Barkhatova and co-workers also have established elevated glutamate levels in the cerebrospinal fluid of patients with multiple sclerosis.³⁴

SUMMARY

It appears likely that, because of earlier iodine deficiencies, multiple sclerosis patients suffer from lifelong dopamine abnormalities. These seem to encourage the production of excessive dopamine metabolites, including dopachrome and other toxic chrome indoles. The excessive oxidation of dopamine may also result in high levels of cytotoxic glutamate.

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From the foldings of its robe, the spirit brought two children; wretched, abject, frightful, hideous, miserable. They knelt down at its feet, and clung upon the outside of its garment. 'This boy is Ignorance. This girl is Want. Beware them both, but most of all beware this boy.'

Charles Dickens, *A Christmas Carol*

CHRONIC INFLAMMATION

One of the very few things agreed upon by conventional and alternative physicians about multiple sclerosis is that it is associated with chronic inflammation that ultimately seems to cause a loss of myelin from nerve surfaces.¹⁻² Understanding why such inflammation occurs will clearly help in unmasking the disorder's cause. In late April 2006, I attended and spoke at the 35th Annual International Conference on Nutritional Medicine Today, held in Vancouver, British Columbia. Fortunately, both Drs. Ron Hunninghake³ and Alex Vasquez⁴ lectured on inflammation at this conference. Much of this chapter draws upon their presentations and upon Hunninghake's book *Basic Health Publication User's Guide to Inflammation, Arthritis and Aging*.⁵

There are two forms of inflammation: acute and chronic. The former is essential for personal survival, while the latter threatens it. The body has a very rapid and orchestrated reaction to injury. Consider, for example, what happens when you accidentally cut your hand while peeling an apple. Bacteria,

living on the knife and your skin's surface, immediately invade the wound. The injury and this infection threat triggers your body's inflammatory system.⁶ Cytokines are activated and released into your bloodstream. These messengers mobilize germ-fighting, white blood cells that rapidly arrive at the injury site. Simultaneously, cytokines loosen the junctions between blood vessels' wall cells. The arriving white cells engulf and eradicate infectious agents in the damaged area, through a process called phagocytosis. Enzymes released from the white blood cells also remove any cellular debris. In a final step, repair and growth chemicals, produced by fibroblasts, coordinate the replacement of damaged cells by scar tissue.⁷ This entire healing process is relatively rapid and results in the prevention of infection, the formation of healthy new tissue, and an almost complete return of function.

In contrast to this type of highly valuable acute inflammation, chronic inflammation is associated with numerous destructive conditions varying from rheumatoid arthritis and multiple sclerosis to colitis and the destruction of the liver by the hepatitis C virus.⁸ In such chronic inflammation, at least one trigger perpetually activates the system. As a result, excessive cytokines are generated continuously, and more and more white cells are mobilized to the trigger site. There is also an ongoing release of excess tissue-damaging enzymes that are not required. Repair chemicals accumulate and continuous scar tissue formation results in granulation tissue, adhesions, and even keloids. To quote Hunninghake⁹ directly:

The five microscopic steps perversely malfunction in chronic inflammation. This pathologic predisposition to persistent inflammation is the basis of hundreds of diseases physicians identify with the “-itis” suffix. Arthritis is chronic joint inflammation. Colitis is chronic colon inflammation. Sinusitis is chronic inflammation of the sinuses, and so on.

It is clear, therefore, that the key distinction between acute and systemic inflammation is the length of time that the initial triggering event continues. Acute triggers are immediate and last a short time. They activate the inflammatory response; as a consequence, repairs are made and healing is achieved. Chronic triggers also activate the inflammatory cascade but keep signalling indefinitely for help, promoting disease, not health. Hunninghake¹⁰ recognizes five categories of such triggers associated with chronic inflammation. These are physical injuries, infections, environmental toxins and irritants, allergies, and sensitivities. Typical chronic inflammation triggers include athletic and overuse injuries, parasitic and viral infections, air pollution, cigarette smoke, carpet out-gassing and food allergies, perfumes, animal danders, and molds and pollens.

THE MODERN PRO-INFLAMMATORY DIET

Hunninghake¹¹ and Vasquez¹² both believe that the modern diet promotes chronic inflammation and is the root cause of the autoimmune illnesses that plague our society. According to the former author, the history of human diet has consisted of four epochs, each of which was more pro-inflammatory than the one that preceded it. The initial hunter-gatherer diet, as shown by Dr. S. Boyd Eaton¹³ who studied the ethnographic records of 229 such cultures, had four important structural characteristics: wholeness; a balanced omega-6/omega-3 ratio; a low glycemic index (a measure of its tendency to stimulate the release of insulin); and a high ORAC score (an ability to reduce oxidative stress). As the human diet changed first to agricultural, then industrial, and finally to fast food, all these beneficial characteristics declined, increasing the tendency for pro-inflammatory illnesses such as multiple sclerosis to occur. The typical fast food diet, consisting largely of highly processed

manufactured products, now has only 40 percent of the wholeness of that of hunter-gatherers; the omega-6/omega-3 ratio has changed from 1:1 to 20:1; the glycemic index has gone from very low to high; and the ORAC score has dropped from high to very low. Each of these trends has encouraged the development of chronic inflammation and its associated illnesses, such as diabetes type 1, asthma, psoriasis, rheumatoid arthritis, and gingivitis.¹⁴

Whole foods, for example, mitigate inflammation because they tend to contain high levels of antioxidants that protect cells from free radicals. They are also fibre rich and therefore lower the glycemic index. Furthermore, eliminating processed foods such as white flour and sugar enhances such benefits. The low omega-6/omega-3 ratio found in our ancestral diet depressed the pro-inflammatory AA precursor and increased anti-inflammatory EPA regulation.¹⁵ As a consequence, it greatly reduced inflammation. A low dietary glycemic index is useful because it helps maintain depressed insulin levels, so slowing the conversion of omega-6 to pro-inflammatory eicosanoids. Such an index also protects against diabetes and the advanced glycation end products associated with this illness, which are very potent free radicals. Finally, high score ORAC foods absorb free radicals and thus limit the excessive inflammatory triggering seen in chronic inflammation. As a consequence of these relationships, the ancestral hunter-gatherer diet prevented inflammatory illness while, in contrast, fast food diets promote it.¹⁶

Autopsy results leave no room for debate over whether or not multiple sclerosis patients suffer chronic inflammation of their myelin sheaths. They do.¹⁷⁻¹⁹ The question to be answered is “Why?”. Jared Diamond,¹⁹ in his book *The Third Chimpanzee*, shows that changing from the hunter-gatherer diet to that of the agriculturalist was associated with a trade-off of quality

for quantity, and with enormous changes in the incidence of specific diseases. Paleopathologists, for example, have demonstrated that this major transition had a negative impact on human health for three reasons. Firstly, hunter-gatherers enjoyed a diversity of foods that provided adequate amounts of essential fatty acids, protein, vitamins, and minerals. In contrast, farmers “gained cheap calories at the cost of poor nutrition,”²⁰ eating a diet rich in starchy, high-carbohydrate plants such as wheat, corn, and rice. Secondly, because of a lack of diversity, farmers ran a greater risk of starvation when one essential crop failed. In contrast, hunter-gatherers could fall back on many other foods if one became scarce. The Irish potato famine, which killed some one million farmers and their families, illustrated the weakness of agriculture overdependence.²¹ Finally, most infectious diseases and parasites persist only in societies of crowded, undernourished, sedentary people who repeatedly reinfect one another through their own wastes. Cholera, measles, tuberculosis, and leprosy do not persist in small, scattered groups of highly mobile hunter-gatherers. According to Diamond, “Tuberculosis, leprosy, and cholera had to await the rise of farming, while smallpox, bubonic plague, and measles appeared only in the past few thousand years with the rise of even denser populations in cities.”²² We are, of course, seeing a repeat of this process as a wave of new diseases – diabetes mellitus, cancer, coronary heart disease, osteoporosis, Alzheimer’s disease, and the rise of obesity – follow the change of diet from industrial to fast food.

It would not be surprising, then, if diets containing insufficient anti-oxidants, a deficiency of omega-3 fatty acids, sugars that overstimulated the release of insulin, and foods that failed to significantly reduce oxidative stress were linked to chronic inflammation and, through it, to multiple sclerosis. To illustrate, the best evidence of the impact of food on the progression of multiple sclerosis comes from the work of Swank.²³

As described previously, with enormous patience Swank has followed the lives of 144 multiple sclerosis patients who had agreed to eat a low fat diet for 50 years. After 34 years, there had been 23 deaths among the 70 dieters who had stuck to a low fat lifestyle; only 14 of these were due to multiple sclerosis. In contrast, 58 of the 74 “poor dieters” were dead, 45 from multiple sclerosis. In summary, only 33 percent of these who strictly adhered to the Swank diet had died, but this figure had risen to 79 percent among those who had not.²⁴ This is very unlikely to have been a matter of chance. Indeed, Navarro and Segura²⁵ have shown that multiple sclerosis patients definitely do suffer from polyunsaturated fat deficiencies. Simply put, the Swank diet is less inflammatory than the typical Caucasian diet and is, therefore, at the very least, likely to slow the progression of multiple sclerosis. In fact, in some cases it appears to have stopped it.²⁶ The same generalization can be made about the Roger MacDougall diet,²⁷ which this professor based on the much healthier foods consumed by our ancestors, the hunter-gatherers.

Another line of evidence supporting the importance of chronic inflammation in multiple sclerosis comes from the links between sunlight, vitamin D, and the incidence and progression of the disorder. As described previously, the prevalence of multiple sclerosis among Caucasians varies greatly with latitude.²⁸ The disorder is much more common where sunlight exposure is relatively low.²⁹ Similarly, there is a strong negative correlation between death from skin cancer and melanoma and mortality from multiple sclerosis.³⁰ It seems, therefore, that multiple sclerosis reflects inadequate exposure to sunlight and, therefore, a deficiency of vitamin D.

Recent research strongly suggests that vitamin D is highly anti-inflammatory. This would explain why it appears protective in multiple sclerosis and why this illness is so rare in tropical and

equatorial regions, even in Caucasians. One way to assess the amount of inflammation in the body is to measure C-Reactive Protein (CRP).³¹ This has been used since the 1930s to help diagnose rheumatoid arthritis and other highly inflammatory autoimmune disorders. It has recently been refined to detect low-grade, systemic inflammation. C-Reactive Protein is a by-product of a specific cytokine, interleukin-6 (IL6), a potent inflammatory activator processed into C-Reactive Protein by liver and abdominal fat cells. Researchers in Belgium³² recently have shown that vitamin D (cholecalciferol) lowers levels of both C-Reactive Protein and its precursor interleukin-6 in critically ill patients. Even small amounts of vitamin D, about 500 IU, lowered inflammation by more than 25 percent in such patients, who were found to be profoundly deficient in this nutrient.

In a more recent German study, Schleithoff and her colleagues³³ did a double-blind, randomized, placebo-controlled trial of 123 congestive heart failure patients who received either 50 micrograms of vitamin D and 500 mg of calcium daily or a placebo and the same amount of the mineral. To quote them³⁴ directly:

We showed for the first time that a daily supplement of 50 micrograms vitamin D for nine months is able to increase serum concentrations of the anti-inflammatory cytokine IL-10 and to prevent an increase in serum concentrations of the pro-inflammatory cytokine TNF-alpha in CHF patients.

