DECLARATION

I confirm that the enclosed thesis is all my own work with acknowledged exceptions.

Signed

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An Examination of the Relationship between the Prevalence of Multiple Sclerosis and the Geological Environment Specifically Exposure to Indoor Radon before the age of 15 years

by

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THIS STUDY IS DEDICATED TO

MR. JAMES DOYLE
1925 – 2005

HE BELIEVED IN ME

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ABSTRACT

AN EXAMINATION OF THE RELATIONSHIP BETWEEN THE PREVALENCE OF MULTIPLE SCLEROSIS AND THE GEOLOGICAL ENVIRONMENT – SPECIFICALLY EXPOSURE TO RADON BEFORE THE AGE OF 15 YEARS

DENIS CARROLL 2005

Multiple Sclerosis (MS) is one of the most common diseases of the Central Nervous System, with no known cause or cure. It is a progressive degenerative disease and it affects people all around the world. It is one of the most common disabling neurological conditions of young adults, affecting almost twice as many women as men. It has been diagnosed more frequently since 1970s.

Worldwide epidemiological and genetic surveys indicate that MS is caused by an interplay between genetic traits and environmental influences. To date, no known environmental agent has been identified. Estimates of total number of cases in Ireland are in the region of 4,000 to 6,500, suggesting a prevalence rate of 100-162/100,000, however, there is no reliable national database of people with MS.

This study was designed to examine the environmental milieu of people with MS, via a questionnaire distributed with MS News to over 5,000 MS News subscribers. The 671 responses received were analysed under various headings including: gender (F:M = 2.2:1); average age at diagnosis (36.8 years); relatives with MS (over 22%); type and location of house (40% single storey) and school (65% single storey).

Based on comparison with the study of Donegal and Wexford by McGuigan et al. (2004), an estimated prevalence rate of 164.25/100,000 has been calculated for the whole country.

Radon levels (RPII data) and Interferon prescribing patterns were also examined. The study observed clustering of MS cases in areas that are known to have high Radon emissions and a sparser distribution of cases in low Radon emitting areas, and therefore, concludes that the potential to develop MS is greater if exposed to high Radon levels in childhood, especially for males, and that the rise in incidence since the 1970s has coincided with greater exposure to indoor Radon.

Key words: Multiple Sclerosis, Radon, environment, Ireland, estimated prevalence

1. INTRODUCTION

1.1 INTRODUCTION

Anyone who encounters Multiple Sclerosis (MS) inevitably asks, "what are the causes? and why this person, at this time and in this place?" Despite extensive studies, especially over the last 50 years, many questions remain unanswered. This study was designed to investigate the epidemiology of one aspect of MS.

1.2 OBJECTIVES OF STUDY

The objectives of this study were

a. To establish the prevalence of MS in Ireland
b. To establish the environmental milieu of MS patients for the first 15 years of their lives
c. To plot this information geographically
d. To examine the relationship between the incidence of MS and factors increasing exposure to natural radiation within the built environment, (specifically – indoor radon)
e. If the hypothesis is proven - to alert national authorities as to what preventative or mitigating actions can be taken.

1.3 MULTIPLE SCLEROSIS RESEARCH OVERVIEW

The history, or mystery, of MS reads like a detective novel spanning more than a century, and to date many clues have been put together. The answers are slowly emerging, but there is still much more work to be done, in order to solve the mystery of MS.

Ever since Charcot first described the disease now called Multiple Sclerosis (MS) in 1868, research has been ongoing into the aetiology of this disease. It has been described as an autoimmune disease i.e., the body's defence mechanism, which is designed to recognise self from non-self, turns from defender to attacker and attacks the myelin sheath that coats the nerves. To date no known cause or cure has been found. This has been frustrating for both the health science community and more particularly, for those diagnosed with MS. MS has been long associated

with geography, insofar as incidence increases with distance from the equator. This project will focus on the epidemiology of MS and radiation in its geographical setting. I will explain what MS is, how it affects one, and from where it is thought to have originated. The global distribution of MS will be described, with already recognised patterns. This study will test the hypothesis that Radon exposure in the first fifteen years influences the onset of MS in later life. It is hoped to demonstrate that there may be an association between the likely exposure to indoor Radon and onset of MS in genetically susceptible individuals.

1.4 Background to Study

My association with this project stems from the pilot study that was carried out by Dr. Margaret Gilmore and Mr. Eamonn Grennan, both lecturers in IT Sligo, whose backgrounds are respectively in Medicine and Geology.

The northwest of Ireland appears to have one of the highest prevalence rates of MS in Ireland. This is speculative, as there is no reliable national database. The area is one of the highest radon-emitting areas in Ireland, with Donegal in particular containing some of the most highly uranium enriched granites in the country. This provided the motivation for the pilot study that was undertaken, i.e. an attempt to refine the well-known geographical association between MS and temperate climates to a more coherent association between MS and geology (Gilmore and Grennan, 2003).

From epidemiologic studies, it has been thought that there is a trigger in early life, possibly in the first fifteen years, in genetically susceptible individuals, which is responsible for the onset of MS. A childhood virus has long been considered one of the main triggers. To date no virus has been positively identified as being this trigger.

1.5 Disease and Geology

The link between disease and geology is nothing new, for example;

a. coal mining – silicosis
b. mining or processing asbestos – asbestosis
c. radon – lung cancer

d. Uranium enriched granites - multiple sclerosis, as postulated by Bolviken, Nilsen and Ukkelberg (1997).

In this current study the hypothesis is posed that radon (a decay product of uranium) exposure, may trigger MS in susceptible individuals, who are exposed to it before the age of 15 years.

If exposure to indoor radon is shown to be an environmental trigger, then it would follow that by eliminating or mitigating exposure to this known contributor to ill health, MS may be preventable, in some if not all of its forms in certain individuals.

Radon gas is generated in the earth's crust by the radioactive decay of uranium within e.g. granites many kilometres below the surface. Radon may become trapped within buildings; it is nine times heavier than air and therefore is more concentrated at ground levels. It follows logically that bedrooms at ground floor level permit a greater degree of exposure, as would floor play by children. Radon has an accepted association with lung cancer, and it is known to be soluble in fat. The myelin tissue coating the nerves in MS is fatty tissue.

1.6 RESULTS

The results of this study are based on the findings of a questionnaire that was distributed via the MS News magazine to people with MS, with a view to establishing their environmental milieu during the first fifteen years. Brady, Dean, Secerbegovic, S. and Secerbegovic, A. (1977) in their paper "Multiple Sclerosis in the Republic of Ireland" suggested "a study based on the birthplace of MS patients".

In this thesis, data on Multiple Sclerosis and Radon will be presented, as will the results from the analysis of the questionnaires.

2. LITERATURE REVIEW

2.1 MULTIPLE SCLEROSIS

2.1.1 Origins and History of Multiple Sclerosis

The first written record of someone with MS type symptoms refers to the Dutch patron Saint of ice skaters, "Lydwina of Schieden" (1380 – 1433), (http://www.mult-sclerosis.org/famous.html) and (http://www.albany.net/~tjc/ms-tory.html). Medical drawings from the late 1830's show what is today recognised as MS. However, the first scientific description and clinical symptoms that are today known as "Charcot's Triad", diplopia (double vision), ataxia (disturbances of balance or co-ordination) and dysarthria (difficulties with, or slurred speech) were recorded by Dr. Jean Martin Charcot (1825 – 1893), who is often referred to as the "Father of Multiple Sclerosis".

One of his many students was a man named Sigmund Freud (1856 – 1939). Freud treated his former Nanny who had what was then known as "*Creeping Paralysis*", thought to be a mental condition caused by "*Female Hysteria*". This misdiagnosis probably explains why little research into MS was conducted until modern times.

MS was originally thought to be more prevalent in men, due to women being diagnosed with "*Female Hysteria*". There is a tendency for MS symptoms to flare each month for many female sufferers. "In a sample of 149 women with MS, 70% of the women said they noted an increase in their neurologic symptoms several days prior to onset of menses. Three or four additional studies of self-reports, support this observation", (http://www.nationalmssociety.org/Brochures-Hormones1.asp).

Louis Ranvier discovered myelin, the fatty tissue that coats the nerves in 1878. In 1925, Lord Edgar Douglas Adrian helped prove that demylinated nerves are unable to carry the electrical impulses by recording the first electrical nerve transmissions, (http://www.ifmss.org.uk/en/research/history_of_ms_research/co-mplexitiesand.html) and (http://www.albany.net/~tjc/mstory.html).

Fig. 2.1 Myelinated Nerve Fibres

Source: Lexi Comp Inc USA Diseases Explained
http://www.diseases-explained.com/MultipleSclerosis/whatisms.html

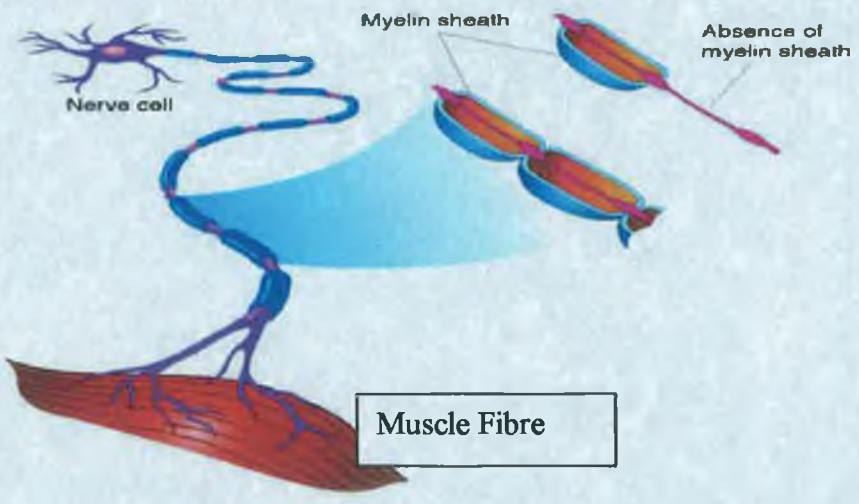

Fig. 2.2 Electrical Impulse from Nerve to Muscle

Source: http://www.ahealthyadvantage.com/topic/ms

In the above illustration, the electrical impulse from the nerve cell may not reach, or only partially reach the muscle, that it is attached to, due to demyelination, thereby causing the muscle to malfunction (shaking) or not function at all.

2.1.2 Description of Multiple Sclerosis

MS is a disease of the central nervous system (CNS), i.e. the nerves that comprise the brain and spinal cord. There is no known single causative factor associated

with the development of MS, therefore there is no way of knowingly preventing it, nor can it be cured. It is one of the most common diseases of the CNS. Its

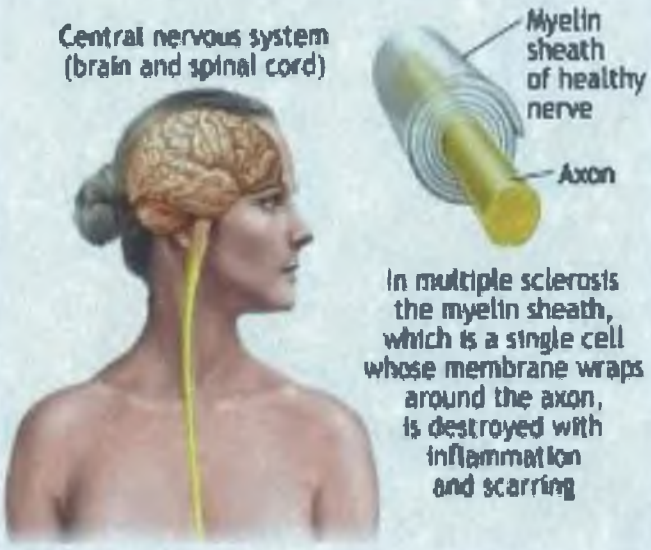

Fig. 2.3 Brain and Spinal Cord

Source: medline plus
http://www.nlm.nih.gov/medlineplus/ency/imagepages/17089.htm

mechanism remains obscure and elusive; it is considered to be an autoimmune disease, attacking the myelin sheath that wraps around the nerves. It affects approximately twice as many women as men, as do most autoimmune diseases and there also exists a familial pattern. The pathogenesis of MS has been attributed to: - infectious agents, environmental exposure, genetic susceptibility and even dietary factors. Viral infections have been suspected of having an influence on developing MS and this is attributed to their known ability to cause demyelination in both humans and animals. Hogancamp, Rodriguez, and Weinshenker, (1977) and Ebers and Sadovnick (1993) in their studies into the epidemiology and geographic distribution of MS, support the theory that both genetics and environment play a part in the development of MS. Compston (2004) has hypothesised that MS evolved from a somewhat related disorder, Devic's disease, or Neuromyelitis Optica.

2.1.3 Pathology

The CNS contains millions of nerve cells joined together by long thin fibres. The electric signals start in the nerve cells and travel along these fibres to and from the brain. A fatty substance called myelin covers these fibres. This myelin (which

works in a similar way that insulation works on electrical wire) becomes damaged and the connection with the nerve fibres is disrupted, resulting in lost, blocked or delayed signals travelling to and from the brain. Hardened tissue called scar tissue forms on the nerve fibres; this process is called "sclerosis", a Latin word meaning scar and that is how the disease gets its name. Multiple refers to the multiple sites that are scarred, leading to a multiplicity of symptoms (Herndon, 2003).

MS is a progressive degenerative disease and it affects people all around the world. According to the World Health Organisation (WHO) and the National Multiple Sclerosis Society (USA), it affects 2.5 million people worldwide. Kurtzke (1977) described it as a geographically related disease, more common in Caucasians. MS development is related to place of residence before 15 years of age (Dean and Elian, 1997). The true cause or causes of the disease are still waiting to be discovered. However, if a cause can be identified, and is eliminated, then MS may be preventable.

2.1.4 Types of Multiple Sclerosis

There are several recognisable patterns of MS that are described below.

2.1.4.1 Benign Multiple Sclerosis: Affects approximately 20% of MS population, (http://www.albany.net/~tjc/multiple-sclerosis.html), or affects 10% of MS population (www.msmeans.ca/faqs.html), depending on which expert you are consulting. Following one or two attacks, there is a complete recovery and no discernable disability. There is no permanent disability for the majority in this category; however, some people in this category will experience disease progression, evolving into the more progressive stages of MS as time passes, some ten to fifteen years hence.

2.1.4.2 Relapsing-Remitting: Affects approximately 25% of MS population. (http://www.albany.net/~tjc/multiple-sclerosis.html), or again depending on who is being quoted, 50% (www.msmeans.ca/faqs.html), and follows a pattern of unpredictable, recurrent attacks during which existing symptoms may become more severe or new symptoms may appear. This is followed by a gradual recovery, generally over weeks or months. Any impairment will not worsen

between attacks. During this stage of the disease, there may be long stages where there are no discernable symptoms, however the disease is not dormant and there is ongoing damage occurring. This can be considered the most common "beginning phase" of the disease. Some 50% of cases will have progression within ten to fifteen years and an additional 40% within twenty-five years of onset (http://www.albany.net/~tjc/multiple-sclerosis.html). This form of the disease then evolves into Secondary Progressive.

2.1.4.3 Secondary-Progressive: Evolving from the relapsing-remitting stage and affecting approximately 40% of MS population. (http://www.albany.-net/~tjc/multiple-sclerosis.html#S/P). Recovery from this stage is not as complete as previous stages and the disability becomes permanent. There is an apparent lessening of clinical attacks and they become less pronounced with little or no remission. This type is associated with more and more central nervous system tissue being destroyed.

2.1.4.4 Primary-Progressive: Affecting approximately 12% of sufferers (http://www.albany.net/~tjc/multiple-sclerosis.html), and is characterised by gradual and increasing impairment. There are no distinct remissions, but periods of relative stability can occur. While not common in younger individuals, this is the most common pattern in late onset cases (i.e. onset after age 40). In this type, unlike the exacerbating remitting types in which the female to male ratio is generally 2:1, the ratio is only about 1.3:1 (Herndon, 2003).

2.1.4.5 Progressive-Relapsing: Presenting a progressive pattern of impairment (once known as Marburg MS), with periods of more rapid deterioration and affecting approximately 3% of people with MS (http://www.albany.net/~tjc/mul-tiple-sclerosis.html). It is the more complex form of the disease, although it is similar in terms of disability to primary progressive. It is probably the most dreaded form of the disease, as lost function never returns. Its severe unrelenting progression can lead to death within a few months to a year (Herndon, 2003).

2.1.5 Diagnostic Categories for Multiple Sclerosis

During the early stages of MS, the symptoms experienced may not be recognised as being associated with MS. They may be mistaken for other conditions that have similar symptoms. As there is no specific non-intrusive diagnostic test for MS, (Fangerau, Schimrigk, Haupts, Kaeder, Ahle, Brune, Klinkenberg, Kotterba, Möhring, and Sindern, 2004) and given the unpredictable nature of the disease, it can be difficult to confirm.

MS is likely to begin with a string of fluctuating, difficult to describe, and what seem to be minor, symptoms that are often forgotten about. They seem to clear up without treatment, but continue to return periodically. Many of the symptoms can be attributed to several different medical conditions, e.g. Lindane Poisoning, as illustrated in Table 2.1 below.

Lindane, formerly known as gamma benzene hexachloride is an insecticide used to treat scabies and head lice infestations. It is also widely used to control insect infestations on livestock, pets and agricultural products. It has been banned in several countries and is severely restricted in others, (http://www.drrichard-hall.com/lindane.htm). It has been described as a persistent organic pollutant by UN Environment Programme and has been classified as a possible human carcinogen, (http://www.foodcomm.org.uk/pesticides_lindane.htm)

Table 2.1 Comparison of Symptoms

Symptoms of Lindane poisoning compared to symptoms of MS	
Lindane poisoning symptom	*MS symptom*
Seizures	Acute flare-ups
Weakness	Fatigue
Paresthesia of face and extremities	Numbness of extremities
Giddiness	Giddiness
Impaired memory	Short term memory loss
Loss of sleep	Sleeping disorders
Headaches	Headaches
Abnormal EEG patterns	Abnormal EEG patterns
2/3 women affected	2/3 women affected
Vertigo	Dizziness (Erratic walking)
Trauma induced	Trauma induced
Loss of libido	Loss of sexual urge
Malaise	Feeling of discomfort or uneasiness
Tremors	Tremors
Apprehension	Uneasy, Anxious
Decreased nerve velocity	Decreased nerve velocity
Musculoskeletal effects	Musculoskeletal dysfunction

Source: http://www.protector.pair.com/ms/

A considerable time may pass before MS is confirmed or even mentioned. However, a diagnosis of MS may be more definite if the patient presents with a concise history of attacks, coupled with known symptoms of MS. What the neurologist requires is clinical evidence that the symptoms point to at least two different areas of the CNS and at least two distinct attacks with a specific timeframe between attacks. All other neurological causes have to be eliminated.

2.1.6 Poser Criteria

The Poser criteria for diagnosing MS were put forward in 1983 to update the 1965 Schumacher criteria (http://thjuland.tripod.com/diagnosis.html). McDonald also developed criteria for diagnosing MS in 2001, however, Fangerau et al. (2004 p. 385) concluded that, "MS according to the McDonald criteria was diagnosed more often than 'clinically definite MS' according to Poser et al., but combining the categories of clinically and laboratory definite MS, the diagnosis of MS could clearly be established more frequently using the Poser criteria". Therefore, only the Poser criteria are included in this thesis.

2.1.6.1 Definite Multiple Sclerosis

a. Consistent course, relapse/remitting, with at least two bouts, separated by at least 1 month; or slow, stepwise progressive course for at least six months.
b. Documented neurological signs of lesions in more than one area of brain or spinal cord white matter.
c. Onset of symptoms between ten and fifty years of age.
d. Absence of other more likely neurological explanations.

2.1.6.2 Probable Multiple Sclerosis

a. History of relapsing/remitting symptoms.
b. Signs not documented and only one current sign commonly associated with MS.
c. Documented single bout of symptoms with signs of more than one white matter lesion.
d. Good recovery, then variable symptoms and signs.
e. Absence of other more likely neurological explanations.

2.1.6.3 Possible Multiple Sclerosis

a. History of relapsing/remitting symptoms.
b. No documentation of signs establishing more than one white matter lesion.

c. Absence of other more likely neurological explanations.

2.1.7 Symptoms

The symptoms can vary from time to time and from individual to individual and can include: bladder dysfunction, bowel dysfunction, cognitive problems, speech and swallowing disorders, dizziness, fatigue, walking problems, headaches, hearing loss, vision problems, numbness, pain and seizures. (Medline: http://www.nationalmssociety.org//Symptoms.asp). Martyn (1991) in a review of published reports, observed the incidence of initial symptoms as:

a. weakness in one or more limbs 40%
b. optic neuritis (inflammation of nerves) 22%
c. paraesthesiae (tingling, pins and needles) 21%
d. diplopia (double vision)12%
e. vertigo 5%
f. disturbance of micturition (urination) 5%

Since the myelin can be attacked in any area of the CNS, the symptoms vary accordingly. The disease, which has been described as an autoimmune disease, i.e. the immune system which is designed to recognise self from non self, turns from being a defender to an attacker, and attacks the myelin sheath that insulates the nerves.

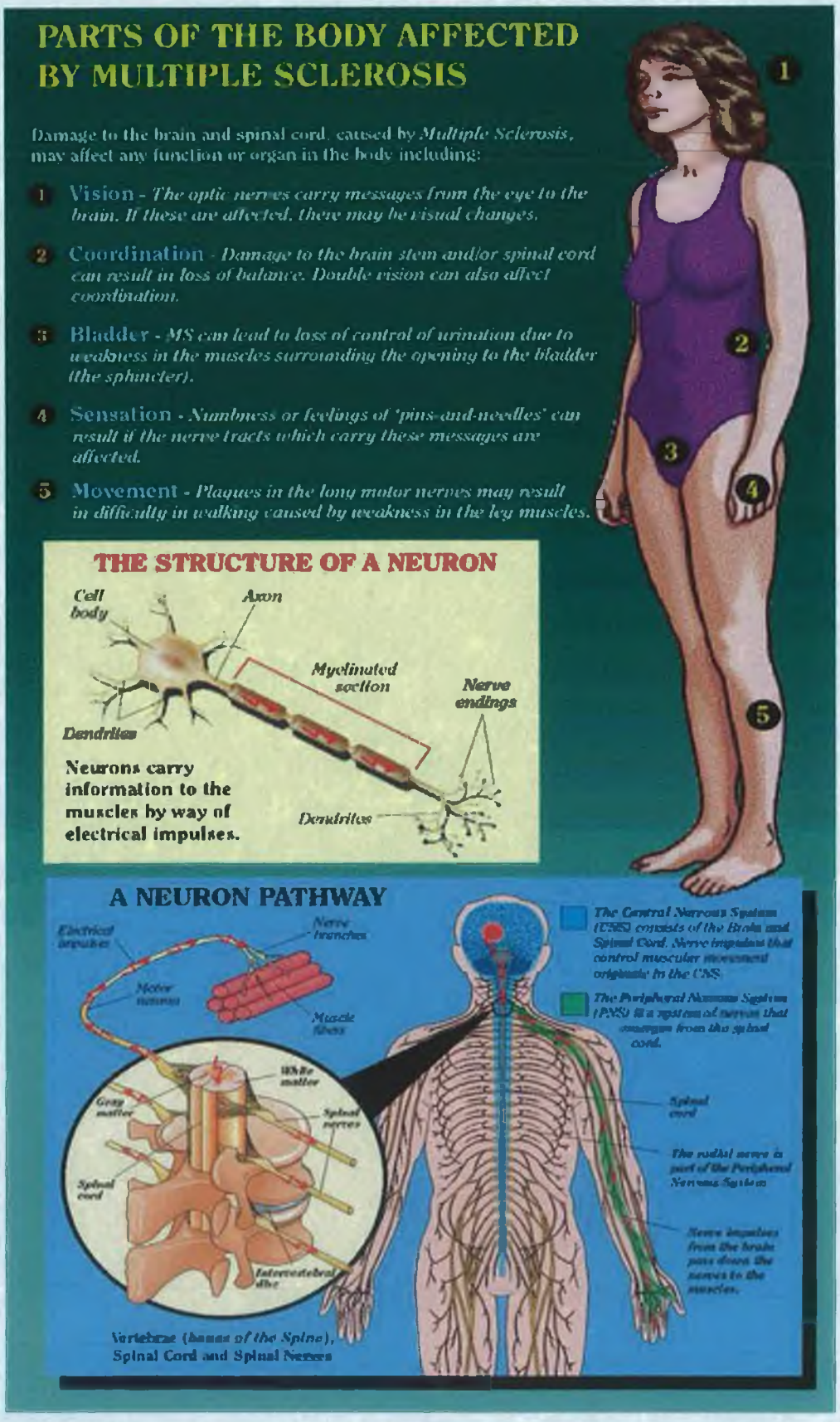

Fig. 2.4 Parts of the Body Affected by MS

Source: Lexi Comp Inc USA
http://www.diseases-explained.com/MultipleSclerosis/whatcausesms.html#

2.1.8 Features Observed in Multiple Sclerosis

The course is unpredictable but some associated features that are known are described below.