It is clear, therefore, that vitamin D can reduce inflammation. Since inflammation plays a key role in multiple sclerosis, it is not surprising that regions of high sunlight, where the skin more easily produces vitamin D, tend to be those where the prevalence of multiple sclerosis is low. This also explains why Goldberg and colleagues' nutritional trial,³⁵ involving 5000 IU of vitamin D daily, was so successful in reducing the exacerbation rates in young multiple sclerosis patients. The ability of

vitamin D to both reduce inflammation and promote calcium deposition probably accounts for the high rates of osteoporosis found in multiple sclerosis patients.³⁶ Vitamin D, either naturally produced from exposure to sunlight or taken as a supplement, has been shown to be anti-inflammatory and capable of preventing, or at least slowing, multiple sclerosis progression. This relationship thus reconfirms the significance of step one, chronic inflammation, in the development of multiple sclerosis. Indeed, in Germany,³⁷ the number of multiple sclerosis lesions has been found to vary seasonally in association with ultraviolet B radiation by a factor of two.

Hunninghake³⁸ has argued further that the omega-6/omega-3 ratio has a significant impact on chronic inflammation. If this is correct, reducing omega-6 intake and increasing that of omega-3 ought to mitigate multiple sclerosis progression and perhaps even reduce the incidence of this disorder. According to Hunninghake, arachidonic acid (AA) is produced by the body from the omega-6 precursor, linoleic acid. Linoleic acid occurs in vegetable oils, such as soy, peanut, safflower, and corn oil, and in processed foods that contain them. Overconsumption of linoleic acid leads to an excess of arachidonic acid (AA) which is then converted into a highly pro-inflammatory eicosanoid called prostaglandin E_2 . As a consequence, a diet high in such vegetable oils tends to be very inflammatory.

In contrast, eicosapentaenoic acid (EPA) is derived from sources such as fish oils. It is converted to prostaglandins E_1 and E_3 , which are anti-inflammatory. Interestingly, arachidonic acid (AA) is converted into the pro-inflammatory eicosanoid prostaglandin E_2 , and eicosapentaenoic acid (EPA) is changed into the anti-inflammatory eicosanoids prostaglandin E_1 and E_3 by the same enzyme, cyclooxygenase (COX). This is why the omega-6/omega-3 ratio is so important in diet. As Hunninghake³⁹ points out:

If your diet contains an excess of AA molecules, COX dishes you out an excess of pro-inflammatory prostaglandins. By increasing your dietary or supplemental intake of EPA molecules, your COX enzymes get tied up and slowed down. Fewer pro-inflammatory prostaglandins are made, and more of the anti-inflammatory species result. AA/EPA is the crucial cytokine-balancing ratio!

What then is the evidence that a diet with a low omega-6/omega-3 ratio is beneficial in multiple sclerosis? The *Agency for Healthcare Research and Quality*,⁴⁰ under its Evidence-based Practice Program, has produced a technology assessment report that reviews the effects of omega-3 fatty acids on cognitive function with aging, dementia, and neurological diseases. Included in this overview is the evidence for the impact of omega-3 fatty acids on multiple sclerosis. To quote the report directly:

Three studies reported on the effects of omega-3 FA intake on the progression of multiple sclerosis. In one study, treatment with an omega-3 FA supplement, MaxEPA, had no effect on disability or relapse rates. However, two other studies reported a significant reduction in disability and one reported improvement on an index of disease progression. Thus, the quantity and strength of evidence for effects of omega-3 FA on outcomes in the conditions assessed varied greatly.

A more recent study⁴¹ attempted to address the impact of omega-3 fatty acid on patients on an otherwise low fat diet. That is, the project tried to find the significance of a low omega-6/omega-3 ratio on multiple sclerosis patients. In a 1 year, double-blind, randomized trial, 31 patients were given either a low (15 percent) fat diet and omega-3 fish oil supplements or a higher (30 percent) fat diet and olive oil supplements. The relapse rate decreased in both groups relative to rates in the previous year. The researchers concluded that a low fat diet supplemented with omega-3 polyunsaturated fatty acids can have moderate

benefits in relapsing-remitting multiple sclerosis patients. The total evidence, therefore, appears to support Hunninghake's⁴² contention that a low omega-6/omega-3 ratio diet should be beneficial in the treatment of multiple sclerosis, probably because it reduces inflammation of the myelin sheath.

INFLAMMATORY TRIGGERS IN MULTIPLE SCLEROSIS

What, then, is the chronic trigger or triggers that activate the inflammatory cascade in multiple sclerosis patients and keep signalling indefinitely for immune system help, so promoting autoimmune disease? As discussed previously, cow's milk is the most likely candidate for this role. Dosch and co-workers⁴³ have noted how the autoimmunity in diabetes mellitus type I and multiple sclerosis appears virtually identical. The former illness is known to be caused by an allergy to a cow's milk albumin peptide.⁴⁴ It seems likely that cow's milk, therefore, may also play this trigger role in multiple sclerosis, which would explain why this disorder is so rare among populations that rarely drink milk, such as the Japanese and Chinese. It would also account for the high prevalence of multiple sclerosis seen in the populations of United States states that drink the most cow's milk.⁴⁵

Of course, it is quite possible that cow's milk triggers multiple sclerosis in many patients, but not all. Gluten is another potential trigger for chronic inflammation. Reichelt and Jensen,⁴⁶ for example, have found that IgA antibodies against gluten occur much more often than normal in the serum of multiple sclerosis patients. This is what would be expected if Braly and Hoggen⁴⁷ are correct and approximately 25 percent of multiple sclerosis patients have increased intestinal permeability that allows gluten protein to leak into their bloodstreams. Since gluten largely is associated with grains such as wheat, oats,

and barley, it is not surprising that multiple sclerosis is rare in Oriental rice-eating societies. A gluten trigger would also explain why Professor Roger MacDougall's diet,⁴⁸ which avoids this protein, is so successful in treating multiple sclerosis. It is possible, of course, that in specific multiple sclerosis patients, other elements, ranging from tomatoes and chocolate⁴⁹ to viral or bacterial infection, may play the role of the chronic trigger.

DYING OLIGODENDROCYTES

If multiple sclerosis is the end result of eating a fast food diet that causes chronic inflammation, triggered by cow's milk or gluten, then it should occur in most of the world's Caucasians. While it is a relatively common neurological disorder, it is thankfully not that common. There must still be a piece of the puzzle missing. This part seems to have been discovered by Barnett and Prineas⁵⁰ at the University of Sydney. These Australian researchers⁵¹ believe that even before the large influx of immune system cells causes inflammation of the central nervous system, the cells that can repair the myelin sheath are dead. Such cells, called oligodendrocytes, are known to be susceptible to oxidative stress, and appear to be killed by it early in the disease process. This conclusion is based on a study of tissue samples taken from 12 multiple sclerosis patients who had died during or soon after a relapse. It was found during this examination that oligodendrocytes, the cells that produce the myelin that makes up the protective nerve sheath, had undergone apoptosis or necrosis, that is, cell death. Naturally, as a result, they were unable to repair any subsequent damage caused by prolonged inflammation.

This, of course, leads us to the key question. What is killing these myelin producing cells? According to Prineas, "The pattern of death that we observed provides little clue to the cause."⁵²

Interestingly, the geography of multiple sclerosis suggests a logical explanation for the premature death of oligodendrocytes that is characteristic of multiple sclerosis. As described at length in Chapters 5 and 10, there is good evidence to suggest that, at some time during gestation or early childhood, future multiple sclerosis patients suffer from inadequate thyroid hormone production. Such a deficiency seems to be due most often to a lack of iodine and, therefore, is most common in those living in recently glaciated regions, where soils tend to be depressed in this trace element.⁵³ In response to this thyroid hormone deficiency, future multiple sclerosis patients likely develop abnormal requirements for dopamine⁵⁴⁻⁵⁵ that ultimately encourage the overproduction of dopamine derivatives such as dopachrome and other toxic chrome indoles. In recent correspondence with Dr. Abram Hoffer, Dr. Yoshihiko Moro-oka of the Tokyo Institute of Technology has described measuring the absolute reaction rates of a series of neurotransmitters subjected to oxidative stress.⁵⁶ Drs. Ohkubo, Fukuzumi, and Moro-oka⁵⁷ have found that L-DOPA, dopamine, norepinephrine, and epinephrine, that is the catecholamines, are very sensitive to oxidative stress and are dehydrogenated by active oxygen species at extraordinarily high speed. This was not true for the other neurotransmitters examined. In short, dopamine breaks down very easily when subjected to oxidative stress.

Beyond this, Khorchid and colleagues,⁵⁸ from McGill University, have shown that, in culture, catecholamines cause a reduction in intracellular glutathione and the production of excess reactive oxygen species. These changes were seen to cause oligodendrocyte cell death. Conversely, Rosin and co-workers⁵⁹ demonstrated that oligodendrocytes were highly vulnerable to oxidative glutamate toxicity and to oxygen/glucose deprivation. Interestingly, oligodendrocyte dopamine D2 and D3 receptor activation seemed to play an important role in oligodendrocyte protection against such oxidative glutamate toxicity.

The triiodothyromine hormone deficiencies seen in multiple sclerosis patients⁶⁰ may also have a direct impact on the absence of viable oligodendrocytes that is characteristic of this disorder. Calza and co-workers,⁶¹ at the University of Bologna, Italy, for example, have shown that in animal experiments it is the thyroid hormones that activate oligodendrocyte precursors and increase the production of a myelin-forming protein.

SUMMARY

Available evidence, therefore, seems to suggest that due to inadequate thyroid hormone production during gestation or early childhood, and probably throughout the illness, multiple sclerosis patients have an abnormal need for dopamine. Dopamine, however, breaks down easily when oxidative stress levels are high, and its resulting metabolites, including dopachrome and other chrome indoles, then cause the death of oligodendrocytes, the cells responsible for repairing the myelin sheath. It also appears likely that multiple sclerosis patients remain chronically short of the thyroid hormone triiodothyromine and that this abnormality reduces the ability to activate oligodendrocyte precursors and produce myelin-forming protein. As a result, multiple sclerosis patients who eat a highly inflammatory diet and foods to which they are allergic are unable to repair the associated myelin damage. The subsequent deterioration of the sheath prevents electrical impulses from travelling normally along nerve fibres, leading to a decline in function of the mind and body that is called multiple sclerosis.

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The tradition of 'peer-review' of articles published in professional journals has degenerated into almost total censorship. Originally, a reviewer could help an author improve his article by pointing out errors in calculation, references, clarity, etc., but scientists, in their fervid attachment to their own theories, have now mostly used their selection as a referee to reject publication of any result that would be unfavorable to their own personal commitment...The press, of course, only reports news from established academic centers that have a strong financial and prestige interest in glorifying the status quo. The result is that real investigative science is mostly now an underground activity.

Halton Arp, What has science come to?
Journal of Scientific Exploration, 14(3), 477-454

PUTTING THE PIECES TOGETHER

“Milk has been called the perfect food.” The statement as it stands is unquestionably true. Milk has been called the perfect food, but who called it that and how much were they paid?

W. Harris, *The Scientific Basis of Vegetarianism*¹

A WORKING HYPOTHESIS: THREE-STEPS FORWARD

People with multiple sclerosis suffer from chronic inflammation of the surfaces of their nerves. This problem seems to be associated with pro-inflammatory diets that contain inadequate antioxidants, a deficiency of omega-3 fatty acids, sugars that overstimulate insulin release, and foods that fail to significantly reduce oxidative stress. These characteristics unfortunately are typical of the current Western diet.² If they were all that was needed to cause multiple sclerosis, this disorder would be almost universal among Caucasians. Those with multiple sclerosis, however, also are exposed repeatedly to an allergen, often cow’s milk or gluten, that continuously triggers their inflammatory cascades, promoting autoimmune disease.

However, if ingestion of highly processed Western foods and allergy to cow’s milk, gluten, or some other trigger caused multiple sclerosis, this disorder would still be far more common than it is. Some 19 percent of adult Caucasians, for example, are allergic to cow’s milk.³ There must be a necessary third step. At some time during gestation or childhood, future multiple sclerosis patients produce, or are also exposed to, inadequate thyroid hormones and, as a consequence, develop an

abnormal need for dopamine.⁴ Dopamine, however, is highly susceptible to oxidative stress and breaks down easily to form toxins such as dopachrome and other chrome indoles. These in turn kill oligodendrocytes, the cells responsible for myelin repair.⁵ Therefore damage to the sheaths surrounding the nerves caused by chronic inflammation cannot be corrected. Beyond this, a continuing shortage of the thyroid hormone triiodothyronine⁶ seems to reduce the body's ability to produce additional oligodendrocytes. Taken together, both processes, an underproduction of oligodendrocytes and an acceleration of their rate of demise, results in an accumulation of myelin damage. Consequently, electrical impulses can no longer travel normally along nerve fibres. Symptoms of multiple sclerosis, therefore, appear and worsen as these biochemical processes continue.

TESTING THE THREE-STEP HYPOTHESIS

The most effective way to test the validity of this three-step multiple sclerosis hypothesis is to use it in attempts to explain the evidence that has been collected about this disorder by disciplines as diverse as genetics and geography—that is, to see whether the multiple sclerosis jigsaw puzzle can be put together successfully using the chronic inflammation-dopachrome three-step hypothesis as its dominant theme. To assist in this process, Table 4 lists the clues identified in earlier chapters.

What follows is my effort to explain each of these clues using the three-step hypothesis as a starting point. There may be some of them that cannot be adequately explained. This may be because the hypothesis is incorrect, or the data the clue was based on was in error, or I am too ignorant to be aware of the true link between the tested hypothesis and the clue. The realistic goal, therefore, must be to explain the majority of the

clues in Table 4, and to do so in a manner that is more convincing than explanations that have been put forward supporting any competing hypotheses.

Table 4: The Pieces of the Jigsaw Puzzle

Chapter 1 Multiple Sclerosis: The Conventional Wisdom

- A. Neurological disease that is first diagnosed in young adults, usually in their 30s
- B. Inflammation and ultimately the loss of myelin from surface of nerves, causes scarring
- C. Attacks or relapses (exacerbations) occur intermittently
- D. Subsequent remissions follow exacerbations
- E. There are various subtypes with differing symptoms
- F. Gender preference: more common in females than in males
- G. Gender ratio varies but preponderance of female over male cases peaks where disease is relatively rare
- H. Risk of developing multiple sclerosis alters with migration
- I. Seems to be an “incubation” or “latency period” after the disease process has been triggered but before symptoms appear

Chapter 2 It’s all my Parents’ Fault: The Mendel Excuse

- A. The average individual in the United States has a 1 in 750 chance of developing multiple sclerosis
- B. Family members of multiple sclerosis patients have a 1 in 100 to 1 in 40 chance of developing the disorder
- C. A monozygotic (identical) twin has a 1 in 4 chance of developing multiple sclerosis if their sibling develops it
- D. APOE-4 allele is associated with more severe disease and rapid progression of symptoms
- E. Appears multigenic in its genetic susceptibility
- F. Geographical belts of multiple sclerosis circle the planet
- G. Multiple sclerosis is common in northern Caucasians

- H. Rare in Inuits, Lapps, Chinese, Japanese, Koreans, Africans, and Mexicans
- I. Clusters occur, for example, in the Orkney and Shetland Islands, Trail, Key West, Bombay, and Poona
- J. Prevalence can vary, seemingly declining in North America and Western Europe, rising in Mediterranean countries, Kenya, and Saudi Arabia

Chapter 3 Just Another Pathogen

- A. Distributions of multiple sclerosis patients in Europe and North America parallel those of the Lyme disease pathogen, *Borrelia burgdorferi*
- B. Birthdates of multiple sclerosis patients mirror seasonal fluctuations in Ixodes ticks
- C. Ticks and Lyme disease spirochetes common in China, Japan, and Korea and multiple sclerosis is not
- D. Shaltenbrand's efforts to show multiple sclerosis is infectious by making Koch's postulates fail

Chapter 4 A Place for Everything

- A. In the United States, multiple sclerosis and Parkinson's disease mortalities have very similar distribution patterns
- B. Strong negative correlations with skin cancer and melanoma
- C. Strong positive correlations with former goitre distribution in the United States
- D. Levodopa, used to treat Parkinson's disease, also reduces multiple sclerosis symptoms dramatically

Chapter 5 Iodine: The Salt of the Earth

- A. During gestation or childhood, multiple sclerosis patients have inadequate levels of thyroid hormones—hypothesis meets Bradford-Hill criteria for cause and effect
- B. Thyroxine deficiency in rat fetus causes serious brain myelin thinning
- C. Exposure to radioactive iodine and fluoride increases risk
- D. Prevalence has strong positive correlation with latitude in Caucasians

Chapter 6 Two Peas in a Pod

- A. Levodopa trial saw major improvements in symptoms
- B. As in Parkinson's disease and Encephalitis lethargica, Levodopa is beneficial but probably causes serious side effects
- C. Hypothyroid rats develop abnormally high number of dopamine receptors in the brain
- D. During pregnancy, dopamine levels increase and rate of relapse declines

Chapter 7 Let the Sun Shine

- A. Sunlight deficiency a risk factor
- B. Vitamin D deficiency a risk factor
- C. Death rate in the United States almost twice as high in low sunlight states
- D. In Europe and Canada, November birthdates most common
- E. Skin cancers rare in multiple sclerosis patients
- F. Multiple sclerosis patients have high risk of developing osteoporosis

Chapter 8 Anomalies: Termites in the Foundations

- A. Global spatial distribution of multiple sclerosis and diabetes mellitus type 1 (juvenile) are very similar
- B. Pancreas and central nervous system both targets of autoimmunity in multiple sclerosis and diabetes mellitus type 1
- C. Consumption of cow's milk a risk factor for multiple sclerosis in 24 countries
- D. Milk from iodine deficient cows a possible risk factor
- E. Saturated fats a risk factor
- F. Populations with high levels of lactose intolerance have low multiple sclerosis risk

Chapter 9 Nothing Succeeds like Success

- A. Omega-3 in diet may reduce symptoms
- B. Vitamin D, calcium, and magnesium supplements reduce the number of exacerbations

- C. Intravenous vitamin B₁ and intramuscular liver extract reverse symptoms
- D. Ascorbic acid, vitamin E, niacin, B complex may help
- E. High protein diet may be helpful
- F. Diet low in saturated fat improves performance and longevity
- G. Gluten free, dairy product restricted diets may reverse symptoms
- H. IgA antibodies against gluten more common in multiple sclerosis patients
- I. Uhthoff's Phenomenon (symptoms worsen as body temperature rises) may be linked to inadequate thyroid hormone levels
- J. Desiccated thyroid may help relieve symptoms

(1) Multiple Sclerosis: The Conventional Wisdom

The first chapter of this book discusses the clinical symptoms of multiple sclerosis, providing nine basic clues. The disorder is most common in White females, in temperate Western climates, and is quite rare in Orientals, especially those living in Asia. While symptoms can vary and several types of multiple sclerosis are recognized, the disease often follows a slow progression into disability. It also displays a latency period, which suggests a trigger(s) is active long before symptoms appear in early adulthood.

Why is multiple sclerosis more common in women than in men, especially in marginal regions? The answer to this question seems obvious. Multiple sclerosis patients are deficient in the thyroid hormone triiodothyronine.⁷ Thyroid hormone deficiency diseases are more common in females than in males because menstruation increases the loss of iodine from the female body, as does the breast feeding of infants.⁸ As a result, for example, females tend to develop goitre more often than men. Since iodine is essential for the production of triiodothyronine, and

this thyroid hormone, in turn, is required for the activation of oligodendrocyte precursors and myelin-forming protein,⁹ it is obvious why multiple sclerosis occurs more frequently in women than in men. They are more likely to be deficient in iodine and, therefore, in the cells that repair myelin.

Why are Caucasian women more susceptible to multiple sclerosis than females of other races? The answer to this question appears to be that White women eat the Western diet. The typical Caucasian diet includes numerous inflammatory triggers, especially dairy products and grains containing gluten.¹⁰ Since other races tend to avoid milk, cheese, and related foods because they are lactose intolerant, they do not suffer from dairy-related allergens.¹¹⁻¹² Similarly, the Oriental diet is rice-based and so does not include the grains that add gluten to the Western diet. The gluten found in oats, wheat, rye, and barley, therefore, is absent from the Oriental diet and so does not trigger chronic inflammation of the myelin sheath.¹³

Why does multiple sclerosis occur most often in the residents of temperate climates? Such areas of moderately cool climates were heavily glaciated in the Pleistocene. As a consequence, most of their soils were removed or buried by newer sediments.¹⁴ Since iodine builds up over time from precipitation which was initially derived from evaporation from the iodine-enriched oceans, new soils tend to be very deficient in this trace element.¹⁵ People living in such regions develop iodine-deficiency diseases, such as goitre, cretinism, Parkinson's disease, and multiple sclerosis.¹⁶ In addition, there is less exposure to sunlight in such temperate zones than in regions nearer to the equator. As a result, these populations are more likely to become vitamin D deficient. Since this vitamin is anti-inflammatory,¹⁷ inadequate levels of it among Caucasians living in temperate zones encourage the myelin damage seen in those with multiple sclerosis.¹⁸

Why are there several recognized types of multiple sclerosis? Since this disorder only occurs in the presence of chronic inflammation and triiodothyronine deficiency, it is not surprising that those with multiple sclerosis can display significant differences in disease progression, varying, for example, from relapsing-remitting to primary progressive forms. The rate of decline is likely to be controlled by numerous variables, as distinct as the quantity of dairy products or omega-3 enriched fish eaten to the amount of time spent in the sun. It is evident that changes in location, lifestyle, and diet are all going to be reflected in multiple sclerosis progression. This is why some patients on the Swank diet¹⁹ remained symptom-free even after 50 years. It is, of course, why young people who move into high iodine, elevated sunshine regions reduce their risk of developing multiple sclerosis. Unfortunately, the reverse is true when movement is in the opposite direction.²⁰

Why is there an “incubation” or “latency period” after the process has been triggered, but before symptoms appear? Once a deficiency of the thyroid hormone triiodothyronine²¹ has developed, the activation of oligodendrocyte precursors and related myelin-forming protein will inevitably be affected adversely.²² However, their inadequacy will only become apparent after chronic inflammation has seriously damaged the myelin sheath. That is, there is a delay between falling out of the hotel window and hitting the ground, but the consequences of the accident are largely predetermined by the initial slip.

Why is multiple sclerosis first diagnosed in young adults? Both dopamine and triiodothyronine are hormones. Strawn and co-workers²³ at the University of Cincinnati have demonstrated that in healthy humans there is a clear relationship between central nervous system concentrations of the major metabolites of dopamine (homovanillic and 5-hydroxyindolacetic acids) and plasma concentrations of total triiodothyronine.