2.1.8.1 Age

"MS is the most common disabling neurological condition of young adults, affecting approximately 6,000 people in Ireland" (http://www.ms-society.ie/what/index.html). The average age at onset is not easy to determine. In approximately 70% of patients onset occurs between 20 and 40 years of age (Simon, 2002). Cottrell, Kremenchutzky, Rice, Koopman, Hader, Baskerville and Ebers, (1999) reported a mean age of onset of 38.5 years. An interesting finding by Kurtzke, Page, Murphy and Norman, (1992) in their study of over four thousand WWII veterans, found the average age at onset for white men was 27 years, 27.7 years for white women and 27.5 years for black men. These average ages rose as one travelled from north to south in the USA, thus the further south one lived the higher the average age at onset. They divided the USA into three horizontal tiers, a northern, middle and southern tier. They divided the MS patients by entry into service by state and found that the average age at onset for white men was 26.4 for northern tier, 27.3 for middle tier and 28.8 for the southern tier. Similar trends were observed for white women and for black men. There was no mention of black women in this study.

2.1.8.2 Gender

It is generally accepted that MS affects more women than men, although reported ratios differ from 1.3:1 to 2.79:1. As cited by Gilmore and Grennan (2003) Robinson (1988) and Benz (1988) suggest that the ratio was on average 3:2, while Burnfield (1991) suggests a ratio of 1.7: 1. Ford, Gerry, Airey, Vail, Johnson, and Williams, (1998) found a ratio of 2.8: 1. A study by McDonnell and Hawkins (2000) in Northern Ireland reports a ratio of 2.1: 1. Totaro, Marini, Cialfi, Giunta, and Carolei, (2000) found a rate of 2:1. The pilot study carried out in the Northwest of Ireland by Gilmore and Grennan (2003) suggests a ratio of 1.6:1. Cottrell et al. (1999) reported a significantly lower ratio of 1.3:1.

Data obtained from the Department of Social, Community and Family Affairs, Ireland, (2004) lists the number of people claiming disability benefit due to MS and shows quite a different picture. The figures given were 133 females and 41 males, a ratio of 3.2:1. However, it must be borne in mind that disability benefit is paid out over the short term, and then the individual is transferred to disability allowance, a long-term payment.

2.1.8.3 Ethnicity

MS can be found worldwide but is most common amongst Caucasian people of northern European origin, particularly those of Scottish descent (Rothwell and Charlton, 1998 and Rosati, 2001). Within the African and Asian populations, it is quite rare. Canadians living in the same regions as indigenous Inuit people have up to twenty times the Inuit prevalence rate. Among the Native American population, it is also relatively rare, as it is in the Aborigines and Maoris of Australia and New Zeland respectively (http://en.wikipedia.org/wiki/Multiple_sclerosis#Prevalence).

2.1.8.4 Geography

The risk for MS varies throughout the world. In general, MS is more prevalent in temperate regions than in the tropics. Prevalence is highest in northern and central Europe (except northern Scandinavia), Italy, southern Australia, New Zeland, and the northern regions of the USA and Canada. Middle-risk areas are southern Europe (except Italy), southern USA, northern Australia, northern Scandinavia, and the Caucasian populations of South Africa (Kurtzke, 1977 and Pozzilli Romano and Cannoni, 2002).

Low-risk areas include most parts of Africa and Asia, the Caribbean, Mexico, and possibly northern South America. Several theories have been put forward to explain this pattern, citing environmental factors, genetics, and/or a combination of both. Kira (2003) noted that the cause of MS can be attributed to an interplay between genetic traits and the environment, and is borne out by epidemiological and genetic surveys. The top ten countries today measured by prevalence rate (per 100,000) are: -

a. UK (143.8)
b. Sweden (134.8)

c. Ireland (125.0)

d. Denmark (112.0)

e. Canada (111.0)

f. Iceland (105.1)

g. Germany (99.0)

h. Finland (98.0)

i. Czech Republic (97.1)

j. Holland (94.9)

(source: http://www.mult-sclerosis.org/explainingms.html).

Fig. 2.5 Global Prevalence of MS

(source http://www.mult-sclerosis.org/ms_world.html)

The first mention that MS prevalence rates increased with distance from the equator was by Limburg in 1950 cited in Ford et al. (1998). "There is good international evidence of geographical variation in prevalence, best described by increasing prevalence with latitude, both north and south of the equator" (Richards, Sampson, Beard, and Tappenden, 2002 p. iii). Poser (1995) suggests that the direct relationship between latitude and prevalence rates can no longer be considered valid and although he does not speculate on what the environmental factor might be, he does acknowledge its existence. It is perhaps just a coincidence that the distribution of MS reflects a latitudinal variation. This idea will be revisited. Rothwell and Charlton (1998 p. 730) state "the prevalence of

MS increases with latitude north and south of the equator", and further that this could be caused by exposure to a causative environmental agent. The causative environmental agent seems to be gaining more ground, Ebers and Sadovnick (1993) in their conclusion noted that there is no known single environmental or genetic factor that explains the geography of MS and McDonald (1986) noted that the environmental factor needed to explain MS still remains obscure.

The differences in prevalence rates observed among different ethnic groups in similar locations, seem to suggest, that along with genetic factors, there may be enhancing and/or protective influences which are probably environmental in nature (Poser, 1995). Even in areas of low prevalence, e.g., Japan, Kira (2003), noted a small, but considered it to be a significant north to south gradient of MS prevalence rates, and believes that it is something in the environment that contributes to developing MS. Rosati (2001) also questions the traditional beliefs, on prevalence/latitude, by looking at the updated distribution of MS in Europe, which shows many exceptions to the previously described north-south gradient. This observation requires a more thorough explanation than simply a prevalence-latitude relationship. Wallin, Page, and Kurtzke, (2004) observed marked changes in the distribution of MS and this they suggest implies a primary environmental factor, and again no suggestion as to what the environmental factor might be. Dean and Elian (1997 p.565) concluded "that the environment during childhood is a major factor in determining the risk of developing MS".

Rosati (2001) acknowledges the difficulty in trying to explain the pattern of geographical differences in MS frequency. Closer to home in a recent study by (McGuigan, McCarthy, Quigley, Bannan, Hawkins and Hutchinson, (2004) they concluded that the latitudinal variation in the prevalence of MS rates between Donegal and Wexford was more likely explained by greater accuracy in diagnosing and/or better case ascertainment. A combination of genetic and environmental factors appears to be needed to explain the data on MS and Geography.

2.1.8.5 Genetics

Descriptions of MS in Scandinavia in the early 18th Century are recounted by Pozzilli et al. (2002), however, the first written record dates back to the 14th Century in Holland (http://www.albany.net/~tjc/ms-tory.html). It appears to have spread across the Baltic States, Northern Europe, and the British Isles over the next 100 years or so, and then on to North America, Australia and Italy. Poser (1995) proposes that MS is a disease of the Scandinavians, as they raided most of Europe and engaged in trade with the Arabs. All this contributed to the genetic distribution of the MS gene or genes.

MS can be described as a complex genetic disorder. Following years of research, no single gene has been identified as being the cause of MS. Several genes have been implicated. Compston (1999) has suggested that interplay between genetic and environmental factors is likely in the onset of MS, with a familial recurrence rate of 15%. Compston's studies into the genetics of MS go back over 15 years and he currently leads the Multiple Sclerosis Genetics Group based in Addenbrooke's Hospital, Cambridge. In April 2000 various groups researching native and migrant European populations came together to identify possible susceptible genes and this collaboration resulted in the Genetic Analysis of Multiple Sclerosis in Europeans "GAMES". A total of 19 GAMES projects have been completed and involved 16 native European and migration European populations.

A large study of Canadian twins (370 pairs), has confirmed that genes and environment both contribute to onset of MS (Willer, C.J., Dyment, D.A., Risch, N.J., Sadovnick, A. D. and Ebers, G. C. 2003). Chataway, Mander, Robertson, Sawcer, Deans, Fraser, Broadly, Clayton, and Compston (2001 p. 757) agree, "genes influence both susceptibility and evolution in MS" and they also recognised the familial tendency. The Canadian Twin Study that spanned two decades has confirmed that the overall risk for identical co-twins is 25%. When both twins were male, the risk dropped to 5% and rose to 34% when the twins were female. The study also found that the majority of identical twins with MS are female. The risk for non identical twins was 5.4%. This would indicate that the disease runs in families, although the risk of someone inheriting all the genetic factors is low. However, as

Compston (1999) points out, if both parents have MS, prevalence in children is higher than if only one parent has MS.

Scientists have identified a gene, which appears to be a risk factor and may contribute to more rapid progression than normal. They also found that people who have two copies of a particular variant of the gene, known as CD24, were significantly more likely to develop MS than other people in the study (Zhou, Rammohan, Lin, Robinson, Li, Liu, Bai, Yin, Scarberry, Du, You, Guan, Zheng and Liu, 2003).

2.1.9 Environment

The environmental link between where a person spent their first fifteen years and the likelihood of developing MS in later life has been well established, most recently by Dean and Elian (1997). This has been borne out by migration studies, which show that migration after 15 years of age, the risk of the area moved from is retained. This is based on their (Dean and Elian 1997) study of immigrants to England from Asia and the Caribbean. They found that MS is rare among the Chinese, finding only two cases of MS among an estimated 45,000 Chinese immigrants. They also found that Pakistani and Indian immigrants who migrated to England younger than 15 years had a higher risk of developing MS than those who migrated after 15 years. On the reverse side, those born in a high risk area and who move to a low risk area, after the age of 15 years, retain the high risk, as cited by Dean's (1969/70) studies of British migrants to South Africa.

2.1.10 Treatment

One of the reasons why people with MS have tough decisions to make as regards treatment is the fact that their disease may be progressing even though there are no visible symptoms, and whilst it might go against the grain to take drugs when there is no apparent problem, medical science tells us that waiting is not a good approach. The main form of treatment for MS is drug therapy, including the interferons, Beta 1a and Beta 1b (see ABC treatments in table 2.2)

The latest bad news for MS patients is the withdrawal of the Biogen/Elan drug, Tysabri. However, this drug is not, nor has it been on the market in Ireland as it has not yet been licensed in Europe. There are however up to 20 patients involved in trials in Ireland (http://www.msireland.com/news/tysabri.html). See Table 2.2

for a complete list of drugs used. MS is big business as it has cost the Irish taxpayer from June 2002 to June 2003 €2,132,496 to supply drugs to MS patients. (Source: General Medical Services Payments Board).

2.1.11 Prognosis

While there are definite types recognised, there is no typical MS and symptoms vary from individual to individual, therefore trying to generalise a specific prognosis is not possible. The course of MS is unpredictable and varies considerably in individuals; however the majority of people with MS can usually expect to live up to 95% of the normal life span (http://www.nationalms-society.org/sourcebook-prognosis.asp). The difficulty in diagnosing MS due to the multiplicity of symptoms can be quite difficult for people with MS to come to terms with.

Most people with MS are mildly affected and can lead reasonably normal lives, although some can lose their sight, the ability to talk, or may be confined to a wheelchair (http://www.ninds.nih.gov/disorders/multiple_sclerosis/multiple_sclerosis.htm#What_is_the_prognosis). However, some people with MS, perhaps with the progressive-relapsing subtype can lose the ability to speak, see, walk, etc., and the severe unrelenting progression can lead to death within a few months to a year (Herndon, 2003). Death from the direct effects of MS on the nervous system is not usual and is more likely from complications as a result of the paralysis caused by demyelination (Matthews, McAlpines MS 1991).

2.1.12 Overview

For the estimated 2.5 million people spread across the five continents, often struck down in the prime of their lives by MS, with its puzzling prevalence and geographic distribution, who have to live with the unpredictability of attacks and remissions, diminished quality of life, daily regime of drug dependency coupled with the unpleasant side effects, no concrete sign of a cause being identified or any sign of a cure on the horizon, this study can do nothing for them, However, for genetically susceptible individuals who have yet to develop the disease this study may offer some hope to them. If the original hypothesis which states "that Radon exposure before the age of 15 years is postulated as a contributory cause in genetically susceptible individuals". (Gilmore and Grennan, 2003 p157) is proven,

it may go some way towards eliminating the suffering that MS brings. It is not a cure but it may be a preventative measure.

Table 2.2 List of Drugs used in Treating Symptoms of MS

ABC Treatments				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Relapsing-Remitting MS, Secondary Progressive MS with relapses	Interferon Beta 1a	30 mcg intramuscular once per week self-injection	Avonex	Biogen
		44 mcg subcutaneous 3 times per week self-injection	Rebif	Ares-Serono
	Interferon Beta 1b	Subcutaneous self-injection once every two days	Betaseron	Berlex
			Betaferon	Schering
Relapsing-Remitting MS	Glatiramer Acetate	20mg subcutaneous daily self-injection	Copaxone	Teva-Marion
Chemotherapeutic Agents				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Secondary Progressive MS, Worsening Relapsing-Remitting MS	Mitoxantrone	Intravenous every 3 months for about 2 to 3 years	Novantrone	Immunex
Corticosteroids and ACTH				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Acute relapses in Relapsing-Remitting MS and occasionally Secondary Progressive MS	MethylPrednisolone	Intravenous high doses tapered off	Depo-Medrol	
			Solu-Medrol	Pharmacia
	Prednisone	Oral administration	Deltasone	Pharmacia
	Prednisolone	Intravenous administration	Delta-Cortef	Pharmacia
	Dexamethasone	Oral administration	Medrol	Pharmacia
			Decadron	Merck
	Adreno-corticotrophic Hormone (ACTH), Corticotropin	Use largely replaced by synthetic corticosteroids	Acthar	Roche, Rhone-Poulenc Rorer
Pain/Altered Sensation (Dysaesthesia)				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Neuropathic/neurogenic pain (pain that arises from nerve dysfunction and not as a result of injury e.g. Trigeminal	Carbamazepine	Anti-convulsant	Tegretol, Epitol, Atretol, Carbatrol	Ciba
	Gabapentin	Anti-convulsant	Neurontin	Pfizer

Neuralgia)	Topiramate	Anti-convulsant	Topamax	Ortho-McNeil
	Zonisamide	Anti-convulsant	Zonegran	Elan
	Phenytoin		Dilantin	
	Desipramine		Norpramin	
	Amitriptyline	Tricyclic antidepressant	Elavil	AstraZeneca
	Imipramine	Tricyclic antidepressant	Tofranil, Imavate, Janimine	Ciba Geigy
	Doxepin	Tricyclic antidepressant	Sinequan, Adapin, Triadapin, Zonalon	
	Protriptyline	Tricyclic antidepressant	Vivactil	
	Cannabis and synthetic cannabinoids	Illegal in many parts of the world	Marinol	
Pain associated with poor circulation	Pentoxifylline		Trental	
'flu-like symptoms associated with Beta Interferon injections	Ibprofen		Neurofen	
			US versions	
	Aspirin		generic	
	Acetaminophen	Often formulated with alkaloid pain killers like codeine and hydrocodone	generic	
Paroxysmal itching	Hydroxyzine		Atarax	

Depression/Anxiety/Insomnia				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Depression without anxiety	Fluoxetine	Selective Serotonin Reuptake Inhibitors	Prozac	Eli Lilly
Mild anxiety, panic attacks, people on multiple medications	Sertraline	Selective Serotonin Reuptake Inhibitors	Zoloft	Pfizer
			Lustral	Pfizer
Moderate depression, anxiety, people for whom other antidepressants don't work	Venlafaxine	Selective Serotonin Reuptake Inhibitors	Effexor XR	Wyeth-Ayerst Laboratories
Depression with mild anxiety	Citalopram	Selective Serotonin Reuptake	Celexa	Forest Pharmaceuticals

		Inhibitors		
Depression with mild anxiety	Parocetine	Selective Serotonin Reuptake Inhibitors	Paxil, Seroxat	Glaxo-Smith-Kline
Depression also agoraphobia, insomnia, essential tremor, some pain syndromes	Trazodone	Similar to SSRIs - works by increasing the amount of serotonin	Desyrel, Trialodine	Pharmacia
Depression	Amitriptyline	Tricyclic antidepressant	Elavil	AstraZeneca
Endogenous depression	Nortriptyline	Tricyclic antidepressant	Pamelor	Novartis
			Aventyl	Eli Lilly
Depression	Imipramine	Tricyclic antidepressant	Tofranil, Imavate, Janimine	Ciba Geigy
Depression particularly when accompanied by anxiety and insomnia	Dothiepin	Tricyclic antidepressant	Prothiaden	Knoll Pharmaceuticals
Depression of varying severity with coexisting anxiety	Lofepramine	Tricyclic antidepressant	Gamanil	Organon
Anxiety, neurosis, manic depression	Doxepin	Tricyclic antidepressant	Sinequan, Adapin, Triadapin, Zonalon	
All types of depression, apathety, withdrawal	Protriptyline	Tricyclic antidepressant	Vivactil	
Moderate to severe depression	Tranylcypromine	Monoamine oxidase inhibitor (MAOI)	Parnate	Glaxo-Smith-Kline
Depression particularly when accompanied by social phobia	Moclobemide	Monoamine oxidase inhibitor (MAOI)	Manerix, Aurorix	Roche
Withdrawn, depression-related fatigue, concentration and attention problems, depression-related sexual dysfunction	Bupropion	Aminoketone antidepressant	Wellbutrin SR	Glaxo-Smith-Kline
			Amfebutamone	
Depression with significant anxiety, panic attacks, insomnia, sexual dysfunction	Nefazodone	Phenylpiperazine antidepressant	Serzone	Bristol-Myers Squibb
Depression with insomnia, moderate to severe anxiety, sexual dysfunction	Mirtazapine	Piperazino-azepine antidepressant	Remeron	Organon

Insomnia	Zolpidem	Imidazopyridine	Ambien	Pharmacia
Anxiety - not indicated if primary complaint is depression	Alprazolam	Benzodiazepine - addictive	Xanax	Pharmacia and Upjohn
Insomnia, Anxiety	Temazepam	Benzodiazepine - addictive	Restoril	Novartis
Anxiety, Insomnia, muscle relaxant	Diazepam	Benzodiazepine - addictive	Valium	Roche
Anxiety	Buspirone	Azaspirodecanedione	BuSpar	Bristol-Myers Squibb
Fatigue				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Multiple sclerosis fatigue. Also dystonia and akathisia	Amantadine	Anti-viral	Symmetrel	Endo Pharmaceuticals
Fatigue	Pemoline	Central Nervous System stimulant	Cylert	
	Modafinil		Provigil	
Urinary Problems				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Urinary Frequency and Urgency	Oxybutynin		Ditropan XL	
	Desmopressin, Vasopressin	Nasal spray	DDAVP	
Urinary Urgency and Incontinence	Tolterodine		Detrol	
	Carbamazepine	Anti-convulsant	Tegretol, Epitol, Atretol, Carbatrol	Ciba
	Imipramine		Tofranil	
	Bethane		Urecholine	
Urinary Hestitancy	Phenoxybenzamine		Dibenzyline	
	Terazosin		Hytrin	
Spastic Bladder	Propantheline	Anticholinergic agent	Pro-Banthine	
	Oxybutynin	Anticholinergic agent	Ditropan	
	Hyoscyamine	Anticholinergic agent	Urispas	
			Cystopas	
	Baclofen	Skeletal muscle relaxant	Lioresal	
	Diazepam	Benzodiazepine - addictive	Vallium	
Urinary Tract Infections (UTI)	Methenamine		Hiprex	
			Mandelamine	
	Nitrofurantoin		Macrodantin	
	Phenazopyridine		Pyridium	
	Ciprofloxacin		Cipro	
Bowel Problems				

Condition/Symptom	Generic Name	Comments	Brand Name	Manufacturer
Constipation	Bisacodyl	Stimulant laxative	Dulcolax	
			Bisacolax	
	Magnesium hydroxide (Milk of Magnesia)	Hyperosmotic laxative	generic	
	Glycerin	Hyperosmotic laxative, suppository	Sani-Supp	
	Psyllium hydrophilic mucilloid	Bulk-forming oral laxative	Metamucil	
	Sodium phosphate		Fleet Enema	
	Docusate	Stool Softener	Colace	
		Suppository	Therevac Plus	
Sexual Dysfunction				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Erectile dysfunction in men and women	Sildenafil		Viagra	
Erectile dysfunction	Alprostadil	Suppository	Prostin VR	
			MUSE	
	Papaverine	Injection into penis		
Spasticity/Clonus/Muscle Tics				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Spasticity	Diazepam	Benzodiazepine	Valium	
	Clonazepam	Benzodiazepine	Klonopin	
			Rivotril	
	Baclofen	Skeletal muscle relaxant	Lioresal	
	Dantrolene sodium	Skeletal muscle relaxant	Dantrium	
	Tizanidine	Skeletal muscle relaxant	Zanaflex	Elan
			Sirdalud	
	Clonidine	Antihypertensive	Catapres	
	Botulinum Toxin	Kills Nerves	Botox, Neurobloc	Elan
Tremor				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Postural tremor	Clonazepam		Klonopin	
			Rivotril	
	Gabapentin		Neurontin	
		Beta blockers		
	Primidone		Mysoline	

	Botulinum toxin	Kills Nerves		
	Acetazolamide		Diamox	
Rest tremor	Levodopaandshy;carbidopa		Sinemet	
		anticholinergics		
Tremor	Isoniazid		Laniazid	
			Nydrazid	

Vertigo, Nausea, Dizziness				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Vertigo, Nausea, Dizziness	Meclizine		Antivert	
			Bonamine	
	Dimenhydrinate		Dramamine	
	Prochlorperazine		Compazine	
	Scopolamine		Transderm	
	Diphenhydramine		Benedryl	

Anti-virals/Vaccinations				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Prevention of Relapses	'flu jabs	Now recommended for people with MS	N/A	N/A
	Acyclovir			

Other Treatments/Experimental Medications				
Condition/Symptom	**Generic Name**	**Comments**	**Brand Name**	**Manufacturer**
Relaspsing-Remitting Multiple Sclerosis and possibly Secondary Progressive MS	Natalizumab	Monoclonal antibody - blocks access for lymphocytes to the central nervous system	Antegren	Elan/Biogen
Relaspsing-Remitting Multiple Sclerosis and Secondary Progressive MS	Alemtuzumab	Monoclonal antibody - kills T Cells	Campath-1H	Schering/Millennium Pharmaceuticals/IL EX Oncology
	4-aminopyridine	Blockspotassium channels in neurons which may improve nerve transmission in MS	Fampridine	Elan/Accorda
	3,4 Diaminopyridine	Blocks potassium channels in neurons which may improve nerve transmission in MS		

	Eliprodil	Might promote remyelination		
	IV Immunoglobin	Reduces severity of viral infections	Gammagard, Gammar-IV, Gamimune N, Iveegam, Panglobulin, Sandoglobulin, Venoglobulin	
		May reduce severity of relapses	AnergiX-MS	Anergen
Neuropathic pain	Pregabalin	Concerns raised over safety because of tumours in mice		Pfizer
Chronic pain	Ziconotide	Non-opioid, calcium channel blocker		Elan/Neurex

Source: http://www.mult-sclerosis.org/mstreatments.html

2.2 DESCRIPTION OF RADON

2.2.1 What is Radon and Where does it come from?

Radon is a common, naturally occurring colourless, odourless, tasteless, radioactive noble gas. It is the heaviest noble gas, being nine times heavier than air and is soluble in water and fat (Gilmore and Grennan, 2003). It is created naturally by the breakdown of uranium and radium (table 2.3) and is continuously released from rocks and soil containing these two elements (Nazaroff and Nero, 1988) and (O'Dea 1997).