The association is negative and significant, so as levels of metabolites of dopamine rise, total triiodothyronine falls. In susceptible young adults, with abnormally high numbers of dopamine receptors from early iodine deficiency, levels of total triiodothyronine are likely to drop as dopamine derivatives increase. This reduction of the thyroid hormone will slow the activation of oligodendrocytes, reducing rates of myelin repair.²⁴ This, of course, ultimately results in the symptoms known as multiple sclerosis.

(2) It's All My Parent's Fault: The Mendel Excuse

The second chapter demonstrated that multiple sclerosis is not predominantly a genetic disease. Incidence and mortality patterns for the disorder are very non-random and clear global zones are obvious. However, genetics are likely to play a role in multiple sclerosis since the disorder is more common in some families than others. That is, while there is no dominant genetic aberration involved in multiple sclerosis, there are a number that seem to play relatively minor, but significant, roles in determining susceptibility to the disorder.²⁵

Most aberrant genes do not, in themselves, cause disease.²⁶ While some clearly increase the probability of developing multiple sclerosis, their significance varies with both location and lifestyle. One can imagine, for example, various aberrant genes that decrease the ability to absorb iodine, or produce triiodothyronine, or to manufacture vitamin D, or to promote allergies to gluten or lactose. If the current three-step hypothesis is correct, inheritance of any one of these genetic aberrations will increase an individual's susceptibility to multiple sclerosis. However, the probability of such individuals to develop this disorder will rise and fall depending on where they live and their choice of diets and lifestyles.

Since the average individual in the United States has only a 1 in 750 chance of developing multiple sclerosis,²⁷ contributing genetic aberrations and deleterious diets and lifestyles must occur concurrently relatively rarely, even in dominantly Caucasian populations. Clearly, though, since family members of those with multiple sclerosis patients have between a 1 in 100 and 1 in 40 probability of developing the disorder, these genetic aberrations must play a fairly significant role. This is even more apparent when it is recognized that monozygotic twins have a 1 in 4 chance of getting multiple sclerosis if it occurs in their identical sibling.²⁸

Do such genetic aberrations, related to the three-step hypothesis, really exist? It is clear that they do. A meta-analysis by the Transatlantic Multiple Sclerosis Genetics Cooperative²⁹ indicated that the highest non-parametric linkage score occurs on chromosome 17q11. That is, the most common genetic abnormality seen in multiple sclerosis occurs at this position on chromosome 17. Apparently at location 17q11.2 “triiodothyroxine receptor mutants selectively impair beta2 isoform function in providing pituitary resistance to thyroid hormone.” The gene name for this location is THRA and a summary of its function reads:

*The protein encoded by this gene is a nuclear hormone receptor for triiodothyronine. It is one of the several receptors for thyroid hormone, and has been shown to mediate the biological activities of thyroid hormone. Knockout studies in mice suggest that the different receptors, while having certain extent of redundancy, may mediate different functions of thyroid hormone. Alternatively spliced transcript variants encoding distinct isoforms have been reported.*³⁰

It has already been shown that multiple sclerosis patients are deficient in triiodothyronine,³¹ that this thyroid hormone has a

negative association with dopamine levels³² and that multiple sclerosis is more common in the populations of iodine deficient regions.³³ The three-step hypothesis, evaluated here, predicts a key role for triiodothyronine in multiple sclerosis. It would be a very strange coincidence if the most common genetic aberration found in multiple sclerosis patients was one that probably adversely affects the biological activities of this hormone, if triiodothyronine deficiency did not play a very significant role in the development of the disorder.³⁴

The Transatlantic Multiple Sclerosis Genetic Cooperative³⁵ also identified another aberration that occurred more often than normally in multiple sclerosis patients. This was the HLA region on chromosome 6p21. A gene called KCNK5 occurs in this area. According to *NCBI Entrez Gene*³⁶ quoted below:

This gene encodes one of the members of the superfamily of potassium channel proteins containing two pore-forming P domains. The message for this gene is mainly expressed in the cortical distal tubules and collecting ducts of the kidney. The protein is highly sensitive to external pH and this, in combination with its expression pattern, suggests it may play an important role in renal potassium transport.

Interestingly, potassium loss may accompany chronic inflammation due to trauma.³⁷ In addition, potassium hydroxide is known to reduce anthralin inflammation without the loss of its therapeutic effects on psoriasis.³⁸ Animal studies have demonstrated that potassium channel agonists also protect against inflammation in rat endothelium and vascular smooth muscle.³⁹ In summary, the evidence suggests that this aberration may adversely affect potassium transport in multiple sclerosis patients and thus reduce their ability to control inflammation. Such a role would ultimately be consistent with the three-step hypothesis.

A similar genetic relationship appears to occur with vitamin D. It has been shown that vitamin D is anti-inflammatory, that supplements of this nutrient can reduce the number of exacerbations suffered by multiple sclerosis patients, and that the probability of developing the disorder increases as sunlight exposure and vitamin D production falls. In Australia, Tajouri and co-workers⁴⁰ have established that, especially in the progressive forms of multiple sclerosis, there appears to be “a role for the vitamin D receptor gene increasing the risk of developing multiple sclerosis.” Their generalization was based on a study of the genotypes of 104 patients and the same number of age, gender, and ethnically-matched controls. Those individuals with specific genetic variants that reduce their ability to produce vitamin D were seen to be far more likely to develop multiple sclerosis. This genotype is likely to be particularly significant at high latitudes, and in those eating diets that are deficient in the vitamin.

Interestingly, the chromosome 19q13 region surrounding the apolipoprotein E (APOE) gene has shown consistent evidence of involvement in multiple sclerosis.⁴¹ Indeed, the APO E4 allele may be associated with more severe disease and rapid progression of symptoms. This is extremely interesting because the APO E4 allele plays a key role in another disorder involving demyelination, Alzheimer’s disease.⁴² In *What Really Causes Alzheimer’s Disease*,⁴³ I wrote:

...animal experiments suggest that the “APO E3 gene is much more effective at promoting regrowth of nerve cell extensions after injury”⁴⁴ than is the APO E4 allele. APO E3 also may be more protective in preventing the loss of connections between neurons.⁴⁵ Beyond this, in cell cultures APO E4 inhibits neurite outgrowth in rabbit dorsal root ganglion neurons.⁴⁶ Simply put, individuals with the APO E4 allele(s) are more likely to suffer from brain plaques and tangles and also

probably are less capable of protecting against associated neuronal damage, or of recovering from it. That is, they are prime candidates for the development of Alzheimer's disease.

It would appear that individuals carrying one or, even worse, two copies of the APO E4 allele also have a higher likelihood of developing multiple sclerosis. This is probably because they are less able than healthy individuals to protect against, or repair, neuronal damage. However, genes are not destiny. Regardless of their alleles, the residents of Maracaibo do not develop Alzheimer's disease.⁴⁷ Similarly, multiple sclerosis is very rare among the Lapps, Chinese, Japanese, Koreans, Africans, and Mexicans. Clearly, diet and environment play a key role in both disorders.⁴⁸

Ever optimistic, in 2005 the genetic community announced the "MS Gene is Identified."⁴⁹ This was claimed to be MHC2TA, a gene associated with increased susceptibility to rheumatoid arthritis, myocardial infarction, as well as multiple sclerosis.⁵⁰ MHC2TA was only one of the several genome regions associated with inflammation of the nervous system identified by researchers at the Karolinska Institute in Sweden. Obviously, any genetic aberration that encourages such inflammation is going to increase the probability of developing multiple sclerosis but, in and of itself, will not be the ultimate cause of the disorder. That is, as Bishop and Waldholz⁵¹ point out, aberrant genes like those just described matter in some environments but not in others.

The significance of clusters of multiple sclerosis patients also was discussed in this book's second chapter. Such abnormally high incidence rates have been identified in the Orkney and Shetland Islands, Trail, Key West, and Bombay and Poona. There is, however, no reason to believe they are of predominantly

genetic or infectious origin. Kurtzke and Hyllested⁵² have argued that the rise in multiple sclerosis incidence rates in the Orkney and Shetland Islands that followed World War II was evidence of an infectious agent spread by soldiers stationed there during this conflict. However, the presence of thousands of troops in what previously had been very isolated rural communities obviously had a great influence on the lifestyle and diet of the local population. The subsequently increased incidence of multiple sclerosis could easily have resulted from the greater exposure of inhabitants to the Western inflammatory diet.

Similarly, the exceptionally high prevalence of multiple sclerosis in Trail, British Columbia⁵³ seems likely to result from air pollution. Trail is a smelter town and its population is constantly exposed to excess fluoride. This goitrogen interferes with the body's ability to produce triiodothyronine⁵⁴ and, as a result, can be expected to reduce the activation of oligodendrocyte precursors and myelin-forming protein, so hindering myelin repair.⁵⁵

Multiple sclerosis is also much more common in the Zoroastrian, largely Parsi, communities of Bombay and Poona⁵⁶ than it is in the general Hindu populations of this region of India. The Parsis are of Iranian origin and, unlike the Hindi, generally eat a diet that is elevated in meat.⁵⁷ They also tend to live a western lifestyle and so suffer high rates of Caucasian diseases, such as osteoporosis, cancer,⁵⁸⁻⁵⁹ and multiple sclerosis.⁶⁰ In summary, the Parsis eat a highly inflammatory Western diet, whereas the Hindi do not and, as a result, the Parsis develop far more multiple sclerosis.

The final piece of the multiple sclerosis puzzle described in the second chapter are the varying prevalence rates for the disorder that appear to be declining in North America and Western

Europe but rising in Mediterranean countries, Kenya, and Saudi Arabia. These fluctuations can be explained quite easily by the three-step hypothesis. Obviously, they will occur when diets alter and when inflammatory triggers, such as cow's milk and gluten, are more or less frequently consumed.

During the Second World War, the German occupation of Belgium, Holland, Norway, and Poland was associated with rationing and the greatly reduced consumption of meat and sugar.⁶¹ Diet changed dramatically and was dominated by potatoes and bread, since the Nazis had taken away all livestock. These forced changes in diet caused significant alterations to disease patterns. Virtually all the atherosclerosis in blood vessels disappeared. Such arterial deposits had been common prior to the Second World War, being present in 70 percent of all autopsies; but from 1942 to 1950 atherosclerosis became virtually unknown in such occupied countries.⁶² Interestingly, the incidence of rates of multiple sclerosis also fell.

The converse of this phenomenon occurs when indigenous populations abandon their traditional diets in favour of Western foods. Diseases of "civilization" follow quickly, often in a predictable order.⁶³ These include obesity, hypertension, atherosclerosis, diabetes mellitus, and cancers of the colon and rectum. Coronary heart diseases appear to be one of the last major Western diseases to emerge. It would seem that multiple sclerosis also can be added to this list.

(3) Just Another Pathogen

As described in Chapter 3, in 1940, internationally known German neurologist Georges Shaltenbrand⁶⁴ tried to apply Koch's postulates to multiple sclerosis by injecting supposedly infected cerebrospinal fluid, taken from monkeys, into six mentally ill patients. Although none of these patients showed any sign of

developing multiple sclerosis, attempts were made to infect 39 more. Highly unethical though this research was, it seemed to provide convincing proof that there is unlikely to be a key causal pathogen involved in multiple sclerosis.

Despite this evidence, there have been recent assertions that, since the distribution of multiple sclerosis and Lyme disease patients in Europe and North America are similar, there might be some common link through the Lyme disease pathogen *Borrelia burgdorferi*.⁶⁵ The birth date excesses in specific months of the year of those who develop multiple sclerosis later in life also appear to reflect the seasonal distribution of the *Borrelia* transmitting Ixodes⁶⁶ ticks. Some of this confusion/similarity⁶⁷ may stem from the fact that “Infection with *Borrelia burgdorferi*, the spirochete responsible for Lyme disease, can involve the central nervous system and the later stages of the disease may mimic the clinical symptoms of multiple sclerosis.”⁶⁸ Beyond this, the seasonality of multiple sclerosis is probably related to fluctuations in vitamin D,⁶⁹ while that of Ixodes ticks also reflect the seasons.⁷⁰ The fact that Ixodes ticks are common in parts of China, Japan, and Korea,⁷¹⁻⁷² where Lyme disease is endemic but multiple sclerosis is not, further supports a dietary, rather than infectious, explanation for the latter illness.

(4) A Place for Everything

Geography has much to offer the study of multiple sclerosis. As previously discussed in Chapter 4, correlations of United States medical and environmental data raise several pertinent questions about the disorder.⁷³ Why do multiple sclerosis and Parkinson’s disease mortality data, for example, have such similar distribution patterns? Why are these two patterns so different from those of skin cancers (including melanoma) and so like those of the former incidence of goitre?

Such “coincidences” appear to be easy to explain if the three-step hypothesis is correct. Multiple sclerosis and Parkinson’s disease rise and fall together spatially in the United States because both involve an exposure to iodine deficiency during fetal development and/or early childhood. The lack of this trace element subsequently results in an abnormally high need for dopamine,⁷⁴⁻⁷⁵ and probably in the inadequate production of triiodothyronine.⁷⁶ Ultimately, these biochemical abnormalities can result in multiple sclerosis and/or Parkinson’s disease in those who eat a diet that causes chronic inflammation of the myelin sheath. Of course, since goitre is endemic in iodine deficient regions,⁷⁷ it used to have very high prevalence in states where multiple sclerosis and Parkinson’s disease also frequently occur. This is because goitre still occurs there in many pregnant women,⁷⁸ since they require elevated levels of iodine during pregnancy.

The negative associations between multiple sclerosis and cancers of the skin are also easy to explain. Multiple sclerosis is less common where exposure to sunlight is high because vitamin D is anti-inflammatory.⁷⁹ Conversely, high levels of exposure to sunlight promotes cancers of the skin.⁸⁰ As a result, low sunlight environments that promote multiple sclerosis are protective against skin cancer. The reverse is true of regions where ultraviolet exposure is high.⁸¹

(5) Iodine: The Salt of the Earth

The fifth chapter provides evidence to show that multiple sclerosis patients suffer from thyroid hormone deficiencies long before their symptoms first appear. It also demonstrates that in rats, thyroxine inadequacy provides serious myelin thinning.⁸² If a similar process occurs in humans, it would be very consistent with the three-step hypothesis because it would facilitate myelin damage by chronic inflammation.

Supporting evidence also is presented in Chapter 5 showing that exposure to fluoride⁸³ and radioactive iodine-131⁸⁴ promotes multiple sclerosis. This is to be expected as both damage the thyroid gland and reduce related hormone production. Under these conditions it is not surprising that some of those exposed to such goitrogens subsequently develop multiple sclerosis. Thyroxine deficiency, for example, appears to promote myelin thinning.⁸⁵ As shown in Chapter 10, thyroid hormone inadequacy also encourages overproduction of dopamine metabolites, such as dopachrome and other chrome indoles,⁸⁶ that can kill oligodendrocytes,⁸⁷ the cells responsible for myelin repair. In addition, a lack of the thyroid hormone triiodothyronine reduces the body's ability to produce oligodendrocytes.⁸⁸ Therefore, a thyroid hormone deficiency caused by fluoride or radioactive iodine-131 may result in an abnormally thin myelin sheath, and few viable oligodendrocytes. The consequence is an inability to repair any subsequent damage the weakened sheath experiences. Since iodine deficiency is common in recently glaciated regions, it frequently occurs at the same high latitudes as does Caucasian multiple sclerosis.⁸⁹

(6) Two Peas in a Pod

Chapter 6 stresses the similarities, both geographical and clinical, of multiple sclerosis and Parkinson's disease. Both commonly occur in iodine deficient regions and seem linked to an abnormal need for dopamine.⁹⁰ This peculiarity is predicted by the three-step hypothesis postulating that such dopamine abnormalities are a reflection of early thyroid hormone imbalances. Beyond this, they result in overload by excessive dopamine metabolites, such as dopachrome and other toxic chrome indoles that kill the oligodendrocytes responsible for myelin repair.⁹¹

As a result, some of the symptoms of multiple sclerosis reflect an inadequacy of dopamine. This is why Swedish multiple

sclerosis patients initially responded so well to L-DOPA supplementation.⁹² It also explains why the rate of relapse falls as dopamine levels rise during pregnancy in women with multiple sclerosis.⁹³

(7) Let the Sun Shine

Years ago, “in a past life,” I worked as a consultant with a colleague, Dr. W.R. Derrick Sewell, to help design a resilient energy policy for Canada. This research took place during the tenure of the Trudeau federal Liberal government in the 1970s. Our major contribution was to assess the benefits and costs associated with renewable energy sources, such as solar and wind power, and conservation.⁹⁴⁻⁹⁵ In one of these projects we coined the word Daedalophobia, fear of the sun.⁹⁶ You may recall that in Greek mythology,⁹⁷ Daedalus built wings for his son Icarus and himself so they could escape imprisonment. Unfortunately, the wax used to hold some of the feathers on Icarus’ wings melted in the strong sunlight and the boy fell to his death in the sea. Derrick and I suggested that the loss of his child caused Daedalus to forever after fear the sun, a phobic condition we, therefore, called Daedolophobia.

Strangely enough, in the 30 years since we wrote *Daedolophobia: Diagnosis and Prognosis*,⁹⁸ fear of the sun has become commonplace among the medical profession, the makers of sunscreens, and researchers who study skin cancer. Despite the fact that excess exposure to the sun can trigger skin cancer,⁹⁹ avoidance of the sun seems far more dangerous. Caucasians are frequently vitamin D deficient¹⁰⁰⁻¹⁰¹ and, as a consequence, cannot utilize calcium effectively. The risks from the resulting diseases, colon and breast cancer, rickets, Seasonal Affective Disorder, osteoporosis, and multiple sclerosis¹⁰²⁻¹⁰³ to name only a few, are far greater than those posed by skin cancer.

Vitamin D is an anti-inflammatory nutrient¹⁰⁴ and, consequently, the link between a deficiency of this vitamin and multiple sclerosis is easy to explain. Consistent with the three-step hypothesis, a lack of either the sunlight required by the body to produce vitamin D, or a direct deficiency of the vitamin, have been linked to the etiology of multiple sclerosis.¹⁰⁵⁻¹⁰⁶ Beyond this, the death rates from the disorder in the United States are approximately twice as high in the northern low sunlight states as they are in the bright south.¹⁰⁷ This also probably helps to explain the seasonality of the birthdates often seen in multiple sclerosis patients.¹⁰⁸ Furthermore, due to their tendency to avoid sunlight, multiple sclerosis patients have low rates of skin cancer but an elevated prevalence of osteoporosis.¹⁰⁹

(8) Anomalies: Termites in the Foundations

Why don't the high multiple sclerosis prevalence zones, which appear to reflect the availability of iodine and sunlight, the drivers that control thyroid hormone and dopamine imbalances and vitamin D and calcium deficiencies, affect those of Oriental and African descent? The answer to this key question seems obvious. These nutritional abnormalities only cause multiple sclerosis in populations that eat an inflammatory diet that includes dairy products or gluten which trigger chronic inflammation. Since such diets also cause diabetes mellitus type 1, it is hardly surprising that both disorders occur at high levels in the same communities.¹¹⁰ Neither is it unexpected that in both multiple sclerosis and juvenile diabetes, the pancreas and central nervous system are targets of autoimmunity.¹¹¹ As milk consumption is depressed in countries with a high prevalence of lactose intolerance, the prevalence of both multiple sclerosis and juvenile diabetes is low in such nations. Conversely, where milk consumption is high, multiple sclerosis and diabetes type 1 are common. This is why cow's milk consumption has been

identified as a risk factor for multiple sclerosis in at least 24 countries.¹¹² It is not surprising that iodine deficient milk is particularly harmful since it combines two risk factors for multiple sclerosis, both a lack of a key protective trace element and a trigger for chronic autoimmune disease.¹¹³⁻¹¹⁴

(9) Nothing Succeeds like Success

If multiple sclerosis is really caused by chronic inflammation associated with dopamine abnormalities that make myelin repair inadequate, then dietary change should have a marked impact on the progression of this disorder. The available evidence clearly demonstrates that it does. In 1986, Goldberg and colleagues¹¹⁵ showed that cod liver oil, vitamin D, and calcium and magnesium supplements could reduce the exacerbations seen in multiple sclerosis patients. This is no surprise. Cod liver oil is a good source of omega-3 fatty acid. As has been argued by Hunninghake,¹¹⁶ the current Western diet is typically far too high in omega-6 and too low in omega-3 fatty acids. This elevated omega-6/omega-3 ratio promotes inflammation. Clearly, adding extra omega-3 in cod liver oil to the diets of multiple sclerosis patients will decrease this ratio and reduce inflammation of the nervous system.

A recent animal study¹¹⁷ has shown that omega-3 fatty acids from fish oils do, indeed, reduce inflammation. This was demonstrated by inducing colitis in 40 rats, which previously had been fed four different diets, for 2 weeks. Ten animals were given fish oil (a 4 percent solution in olive oil for a 4.5 to 1 omega-6 to omega-3 ratio). Another 10 animals received this fish oil blend and the antioxidant quercitrin. The remainder were given soybean oil, with or without quercitrin, and so had an omega-6 to omega-3 ratio of 15.7 to 1. After 10 days, the authors¹¹⁸ measured inflammatory response markers. It was found that:

1. *In the group fed fish, inflammatory response marker levels were lower than for those fed soybean oil by 49 percent for TNF-alpha, 31 percent for IL 1-beta, and 39.5 percent for LTB4.*
2. *And for the animals fed fish oil plus quercitrin, these levels were reduced versus those fed soybean oil by 57 percent, 62 percent, and 45 percent, respectively. (Quercitrin has been shown to inhibit the production of TNF-alpha and IL 1-beta in the colon, while the fish oil acts to inhibit TNF-alpha and LTB4. The quercitrin provides a protective antioxidant factor while adding a synergistic effect.)*

Omega-3 fatty acid also has been shown to be very useful in the treatment of neck and back pain because of its ability to reduce inflammation.¹¹⁹

The patients taking part in the Goldberg and co-workers¹²⁰ trial also received elevated vitamin D, the anti-inflammatory nutrient. Obviously, since the Klenner,¹²¹ Swank,¹²²⁻¹²³ and MacDougall¹²³ diets all tend to be higher than the typical Western diet in omega-3 and lower in omega-6, they will protect against inflammation. Swank and Dougan¹²⁵ in particular promote a diet that is very low in saturated fat. Patients who follow such diets will also receive more vitamin D than is usual. In addition, they will be less exposed to gluten and dairy products, allergens that frequently appear to trigger the chronic inflammation typical of many autoimmune diseases, including multiple sclerosis.¹²⁶⁻¹²⁷