Table 2.3 Uranium-238 Decay Chain

Symbol	Element	Radiation	Half-Life	Decay Product
U-238	Uranium-238	alpha	4,460,000,000 years	Th-234
Th-234	Thorium-234	beta	24.1 days	Pa-234
Pa-234	Protactinium-234	beta	1.17 minutes	U-234
U-234	Uranium-234	alpha	247,000 years	Th-230
Th-230	Thorium-230	alpha	80,000 years	Ra-226
Ra-226	Radium-226	alpha	1,602 years	Rn-222
Rn-222	Radon-222	alpha	3.82 days	Po-218
Po-218	Polonium-218	alpha	3.05 minutes	Pb-214
Pb-214	Lead-214	beta	27 minutes	Bi-214
Bi-214	Bismuth-214	beta	19.7 minutes	Po-214
Po-214	Polonium-214	alpha	1 microsecond	Pb-210
Pb-210	Lead-210	beta	22.3 years	Bi-210
Bi-210	Bismuth-210	beta	5.01 days	Po-210
Po-210	Polonium-210	alpha	138.4 days	Pb-206
Pb-206	Lead-206	none	stable	(none)

Source: New York State Department of Health

Uranium and radium may be found in almost all soil and rock, but are most often associated with those containing granite, shale and phosphate. Soil gas represents the predominant source of indoor Radon and the main site for Radon exposure is the home (Field, 1999). In a study by Nicholls (1999) it was noted that the high indoor radon levels were discovered to be associated with limestone, shale and sandstone as well as a variety of clays. It is emitted from all ice-free land surfaces. Ice cover inhibits its emissions (Conen, 2003).

Radon spontaneously decays to produce Radon progeny (daughters) and it is these progeny, rather than the Radon itself, which are responsible for the adverse health effects of indoor Radon exposure. These progeny are minute solid particles (alpha particles) and can adhere to dust particles in the air (O'Dea, 1997).

The rate at which a radioactive element decays is known as its half life, i.e., the time taken for half of a radioactive element in a sample to decay into another element. Radon has a half-life of 3.8 days and its progeny have a half-life of about 30 minutes (Nazaroff and Nero, 1988).

The amount of Radon in air is measured in Becquerels per cubic metre (Bq/m^3). One Becquerel (Bq) represents one radioactive disintegration, (a nucleus giving off a ray or particle) per second. Outdoors, Radon is not a problem as it dissipates and is considered harmless. It is estimated that every square mile of soil to a depth of 6 inches contains about 1g of radium, which releases Radon in tiny amounts into the atmosphere (http://ww-w.scescape.net/~woods/elements/general).

The discovery of Radon has been credited to Fredrich Ernst Dorn who called it "radium emanation" circa 1898. By 1908 it had been renamed "niton" by Ramsay and Gray, who isolated the element and determined its density. Since 1923 it has been called Radon. Since its discovery, many uses have been found for Radon, one of the first being as a supposed therapeutic aid. Many people believed that inhaling Radon had beneficial effects. Some towns, e.g. Hot Springs, Arkansas, USA, attracted many tourists on the strength of the Radon in its thermal waters. As more has become known about Radon, so the potential uses of it in geological and environmental applications have grown. Some of its uses include; monitoring

atmospheric mixing, investigating monsoon circulation patterns, predicting earthquakes and volcanic eruptions and mapping geological faults (http://www.geol-soc.org.uk/pdfs/Radon.pdf).

2.2.2 Is it Dangerous to Humans?

The link between Radon (although not officially discovered until circa 1898), and lung cancer was first postulated, as early as 1556 by Georgius Agricola (1494 – 1555) (Field, 1999). He described high mortality rates from respiratory diseases among underground metal miners as "an angel choking old miners to death" (Weber, 2002), at Schneeberg in the Erz Mountains of Central Europe. Harting and Hesse in 1879, based their finding on post-mortems which showed pulmonary malignancies as being the cause of the high mortality rates at Schneeberg (Commission on Life Sciences 1999), in 1921 Uhlig proposed that radium emanation might be the cause of the lung cancers (Field 1999). In 1939 Peller first reviewed and described mining related cancers, in Schneeberg and Joachimsthal miners, and finally, in the mid 1950s ^{222}Rn progeny inhalation rather than ^{222}Radon gas was cited as the causative agent in the excessive lung cancer deaths for miners in both the United States and Europe (Field, 1999). There is little disagreement that breathing air containing Radon caused thousands of uranium miners to get lung cancer. The known ill-health effects from Radon exposure include lung cancer from breathing the gas and a significant risk of stomach cancer from drinking Radon contaminated water (Kendall and Smith, 2002).

2.2.3 Radon and Lung Cancer

Radon decay products attach to dust particles present in air. The particle is then inhaled into the lungs where it lodges. Once in the lungs, these decay products deliver a small burst of radioactive energy. These emissions of energy are the source of lung cancer caused by Radon decay products. As these progeny are radioactive and have half-lives of less than 30 mins there is the likelihood that before they can be cleared from the lung that the deposition of ^{210}Pb by decay, on the lining of the lung will occur (Nazaroff and Nero, 1988). Information gleaned from the American Association of Radon Scientists and Technologists shows that the "average person in the U.S. gets more radiation dose from exposure to indoor

Radon than from any other source of natural or man-made radiation" (Radon Risks and Health Effects 1987), (See Fig. 2.8).

There is an abundance of literature e.g. BEIR VI published by the Commission on Life Sciences 1999, that implicates Radon as a causative agent in the contraction of lung cancer. It cannot be proven without an unethical trial, but there is little doubt that exposure to excessive amounts of Radon will cause lung cancer in susceptible individuals. Experimental animal studies show higher rates of lung tumours among rodents exposed to high Radon levels (Cancer Facts – National Cancer Institute 2004). Kendall and Smith (2002) suggested that exposure to Radon could lead to increased risk of lung cancer. Barros-Dios, Barreiro, Ruano-Ravina and Figueiras, (2002) in their study suggest that, even at concentrations far below official guideline levels, that exposure to Radon may lead to a 2.5 fold rise in the risk of lung cancer. Furthermore, they also point to more recent case control studies in locations as far apart as Sweden, Moscow, Germany, England, Missouri and Iowa, that seem to add greater support for the idea that there is an association between Radon and lung cancer. In the Iowa lung cancer study carried out by Field, Steck, Smith, Brus, Fisher, Neuberger, Platz, Robinson, Woolson and Lynch, (2000) it was suggested that Radon exposure is a significant risk factor for lung cancer in women. The UK Radiological Protection Board concluded, because of higher than expected concentrations of Radon in houses in a study entitled "Radon and Health" that Radon is more dangerous than has previously been thought (Bowie and Bowie, 1991).

2.2.4 Radon and Water

Radon, being soluble in water can also be considered a health risk and it is considered the second most important source of indoor radon (http://www1.umn.-edu/eoh/hazards/haz-ardssite/radon/radonintro.html). In some areas depending on local geology, it dissolves, often in high concentrations in ground water. These concentrations will be higher if the groundwater is in contact with uranium bearing rock. Ground water is more likely to have high levels of Radon than surface water, i.e., streams, rivers, lakes. The more water is agitated the lower the Radon concentrations are. Therefore, households that use private water sources,

e.g. wells are more likely to be exposed to large amounts of Radon, and this may be either ingested or inhaled.

The main risk from Radon in water comes from breathing Radon released to indoor air from household water uses. American EPA studies concur (US EPA, 2003) as their greatest concern about Radon in water is not from ingestion, but from the release of Radon into the air, during normal household water uses. However, if such water is ingested, the Radon remains in the stomach from where it is passed to the small intestine and from there to the blood (Kendall and Smith, 2002).

Kohli, Noorlind Brage and Löfman, (2000) in their study of childhood leukaemia and Radon, cite a US study that found the association between groundwater Radon concentration and overall cancer mortality in children under 15, was the strongest for leukaemia.

There seems to be little direct information relating to cancer of the stomach from ingesting Radon enriched water, though Kjellberg and Wiseman (1995) observed in an ecological study set in Pennsylvania a correlation between stomach cancer and Radon levels, cited in (Kendall and Smith, 2002).

2.2.5 Other Adverse Effects of Radon Exposure

2.2.5.1 Radon and Other Cancers

According to the World Health Organisation, Radon is classified as a Class A known human carcinogen; however, with indoor Radon, the levels of Radon present in the air and the length of time one is exposed to it are important factors to be borne in mind.

In a study carried out by the American Academy of Paediatrics (1989) entitled "Radon Exposure – A Hazard to Children" it is considered plausible that exposure before the age of 20 might have greater effects than exposure at later ages. This hypothesis was derived at by studying the evidence of Japanese atomic bomb survivors who were exposed to radiation before the age of 20. It was found that

they had higher relative risks of developing radiation-induced cancers than those exposed later in life.

Several studies mentioned in a study by Kohli et al. (2000) confirm an association between Radon and malignancies. They postulated that there is a relationship between the incidence of Acute Lymphatic Leukaemia (ALL) in children and exposure to radiation from background Radon. They also saw a stronger association between incidence of leukaemia and remaining in high-risk areas than the risk level at place of birth they concluded that children are less likely to develop ALL if they are born in and stay in areas where the risk from ground Radon has been classified as low than if they are born in and stay in areas that are deemed to be normal to high risk areas. This can also be said of MS. There is epidemiological evidence which shows that moving from an area of low/high MS prevalence after the age of 15, the risk of developing MS is as for the area moved from (Dean and Elian, 1997). This will be expanded on later.

A study carried out by Etherington, Pheby and Bray, (1996) entitled "An ecological study of cancer incidence and Radon levels in South West England" reported a correlation between Radon levels and non-melanoma skin cancer. There seems to little doubt that exposure to Radon and its daughters have adverse health effects.

2.2.5.2 Radon and Fat

Another characteristic of Radon is its solubility in fat. In animal studies, Radon was shown to be highly soluble, in fact reaching concentration levels five times that of the atmosphere within 24 hours (Bowie and Bowie, 1991). Fat receives the highest dose of all tissues except the lung (Kendall and Smith, 2002), because Radon is more soluble in fat than in other tissues, including blood. Radon permeates cell membranes with ease, including endothelial cells of capillary walls. Blood transport around the body takes approximately one minute, thereby distributing Radon throughout the body. The fat content in tissues then governs radon concentration. Red bone marrow has a reasonably high fat content as does the female breast and consequently, both receive a high dose of alpha radiation from the decay products of Radon (Kendall and Smith, 2002). Myelin, the

substance that coats the nerves and the target for destruction in Multiple Sclerosis, is a fatty substance and therefore its reaction to Radon exposure should not be underestimated.

If the bone marrow is harmed by exposure to alpha radiation, and studies by Zhou, Suzuki, Randers-Pehrson, Vannais, Chen, Trosko, Waldren and Hei, (2001 p. 1415), show "clear evidence that a single alpha particle can induce mutations, and chromosome aberrations in cells that received no direct radiation exposure to their DNA". Therefore, this provides clear evidence that "irradiation can induce a huge bystander mutagenic response in neighbouring cells not directly traversed by alpha particles" (Zhou et al. 2001 p.1415). Therefore, the myelin damage, the cause of the symptoms of multiple sclerosis, has to be considered, given that stem cells come from bone marrow which may or may not have been damaged by exposure to alpha radiation from a very early age, perhaps even prior to birth. Recent studies by Willer, Dyment, Sadovnick, Rothwell, Murray and Ebers, (2005) agree with other studies in twins and half siblings which suggest that the neonatal and/or the gestational environment influence the risk of MS in later life.

2.2.5.3 Radon and Buildings

People typically spend more time indoors in winter and therefore are likely to be exposed to higher concentrations of Radon that at other times of the year. With modern building methods and home improvements throughout the years, homes have become more sealed than ever before. This leads to less home air exchanges per hour and consequently more exposure to Radon. Radon being nine times heavier than air will also be more concentrated at ground floor levels (Gilmore and Grennan, 2003).

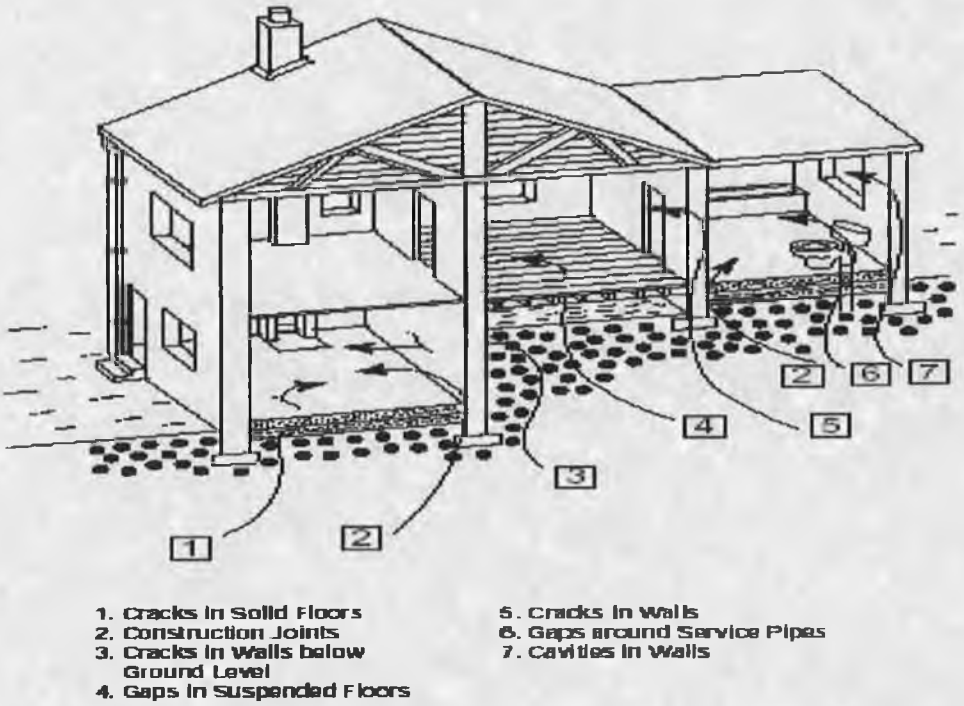

Fig. 2.6 How Radon enters Buildings

Source: *(Geological Society of London, July 2001).*

Radon enters buildings because the air pressure inside buildings is slightly lower than in the ground and they can draw in radon gas from several feet away. Stoves, hot water heaters and fireplaces, reduce the pressure indoors. Warm air inside buildings moves upwards similar to a chimney and this reduces the indoor air pressure. Wind creates a vacuum on the downwind side by the Bernoulli effect. When the ground is frozen or soaked by rain, the radon in the ground moves to the warm and permeable gravel and disturbed ground underneath the house. The resulting advection (pressure driven flow) draws in radon through openings or cracks and through the pores in concrete. Radon is also pulled in by diffusion as it tries to equalise the indoor concentration (Commission on Life Sciences, 1999).

Approximately 18,000,000 homes across the United States have been tested for Radon (Gregory and Jalbert 2003), and of these, almost 800,000 have had remedial measure taken to reduce the occupants' exposure to Radon. In Ireland 11,319 homes have been tested by the Radiological Protection Institute of Ireland

in their National Radon Survey. County Sligo had the largest amount of high radon houses where 20% of the houses exceeded the Reference Level.

The contradictory literature on Radon, where on the one hand Radon is being cited as being dangerous to health, and on the other, where in places like Germany, Austria, and the USA, people flock in their thousands to Radon spas for medical purposes every year is quite interesting. They go seeking miracle cures for diseases such as rheumatoid arthritis, multiple sclerosis, cataracts, depression, to name but a few (Erickson, date unknown). This only goes to show that much more work needs to be carried out on assessing the true nature of Radon and its effects on human health.

The growing concern for Radon related illness continues. Recently in the Castleisland area of Co. Kerry where one of Europe's most radioactive homes is, both the residents in this home lost their battle against lung cancer. Neither of them were smokers. One of the residents was in her mid 40's and her husband was 54. Last year the RPII wrote to 2,500 homes, urging them to have their homes tested. A mere 16% of householders had their homes tested. Nine people have died of cancer along a mile stretch of road near this home, many of them young (O'Connor 2004).

SOURCES OF EXPOSURE TO RADIATION

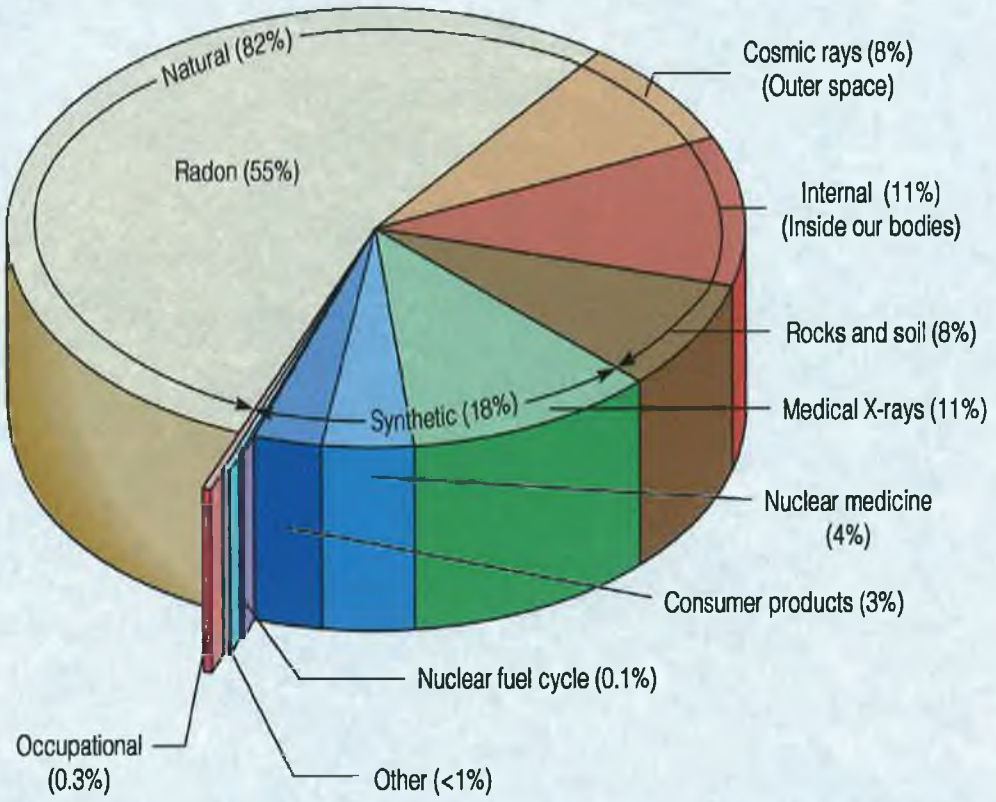

Fig. 2.7 Sources of Exposure

Source: Burns, FUNDAMENTALS OF CHEMISTRY 4/E, (c)2002, p.551. Reprinted by permission of Pearson Education, Inc., Upper Saddle River, New Jersey.

3. METHODOLOGY

3.1 SUMMARY

Following an extensive literature review, data was gathered directly from MS patients, via a questionnaire, distributed with MS News, which is the quarterly magazine of the Multiple Sclerosis Society of Ireland. Its purpose is to provide a forum whereby news and views relating to MS can be discussed. The questionnaire was designed to establish the environmental milieu of MS patients during the first fifteen years of their lives. The information provided would be used, in conjunction with information supplied by the Radiological Protection Institute of Ireland (RPII) to either refute or confirm that exposure to indoor Radon is potentially one of the environmental agents that triggers the onset of MS. The childhood home addresses of MS patients were mapped and the results overlaid onto the map of Ireland, detailing Radon distribution which was produced by the RPII. This data was then entered into an SPSS database for analysis.

3.2 QUESTIONNAIRE DESIGN AND PILOTING

The small-scale study, (Gilmore and Grennan, 2003) via a questionnaire survey, of users of the NW MS Therapy Centre, was studied and analysed. A new questionnaire was designed. Colleagues in the Dept. of Public Health NWHB, provided some professional advice on this aspect of the project. The resulting questionnaire was sent to twenty known MS patients for testing. No apparent problems arose with the questionnaire. It was considered feasible to proceed with the larger study designed to ascertain the true picture of the distribution of MS in Ireland.

3.3 MS SOCIETY – IRELAND AND REGIONAL OFFICES

Dr. Margaret Gilmore and Mr. Eamonn Grennan had built up a working relationship with the CEO of MS Ireland, Mr. Michael Dineen over the years. This made the author's task less onerous, as there was no cold-calling. The MS Society and regional offices were written to in early December 2002, informing them of the current project. *(Appendix 4)*. The author had regularly visited the MS Ireland website, with a view to finding

out as much as possible about current research into MS in Ireland and general MS facts. This turned out to be one of the more fruitful contacts cultivated during the completion this project, for without their help, the project could have floundered. There followed several meetings with Mr. Dineen, culminating in an invitation to attend the Pringle Lecture in UCD and an agreement to distribute the questionnaire, see para 3.7.

3.4 PRINGLE LECTURE

Dr. Robert Pringle (R.I.P) was the founder of the Multiple Sclerosis Society of Ireland and was among those responsible for the development of the International Federation of MS Societies. The theme of the lecture was "epidemiological studies and a statistical analysis of MS in various countries", and was delivered by the renowned neurologist, Prof. Geoffrey Dean on October 16th 2003. His lecture examined the history of MS and he spoke about his research and findings in South Africa, Malta, Sicily and Ireland to name but a few.

His continued research showed that no Maltese people had ever been diagnosed with MS in the UK. This led him to Malta where he found that MS was very rare, finding only 16 patients. He believes that is due to genetics as Malta differs from the rest of Europe in that it has a history of settlement of people from North Africa. On the contrary, his studies in Sicily which is only approximately 60 miles away, found high prevalence rates for MS, and even higher for Sardinia and the rest of Italy. He also carried out studies in Cyprus and Spain.

The lecture finished with a question and answer session. Overall this lecture was most informative and the information gathered has been beneficial to this project. It was also a privilege to meet Prof. Dean and to have a chance to talk informally with him before the lecture.

3.5 NEUROLOGISTS

The first challenge was to access MS patients. The country's neurologists were considered the best route to these. Fifteen neurologists were identified and located using the Irish Medical Directory and written to in December 2002 *(Appendix 1)*. They were informed of the study and their cooperation was requested.

Eight replies were received. Of these, three would consider helping, one had retired and the other four had ethical concerns. Below are extracts from the replies.

> *"Any potential research project would have to go through the ethics committee. It otherwise would not be possible to be involved with this project".*
>
> *"There would be major ethical concerns about releasing any information pertaining to patients. – The other possibility would be to contact the MS Society".*
>
> *"Most of our information was obtained from the local organisers both in Wexford and Donegal and I would suggest that this might be the best route for you".*
>
> *"I actually feel that you would be better served by approaching the MS Society".*
>
> *"I would be grateful if you could send me the pilot study and after reading that I might be willing to help".*
>
> *"I find your research project of great interest. Perhaps at some stage you might like to present your data at our Dublin Neuroscience meeting"*, also pointing out that *"I have discussed*

your project with the ethics committee and you would need to apply formally for access to patient information".

"I think this is certainly an interesting project and would be happy to cooperate in any way I can, however I am not at liberty to divulge any demographic information without the written consent of the patients and consent of the Health Board".

An invitation to present the data, i.e. the data from the small-scale study mentioned in para 3.2, to the Dublin Neuroscience Meeting was accepted. This was arranged for the 28th March 2003. The presentation *(Appendix 2)* was well received.

There were follow up meetings with neurologists in St. James' Hospital and the Beaumont Hospital, both in Dublin. Again, the ethics question came up and it was acknowledged to be an important obstacle. Even though the author felt that no ethical guidelines were being breached, the neurologists had some very understandable reservations about becoming involved in the study. The various ethical committees were identified and two applications were made. However, it was concluded by author and supervisors that this process was far too cumbersome for what the project was aiming at.

Having considered this route it was concluded

1) That such a route would be too cumbersome, albeit for very good reasons
2) It was too complicated and
3) That it would take a long time to complete
4) That a successful outcome was not guaranteed, and
5) Since only about one third of neurologists had indicated support, the eventual survey might not be fully representative.

3.6 General Practitioners and Local Medical Staff and Lists

A team from St. Vincent's University Hospital had just completed a study of MS prevalence in Counties Wexford and Donegal (McGuigan, et al. 2004). Having accessed this via the researchers, it was decided, for ascertaining the prevalence rates for the country as a whole, that some of the methods employed were worth replicating. The method used to access the target audience included communications with General Practitioners, Neurologists, County Physicians, Hospital Coding Lists, Local MS Societies, Respite Care Facilities and Interferon Prescription Lists.

Having approached the neurologists and failed due to ethical considerations, the author thought that the General Practitioners would be a worthy alternative. Having discovered that there are approximately 1,500 practices in the country (plus private ones) and given the previous responses plus the cost and practicalities involved in writing to all of these, the author decided that this course of action would be too onerous and unlikely to yield a positive outcome. County Physicians and Hospital Coding Lists were also considered to be avenues that would entail more hurdles than could be dealt with, e.g., ethical committees. That left the MS Society, Respite Care Facilities and Interferon Prescription Lists. Having had the co-operation from the MS Society, it was decided that this would be the best route for the success of this project. Information was also obtained from the GMS (P) Board and this will be revisited.

3.7 Questionnaire Distribution

One of the outcomes of the meetings with the CEO MS Ireland, was an agreement whereby the MS Society Ireland consented to distribute the questionnaire with their magazine "MS News" in Jan 2004. Addressed envelopes were included, to aid responses. It was agreed following discussions with MS Ireland staff and other polling bodies, that there was no need to include stamped envelopes. Furthermore, the impression of the staff of MS Ireland is, that the membership are quite good about taking part in surveys and this proved to be correct. No prior knowledge of where, or to

whom the questionnaires were going to was made available, nor was it sought. The only information sought was the number by county of subscribers to MS News. This would help to work out the response rate by county, rather than the overall response rate, thereby helping to give a more accurate picture. The CEO also suggested that an accompanying article, explaining the rationale for the research project *(Appendix 5)* should be included. However, unfortunately the article was inadvertently omitted from the magazine. This may have contributed to the lower than expected response rate, but nevertheless it should be emphasised that the response rate was still very satisfactory.

3.8 Radiological Protection Institute Ireland (RPII)

The RPII carried out a survey between 1992 and 1999 to identify the areas most at risk from elevated indoor Radon levels. (See table 3.1) It was a geographically based survey using the 10km grid squares of the Irish National Grid. Based on statistical advice, it was determined that a minimum of five samples was required from each 10km grid square to make valid predictions. Measurements were carried out for 12 months and the results were used to predict the percentage of dwellings for each grid square that exceeded the (safe?) reference level of 200 Bq/m^3. Therefore, if more than 10% of dwellings in any given grid square are predicted to have Radon levels above the reference level, then that grid square is considered a high Radon area and coloured light brown, or dark brown (Fennell, Mackin, Madden, McGarry, Duffy, O'Colmáin, Colgan, and Pollard, 2002)

"For squares in which there were fewer than five valid measurement results the Geometric Mean and Geometric Standard Deviation were estimated from data in the surrounding squares. A smoothing algorithm, optimised on the Irish data set using the cp-criterion, was used" (Fennell, et al. 2002 p.40).

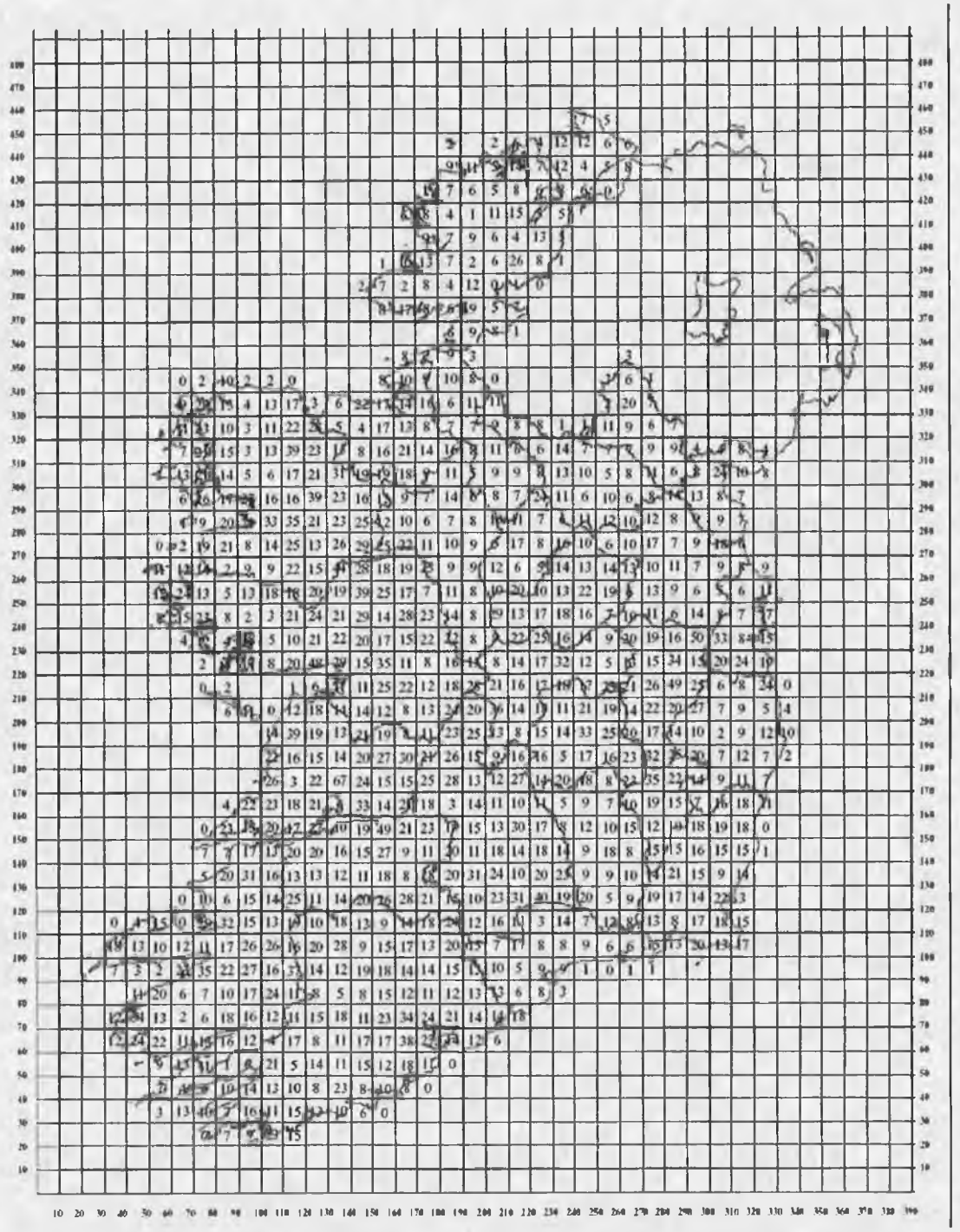

Fig. 3.1 Map of Ireland showing the valid number of measurements of Radon in dwellings per 10Km grid square. (Source: RPII 2002)

There are 837 grid squares covering the Republic of Ireland and fig 3.1 shows the number of valid measurements per 10Km grid square. These measurements were taken in domestic dwellings to predict the percentage of dwellings that are likely to exceed the reference level. Of these 837 grid

squares 28% (n = 234 have been classified as being High Radon Areas. The counties that stand out are, Carlow, Kilkenny, Waterford, Wexford and Wicklow, and in the west the counties that stand out are Clare, Galway, Mayo and Sligo (Fennell, et al. 2002) (See fig 4.6)

Table 3.1 Summary of Results by County. (Source:RPII 2002)

County	No. of Dwellings Measured	No. >200Bq/m^3 (% of dwellings measured	Mean(Bq/m^3)	Max (Bq/m^3)
Carlow	194	30 (15%)	123	1562
Cavan	180	5 (3%)	67	780
Clare	742	66 (9%)	88	1489
Cork	1211	71 (6%)	76	1502
Donegal	487	18 (4%)	69	512
Dublin	155	6 (4%)	73	260
Galway	1213	181 (4%)	112	1881
Kerry	932	52 (6%)	70	1924
Kildare	480	29 (6%)	90	1114
Kilkenny	181	16 (9%)	100	717
Laois	334	17 (5%)	83	565
Leitrim	145	6 (5%)	60	433
Limerick	524	41 (8%)	77	1102
Longford	132	8 (6%)	75	450
Louth	124	14 (11%)	112	751
Mayo	1184	152 (13%)	100	1214
Meath	233	18 (8%)	102	671
Monaghan	120	4 (3%)	68	365
Offaly	286	7 (2%)	68	195
Roscommon	235	17 (7%)	91	1387
Sligo	270	54 (20%)	145	969
Tipperary	852	63 (7%)	79	1318
Waterford	162	20 (12%)	119	1359
Westmeath	289	20 (7%)	91	699
Wexford	469	54 (12%)	99	1124
Wicklow	185	24 (13%)	131	1032

The RPII provided an up to date Radon Map of Ireland and gave permission to use their map in whatever way was deemed suitable. They provided the information that enabled the coding of their radon map of Ireland into 5% intervals. They also provided on CD their Radon map of Ireland that was required by Dr. Dennis Pringle, Dept of Geography, NUI, Maynooth, to plot the cases of MS.

3.9 National Cancer Registry

Data was obtained on lung cancer from the National Cancer Registry. As mentioned previously, Radon is known to cause lung cancer. The high Radon areas are known, but whether or not the lung cancer patients were smokers, and data on how much time they spent in a particular area/home, was not available. However, the data gleaned from this source provided some interesting and possibly comparable figures.

3.10 Health Boards

The Health Boards and the National Physical and Sensory Disability Database were contacted. It should be pointed out that that not everyone with a disability will be included in the database, as inclusion is voluntary. It was also pointed out that quite often people with MS do not like to advertise their condition. Furthermore, when a person reaches sixty-five, they are removed from the database. Also, the database in each Health Board area is incomplete, at the time of writing. This appears to be a serious deficiency worthy of further consideration. This line of enquiry was closed.

3.11 Drug Companies

Schering AG who produce Betaferon, were contacted with a view to obtaining prescribing patterns for Ireland. One of their representatives informed the author that Schering AG produce only one of the four products used in the treatment of MS. Furthermore, he also intimated that the information sought was commercially and ethically sensitive and felt that it could not made public. Similar responses were received from Serona who

produce Rebif, and from Biogen who produce Avonex. Yet again, a cul-de-sac.

3.12 GMS (P) Board

The GMS payments board were contacted and they sent a breakdown by county, gender and age of the numbers of patients being prescribed interferon *(Appendix 6)*. As this is the main drug used for treating the symptoms of MS, this information was used to compare drug use with MS distribution rates. This data will be presented and discussed later.

3.13 Dept of Geography – NUI Maynooth

An outline of the project and presentation of the preliminary results was given at the 10th annual ENRGHI conference in June 2004. Great interest in the project was shown at this conference and some interesting contacts were made. These contacts have turned out to be very worthwhile, as they were helpful in plotting the cases of MS on to the Radon map of Ireland. The technology needed to do this is not available at IT Sligo.

3.14 Multiple Sclerosis International Federation (MSIF)

The author subscribes to "World of MS Update Service" and weekly reports are posted via email, with details of the latest research into MS. This site has been very informative and has provided an insight into the scale of research that has been and is currently being undertaken throughout the world. To date no notification of any research similar to this work has been reported.

3.15 Analysis of Questionnaire

A total of 671 responses have been received and the data has been entered into an SPSS database. Excel is also being used as a tool for analysis and presentation of data. Ongoing assistance from experts in this field is being received and is acknowledged elsewhere.

The address data provided on the questionnaires has been geocoded by Gamma Ltd., Dublin. Geocoding is a process whereby addresses are

assigned map co-ordinates (Eastings and Northings). This method was used as it was considered too onerous to manually plot 671 addresses, plus 87 second home addresses. However, Co. Donegal was manually done to cross-reference data from Gamma Ltd., and the results were the same. The geocoded data was sent for plotting to Dr. Pringle of NUI Maynooth. Dr. Pringle has made the computer software and expertise for plotting the cases of MS available *(Fig 4.5)*. The author also plotted the geocoded data manually (*Fig 4.6*). This geocoded data has been added to the database along with codes for each 10Km grid square on the map of Ireland on which the Radon data has also been plotted.

An inconsistency on this map was identified (Grennan, pers comm.) and data to rectify it was supplied by RPII. It was that the grid squares were colour coded depending on their radon readings, e.g. <1% (of houses containing Radon levels above 200Bq/m^3), 1-5%, 5-10%, 10-20% and >20%. The ratings increase in increments of 5% except for the 10-20%, which is obviously an increment of 10%. Based on information supplied from RPII this inconsistency was circumvented and the information provided enabled the subdivision of the 10-20% grid squares. Therefore, the coding system used is based on six divisions numbered 1 – 6, 1 being the lowest Radon reading and 6 being the highest.

3.16 Conclusion

The road from questionnaire design to final analysis was fraught with obstacles, which at times were seen as almost insurmountable. However, each problem was considered a challenge, and each challenge met with tenacity. As mentioned previously, this project could have floundered had it not been for the good offices of the many people that were befriended during the preparatory stages of the project. The willingness of the many over the insouciance of the few were what kept the project rolling on to the stage of finality that it has now reached. One of the objectives that will not be met, and for the author is regrettable, is that the overall prevalence rate for MS in Ireland is still unknown.

4. RESULTS

4.1 RESPONSE RATE

The questionnaire was distributed with MS News to 5,342 members. (Table 4.1 shows distribution and response rate by County). Of these approximately 3,000 have been diagnosed with MS (source: MS Ireland 2004, pers. comm.), which represents approximately 56% of readership of MS News. From this 56% or 3,000, 671 responses were received. This represents a response rate of over 22%. For statistical inference, a higher response rate would have been desirable.

4.1.1 Response by County

The county with the highest response rate was Clare with a response rate of 32.8% and the lowest was Carlow at just 3.5%. Analysing by county will enable a more detailed comparison between counties with high and or low radon levels and give a more accurate reading of the true picture of MS. Of the 671 responses, 56 were excluded in this section as the county of origin could not be established, or they were from outside the 26 counties. Data by county was therefore analysed for 615 respondents as per table 4.1.

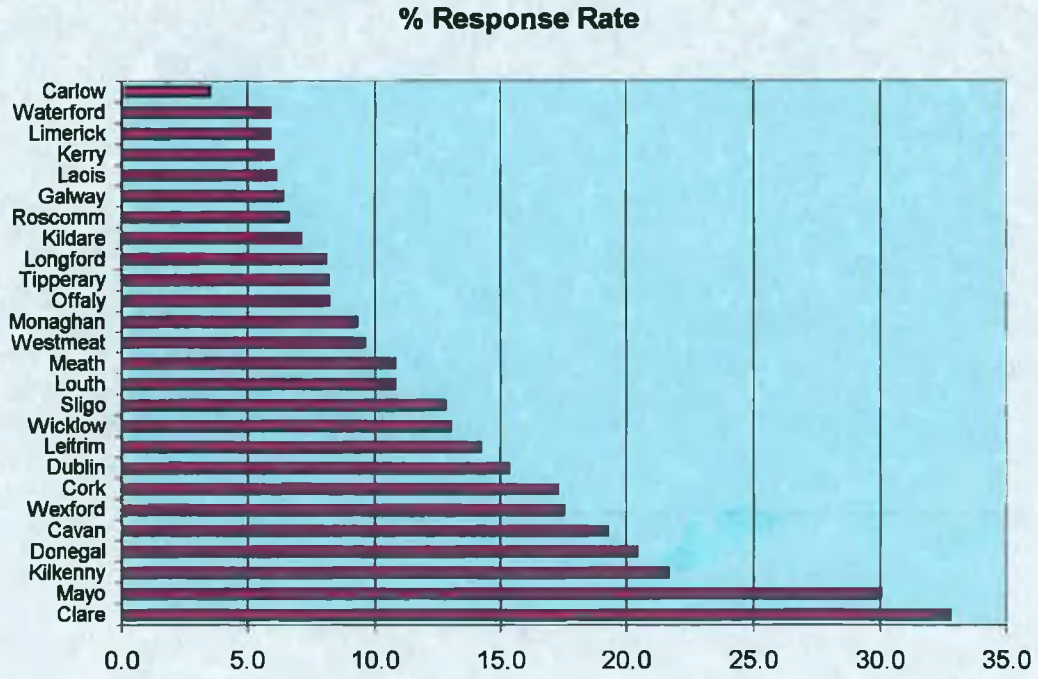

Fig. 4.1 Response Rate by County

Table 4.1 Distribution and Response Rate by County

County	Q's Distributed	No of Responses	% Response Rate
Carlow	139	**5**	3.5
Cavan	78	**15**	19.2
Clare	64	**21**	32.8
Cork	423	**73**	17.3
Donegal	186	**38**	20.4
Dublin	797	**122**	15.3
Galway	480	**31**	6.4
Kerry	380	**23**	6.0
Kildare	181	**13**	7.1
Kilkenny	83	**18**	21.6
Laois	179	**11**	6.1
Leitrim	98	**14**	14.2
Limerick	469	**28**	5.9
Longford	86	**7**	8.1
Louth	101	**11**	10.8
Mayo	139	**43**	30.0
Meath	148	**16**	10.8
Monaghan	193	**18**	9.3
Offaly	85	**7**	8.2
Roscommon	195	**13**	6.6
Sligo	156	**20**	12.8
Tipp	193	**16**	8.2
Waterford	186	**11**	5.9
Westmeath	83	**8**	9.6
Wexford	97	**17**	17.5
Wicklow	123	**16**	13.0
Total	**5342**	**615**	

4.2 DISTRIBUTION OF MS BY COUNTY

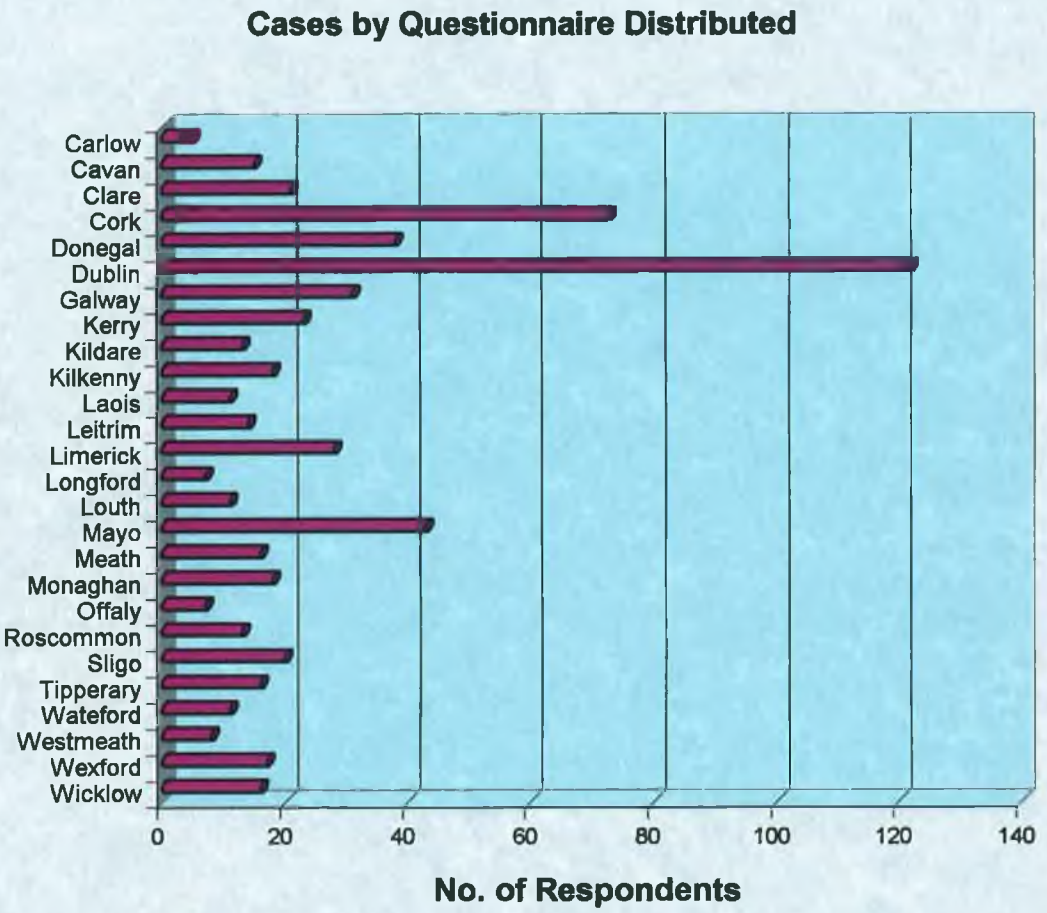

Fig. 4.2 Distribution of Respondents by County

As expected, the majority of responses came from Dublin (n = 122), followed by Cork (n = 73) and this mirrors population statistics. If the number of responses were to mirror population statistics throughout Ireland, the third highest response rate should be from Galway, but Mayo comes third with (n = 43) responses, even though it ranks 10th in size of population. Donegal had the fourth highest response rate with (n = 38) responses and it ranks 7th by population. Interestingly, Kildare which ranks 5th in terms of population, had a low response rate (n = 13), joint eighteenth. It also has relatively low radon levels. Table 4.2 below shows the counties ranked by population and by number of responses. If there were an even distribution of MS throughout the country, one would expect to see similarities between response rate and population size. The contrasting data is perhaps indicative of the uneven distribution of MS throughout the country.

Table 4.2 Counties by Population and Number of Responses

Ranked by population		County	Ranked by number of response
1st	1,122,821	Dublin	1st
2nd	447,829	Cork	2nd
3rd	209,077	Galway	5th
4th	175,304	Limerick	6th
5th	163,994	Kildare	Joint 18th
6th	140,131	Tipperary	Joint 13th
7th	137,575	Donegal	4th
8th	134,005	Meath	Joint 13th
9th	132,527	Kerry	7th
10th	117,446	Mayo	3rd
11th	116,596	Wexford	12th
12th	114,676	Wicklow	Joint 13th
13th	103,277	Clare	8th
14th	101,821	Louth	20th
15th	101,546	Waterford	Joint 20th
16th	80,339	Kilkenny	Joint 10th
17th	71,858	Westmeath	23rd
18th	63,663	Offaly	Joint 24th
19th	58,774	Laois	Joint 20th
20th	58,200	Sligo	9th
21st	56,546	Cavan	16th
22nd	53,774	Roscommon	Joint 18th
23rd	52,593	Monaghan	Joint 10th
24th	46,014	Carlow	26th
25th	31,068	Longford	Joint 24th
26th	25,799	Leitrim	17th

4.2.1 Response Frequency

Surprisingly, Leitrim which is considered to be a low radon county showed the highest response frequency (54.3), *i.e., cases per 100,000* although with a population of only 25,799 a few cases more or less would skew the results for this county. Mayo, which is a high radon county, had the second highest response frequency with (36.6), followed by Sligo, again a high radon county with a rate of 34.4. Monaghan was fourth with a rate of (34.2) and Donegal came fifth with a rate of (27.6).

The five counties with the lowest response frequency were Kildare (7.9), Louth (10.8), Dublin (10.9), Carlow (10.9) and Offaly (11.0), mostly considered low Radon emitting counties with the exception of Carlow and parts of Louth.