Both Mount¹²⁸ and Klenner¹²⁹ insist upon daily vitamin B₁ injections. Why this vitamin may be so beneficial is obvious if the three-step hypothesis is correct. This model suggests that it is the oxidation products of dopamine, such as dopachrome and other chrome indoles, that are responsible for much of the damage that ultimately deprives multiple sclerosis patients of

viable oligodendrocytes and so of their ability to repair their own myelin sheaths.¹³⁰ If this hypothesis is correct, it follows that high doses of natural methyl acceptors, such as thiamin (vitamin B₁), riboflavin (vitamin B₂), niacin (vitamin B₃), and ubiquinone (coenzyme Q₁₀), should slow or even stop multiple sclerosis progression by greatly reducing the breakdown of dopamine.¹³¹ If this is the case, then the vitamin B₁ injections promoted by Mount¹³² and Klenner¹³³ must ultimately improve the myelin repair capabilities of multiple sclerosis patients, so preventing exacerbations. Interestingly, it has been shown recently that high doses of coenzyme Q₁₀ can play a similar role in Parkinson's disease patients.¹³⁴

In summary, the diets that appear to work the best for those who suffer from multiple sclerosis are anti-inflammatory, rich in antioxidants (such as selenium and vitamins C and E), having a low omega-6/omega-3 ratio, depressed glycemic index, and a high capability to quench free radicals. In addition, such diets do not include dairy products or grains containing gluten, substances that may act as chronic inflammatory "triggers."¹³⁵

As multiple sclerosis patients tend to be deficient in total triiodothyronine,¹³⁶ it is hardly surprising that they benefit from desiccated thyroid.¹³⁷ Thyroid hormones also play a key role in controlling body temperature.¹³⁸ As a result, thyroid hormone deficiency may account for Uhthoff's Phenomenon, the worsening of multiple sclerosis symptoms as temperature rises.¹³⁹

SUMMARY

It is apparent from this overview that virtually all of the evidence, presented from disciplines as diverse as geography and genetics, is consistent with the three-step hypothesis. That is, multiple sclerosis patients suffer from chronic inflammation

caused by diets that contain inadequate antioxidants, omega-3 deficiencies, excess sugar, and foods that fail to significantly reduce oxidative stress. In addition gluten, cow's milk, or some other allergen further promotes autoimmune disease. The coup de grâce, however, is a thyroid hormone deficiency that causes an abnormal need for dopamine.¹⁴⁰ Dopamine is very susceptible to oxidative stress and can break down to form toxins such as dopachrome and other chrome indoles. These, in turn, kill oligodendrocytes,¹⁴¹ the cells needed to repair the damage to myelin caused by chronic inflammation. Beyond this, a shortage of triiodothyronine in multiple sclerosis patients appears to reduce their ability to produce new oligodendrocytes.¹⁴² Therefore, myelin deteriorates and the symptoms of multiple sclerosis worsen. Wilcoxon and Redei have shown that such thyroid malfunctions in adults may be triggered by environmental challenges early in life.¹⁴³ This process is termed fetal programming.

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Genes are not destiny! Environmental influences, including nutrition, stress and emotions, can modify those genes, without changing their basic blueprint. And those modifications, epigeneticists have discovered, can be passed on to future generations, as surely as DNA blueprints are passed on via the Double Helix.

Bruce H. Lipton, *The Biology of Belief*¹

INTRODUCTION

For over 20 years²⁻⁵ I have been arguing that chronic degenerative diseases are primarily geographical, not genetic. The spatial distribution patterns of these illnesses cannot be adequately explained by genetic determinism, but greatly reflect the environment and the lifestyles associated with particular cultures and individuals. This, of course, has been a fringe viewpoint, pushed aside by the massive financial and academic support given to those who were certain that all you had to do to prevent a disease was to discover which defective gene was responsible for it. However, as Dr. Bruce Lipton⁶ points out in his brilliant book, *The Biology of Belief*:

Of course there is no doubt that some diseases, like Huntington's chorea, beta thalassemia and cystic fibrosis, can be blamed entirely on one faulty gene. But single-gene disorders affect less than two percent of the population; the vast majority of people come into this world with genes that should enable them to live a happy and healthy life. The diseases that are today's scourges—diabetes, heart disease and cancer—short

circuit a happy and healthy life. These diseases, however, are not the result of a single gene, but of complex interactions among multiple genes and environmental factors.

What about all those headlines trumpeting the discovery of a gene for everything from depression to schizophrenia? Read those articles closely and you'll see that behind the breathless headlines is a more sober truth. Scientists have linked lots of genes to lots of different diseases and traits, but scientists have rarely found that one gene causes a trait or a disease.

The one-gene, one-protein concept, however, has been fundamental to the “religion” of genetic determination. Genetic conventional wisdom argued that since there are more than 100,000 different proteins in the body, together with at least another 20,000 regulatory proteins orchestrating their activity, the human genome must contain at least 120,000 genes within its 23 pairs of chromosomes. What a shock to so many geneticists when, contrary to the expected 120,000 or more, they discovered that the entire human genome consisted of approximately 25,000 genes.⁷ That is, the human genome has only slightly more genes than that of the primitive *Caenorhabditis* worm, with a genome composed of approximately 24,000.⁸ While the human body consists of roughly 50 trillion cells, microscopic *Caenorhabditis* has only 969 cells. How can this be? The activity of each human gene is “controlled” by the presence or absence of ensleeping proteins, which in turn are “controlled” by signals from the environment. As Lipton⁹ points out, “studies of protein synthesis reveal that epigenetic ‘dials’ can create 2,000 or more variations of proteins from the same genetic blueprint.” Simply put, ensleeping proteins, which are controlled by the environment, create much of the complexity of the human body. The majority of patients suffering from chronic diseases, including those with multiple sclerosis, probably do so because of environmentally-induced epigenetic

alterations, not defective genes. To quote Lipton¹⁰ yet again, “DNA does not control biology and the nucleus itself is not the brain of the cell. Just like you and me, cells are shaped by where they live. In other words, it’s the environment, stupid.” Just before this book was typeset, in the August 2006 volume of *Scientific American*, Gerstein and Zheng¹¹ wrote “Humans have only an estimated 21,000 protein-coding genes.” If this figure is now considered correct then we are clearly outcoded by the primitive *Caenorhabditis* worm. After this chapter was typed, the *National Post*, September 15, 2006, pA9, announced that researchers from the University of British Columbia and Vancouver’s Genome Sciences Centre had completed the first genome of any tree. The black cottonwood was found to have more than 45,000 genes; that is, twice as many as you or I. Why is it that I keep expecting to see P.T. Barnum announce his new and exciting “Shrinking Human Genome Show”?

FACING UP TO REALITY

This new reality is a blow to more than just most geneticists. I recall seeing the interview of a man so obese he could not turn over in his bed. He explained to the reporter that his problems were genetically controlled. His weight had been preordained, his fate since birth. When further questioned about what he had eaten for his last meal he replied “24 pork chops.” I mention this because it was such a perfect example of how genetic determination allows an unwarranted escape from reality. We are all dealt genetic cards, but they can still be played well or badly, greatly affecting their consequences in the game of life. While inheriting certain genes increases the probability of developing cancer, heart disease, stroke, diabetes mellitus, Alzheimer’s disease, schizophrenia, osteoporosis, and multiple sclerosis, such genes do not determine the future. It is quite possible to alter personal environments and lifestyles

so that they prevent these illnesses. This is the truly important good news associated with the intellectual collapse of genetic determinism.

Unfortunately, as Horrobin¹² has pointed out, this is not an approach most people are willing to take. When faced with illness, the majority of the population still would much sooner blame their genes and “pop a pill.” The results of this approach are inevitable:

The escalating costs of the health care system will bankrupt both states and individuals. These costs largely arise because we are spending vast amounts on marginally useful treatments that ensure that patients return to the health care system again and again. The only way this will change is if we find dramatically effective treatments that remove patients from the health care system altogether. And the only way to make such discoveries will be to test greater numbers of scientifically much more diverse approaches to treatment. That, I believe, is the ethical imperative of all involved in medical research. And because the introduction of highly effective treatments is the only possible basis for a dramatic reduction in costs, it happens to be a financial imperative as well.

PREVENTION AND TREATMENT OF MULTIPLE SCLEROSIS

If the three-step hypothesis is correct, then multiple sclerosis should be easy to both prevent and reverse. To achieve these goals, however, involves a great deal of both societal and personal commitment. Above all, it requires a willingness to take responsibility for one’s own health. While the remainder of this book focuses on the avoidance and mitigation of the symptoms of multiple sclerosis, it must be pointed out that every case is unique. As Dr. Roger J. Williams¹³ in his pioneering book

Biochemical Individuality pointed out, we are all unique and, as a result, there can never be a one-size treatment that fits all. Multiple sclerosis patients need to vary their intakes of potentially beneficial nutrients to determine their own optimum levels. In *Your Personal Life*, Dr. Greg Tafft and Bill Quateman¹⁴ describe an interesting scientific approach that can assist in this process.

(1) Anti-inflammatory diets

There is a great deal of recent information on inflammation and diet. The link between foods and autoimmune disease has stimulated publications such as Monica Reinagel and Julius Torelli's¹⁵ *The Inflammation Free Diet Plan* and Barry Sears'¹⁶ *The Anti-Inflammation Zone*. While diets such as those designed by Drs. Swank¹⁷ and Klenner¹⁸ are certainly less inflammatory than those normally eaten by Caucasians, they were not specifically designed with this objective in mind. In contrast, the Reinagel and Torelli dietary approach has one major goal: the reduction of inflammation. Their book gives IF ratings of some 1,500 foods that represent the total inflammatory or anti-inflammatory potential of each. This rating integrates more than 20 different factors that influence the inflammatory impact of any particular food. The data on which these ratings are based was obtained by Reinagel and Torelli from two major sources: the *National Nutritional Database for Standard Reference*, developed by the US Department of Agriculture, and the Glycemic index Research Institute at the University of Sydney, Australia.

Reinagel and Torelli emphasize seven key points about the impact of diet on chronic inflammation. These are listed here, but readers should consult *The Inflammation Free Diet Plan* for more details:

1. *The amount of fat matters, but the type of fat is more significant.*

2. *Certain fatty acids play key roles in creating or preventing inflammation.*

As discussed earlier in this volume, four fats are of particular interest in terms of the creation of inflammation. Eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and gamma-linolenic acid (GLA) are anti-inflammatory, while arachidonic acid (ARA) encourages inflammation.

3. *Antioxidants are anti-inflammatory.*

This seems particularly true of vitamins C, E, selenium, and beta-carotene.

4. *High homocysteine levels promote inflammation.*

The B vitamins, especially B₆, B₁₂ and folic acid effectively reduce homocysteine levels.

5. *Sugar promotes inflammation.*

Artificial sweeteners are to be avoided.

6. *Vitamin K, found in vegetables such as kale and broccoli, is anti-inflammatory.*

7. *Certain phytochemicals are anti-inflammatory.*

Some foods such as ginger, turmeric, chili peppers, garlic, pineapple, and related plants have dramatic anti-inflammatory impacts. Many of these foods have been used by traditional healers to treat auto-immune diseases for hundreds, if not thousands, of years. While anyone wishing to eat an anti-inflammatory diet should consult Reinagel and Torelli's¹⁹ *The Inflammation Free Diet Plan* and Sears'²⁰ *The Anti-Inflammation Zone*, Table 5 provides a few examples of foods with high and low IF ratings. A positive value in this table is indicative of an anti-inflammatory impact, while a negative value means that the food promotes inflammation.