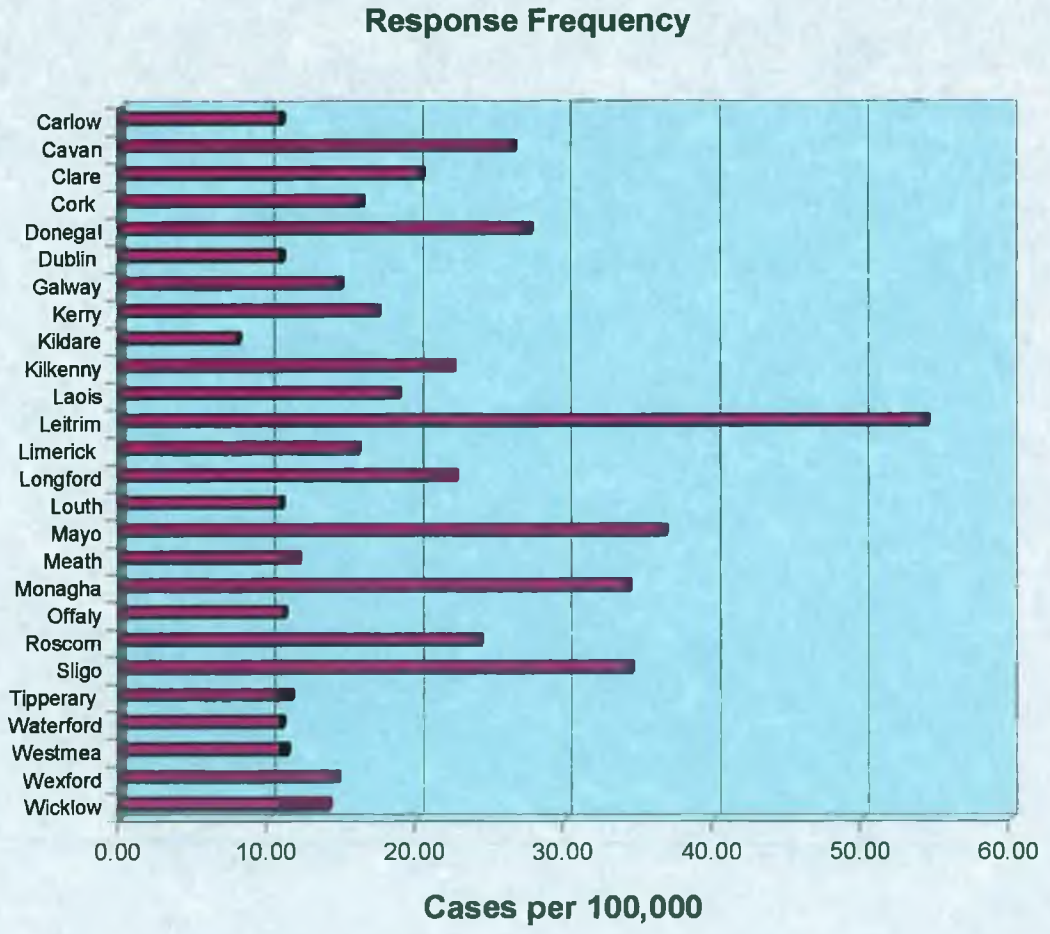

Fig. 4.3 Response Rate/100,000 of MS by County

4.2.2 Interferon Use

Interferon is prescribed for MS patients and data from GMS Payments Board show a distribution as per fig. 4.4. There are some similarities with fig 4.3, the five counties with the highest usage of interferon are: Leitrim at (158.9), Dublin (124.9), Wicklow (108.1), Kildare (107.3) and Sligo (106.5).

Waterford showed the lowest usage of interferon (37.4) followed by Offaly (39.3), Roscommon (40.0), Mayo (46.8) and Cavan (47.7). Table 4.3 shows all the data for responses by county, response rate/100,000, interferon users, interferon rate/100,000, and percentage of interferon users. The higher the figure is in column 6, the more accurate the data is for that county.

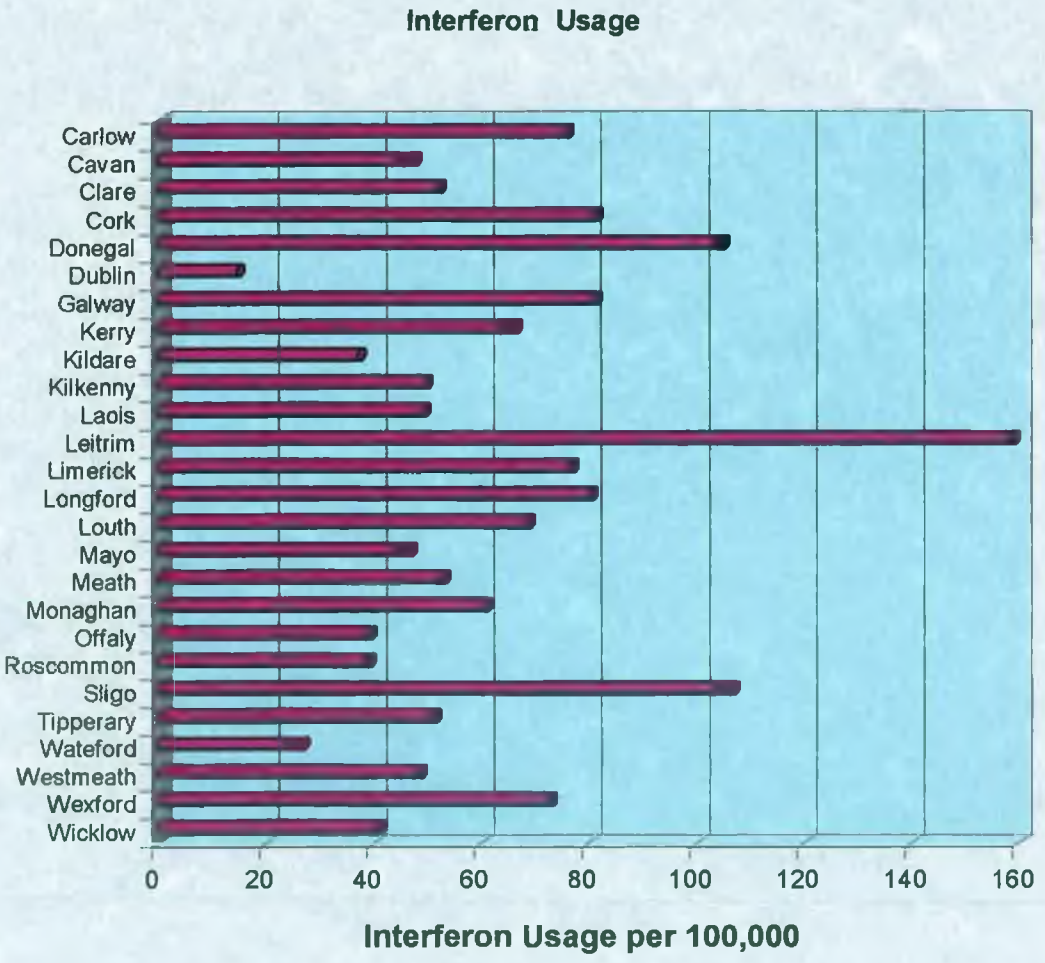

Fig. 4.4 Usage rates for Interferon

The usage rates for Dublin, Kildare and Wicklow are not accurate as there are 963 out of 1,703 interferon users that were not categorised by county in data received

from GMS (P) Board. However, when the 963 unallocated people with MS are distributed among the three counties based on population statistics, i.e. Dublin with a population of 1,122821 will get 80% or 770, Kildare with a population of 163,994 gets 12% or 115 and Wicklow with a population of 114,676 gets 78. These adjusted figures are shown in red in table 4.3.

Table 4.3 Counties by Questionnaire Response, Response Rate/100,000, Interferon Users, Interferon Rate/100,000, and percentage of Interferon Users, e.g. Carlow with 5 cases by Questionnaire expressed as a percentage of 35 interferon users = 14.2%

blue = high green = low

County	Cases by Q	Response Frequency Rate /100,000	Interferon Users	Interferon Rate /100,000	% of Interferon Users
Carlow	5		35	76.1	14.2
Cavan	15	26.5	27		55.5
Clare	21	20.3	54	52.3	38.8
Cork	73	16.3	365	81.5	20.0
Donegal	38	27.6	144	104.7	26.3
Dublin	122	10.9	1,402	124.9	8.7
Galway	31	14.8	170	81.3	18.2
Kerry	23	17.4	88	66.4	26.1
Kildare	13	7.9	176	107.3	7.3
Kilkenny	18	22.4	40	49.8	45.0
Laois	11	18.7	29	49.3	37.9
Leitrim	14	54.3	41	158.9	34.1
Limerick	28	16.0	135	77.0	20.7
Longford	7	22.5	25	80.5	28.0
Louth	11		70	68.7	15.7
Mayo	43	36.6	55		78.1
Meath	16	11.9	71	53.0	22.5
Monaghan	18	34.2	32	60.8	60.0
Offaly	7	11.0	25		28.0
Roscommon	13	24.2	21		61.9
Sligo	20	34.4	62	106.5	32.2
Tipperary	16	11.4	72	51.4	22.2
Waterford	11		38		28.9
Westmeath	8	11.1	35	48.7	22.8
Wexford	17	14.6	85	72.9	20.0
Wicklow	16	14.0	124	108.1	12.9

When one considers that Interferon is the main drug prescribed to people diagnosed with MS, and that MS is a long term illness and therefore the cost of drugs is borne by the State (€2,132,496 from June '02 to June '03, and €2,492,200 from June '03 to June '04) it is probably safe to assume that not many pay for drugs for MS. That being the case, deductions can be made as to the percentage of people with MS who replied to the questionnaire, e.g., Carlow with 5 replies and 35 people on interferon, approximates to 14%, whereas Clare with 21 replies out of 54 people on interferon approximates to 38%. The total number of people on interferon is 3,422 (GMS (P) Board June '03), which only represents approximately half the total number of estimated people with MS countrywide. Furthermore, not every case of MS is considered suitable for Interferon, type and stage of MS has to be considered.

4.2.3 MS Cases Plotted on Radon Map

At first glance, there appears to be a haphazard spread of MS cases, as per fig 4.5, *(the blue dots represent second home addresses. These were only used, where the respondent spent most of their childhood, or where the second address was in an area with a similar radon level)*. When the information is transferred to the map of Ireland showing radon areas, as per fig 4.6, there appears to be a definite trend. There are considerably more MS cases clustered in the darker areas of the map than in the lighter areas, with the exception of Monaghan, west Clare and perhaps Leitrim.

This matter will be discussed further (cf Chapter 6 below), where prevalence rates for each county will be estimated.

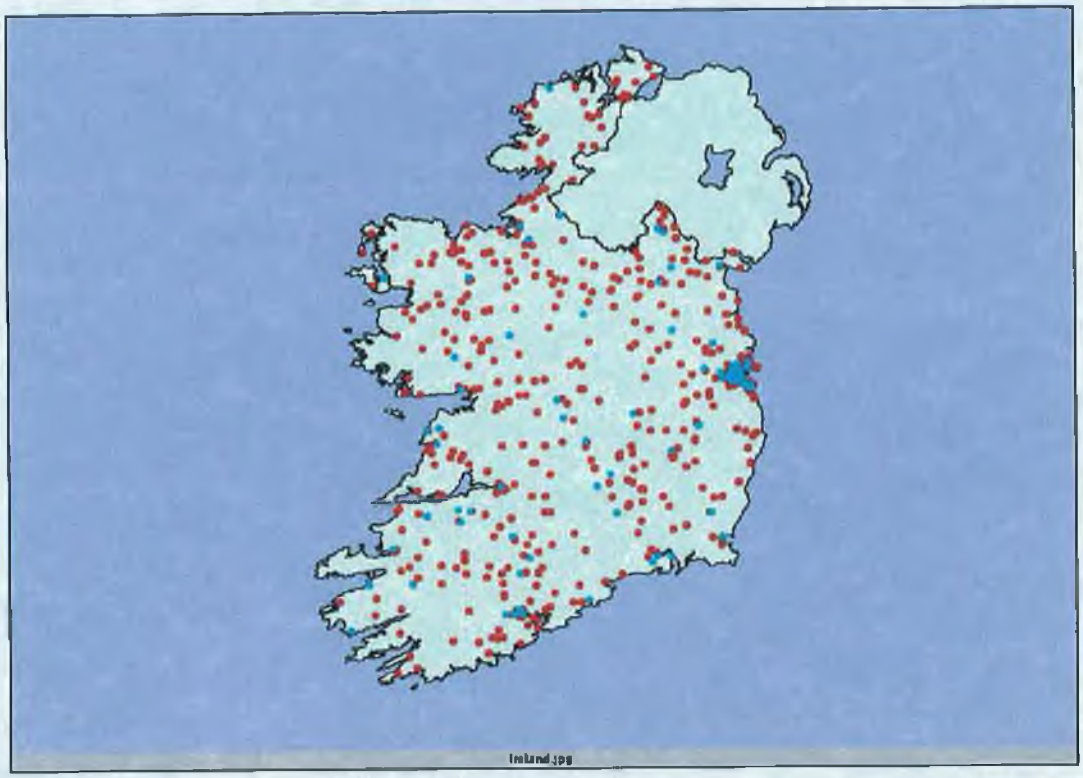

Fig. 4.5 MS cases plotted on map of Ireland

Note: The blue dots represent second home addresses and as can be seen from the illustration are more confusing that illustrative.

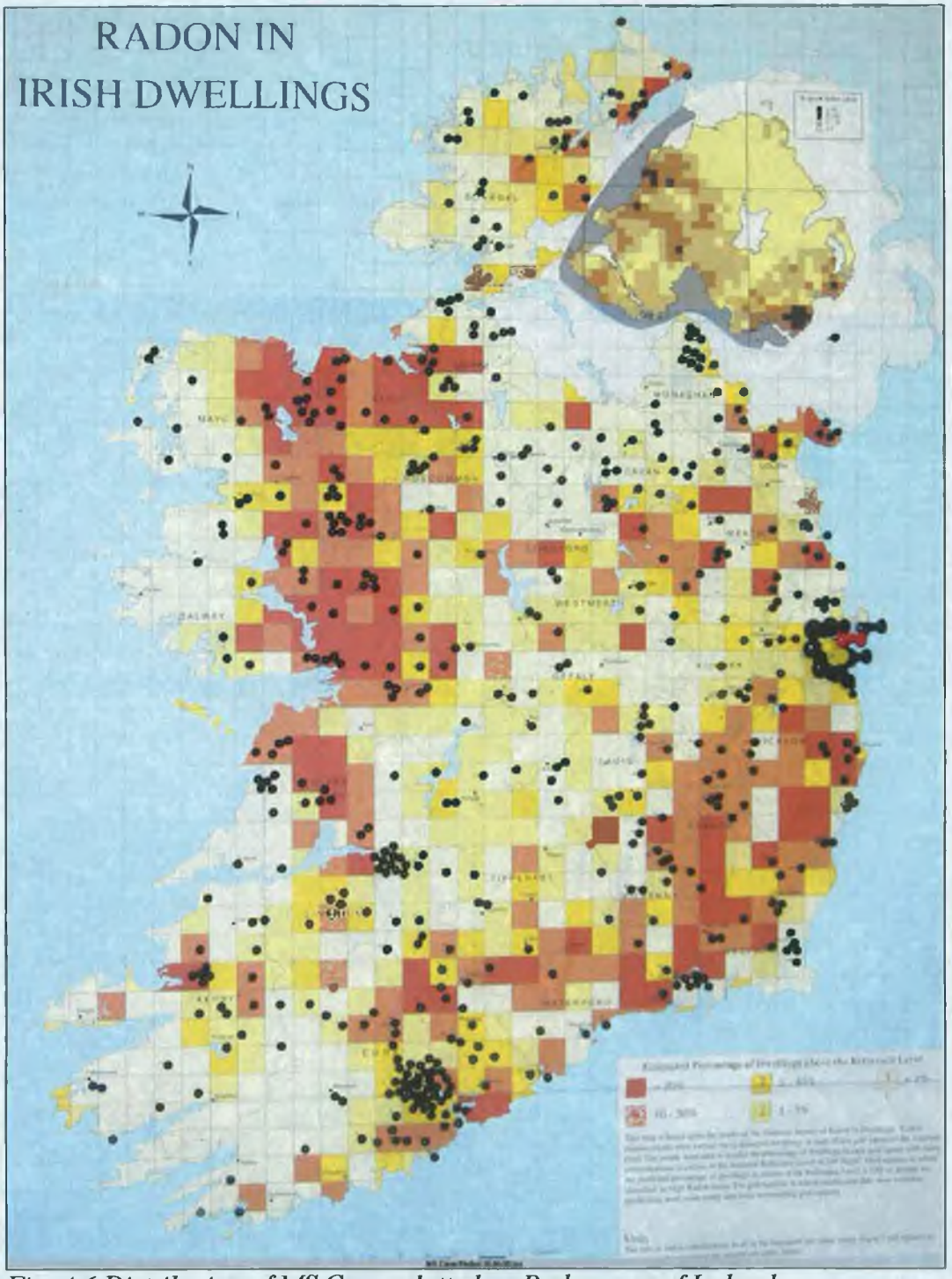

Fig. 4.6 Distribution of MS Cases plotted on Radon map of Ireland

A black dot represents each respondent's childhood home address. Larger coloured pins (Dublin) were used to represent multiple respondents' addresses.

4.3 GENDER

Of the 671 responses, 29.2% (n = 196) were male, 64.2% (n = 431) were female and 6.6 % (n = 44) gave no indication. Of the 627 respondents who indicated gender 31.3% were male and 68.7% were female. This represents a ratio of female to male of 2.2:1 which concurs with previous studies as mentioned in para 2.1.8.2 where ratios ranged from 1.3:1 to 2.8:1. The seemingly higher ratio reported in this study could be due to the propensity of women to attend their doctor more regularly than men (Gilmore, pers comm.).

Table 4.4 Response by Gender

Gender	Frequency = N	Percent	Valid Percent
Male	196	29.2	31.3
Female	431	64.2	68.7
Sub total	627	93.4	
No response	44	6.6	
Total	671	100.0	100.0

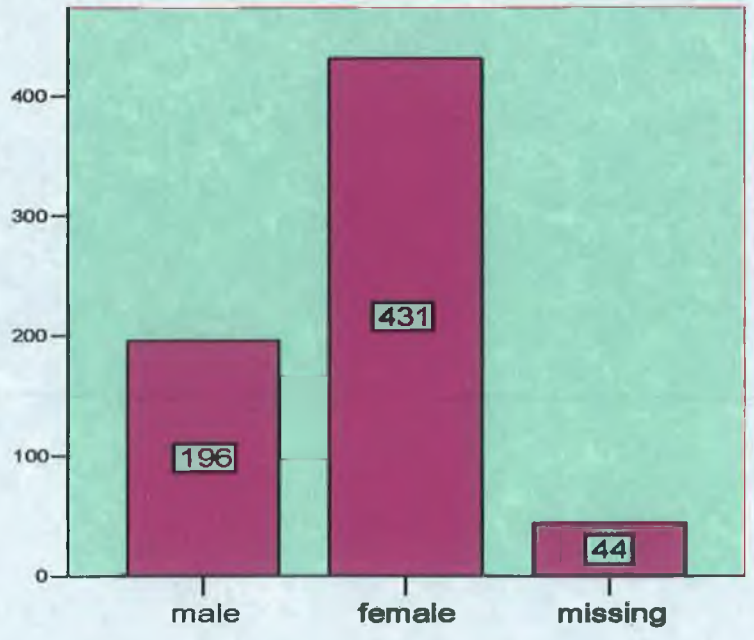

Fig. 4.7 Respondents by Gender

4.4 YEAR DIAGNOSED AND AGE AT DIAGNOSIS

The earliest diagnosis was made in 1949 and the latest was in 2003. In the 20-year period between 1949 and 1968, cases reported in this study as diagnosed per year were in single figures, totalling 24 cases. This low figure could be because diagnostic capabilities were not as good then as they are now, or because there may be less people alive today with MS who were diagnosed in this period. In the 20-year period between 1969 and 1988, those responding were still low, mostly in single figures (14 years out of the 20 year period registered single figures) varying from 3 cases in 1971 to 19 cases in 1980. Total cases in this period amounted to 242. The 14-year period from 1989 to 2003 accounted for the bulk of responses, with 366 cases in this period. This is quite a jump from the previous periods, and may be due to better diagnostic capabilities or greater levels of exposure to indoor radon due to home improvements. (Aluminium and uPVC windows and doors began to proliferate the country from the early 1980's). The year with the most cases diagnosed was 1999 with 42 cases. The youngest age at diagnosis was 3 years and the oldest was 74 years, the median age was 38 years and the average age was 36.8 years. Again previous studies concur, Cottrell et al. (1999) reported a mean age of onset of 38.5 years in para 2.1.8.1. Not surprisingly 62% n = 418 of cases reported being diagnosed between the ages of 27 and 47

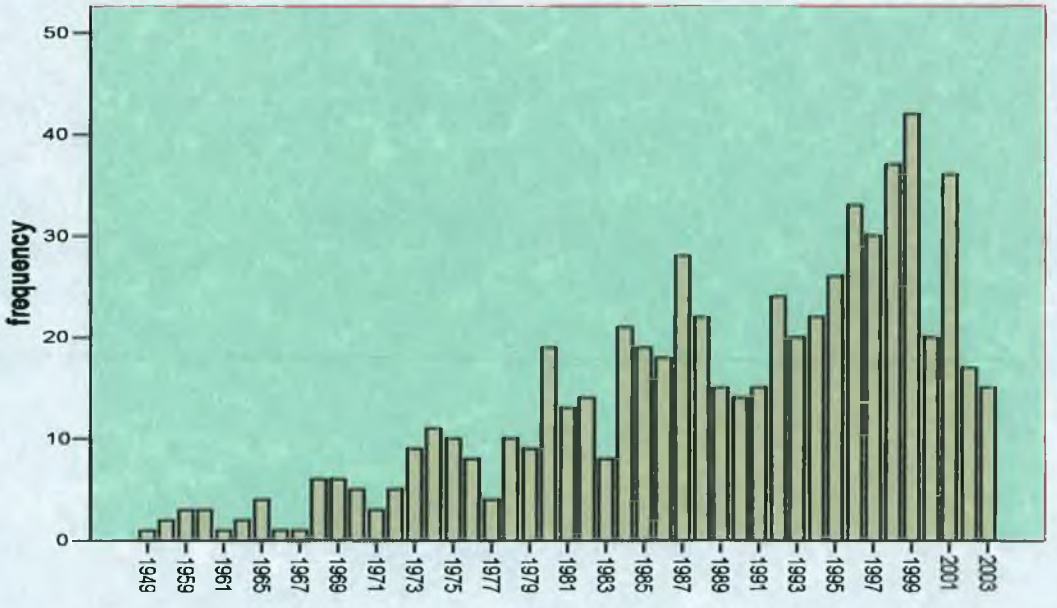

Fig. 4.8 Year Diagnosed

Table 4.5 Age at Diagnosis

Age at Diagnosis	Frequency
3	1
4	2
14	1
15	2
16	4
17	2
18	10
19	7
20	6
21	5
22	10
23	7
24	15
25	19
26	13
27	21
28	21
29	14
30	26
31	22
32	21
33	18
34	20
35	17
36	23
37	21
38	23
39	26

Age at Diagnosis	Frequency
40	19
41	17
42	14
43	17
44	20
45	22
46	14
47	22
48	15
49	9
50	7
51	12
52	15
53	8
54	5
55	10
56	4
57	4
58	1
59	3
60	3
62	1
63	1
67	2
74	1
Sub total	623
Missing	48
Total	671

4.5 FAMILY DIAGNOSED

Over 22% (n = 152) of respondents had a family member with MS. This is higher than the average of approximately 15%, (Compston, 1999). In addition some respondents reported second, and even third cousins with the disease. One hundred female respondents reported having 135 relatives with MS, 61 female, 33 male, (a ratio of 1.8:1) and 41 of unspecified gender. Forty five male respondents reported having 52 relatives with MS, 30 female and 12 male, (a ratio of 2.5:1) and 10 of unspecified gender.

Seven respondents of unspecified gender reported having 8 relatives with MS, 1 male, 4 female and 3 of unspecified gender.