**Table 5: Inflammatory Rating for Sample Foods
(data after Reinagel and Torelli, 2006)²¹**

<i>Food</i>	<i>Amount</i>	<i>IF Rating</i>
Acerola cherries	10	340
Anchovies, canned in oil	1 oz.	297
Bacon, pan-fried	1 lb (uncooked weight)	-138
Baked beans	16 oz. can	-227
Banana	1 medium	-118
Bass, sea baked	3 oz.	331
Beef lungs, braised	3 oz.	-130
Bluefin tuna baked or grilled	3 oz.	591
Brazil nuts, raw	4 oz.	698
Bread, Vienna	1 slice	-261
Brown sugar	½ cup	-746
Butter	1 cup	-716
Cabbage, green, raw	1 small head	260
Carrot juice	8 oz.	396
Chocolate chips	1 cup	-598
Coconut oil	½ cup	-899
Collard greens	½ cup, chopped	205
Ginger, ground	1 tsp.	501
Herring, Atlantic baked or grilled	3 oz.	790
Lamb leg (New Zealand) roasted, lean	3 oz.	-15
Margarine, corn	¼ lb.	-200
Pepper, red chili	½ cup	488
Pork ribs, country style	3 oz.	-7
Pretzels, hard, regular	8 oz. bag	-1,434
Rice, white parboiled	½ cup	-246
Sardines, canned in oil	3 oz. can	470
Sour cream	16 oz.	-290
Turkey breast, roasted with skin	1 breast	-2155

Obviously, designing an anti-inflammatory diet to prevent or reverse the symptoms of multiple sclerosis is not simple and requires the guidance of more than this book. However, the information to achieve this goal is now readily available.²²⁻²³ I would just like to add three more points to the discussion. Firstly, while fish, because of its high levels of omega-3 (EPA) fatty acids, should play a key role in any anti-inflammatory diet, heavy metals and other toxins are a problem for those who eat it on a regular basis. They may accidentally become adversely affected, for example, by mercury, PCBs, dioxins, and other contaminants. Fortunately, Antarctic krill, small shrimp or prawn-like creatures that nourish the great whales, contain few such toxins because they feed much lower down the food chain. As a result, Antarctic krill are a very good source of omega-3 essential fatty acids, and their oils are much purer than those derived from cod or other fish.²⁴ However, krill oil should not be taken by anyone who is allergic to shellfish, has a blood coagulation disorder, or is taking anticoagulants such as warfarin.²⁵ Apart from the elevated levels of omega-3 fatty acids in krill oil, it is also known to have a very high ORAC value (oxygen radical absorbance capacity). It has, for example, 34 times the antioxidant capacity of coenzyme Q₁₀.

Krill oil, however, has one obvious drawback. It does not contain significant vitamin D.²⁶ Since this vitamin is strongly anti-inflammatory, it is important in any multiple sclerosis diet. Exactly how much vitamin D is required is still uncertain, although Dr. Mercola²⁷ has pointed out that:

The old RDA of 400 units was only put together to prevent rickets. It was established long before the appreciation of sun exposure and optimized vitamin D levels. The requirements for vitamin D are far closer to 10 times the current RDA, or 4,000 units. If you only took the RDA of 400 units of vitamin D and avoided the sun you can be virtually guaranteed you would be

vitamin D deficient, just like over 85 percent of the country (USA) currently is.

This is why it is crucial that you have your vitamin D levels tested now. By far, the vast majority of people reading this right now have far too little vitamin D in their blood. Over 85 percent of people have levels below 32, which is considered deficient, but it is possible to overdose on vitamin D.

In my practice we don't like to see patient levels go much above 50, but 55 is probably a perfect level and anything above 60 is likely to be toxic. One study found cancer started to occur at 80. So, be smart and get your vitamin D level tested.

We routinely put people on 10,000 units a day or more of vitamin D safely as long as we monitor them. It is important to understand that most of us get 10,000 units on a sunny summer day if we have significant exposure.

It might be recalled that, as early as 1986, Goldberg and co-workers²⁸ were able to more than halve the expected number of exacerbations (declines in neurological abilities) in a group of 16 young multiple sclerosis patients using dolomite tablets and cod liver oil. The latter provided patients with 5,000 International Units of vitamin D each day. The 10,000 units of this vitamin suggested by Mercola, therefore, is probably not excessive, although body levels require monitoring.²⁹ More recently, Nordvik and colleagues³⁰ have been able to greatly reduce mean annual exacerbation rates in 16 newly diagnosed multiple sclerosis patients with 0.9 grams per day of long-chain marine fatty acids and vitamin supplements. Clearly, an anti-inflammatory diet needs both omega-3 fatty acids and vitamin D.

One final comment seems appropriate here. Omega-3 fatty acids have been demonstrated to be valuable in the treatment

of schizophrenia.³¹⁻³² Interestingly, Rudin and co-workers³³ have argued that supplementing the diets of schizophrenics with essential fatty acids is successful only when selenium intake is optimum.

If a primate is deficient in the antioxidant element selenium, providing supplemental essential fatty acids will only make the selenium deficiency worse. Whatever selenium stores are in the body will be used up that much sooner in an attempt to protect the EFA [essential fatty acids] from oxidative damage.³⁴

Since multiple sclerosis patients are thought to be selenium deficient,³⁵ it is apparent that any use of either fish or krill oils must be accompanied by adequate selenium supplementation. This trace element will also be useful in helping to reduce the inadequacies of the selenoenzyme glutathione peroxidase so typical of multiple sclerosis patients.³⁶ Antioxidant therapy, including selenium, as one would expect, is known to be of value in the treatment of multiple sclerosis.³⁷

(2) Avoiding Triggers

In addition to eating the typical pro-inflammatory Western diet, multiple sclerosis patients seem to be repeatedly exposed to an allergen that continuously triggers the inflammatory cascades that promote this autoimmune disease.

As described in *What Really Causes Schizophrenia*, almost anything that is ingested, inhaled, or touched by a susceptible person can trigger allergies. Such allergens include drugs, foods and their additives and colourings, insects, dust, plant molds, household cleaners, metals, fabrics, latex, and industrial vapours.³⁸ In susceptible individuals, such substances can result in one of four types of antibody-mediated reactions.³⁹

In Type I, (IgE-Mediated) Immediate Hypersensitivity allergies, the antibody immunoglobulin E (IgE) is produced within minutes of exposure. When an allergic individual breathes in the pollen or other allergen causing his problem, his immune system signals B lymphocytes to produce IgE antibodies specifically designed to target the allergen's protein molecules. These IgE antibodies then become attached to the surfaces of mast cells in the respiratory and gastrointestinal tracts and to eosinophils, comparable cells in the bloodstream. During future exposures, the allergen will bind to the waiting IgE antibody receptors, triggering the release of histamine from mast cells and eosinophils. As a result, swelling, itching, redness, pain, watery eyes and nose, muscle contractions, and capillary permeability occurs as the body tries to rid itself of the allergen.

Type I "classic" allergies are usually the result of reactions to airborne allergens including mold, pollen, dust mites, and animal dander. The same type of allergic reactions are also caused, in some people, by milk, eggs, corn, nuts, peanuts, strawberries, and chocolate. Pharmaceuticals such as penicillin (derived from mold) and aspirin, together with insect stings and latex, can also cause the worst form of Type I allergic reaction, anaphylaxis.⁴⁰ This requires immediate adrenaline injections to reverse the symptoms caused.

In Type II, Cytotoxic Allergies, antibodies inject toxic protein enzymes (cytotoxin) into antigen cells, which kills them. If this process occurs in blood or tissue cells, it can result in immune hemolytic anaemia when too many red blood cells die. Intestinal cells often suffer the most damage from cytotoxic reactions because many of the allergens involved are foods.

In Type III, Arthus Allergies, the reaction may occur as much as 10 days after exposure. As in Type II, the antibody IgG binds to an invading protein, but in this case forms a circulating

immune complex. In persons with weakened immunity, such complexes can build up in the bloodstream. If the kidneys cannot excrete them adequately they accumulate in the soft tissues, causing inflammation and symptoms such as hives, joint pain, headaches, fatigue, and even arthritis. It is estimated that approximately 80 percent of food allergies are Type III reactions.⁴¹

In Type IV, Cell-Mediated Allergies, symptoms typically appear 2 to 3 days following exposure. The main triggers of such allergies are various plants, including poison ivy, and some pharmaceutical drugs. These allergies can result in allergic contact dermatitis, allergic colitis, Crohn's disease, and graft-transplant rejections. In such reactions, T cells directly attack an antigen. Since it takes about a day for the body to amass adequate T cells in the affected area, allergic symptoms (usually allergic contact dermatitis) are experienced some 1 to 3 days after exposure. Approximately 3,000 substances are known to be able to cause this type of allergy, ranging from mercury and nickel, through rubber and plastic, hair dyes, cosmetics, and latex. Various foods, such as pineapples, bananas, papaya, kiwi, and avocado, are also contact allergens in some sensitive individuals.⁴²

It is very likely that in all multiple sclerosis patients this neurological disorder is being triggered by one or more types of allergic reaction. Given the far higher rate of multiple sclerosis in Caucasians than in Asians,⁴³ it is very likely that the allergen involved is either a dairy product (especially cow's milk) or gluten from grains such as wheat, oats, or barley. One way of discovering the allergen involved is by fasting. Foods should be returned to the diet one at a time after the fast is over. When a patient again begins to eat a food to which she is allergic, some symptoms may quickly reappear. Other symptoms may take several days to reoccur, as, for example, in the

case of certain grains. Once a patient has been shown to be allergic to a particular food, it should be permanently avoided, although it may be possible to develop less sensitivity to it with treatment.⁴⁴

In addition to fasting, there are a multiplicity of available ways to identify allergens. The simplest of these is to take a patient history, including the circumstances that surround original symptoms. Others include the scratch or prick skin test, the patch test, serial endpoint titration (SET), the radio allergosorbent test (RAST), ELISA test, cytotoxic testing, the ALCAT, provocative neutralization, and electrodermal screening (EDS). This is not the place to review the merits and drawbacks of such tests, but all are discussed in *Allergy Free: An Alternative Medicine Definitive Guide*.⁴⁵ What is important here is the need to identify what a multiple sclerosis patient is allergic to and then to treat them by completely removing, when possible, this allergen from their environments and/or diet.

If no allergen can be identified, it would still seem prudent to remove dairy products and gluten from the diet, since these are the most likely triggers.

(3) Dopamine and the Thyroid

The global prevalence patterns of multiple sclerosis are very suggestive of a link between this disorder and iodine deficiency. It seems that, as a result of a lack of this trace element, some time during gestation or childhood, future multiple sclerosis patients produce, or are exposed to, inadequate levels of thyroid hormones. As a result, they develop an abnormal need for dopamine.⁴⁶ However, dopamine is very susceptible to oxidation⁴⁷ and easily breaks down to create toxins such as dopamine and other indoles. These in turn appear to kill

oligodendrocytes, cells which repair myelin.⁴⁸ As a consequence, myelin damage caused by chronic inflammation is not corrected. Beyond this problem, multiple sclerosis patients also suffer a continuing shortage of the thyroid hormone triiodothyronine,⁴⁹ which reduces their ability to produce oligodendrocytes,⁵⁰ and an acceleration of the demise of these cells. This inevitably leads to increased myelin damage.