Table 4.6 Family Diagnosed

Family Diagnosed	Frequency = N	Percent	Valid Percent
Yes	152	22.7	24.7
No	463	69.0	75.3
Sub total	615	91.7	
Don't know	25	3.7	
No response	31	4.6	
Total	671	100.0	100.0

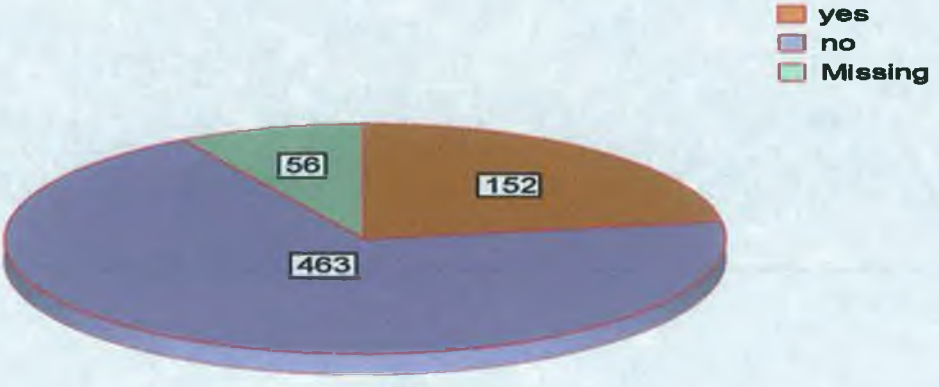

Fig. 4.9 Family Diagnosed

Respondents reported sixty three first degree relatives, (mother, father, brother and sister) with MS. Fifty six respondents reported having an affected relative living in the same house.

One hundred and fifteen respondents reported having one relative with MS, twenty-four respondents had two relatives with MS, six respondents had three relatives with MS and two respondents had four relatives with MS. One respondent reported having six relatives with MS.

Table 4.7 Relatives with MS

Relatives with MS	Frequency = N	Male	Female	Unspecified
1	115			
2	24			
3	6			
4	2			
5	0			
6	1			
Total	195	46	95	54

4.6 TYPE OF HOUSE

Almost 40% (n = 263) of respondents lived in single storey houses, while 53.9% (n = 362) lived in two storey houses. There was no response to that question from 6.9% (n = 46) respondents. Therefore, of the 625 respondents to that question 42.1% spent their childhood in single storey houses.

Table 4.8 Type of House

Type of House	Frequency = N	Percent	Valid Percent
Single	263	39.2	42.1
Two storey	362	53.9	57.9
Sub total	625	93.1	
No response	46	6.9	
Total	671	100.0	100.0

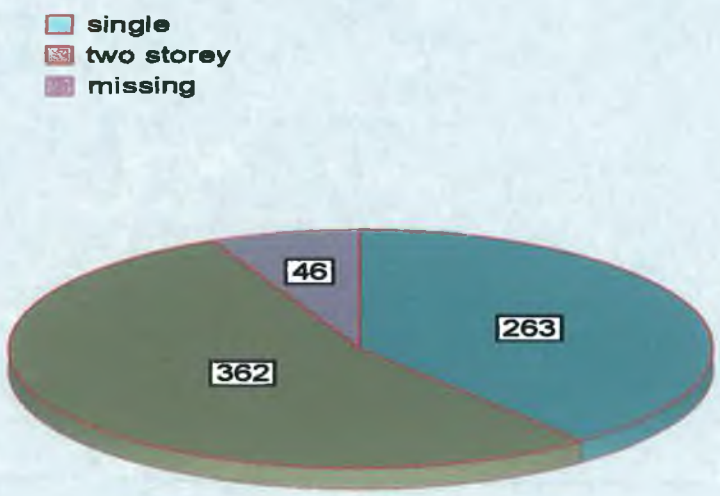

Fig. 4.10 Type of House

4.7 AGE OF HOUSE

Of the 588 respondents who indicated the type of home they were raised in over 85% were raised in homes built prior to 1960, with 45.2% being raised in homes built before 1920. Approximately 3% (n = 18) respondents reported living in homes with a basement.

Table 4.9 When House Built

When House Built	Frequency = N	Percent	Valid
Before 1920	266	39.6	45.2
1921 – 1960	239	35.6	40.6
1961 – 1980	70	10.4	11.9
Since 1980	13	1.9	2.2
Sub total	588	87.6	
Don't know	32	4.8	
No response	51	7.6	
Total	671	100.0	100.0

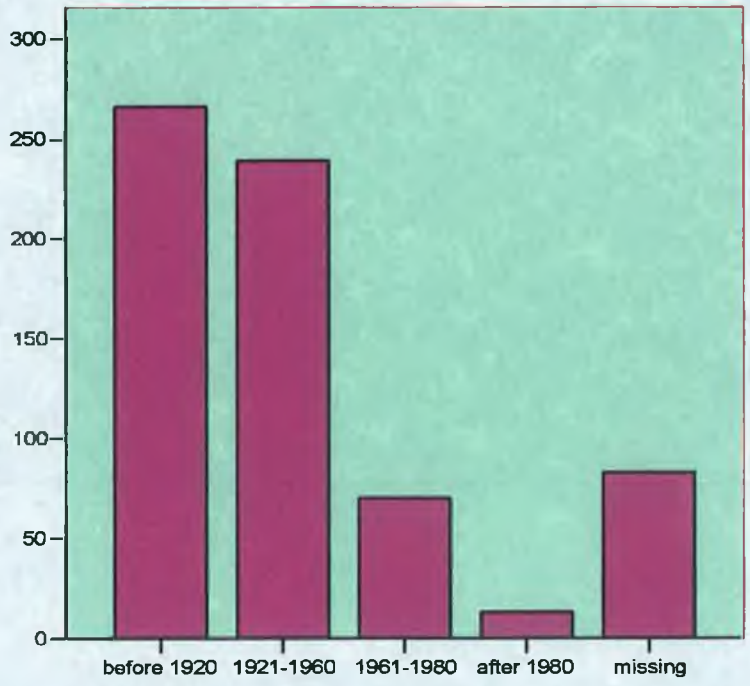

Fig. 4.11 When House Built

4.8 WATER SUPPLY

There was a fairly even divide between private and public water supplies. Of the 600 respondents who indicated a water supply over 50% (n = 303) of homes had a public water supply while 45% (n = 273) had either private or group water scheme supplies.

Table 4.10 Water Supply

Water Supply	Frequency = N	Percent	Valid Percent
Group	52	7.7	8.7
Private	221	32.9	36.8
Public	303	45.2	50.5
More than one	24	3.6	4.0
Sub total	600	89.4	
Don't know	25	3.7	
No response	46	6.9	
Total	671	100.0	100.0

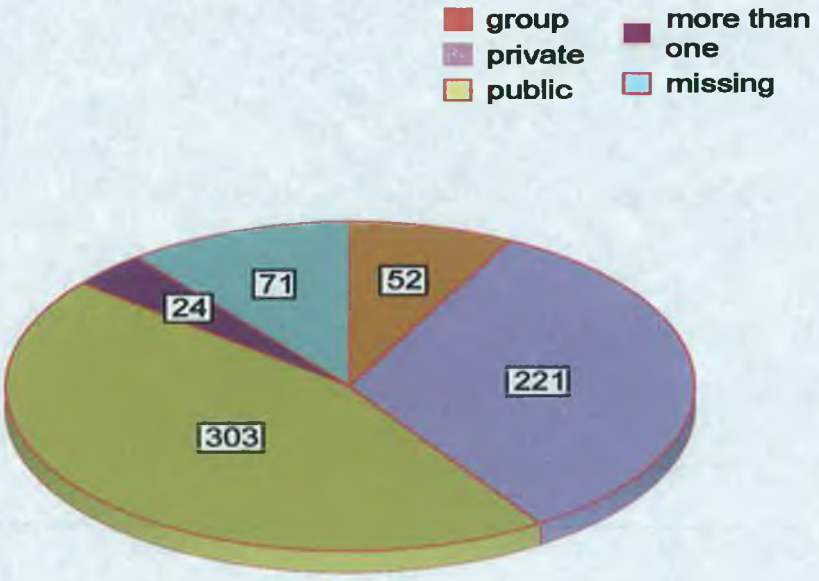

Fig. 4.12 Water Supply

4.9 TOILET FACILITIES

Over 55% (n = 371) reported having indoor flush toilets in their homes, with 6.7% (n = 45) reporting outhouse flush type. Almost 15% (100) reported having a dry toilet and 11% (n = 74) had none. Over 5% (n = 37) had a combination of the above and 6.6% (n = 44) did not respond to that question.

Table 4.11 Toilet Facilities

Toilet Facilities	Frequency = N	Percent	Valid Percent
Indoor flush	371	55.3	59.2
Out-house flush	45	6.7	7.2
Dry	100	14.9	15.9
None	74	11.0	11.8
More than one	37	5.5	5.9
Sub total	627	93.4	
No response	44	6.6	
Total	671	100.0	100.0

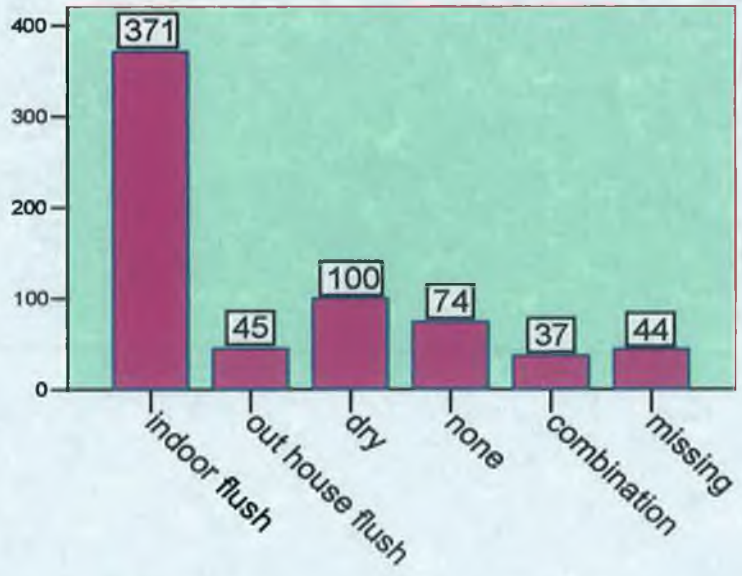

Fig. 4.13 Toilet Facilities

4.10 HEATING SYSTEMS

Of the 622 respondents who answered this question over 70% (n = 462) reported having a range or open fire as the main heating system. Oil fired accounted for 5.5% (n = 34), gas 3.4% (n = 21) and electric storage 0.6% (n = 4). Just over 16% (n = 101) reported a combination of systems.

Table 4.12 Heating Systems

Heating System	Frequency = N	Percent	Valid Percent
Oil fired	34	5.1	5.5
Gas	21	3.1	3.4
Electric storage	4	0.6	0.7
Range/open fire	462	68.9	74.2
More than one	101	15.1	16.2
Sub total	622	92.7	
No response	49	7.3	
Total	671	100.0	100.0

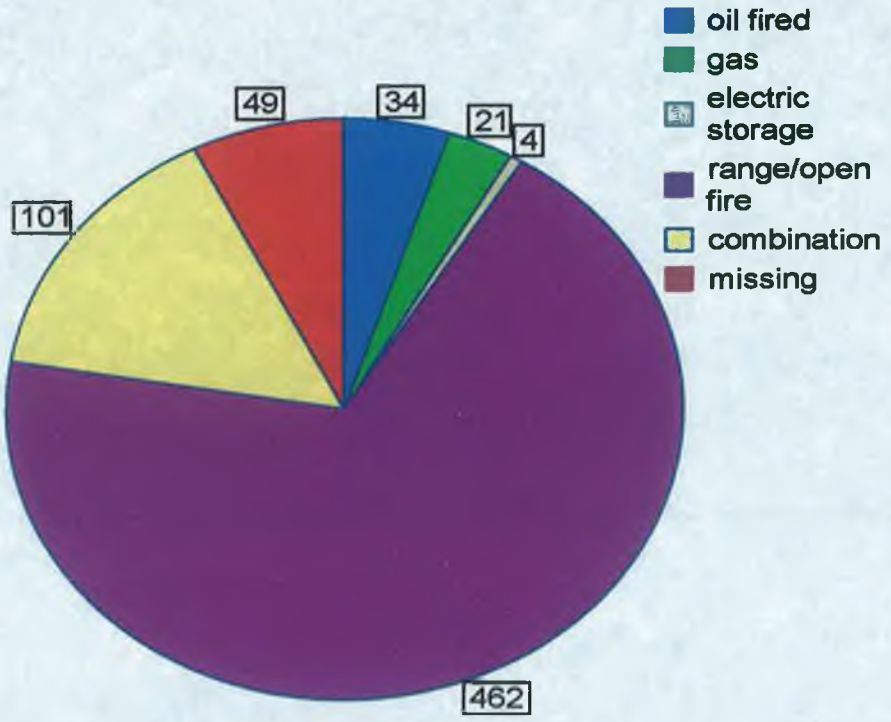

Fig. 4.14 Heating Systems

4.11 TYPE OF FUEL

Over 18% (n = 116) of the 605 respondents to this question reported burning turf only, and almost 18% (n = 108) reported burning coal. Wood and briquettes accounted for just over 3% (n = 19). Over 60% (n = 367) used a combination of fuels.

Table 4.13 Type of Fuel

Type of Fuel	Frequency = N	Percent	Valid Percent
Turf	116	16.5	18.3
Coal	108	16.1	17.9
Wood	14	2.1	2.3
Briquettes	5	0.7	0.8
Mixture	367	54.7	60.7
Sub total	605	90.2	
No response	66	9.8	
Total	671	100.0	100.0

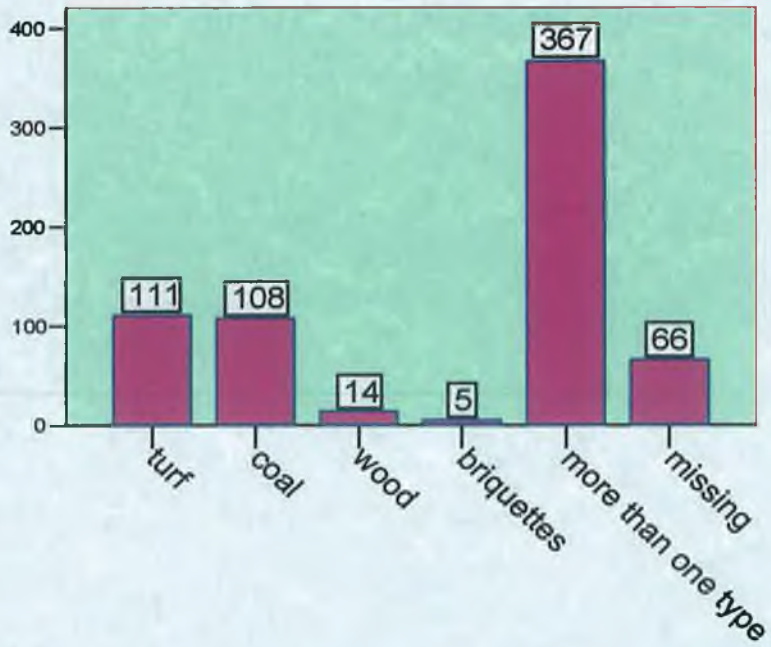

Fig. 4.15 Type of Fuel Used

4.12 AIR FLOW/DRAUGHT

Of the 621 respondents who responded to this question over half 53.1% (n = 330) reported living in draughty homes, with another 20.8% (n = 129) living in very draughty homes. A sizeable proportion, 20.5% (n = 127) reported living in homes that were not draughty and 5.6% (n = 35) were uncertain.

Table 4.14 Air Flow/Draught

Air Flow	Frequency = N	Percent	Valid Percent
Very draughty	129	19.2	20.8
A bit draughty	330	49.2	53.1
Not draughty	127	18.9	20.5
Uncertain	35	5.2	5.6
Sub total	621	92.5	
No response	50	7.5	
Total	671	100.0	100.0

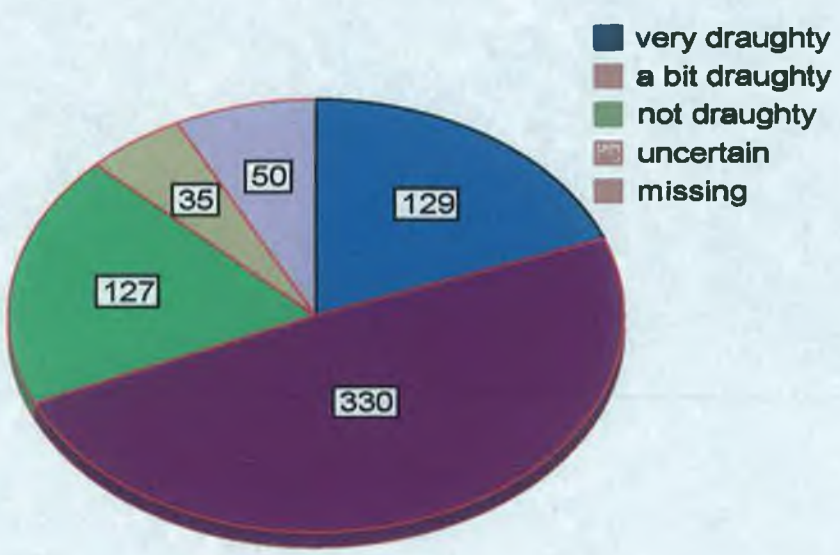

Fig. 4.16 Air Flow Draught

4.13 TYPE OF WINDOWS

There were 617 responses to this question and almost 80% (n = 493) of these reported having wooden windows, with over 50% (349) having wooden sash type and over 20% (n =144) having wooden opening out type. The remainder reported having aluminium, uPVC, single or double glazed.

Table 4.15 Type of Windows

Window Type	Frequency =N	Percent	Valid Percent
Wooden sash	349	52.0	56.5
Wooden opening	144	21.5	23.3
Double glazed	43	6.4	7.0
Single glazed	48	7.2	7.8
Other	33	4.9	5.4
Sub total	617	92.0	
No response	54	8.0	
Total	671	100.0	100.0

4.14 TYPE OF SCHOOLS

Almost 65% (n = 402) of the 621 respondents who replied to this question reported attending single storey schools, while just over 35% (n = 219) attended two storey schools, while 7.5% (n = 50) did not respond to that question.

Table 4.16 Type of Schools

Type of School	Frequency = N	Percent	Valid Percent
Single storey	402	59.9	64.7
Two storey	219	32.6	35.3
Sub total	621	92.5	
No response	50	7.5	
Total	671	100.0	100.0

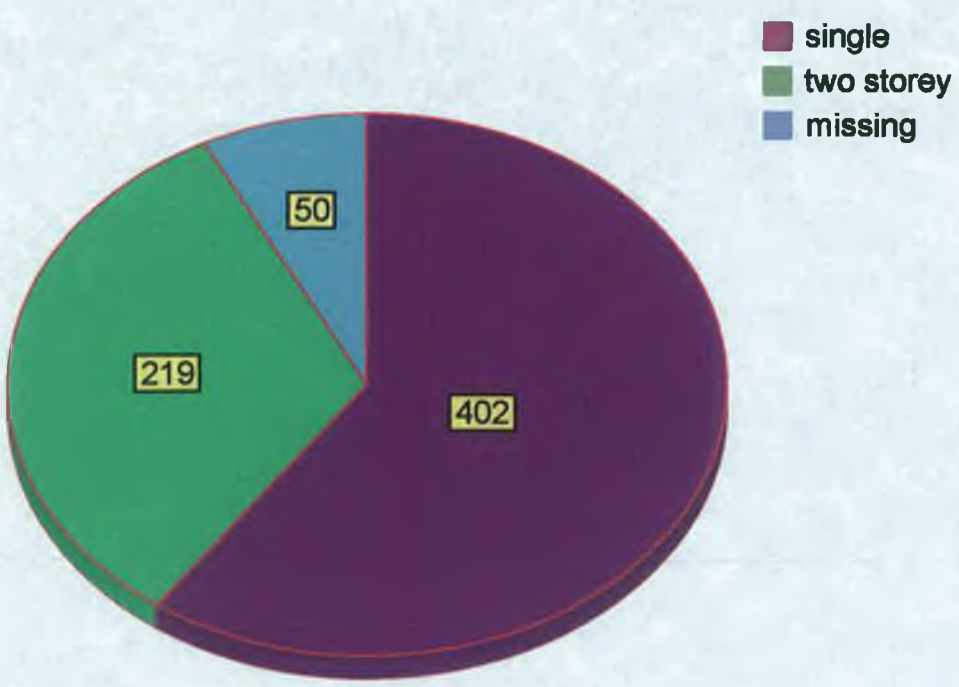

Fig. 4.17 Type of Schools

4.15 AGE OF SCHOOLS

Of the 541 respondents to this question who indicated a school age, almost 90% (n = 483) attended a school built prior to 1960, with over half 54.9% (n = 297) attending a school built prior to 1920. Less than 10% or respondents attended schools built after 1980.

Table 4.17 Age of Schools

When School Built	Frequency = N	Percent	Valid Percent
Before 1920	297	44.3	54.9
1921 – 1960	186	27.7	34.4
1961 – 1980	57	8.5	10.5
Since 1980	1	0.1	0.2
Sub total	541	80.6	
Don't know	81	12.1	
No response	49	7.3	
Total	671	100.0	100.0

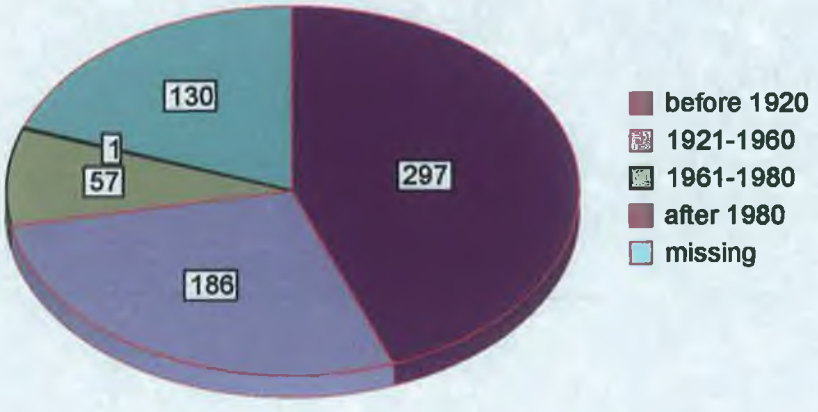

Fig. 4.18 Age of Schools

4.16 WATER SUPPLY TO SCHOOLS

Just over 70% (n = 488) of control group responded to this question and of these 28% (n = 137) reported either group or private as being the water source. By far the greatest majority, over 70% (n = 342) reported having a public water supply in their school, while 1.8% (9) had no water supply.

Table 4.18 Water Supply to Schools

Water Supply	Frequency = N	Percent	Valid Percent
Group	46	6.9	9.4
Private	91	13.5	18.6
Public	342	51.0	70.2
None	9	1.3	1.8
Sub total	488	72.7	
Don't know	128	19.1	
No response	55	8.2	
Total	671	100.0	100.0

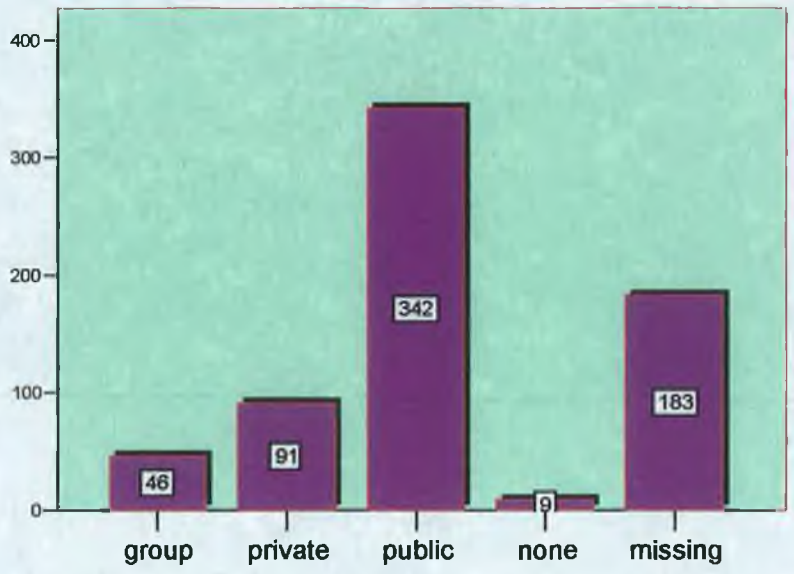

Fig. 4.19 Water Supply to Schools

4.17 TOILET FACILITIES AT SCHOOLS

There were 625 replies to this question and over half (n = 345) of these indicated indoor flush toilets, with outdoor flush accounting for over 16% (n = 104). Almost 24% (n = 149) reported having dry toilets, with 0.7% (5) reporting having none.

Table 4.19 Toilet Facilities at Schools

Toilet Facilities	Frequency = N	Percent	Valid Percent
Indoor flush	345	51.4	55.3
Out-house flush	104	15.5	16.6
Dry	149	22.2	23.8
None	5	0.7	0.8
More than one	22	3.3	3.5
Sub total	625	93.1	
No response	46	6.9	
Total	671	100.0	100.0

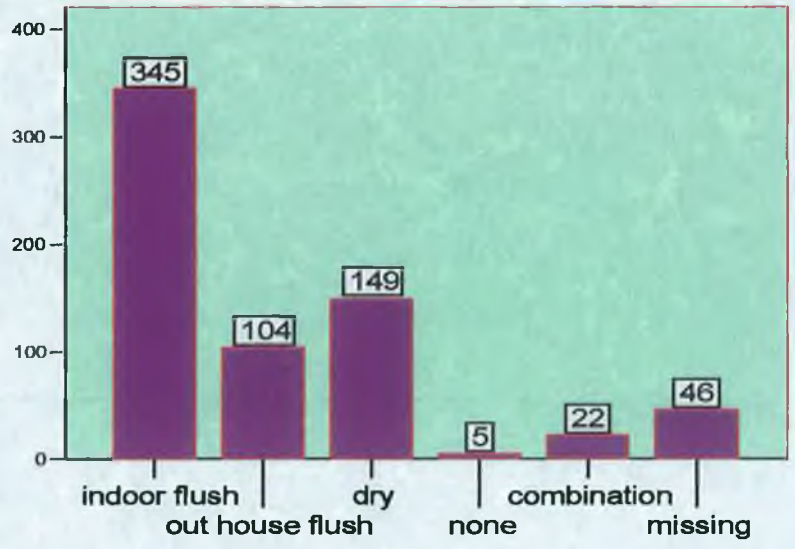

Fig. 4.20 Toilet Facilities at Schools

4.18 HEATING FACILITIES IN SCHOOLS

Over 46% (n = 268) of the 579 respondents to this question reported as having had either range or open fire as the heating system, oil fired accounted for over 35% (n = 212), a small amount 8.3% (n = 48) reported having electric storage heaters as the heating system. Gas heating accounted for 1.7% (n = 10).

Table 4.20 Heating Facilities in Schools

Heating System	Frequency = N	Percent	Valid Percent
Oil fired	212	31.6	36.6
Gas	10	1.5	1.7
Electric storage	48	7.2	8.3
Range/open fire	268	39.9	46.3
More than one	41	6.1	7.1
Sub total	579	86.3	
No response	92	13.7	
Total	671	100.0	100.0

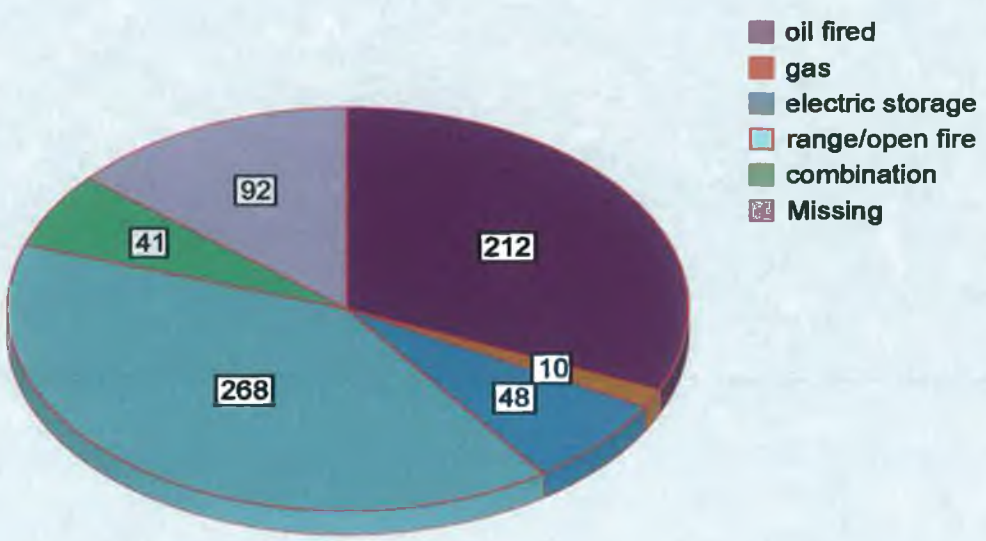

Fig. 4.21 Heating Facilities in Schools

4.19 TYPE OF FUEL USED BY SCHOOLS

The responses to this question were quite low, with only 305 people responding to it, of these 15.6% (n = 104) reported turf as being the fuel used to heat the school and 10.6% (n = 71) used coal, while 17.4% (n = 117) used a combination of solid fuels. Quite a large number of respondents did not reply to this question 54% (n = 366)

Table 4.21 Type of Fuel used by Schools

Type of Fuel	Frequency = N	Percent	Valid Percent
Turf	104	15.6	34.1
Coal	71	10.6	23.3
Wood	13	1.9	4.3
Mixture	117	17.4	38.3
Sub total	305	45.5	
No response	366	54.5	
Total	671	100.0	100.0

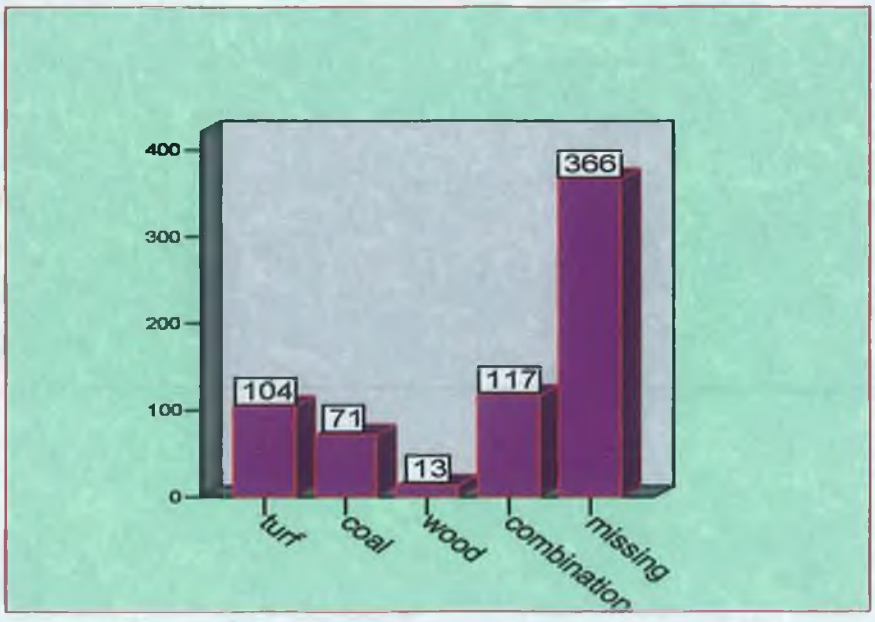

Fig. 4.22 Type of Fuel Used by Schools

4.20 AIR FLOW/DRAUGHT AT SCHOOLS

Almost 45% (n = 273) of the 615 respondents who responded to this question, reported attending schools that they considered a bit draughty, while 27% (166) reported being in very draughty schools and over 16% reported attending schools that were not considered draughty.

Table 4.22 Air Flow/Draught at Schools

Air Flow	Frequency = N	Percent	Valid Percent
Very draughty	166	24.7	27.0
A bit draughty	273	40.8	44.4
Not draughty	102	15.2	16.6
Uncertain	74	11.0	12.0
Sub total	615	91.7	
No response	56	8.3	
Total	671	100.0	100.0

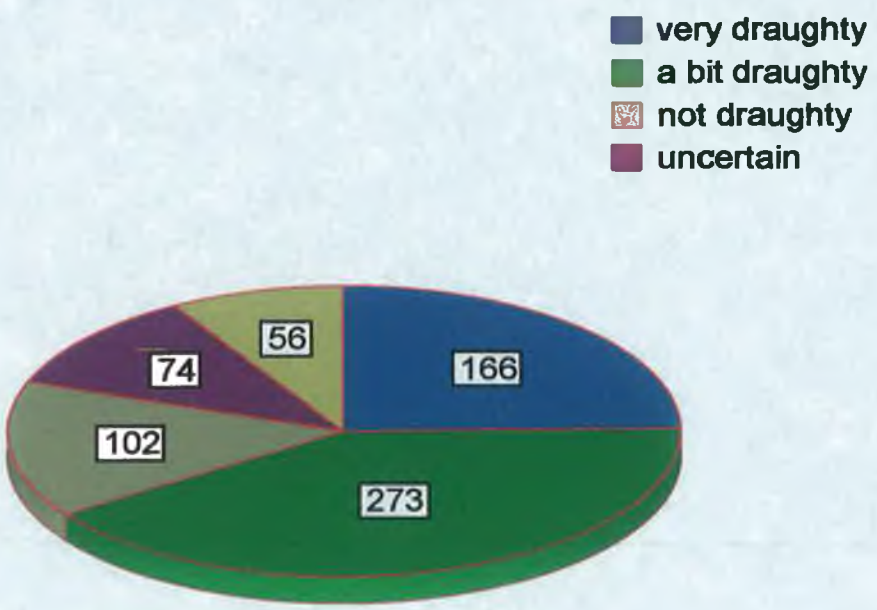

Fig. 4.23 Air Flow/Draught at Schools

4.21 TYPE OF WINDOWS IN SCHOOLS

There were over 600 replies to this question with over 67% (n = 406) indicating that their school had wooden sash windows, with over 18% (n =112) having wooden opening out type.

Table 4.23 Type of Windows in Schools

Window Type	Frequency =N	Percent	Valid Percent
Wooden sash	406	60.6	67.1
Wooden opening	112	16.7	18.5
Double glazed	8	1.2	1.4
Single glazed	46	6.8	7.6
Other	33	4.9	5.4
Sub total	605	90.2	
No response	66		
Total	671	100.0	100.0

5. RADON LEVELS

5.1 RADON LEVELS

Of the 615 respondents who indicated their home county during their first fifteen years, almost 13% (n = 84) spent their first fifteen years living in an area, where greater than 20% of homes are predicted to have radon levels in excess of the National Reference level of 200Bq/m^3, *(Radon Level 6)*.

Just under 3% (n = 16) spent their childhood in areas that are predicted to have 15% of homes above the reference level of 200Bq/m^3, *(Radon Level 5)*.

Over 12% (n = 84) came from areas where between 10 – 15% of homes are predicted to exceed the reference level of 200Bq/m^3, *(Radon Level 4)*. See Table 5.1.

Therefore, almost 30% (n = 184) of respondents spent their childhood in areas that are considered high Radon areas by RPII.

Author is not suggesting that respondents spent their childhood in homes with high Radon Levels; however they did spend their childhood in high Radon areas and therefore may have been exposed to high levels of Radon.

Table 5.1 Distribution of Cases by County and by Radon Level

	Radon Levels						
County	6	5	4	3	2	1	Total
Carlow			5				5
Cavan				2	5	8	15
Clare	3	1	5	1	2	9	21
Cork	1	5	13	17	29	8	73
Dublin				44	63	15	122
Donegal		1	8	1	6	22	38
Galway	14	5	3	3	4	2	31
Kerry	5	1	2		6	9	23
Kildare			3	1	7	2	13
Kilkenny			8	2	2	6	18
Laois			2	1	6	2	11
Leitrim					1	13	14
Limerick			1	8	17	2	28
Longford			3		4		7
Louth	5			1	3	2	11
Mayo	18	1	9	6		9	43
Meath	6	1	2		2	5	16
Monaghan			2	2		14	18
Offaly				1	2	4	7
Roscommon	1			4	4	4	13
Sligo	11	1	1	1	4	2	20
Tipperary			2	3	6	5	16
Waterford	8		1		2		11
Westmeath	1		3		4		8
Wexford	5		6	1		5	17
Wicklow	6		5	2	3		16
Total	84	16	84	101	182	148	615

Logically, one can assume that if an area (10 km grid square) has been classified as a high Radon area, then all the people with MS and all other unexplained ailments can cite exposure to Radon as being the harbinger of disease. However, that's not scientific, but out of the top three counties by response frequency/100,000 of MS, two of them, namely Sligo and Mayo also happen to be high Radon counties. Leitrim is considered a low Radon county and as mentioned previously (4.2.1) with its low population, one or two cases more or less could skew the results. Furthermore, looking at the three counties, reflecting the lowest response frequency/100,000, Kildare, Dublin and Louth, both Dublin and Kildare are considered as low Radon areas, with Louth being in the mid range. The population of Louth by virtue of its proximity to Sellafield Nuclear Processing Plant may be subject to higher levels of ionizing radiation. Perhaps it is just a coincidence that there are more MS cases clustered in high Radon areas, the main exception being Monaghan. The findings presented in this thesis have to be considered in light of the literature presented about MS and Radon. They also have to be considered in light of what is unknown about MS and Radon.

Further analysis will demonstrate that the risk of developing MS is greater in the areas with a high radon level. Galway, Mayo, Sligo, Wicklow, Carlow and Wexford all have known high Radon levels, while Tipperary, Leitrim, Offaly, Laois, Kildare and Cavan, are all considered low Radon emitting counties. Looking at the percentages of MS cases in each of the Radon Levels in these counties it can be postulated that the likelihood of developing MS is greater in the higher Radon level areas.

Take Sligo for example, where the author lives and works, 55% of MS cases reported are in Radon level 6, with only 10% reported in Radon level 1. Wicklow, Galway and Mayo all have at least 40% of reported MS cases in Radon level 6. Conversely, take Leitrim for example, 93% of its reported MS cases are in Radon level 1 and the other 7% in Radon level 2. As mentioned previously, Leitrim with its relatively low population, one or two cases more or less could skew the results. Table 5.2 below shows the approximate percentage of MS cases in each Radon level.

Table 5.2 Percentage of MS cases by questionnaire in each Radon Level

County	Radon Levels						Total MS Cases
	6	5	4	3	2	1	
	%	%	%	%	%	%	
Galway	44	18	9	9	15	5	31
Mayo	42	2	21	14		21	43
Sligo	55	5	5	5	20	10	20
Wicklow	40		26	14	20		16
Carlow			100				5
Wexford	29		36	6		29	17
Waterford	73		9		18		11
Meath	37	6	13		13	31	16
Louth	45			9	28	18	11
Kerry	21	4	8		26	39	23
Westmeath	13		37		50		8
Roscommon	7			31	31	31	13
Monaghan			11	11		78	18
Longford			43		57		7
Limerick			4	28	60	8	28
Clare	14	5	24	5	9	43	21
Dublin				36	52	12	122
Cork	2	7	18	22	40	11	73
Kilkenny			45	11	11	33	18
Donegal		3	22	3	15	57	38
Tipperary			12	19	38	31	16
Leitrim					7	93	14
Offaly				14	28	58	7
Laois			15	8	54	23	11
Kildare			23	8	54	15	13
Cavan				12	31	57	15

Counties shaded in blue are considered to be high Radon emitting counties and the counties shaded in green are considered to be low Radon emitting counties. However, it was not possible to take Radon measurements of respondent's childhood homes as part of this study. (See recommendation 8. f)

6. DISCUSSION

6.1 DISCUSSION

In this study, there were areas that were not studied, e.g., childhood viruses or genetics. The author accepts that genes play a vital role in the onset of MS, (Chatway et al., 2001 and Zhou et al., 2003)) but for this study the childhood environment was the main focus of study. Although the home environment of respondents was not measured for Radon as part of this study, the discussion therefore is based on circumstantial evidence of Radon exposure leading to conjecture and conclusions. This study set out to ascertain if there was any connection between onset of MS and childhood exposure to Radon. Having reviewed the literature and findings, it seems reasonable to propose that there is a connection and furthermore, if this risk is eliminated then MS may be preventable in some if not all of its forms.

The fact that the identical twin of a person with MS, sharing all the same genes, does not always develop MS, and that upwards of 80% of people with MS do not have a first degree relative with MS, strongly suggests that genes are not the only factor involved in developing MS. The pattern of MS inheritance has not been clearly defined. If genes were the only factor in developing MS, the identical twin of a person with MS should always get MS.

6.2 INCIDENCE

The steady rise in the incidence of MS with the passing of time, Fig. 6.1 (as per Fig 4.8) is graphically displayed and there seems to be little doubt that there is a steady rise. From 1949 up to the early 1970's there appears to be a steadily rising, low incidence of MS. Then the numbers increased significantly up to the early 1990's. As mentioned in 4.4 this could be because the diagnostic capabilities improved, or there were more people alive with MS in this period or there are more people contracting MS.

Then there appears to be another shift upwards. This could be attributed to the steady rise in home improvements that were carried out since the 1970's and right up to the present. It is also reasonable to assume that home improvements were carried out in homes of people who now have MS, given that 45% of those who responded to the questionnaire lived in homes that were built prior to 1920 and that another 40% lived in homes that were built between 1921 and 1960.

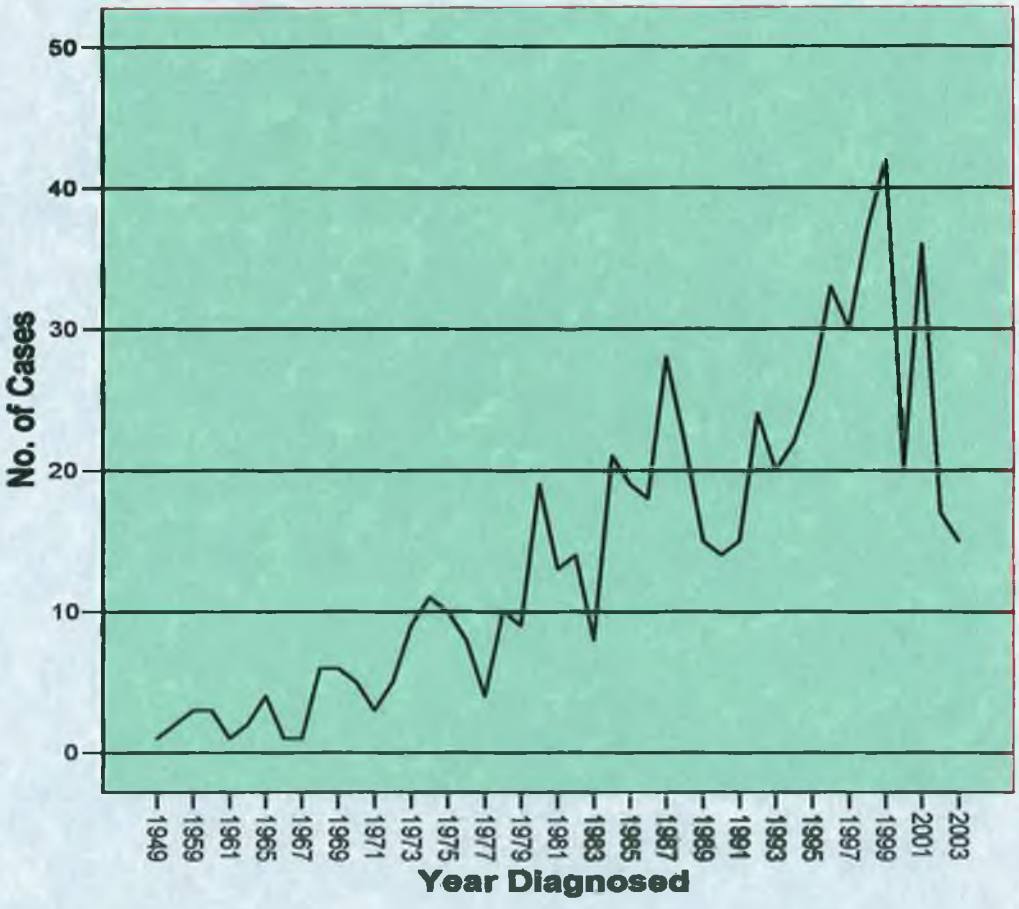

Fig. 6.1 Year Diagnosed

Donegal, although seemingly a medium radon (4% n = 18 out of 487 measurements taken had Radon levels greater than the *safe* reference level of 200 $Bq/m^{3)}$ area seems to have a higher than average response frequency. I suspect that this might be due more to genetics than environment. Traditionally, people from Donegal migrated to Scotland to work and will probably have intermarried

with people of Scottish descent and as Scotland has one of the highest prevalence rates in the world there are probably more Scottish people carrying the genes that are responsible for the development of MS. This mixing of the genes may have contributed to the higher than expected prevalence rate in Donegal. McGuigan et al. (2004) reported a prevalence rate for Donegal of 184.6/100,000

6.3 HOME IMPROVEMENTS

Home improvements usually include new draught proof windows and doors. Obviously this means that there will be less home air exchanges per hour. This, in an area that is considered a high Radon area is likely to lead to greater exposure to Radon. Bowie and Bowie (1991) suggest that draught proofing and double glazing may lead to a 30% increase in Radon levels. In another study, the highest concentrations of Radon were found during the winter months when there is less ventilation and central heating is used, (Law, Kane, Roman, Smith, and Cartwright, 2000).

6.4 WINTER

In the winter months more time is spent indoors and exposure to Radon will be greater. This is significant, as a recent study by Willer, Dyment, Sadovnick, Rothwell, Murray and Ebers, (2005) has shown that there is an association between month of birth and the risk of developing MS. The study found for the northern hemisphere that for the month of May there was a 13% increase in risk of MS compared with November. The study also suggests a reversal for MS patients born in the southern hemisphere. This would mean that the mother carrying the developing foetus during the winter months was more likely to be indoors for the greater portion of the pregnancy and consequently be exposed to Radon for longer periods.

As mentioned previously in para 2.2.5.2, Radon is more soluble in tissues with a high fat content. Both bone marrow and the female breast have a high fat content and consequently receive the highest dose of all tissues outside the lung. Stem cells, which develop into all types of tissue in the body, originating in the bone

marrow may be harmed by exposure to Radon. The evidence presented by Zhou, et al., (2000), showed that a single alpha particle can induce mutations and chromosome aberrations in cells that receive no direct radiation exposure to their DNA. Willer, et al., (2005) also support the suggestion that the gestational and/or neonatal environment influence the risk of MS in later life. A developing foetus is quite a delicate organism and exposure to elevated levels of radiation during this stage is probably not the best start in life.

6.5 WATER

Over 45% of respondents depended on ground water for their domestic supply and the RPII concluded in their report on Radon in drinking water in Wicklow (2003) "that Radon in drinking water may pose a significant additional health risk, in the longer term, to certain consumers who depend on drinking water supplies derived from groundwater as their primary source of drinking water". Bottle feeding of infants and/or breast feeding in such areas is likely to be a further health risk to the developing infant and as Kendall and Smith (2002) noted, that water with a high Radon content if ingested can remain in the stomach quite a while before it is passed to the small intestine and the on to the blood stream.

6.6 HOME ENVIRONMENT

Another significant finding is that over 40% of respondents spent their childhood in single storey houses. Radon being nine times heavier than air is therefore more likely to be a health hazard in single storey houses, particularly for children who spend quite a lot time in their first few years very close to the ground. Even in draughty homes, at night when doors and windows are usually closed there is likely to be a build-up of Radon and consequently more exposure to it. Children in the first ten years of their lives spend quite a large proportion of time indoors and again, there is the likelihood of further Radon exposure. Modern homes that have no Radon barriers or Radon remediation measures taken, and are tightly sealed, well insulated, single storey and built on uranium rich soil are quite frankly, health hazards.