If this hypothesis is correct, there are several steps that should be taken to reduce the incidence of multiple sclerosis and/or mitigate its symptoms. The first of these precautions is a reduction of iodine deficiency in pregnant women. This goal might be achieved in many ways, including adding this element to fertilizers, increasing use of table salt by expectant mothers, or by ensuring that their diets contain a variety of seafoods, including seaweeds. It also appears logical to avoid goitrogens. It should be pointed out that the soybean, often included in baby foods, is a goitrogen, and that soybean milk, for example, can cause hypothyroidism in susceptible infants.⁵¹ Increasing iodine intake by reasonable amounts in the fetus and infant seems likely to have other major benefits, beyond reducing the incidence of multiple sclerosis. These include decreases in crib death (SIDS), the prevention of deafness, and an increase in the IQ of the general population.⁵²

A second issue to be addressed is the obvious dopamine deficiency in multiple sclerosis. Berne-Fromell and co-workers⁵³ have described a clinical study, conducted in Linköping, Sweden, in which 300 multiple sclerosis patients were treated with levodopa and tri- and tetracyclic antidepressants. After only one or two months, 75 percent of the patients had substantial sensory, motor, and autonomic symptom improvements. To me, this study illustrates two key points. Firstly, multiple sclerosis patients definitely suffer from a deficiency of dopamine and could benefit greatly from levodopa in the same way that

Parkinson's disease patients do. Secondly, since, beyond the Swedish trials, levodopa was never used for this purpose, it seems probable that, similarly to Parkinson's sufferers, the trial patients subsequently suffered from adverse side-effects. In our paper on the two faces of L-DOPA, Abram Hoffer⁵⁴ and I argue:

At least part of the neurological damage seen in Encephalitis lethargica, Parkinson's disease, multiple sclerosis and amyotrophic lateral sclerosis appears to be caused by dopachrome and other chrome indoles, produced by the oxidation of dopamine. The use of L-DOPA in these patients probably accelerates production of such neuro-toxins. If this hypothesis is correct, it follows that combining L-DOPA with very high dose antioxidants may permit the beneficial use of this drug in all four neurological disorders. This protocol may also extend the time period over which L-DOPA is of value in the treatment of Parkinson's disease.

As yet, the necessary doses of antioxidants are unclear. They must be high. Shults and colleagues,⁵⁵ for example, have shown that daily doses of 1,200 mg of coenzyme Q₁₀ are very beneficial in the early treatment of Parkinson's disease. Clearly, this is a promising area of research that requires clinical trials capable of determining the correct dosages of levodopa and antioxidants to obtain the best net benefits for multiple sclerosis patients.

There is, of course, another reason why coenzyme Q₁₀ may be slowing down the progression of Parkinson's disease⁵⁶ and would probably do the same for multiple sclerosis. High doses of methyl acceptors, such as thiamin (vitamin B₁), riboflavin (vitamin B₂), niacin (vitamin B₃), as well as coenzyme Q₁₀ (ubiquinone) are likely to slow the breakdown of dopamine.⁵⁷ It is probably no coincidence that the successful multiple sclerosis dietary treatments developed by Mount⁵⁸ and Klenner⁵⁹ both involve repeated vitamin B₁ injections.

Beyond this, perhaps related to this shortage of dopamine observed in multiple sclerosis patients, there also appears to be an imbalance of thyroid hormones, especially a lack of triiodothyronine.⁶⁰ Unfortunately, there is doubt that these imbalances can be monitored using standard testing. As early as 1974, Dr. John A. Thompson⁶¹ wrote in *Clinical Tests of Thyroid Function*:

In the light of the present lack of knowledge it is unfortunate that there is a tendency for the definition of hypothyroidism in recent papers to be that of a raised TSH level. It would seem preferable to define hypothyroidism as a symptom/sign complex resulting from deficiency of thyroid hormones and responsive to replacement therapy, and to use some other term for cases in whom the raised TSH is the only abnormal finding. Perhaps the inelegant term 'hyper-TSH-anemia' is the most descriptive.

This point has been stressed by Derry,⁶² who in an interview is quoted as saying:

Why are we following a test which has no correlation with clinical presentation? The thyroidologists by consensus have decided that this test is the most useful for following treatment when in fact it is unrelated to how the patient feels. The consequences of this have been horrendous. Six years after their consensus decision Chronic fatigue and Fibromyalgia appeared. These are both hypothyroid conditions. But because their TSH was normal they have not been treated. The TSH needs to be scrapped and medical students taught again how to clinically recognize low thyroid conditions.

When his interviewer, Mary Shomon,⁶³ asked “What type of thyroid hormone replacement therapy do you favor? Levothyroxine, levothyroxine plus T3, or natural thyroid hormone replacement, and why?” Dr. Derry responded:

I use any of the above. In Canada we have only Eltroxin (levothyroxine) or desiccated thyroid (Parke-Davis). T3 is available through specialty pharmacies but is not as readily available as in the US. If I don't get the response that I am looking for, I will often switch either way in order to try and make the patient better.

Multiple sclerosis patients generally seem to be triiodothyronine deficient, preventing myelin repair.⁶⁴⁻⁶⁵ Derry's protocol appears an extremely logical approach to this problem.

(4) Enzyme Deficiencies

Probably because multiple sclerosis patients are continuously forced to cope with an excess of dopachrome and other damaging chrome indoles, they typically show deficiencies of the enzymes that protect against oxidative stress. Syburra and Passi,⁶⁶ for example, have established that such patients suffer from depressed erythrocyte glutathione peroxidase. The presence of this deficiency has also been reported by Shukla and co-workers⁶⁷ and Szeinberg and colleagues.⁶⁸ Beyond this, abnormal catalase activity has been seen in the granulocytes and erythrocytes of patients with multiple sclerosis, being decreased in the former and increased in the latter compared to healthy controls.⁶⁹ It seems intelligent, therefore, for the diets of multiple sclerosis patients to be elevated in the nutrients required to increase production of glutathione peroxidase, superoxide dismutase, and catalase.

Since writing "*What Really Causes AIDS*,"⁷⁰ I have been involved in several trials designed to study the beneficial impact of increased glutathione peroxidase levels in HIV/AIDS patients.⁷¹ How to achieve this elevation of the enzyme is discussed at length in "*What Really Causes AIDS*." Briefly, it involves increasing the intake of selenium and the three amino acids,

glutamine, tryptophan, and cysteine. In most of our African trials, selenium has been provided as the easily bioavailable selenomethionine. Patients in the later stages of AIDS have responded remarkably well to 600 micrograms of selenomethionine daily. After one month, the dosage has been reduced to 400 micrograms. The cheapest way to provide the amino acids has been desiccated beef liver. I am not certain, for inflammatory reasons, whether this is appropriate for multiple sclerosis patients. Good alternative amino acid sources include cold processed whey, unfortunately a dairy product, and the algae spirulina. Despite doubts about the inflammatory nature of liver,⁷² it should be recalled that both Mound⁷³ and Klenner⁷⁴ developed apparently effective treatments for multiple sclerosis that involved injection of liver extract. Mound's⁷⁵ patients, for example, received 1 millilitre of intramuscularly injected liver extract at 7 to 10 day intervals. Such injections, of course, would allow these patients to increase their glutathione peroxidase production, provided they were not selenium deficient.

The same amino acid sources should also be adequate for elevating superoxide dismutase and catalase levels. However, these enzymes are not cofactored with selenium. Three forms of superoxide dismutase exist in humans.⁷⁶ These have either copper and zinc or manganese in their reactive centres. The cofactor for catalase is iron.⁷⁷ It is obvious, therefore, that multiple sclerosis patients attempting to increase body levels of glutathione peroxidase, superoxide dismutase, and catalase should consider adding supplements of selenium, copper, zinc, manganese, and possibly iron to their diets, in addition to proteins from a non-inflammatory source.

SUMMARY

Multiple sclerosis is caused, in those eating pro-inflammatory diets, by an excess of dopamine-derived oxidation products that prevent myelin repair. The ultimate cause of this dopamine imbalance is an iodine (and thyroid hormone) deficiency that begins in the fetal or early childhood developmental stages. The value of measuring thyroid stimulating hormone (TSH) levels in blood to identify such hypothyroidism is in doubt and may lead to underestimation of thyroid problems.⁷⁸

The multiple sclerosis three-step model presented here allows the identification of a variety of strategies to prevent the disorder and reverse its symptoms. These include avoiding inflammatory foods and allergens, thyroid hormone supplementation, and the addition of a variety of minerals, vitamins, and omega-3 fatty acid to diet. The evidence behind these recommendations is provided throughout this volume.

There is a violent, ongoing debate about whether use of the artificial sweetener aspartame may cause a pseudo-multiple sclerosis. Dr. Russell L. Blaylock⁷⁹ is a strong supporter of this belief. He argues that aspartame and monosodium glutamate produce excitotoxins, similar in their effects to dopachrome and glutamate, that can also kill oligodendroglia and so prevent myelin repair. The National Multiple Sclerosis Society⁸⁰ rejects this hypothesis. My only comment is that Blaylock's argument seems feasible and it would be a major step backwards for multiple sclerosis patients to reduce their sugar intake in order to avoid inflammation by increasing their use of excitotoxin-producing artificial sweeteners.

Just as I was completing this volume, news was released of a preliminary study that involved treating 27 later stage multiple sclerosis patients with the anticancer drug mitoxantrone and

with copaxone.⁸¹ This initial trial was conducted at the Walton Centre for Neurology in Liverpool. Its objective was apparently to seriously damage the immune systems of multiple sclerosis patients to the point that they could no longer cause autoimmune disease.⁸² This is a very hazardous approach to the treatment of multiple sclerosis. One of the patients given this drug cocktail developed acute leukemia and, according to Humphreys,⁸³ another died of liver failure. Nevertheless, a further 10 controlled studies involving this cocktail are starting in other medical centres in the United Kingdom. Anyone reading this book can hardly fail to realize that there are much simpler and less deadly ways of preventing the inflammation and associated autoimmune effects seen in multiple sclerosis. Fortunately, at more or less the same time, researchers from the Children's Hospital Boston⁸⁴ demonstrated that mice with multiple sclerosis-mimicking autoimmune encephalitis could be protected by nicotinamide shots. This vitamin, as predicted by the three-step model, protected the animals' nerve cells from myelin loss.

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*It cannot be said too often: all life is one.
That is, and I suspect will forever prove to be,
the most profound true statement there is.*

*Bill Bryson, A Short History of
Nearly Everything (2004)*

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His many books include *Disaster Planning: The Preservation of Life and Property*, Springer Verlag, New York; *Reducing Cancer Mortality: A Geographical Perspective*, Western Geographical Press, Victoria; and *The Ozymandias Principles*, Southdowne Press, Victoria. Further books by the author include *Health, Disease, and the Environment*, Bellhaven Press (now John Wiley), London, and *What Really Causes AIDS, What Really Causes Schizophrenia, and What Really Causes Alzheimer's Disease*, Trafford Publishing, Victoria.

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He has been a consultant to numerous organizations, including the United Nations, NATO, and the governments of Canada, Ontario, and British Columbia. Every day he takes at least the recommended daily allowance of the known essential nutrients, in the belief that this will slow the aging process. As a consequence, most of his salary is spent in health food stores. His other bad habits include providing treats to all the neighbourhood dogs; losing at chess to his computer; being regularly beaten by his stepson Dan at video games; and, with the assistance of @Derby and various computer models, failing to correctly predict the outcomes of horse races. For a more complete curriculum vitae visit <http://www.hdfoster.com>. Free copies of this book and *What Really Causes AIDS*, *What Really Causes Schizophrenia*, and *What Really Causes Alzheimer's Disease* can be downloaded at this website.

The man who discovers a new scientific truth has previously had to smash to atoms almost everything he had learned, and arrives at the new truth with hands blood-stained from the slaughter of a thousand platitudes.

José Ortega y Gasset,
The Revolt of the Masses, 1930



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