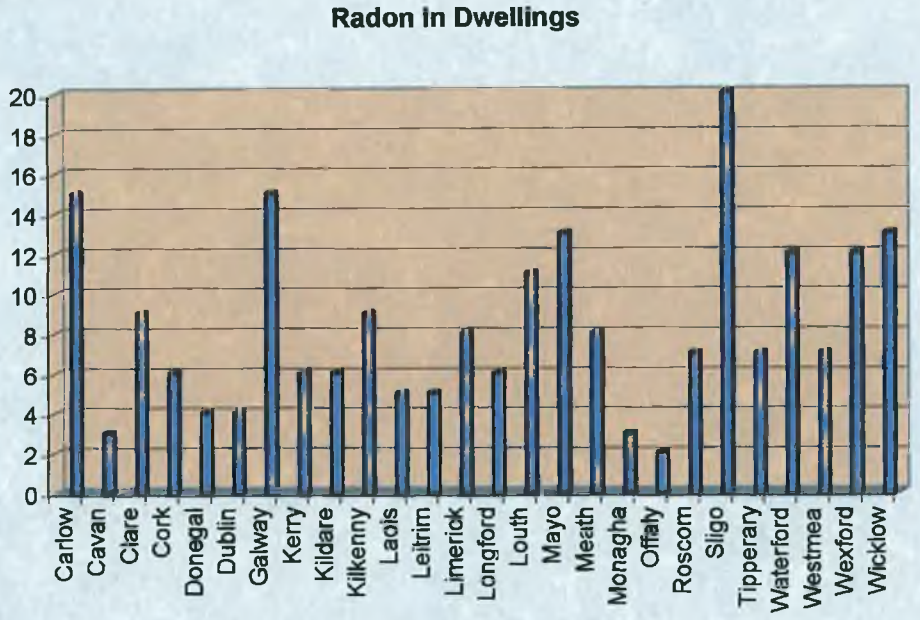

Fig 6.2 Percentage of dwellings by county that exceeded the reference level (Source RPII)

6.7 SCHOOLS

Outside the home, school buildings are where children are most likely to spend most of their time. The majority of respondents (over 60%) attended single storey schools, and *Fig 6.2* shows the percentage of schools with one or more rooms above the reference level of 200 Bq/m3. Galway was found to have the highest number of schools with one or more rooms above the reference level, with 43% of schools falling into this category. Also over 70% of respondents from Galway lived in the upper Radon level areas, 6, 5, and 4, as per Table 5.1, and over 60% also lived in single storey houses. Over 70% of Galway respondents also indicated that their water supply was from groundwater, with over 50% indicating a private well as being the water supply. The response frequency rate for Galway was low at just 14.8/100,000, but it had one of the lowest response rates at just 6.4%. Figures similar to Mayo would be expected with an improved response rate.

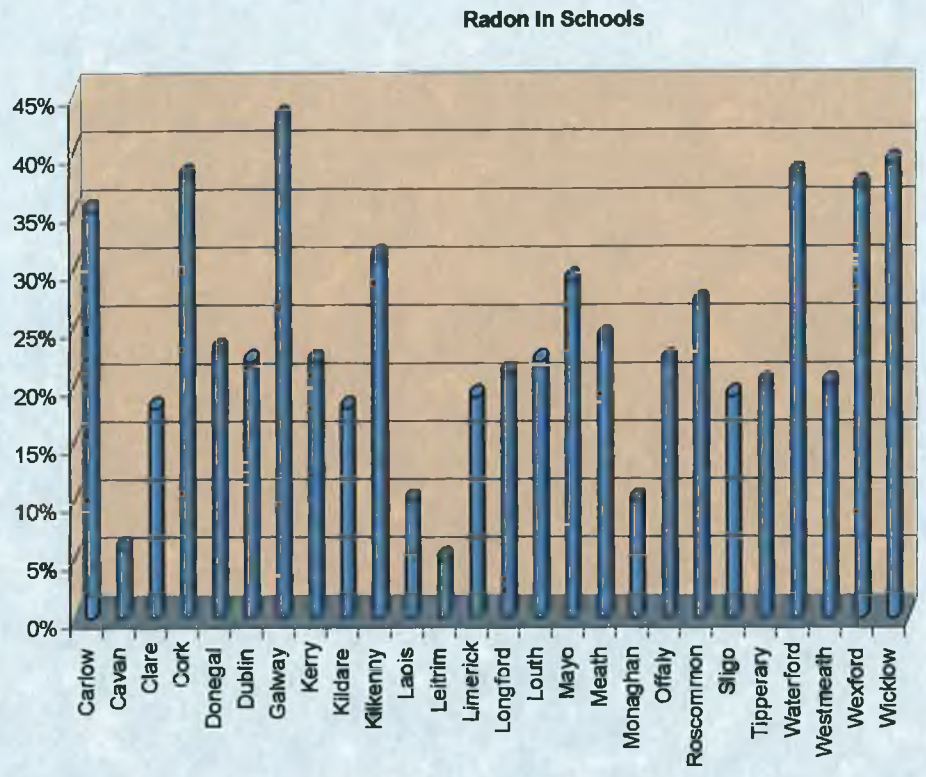

Fig. 6.3 Percentage of schools by county with one or more rooms above reference level (Source RPII)

Mayo, with almost 30% of its schools having one or more rooms above the reference level also had 65% of its respondents living in the upper Radon level areas and over 60% living in single storey houses. Over 50% of Mayo respondents indicated groundwater as their supply with over 40% indicating a private well as being the supply. The clustering of MS cases is quite evident (fig. 4.6) but not exclusive, for both these counties. The response frequency rate for Mayo was second highest at 36.6/100,000 and Mayo also had the second highest response rate at 30%.

Kildare had 18% of its schools with one or more rooms above the reference level and over 75% of its respondents living in Radon level areas, 3, 2, and 1, with over 50% or its respondents living in single storey houses. The response frequency rate for Kildare was the lowest at just 7.9/100,000, although it also had a low response rate of 7.1%.

Cavan had only 6% of its schools with one or more rooms above the reference level and 100% of respondents lived in the lower Radon level areas, 3, 2, and 1 and over 50% of its respondents lived in single storey houses. The response frequency rate for Cavan seemed higher than expected at 26.5/100,000 and it also had a high response rate of 19.2%. However, with its relatively low population, a few cases plus or minus could skew results for this county.

6.8 AGE AT DIAGNOSIS

The was no apparent difference noted in age at diagnosis in areas of differing Radon levels for females. However, there was a difference for males, with average age of diagnosis of 38.4 in Radon level 1 areas and average age of diagnosis of 29.8 in Radon level 5 areas and average age of 33.5 in Radon level 6 areas. In Radon level 5 and Radon level 6 areas males are being diagnosed approximately 7 years earlier than in the other Radon level areas. This would seem to suggest that there is a significant or critical level at which Radon exposure can cause harm to young males. In the areas where greater than 15% of homes are predicted to have Radon levels above the reference level, it seems that males are being diagnosed at a younger age with MS than males in the areas where less than 15% of homes are likely to have elevated Radon levels. Table 6.1 shows the average ages for both males and females for each Radon level area.

Table 6.1 Average Age at Diagnosis

	AVERAGE AGE AT DIAGNOSIS	
Radon Levels	**Male**	**Female**
1	38.4	35.3
2	38.4	36.7
3	38.8	37.4
4	38.6	36.1
5	29.8	37.4
6	33.5	36.8

6.9 CANADA

As pointed in 2.1.8.4, Canada displayed the fifth highest global prevalence rate for MS and is included here because there are startling differences in prevalence rates among native indigenous Canadians and the immigrant community. This again would suggest that the risk factor is genetic and/or environmental. Native Canadians, e.g., Eskimos have very low incidence rates of MS, but the incidence among the mainly European settlers is very high. The difference between these two communities is that Eskimos live predominately outdoor nomadic lives on ice, and ice cover inhibits Radon emissions (Conen, 2003). They will also have a narrower gene pool. Settlers live static indoor lives with the hazard of exposure to Radon, and will have evolved from a mixed European community with a larger gene pool. The fact that MS is not unknown among the Eskimo community proves that the defective gene or genes are present in their gene pool, and therefore one could speculate that Radon is a factor in the high prevalence rates within the immigrant community.

6.10 ESTIMATED PREVALENCE RATE

The estimated prevalence rate was derived at by comparing the results in this study (see table 6.2) with the data in McGuigan et al. (2004). They established that there were 240 MS cases in Co. Donegal giving a prevalence rate of 184.6/100,000 and 126 MS cases in Co. Wexford, giving a prevalence rate of 120.7/100,000. The ratio of cases therefore for Donegal to Wexford is **1.904:1**. This figure was compared to the MS News distribution list, which showed that Donegal had 186 members and Wexford had 97 members. The ratio of MS members for Donegal to Wexford is **1.917:1**. Furthermore, when the response frequency rates (RFR) in this study were examined for Donegal and Wexford, which were 27.6 and 14.6 respectively, they showed a ratio of **1.890:1**. Even more strikingly, when the RFR for Donegal and Wexford in this study were divided into the number of cases identified in McGuigan et al. (2004), Donegal with 240 cases identified divided by the RFR in this study of 27.6, a ratio of **8.69** is the result. Similarly for Wexford with 126 cases identified, divided by RFR of 14.6, a ratio of **8.63** results. Therefore, by using the prevalence rates in McGuigan et al. (2004), and the RFR in this study, the author was able to estimate a prevalence

rate for the country. This was achieved by establishing the ratios between the prevalence rates in (McGuigan et al. 2004) and the RFR (this study) for Wexford and Donegal (184.6 divided by 27.6 = 6.68 and 120.7 divided by 14.6 = 8.26 and averaging the two answers gives a figure of 7.47, rounded up to 7.5) and using the resulting average figure of 7.5 as a multiplier for the RFR to arrive at an estimated prevalence rate for the country. However, Leitrim by virtue of its exceedingly high RFR coupled with its low population, was excluded, and consequently all other counties that had a lower percentage response rate than Leitrim at 14.2% (Table 4.1). That left eight counties namely, Cavan, Clare, Cork, Donegal, Dublin, Kilkenny, Mayo and Wexford. These eight counties account for 2,182,429 persons or 56% of the population of Ireland. When the RFR for these eight counties were multiplied by 7.5 and the resulting answers were totalled and divided by 8 the result was 164.25. Therefore, according to this study the estimated prevalence rate for Ireland is calculated as **164.25/100,000**. If the reported prevalence rates in McGuigan et al. (2004) for Donegal and Wexford are averaged the result is **152.65/100,000** and if the same is done for this study the result is **158.25/100,000**. It was also noted that the eight counties with the highest estimated prevalence rates, namely Leitrim, Mayo, Sligo, Monaghan, Donegal, Cavan, Roscommon and Longford all border each other and are more or less in the North West of the island of Ireland.

Table 6.2 Estimated Prevalence Rate

County	Population CSO	MS News Dist	MS News Dist. Rate per 100,000	Cases by Q	Response Frequency Rate per 100,000	Interferon Use	Rate per 100,000	Estimated MS Prevalence Rate per 100,000
Kildare	163,994	181	110.3	13	7.9	176	107.3	59.2
Louth	101,821	101	99.1	11	10.8	70	68.7	81.0
Waterford	101,546	186	183.1	11	10.8	38	37.4	81.0
Dublin	1,122,821	797	70.9	122	10.9	1402	124.9	81.7
Carlow	46,014	139	302.0	5	10.9	35	76.1	81.7
Offaly	63,663	85	133.5	7	11.0	25	39.3	82.5
Westmeath	71,858	83	115.5	8	11.1	35	48.7	83.2
Tipperary	140,131	193	137.7	16	11.4	72	51.4	85.5
Meath	134,005	148	110.4	16	11.9	71	53.0	89.2
Wicklow	114,676	123	107.2	16	14.0	124	108.1	105.0
Wexford	116,596	97	83.1	17	14.6	85	72.9	109.5
Galway	209,077	480	229.5	31	14.8	170	81.3	111.0
Limerick	175,304	469	267.5	28	16.0	135	77.0	120.0
Cork	447,829	423	94.4	73	16.3	365	81.5	122.2
Kerry	132,527	380	286.7	23	17.4	88	66.4	130.5
Laois	58,774	179	304.5	11	18.7	29	49.3	140.2
Clare	103,277	64	61.9	21	20.3	54	52.3	152.2
Kilkenny	80,339	83	103.3	18	22.4	40	49.8	168.0
Longford	31,068	86	276.8	7	22.5	25	80.5	168.7
Roscommon	53,774	195	326.6	13	24.2	21	40.0	181.5
Cavan	56,546	78	137.9	15	26.5	27	47.7	198.7
Donegal	137,575	186	135.1	38	27.6	144	104.7	207.0
Monaghan	52,593	193	366.9	18	34.2	32	60.8	256.5
Sligo	58,200	156	268.0	20	34.4	62	106.5	258.0
Mayo	117,446	139	118.3	43	36.6	55	46.8	274.5
Leitrim	25,799	98	379.8	14	54.3	41	158.9	407.2

Table 6.3 Facts and Statements in Summary Form

Multiple Sclerosis Facts	Radon Facts	Statement
It affects approximately twice as many females as males	It is harmful when it becomes trapped in buildings	Females traditionally spend more time in the home than males
The myelin coating on the nerves is the target for destruction in MS	It is soluble in fat	Myelin is a fatty substance, as is bone marrow and the female breast
It is most common amongst Caucasian people of northern European origin	Ice cover inhibits its emissions	MS is rare amongst Eskimos
It is more prevalent in temperate regions than in tropical regions	It is considered harmless in the atmosphere	It is rare amongst people who live outdoor nomadic lives
It is a complex genetic disorder	It is a radioactive gas and emits alpha particles when it decays	A single alpha particle can induce mutations and chromosome aberrations in cells that receive no direct radiation exposure to their DNA
There is no known cause	It is a known carcinogenic	Radon? Hypothesis: Exposure to Radon during the first 15 years of life may be one of the environmental triggers that is responsible for the onset of MS in later life

Multiple Sclerosis Beliefs		
It is believed that an environmental trigger in the first 15 years of life is responsible for its onset	It is generated by the decay of uranium within the earths crust and ascends to the atmosphere	Radon is in the environment

7. CONCLUSIONS

The initial aims of this study were to:

a. **To establish the prevalence of MS in Ireland**: - this aim was not realised. Due to ethical considerations full co-operation from the country's neurologists was not possible I am however, very appreciative of the co-operation received. It is difficult for a non-medical researcher to obtain access to medical data. However, to circumvent this problem an estimated prevalence rate of **164.25/100,000** (see para 6.9) was calculated based on data from McGuigan et al. (2004), which reported prevalence rates for Donegal and Wexford.

b. **To establish the environmental milieu of MS patients for the first 15 years of their lives**: - this aim was achieved. However, one of the more interesting findings, although more from a sociological point of view was the fact that, 100 respondents reported having a dry toilet (one wonders how many of today's students know what a dry toilet is), and an even more startling revelation, was, that 74 respondents reported having no toilet.

c. **To plot this information geographically**: - this aim was achieved and for the most part there were no real surprises. A trend was recognised whereby there appears to be more clustering of MS cases in the areas of Ireland, where it is known that there are high radon levels.

d. **To examine the relationship between the incidence of MS and factors increasing exposure to natural radiation within the built environment, (specifically – indoor radon)**:- this aim was also achieved; as the author infers that there is a relationship between MS and exposure to indoor radon. Given what is known about MS and what is known about Radon, especially the lack of data about how the human body, from conception to maturity, reacts to exposure to radon and its progeny, then, unless it can unequivocally be ruled out as being the environmental trigger that precipitates the onset of MS, it must be treated as if it could be one

of the environmental triggers. Environmental factors that have been ruled out include; exposure to Zinc, childhood illnesses, canine distemper, slow viruses, sinusitis, herpes zoster, herpes simplex and climate, (Martyn, 1991). However it was also noted that climate has an influence on many aspects of a population e.g. house design, and that differences in one or more of these could provide the mechanism for environmental triggers to influence the onset of MS. Martyn (1991 p.35) concludes with "epidemiologists now need to formulate specific hypotheses about causal environmental factors". A recent American study has shown a strong potential causality relationship between MS and exposure to ionising radiation, (Eidbo and Prater, 2004). That study found high prevalence rates of MS in US counties that also had high indoor Radon levels. Extremely high prevalence rates were found in the States of Washington and Idaho and both had high indoor radon levels. The study also noted low prevalence rates coinciding with low indoor radon levels, and to advance the radon connection, cases of MS were reported as being rampant among National Park Service personnel at the Mammoth Hot Springs, Yellowstone National Park headquarters in the late 1980's. Radon ground readings there reached 1,000 p/Ci/l, or 200 times the Environmental Protection Agency health standard, (Eidbo and Prater, 2004)

e. **If the hypothesis is proven - to alert national authorities as to what preventative or mitigating actions can be taken**: - no, the hypothesis is not proven beyond all reasonable doubt. There are still too many unknowns to say without doubt that the hypothesis is proven. However, perhaps there is enough circumstantial evidence to form an educated guess. A number of respondents have given permission for measurements to be taken in their childhood homes. The technology to make accurate retrospective Radon measurements is available even if the homes have been

modernised. This can be achieved provided the glass in the windows is original.

The US Congress, in 1988 passed an Act entitled "The U.S. Radon Abatement Act". This Act directed that the EPA identify and measure indoor Radon levels in each of the 3,141 counties in the U.S.A. To date 18,000,000 homes across the United States have been tested for Radon and Almost 800,000 have had remedial measures taken to reduce the occupants' exposure to Radon (Gregory and Jalbert, 2003). The U.S. Congress recognises the threat to public health that Radon poses. In Ireland 11,319 homes have been measured by the RPII in the national radon survey.

This present study now adds to the body of knowledge that recognises the threat to public health from continued exposure to indoor Radon. Already the relevant authorities know this, as there are building regulations directing that Radon preventative measures be taken in all new homes in known high radon areas. These regulations came into force on the 1st July 1998. If these regulations are applied fully, the author would expect to see a decline in the incidence of MS over the next twenty to thirty years, perhaps back to the levels observed before home improvements with double glazing and draught proofing, trapped Radon in homes.

8. RECOMMENDATIONS

Any measures aimed at reducing the hazard of Radon exposure should include:-

a. A government sponsored measuring of all homes in known high Radon areas.

b. Grant assisted remedial measures to eliminate Radon exposure in homes that have elevated Radon levels.

c. A raising of the level of awareness of Radon and its perceived health related risks. The apathy shown towards Radon is probably because it is invisible and therefore not perceived as a threat to health. On the other hand, radiation is known to be dangerous, even though it cannot be seen.

d. As not enough is known about Radon and its perceived health related risks, a multifaceted Radon research plan is needed.

e. The author would also concur with Dr. Colgan of the RPII, in recommending that as part of the home buying process that a Radon Survey be included in the architectural survey of the house.

f. The author recommends that radon measurements be taken in the homes of respondents that gave permission.

g. Given the economic burden of MS on the state, the author definitely recommends that MS becomes a notifiable disease, as should all diseases, and that more use be made of mapping illnesses. After all mapping disease is nothing new. In 1848 when John Snow mapped the incidence of Cholera in Soho, London it was observed that there was a clustering of Cholera cases around a water pump in Broad Street. Once this pump was shut down the epidemic of Cholera subsided rapidly. Obviously the more that is known about a disease the greater the chances are of finding a cure, if not preventing it altogether. The mystery of MS can only be solved by continued painstaking research and full co-operation between all the interested parties.

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Appendix 1

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Ballinode, Sligo, Ireland.

Stiurthoir/Director: Richard Thorn, BA (Mod), MA, PhD, MCIWEM
Tel: 353 71 55222 Fax: 353 71 45704

Dear Dr._____

I am carrying out research for a Masters Degree (A study of the prevalence of Multiple Sclerosis and its relationship with the natural/geological environment), under the supervision of

Eamonn Grennan (geologist – School of Science) Institute of Technology, Sligo and
Margaret Gilmore (medical doctor – Social Studies Department) Institute of Technology, Sligo.

As you are aware, Multiple Sclerosis is considered likely to have an environmental component in addition to a genetic predisposition and so the first objectives of the study are

1. to establish the prevalence of MS in Ireland
2. to establish the natural environmental milieu for the first 15 years of life of people who have MS.

Background Information

The northwest of Ireland appears to have one of the highest prevalence rates of MS in Ireland, but as yet there is no reliable database. The area is one of the

highest radon emitting areas in Ireland with Donegal in particular containing some of the most highly uranium enriched granites in the country. This has provided the motivation for the pilot study that was undertaken by E. Grennan and M. Gilmore i.e. an attempt to refine the well known geographical association between MS and temperate climates to a more coherent association between MS and geology.

It is in relation to objective one that I feel that you can be of great assistance to my study, as we need to survey MS patients to establish their home townlands during childhood. As the majority of patients surveyed in the pilot study (a copy of which can be made available to you on request), had not moved from their childhood home or locality, it would be of great help to us if you could let us have a printout of their present townland. I realise that there may be ethical and legal considerations that may cause problems in divulging such information. If this is not directly possible, I am quite happy to carry it out in a mutually acceptable manner. However, given that this is a worthwhile research project which will fill a major void in our medical statistics I feel that these problems should not be insurmountable. Also, I would like to stress at this time that any information furnished will be treated confidentially and will not be used for any other purpose. A copy of this survey will be made available to you when it is completed.

I have also written to the Health Boards and the MS Society of Ireland, from which I expect to get people to take part in the survey to fulfil the second objective as outlined above.

Should you require any further information, please do no hesitate to contact me at

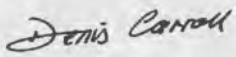
Public Health Department
North Western Health Board
3rd Floor, Bridgewater House
Sligo

Phone – 071 74762 or email – denis.carroll@nwhb.ie

or

Denis Carroll
Department of Business and Humanities
Institute of Technology
Sligo

Kindest Regards
Yours Sincerely



Denis Carroll

MULITIPLE SCLEROSIS and RADON: Is there a connection?

- Eamonn Grennan
  B.Sc., M.Sc., Dip. Admin.Sc.
- Margaret Gilmore
  M.B., B.Ch., B.A.O., D.C.H.,D.Obs.
- Denis Carroll B.A.

Background

- Institute of Technology, Sligo
- Environmental Science
- 30 years world-wide experience
- Geology and Living

Initial Interest

- Bolviken (1997)
- Magnesium and fish eating with low prevalence of MS
- High prevalence of MS with Radon emanating from granites in Norway
- "That the content of Rn in inhaled air is a risk factor in MS" (Neuroepi.2003)

Geology and Health

- ASBESTOSIS
- COAL MINER'S LUNG DISEASE
- Rn and LUNG DISEASE
- ZEOLITES and CARCINOMA

Topics Requiring Focus

- Radon
- Geology
- Environment
- Maps

Early Studies

- Burnfield(1991) and Robinson(1998)
- Medline and Acta. Neur. Scand.
- McAlpine's Multiple Sclerosis
- Latitudinal Effect
- Environmental Trigger

MS Distribution

- Latitudinal effect = Geological Effect
- Europe South to North
- USA Southeast to Northeast
- Australia Queensland to Tasmania

Britain

- Compston and Swingler(1986)
- Prevalence rate for UK increases N
- Appleton and Ball(1995)
- Rn map for Britain

Miller in N.I.(1966)

- 2 areas of high incidence "H" & "D"
- NIPB High Rn in Mourne Mtns
- Mourne Mtns – "rock is Silurian, the soil brown podsolic"
- Sperrin Mtns – "rock is mainly schist, the soil brown podsolic"

Reviewing evidence to date

Redefined influence of Rn to include ionising radiation

European Data-

- Aberdeen - granite city
- Orkneys - major U exploration effort
- Sardinia - unusally high MS, highest indoor bequerel count in Europe

Irish data

- Sligo - very high Rn values
- Donegal - significant U discoveries
- Wicklow - Rn in water recent rediscovery

MS puzzle

- Cause unknown, probably multi-factorial including environmental agent
- Prevalence in temperate latitudes is high

Environmental agent

- Trigger for MS before age 15 e.g.

Migration after age 15 years –

MS rate remains as for area of origin

Race vs Place

- Low incidence of MS among Eskimos, Bantus and Gypsies –

live outdoor, nomadic lives in low radon areas

Geography

Areas of high MS prevalence are underlain by rocks of

- Same age (300-500m. years old)
- Similar mineral composition
- High radon emission

e.g.

- Orkneys (>250/100,000)
- N.E. Scotland (>170/100,000)
- N. Ireland (>130/100,000)

Other links

- "...environmental factors ... possible triggers for various autoimmune disorders e.g. ...
- Ultraviolet radiation and MS
- Ionising radiation and SLE...
- Heavy metals and autoimmune glomerulonephritis" (NIHS 1999)

HYPOTHESIS

- That risk of developing MS (if genetically susceptible) is increased by exposure to natural ionising radiation before age 15 years

Study 1

- Membership of MS Society of Ireland on county basis
  - Broad correlation with areas of greater radon emissions:

However -

- Study needs to be more accurate
- May not be totally representative

Study 2

Prevalence (unquantified) was thought to be high in NW Ireland

- A questionnaire survey of users of N.W. M.S. Therapy Centre showed:

Results of Study 2

67 respondants (33%)

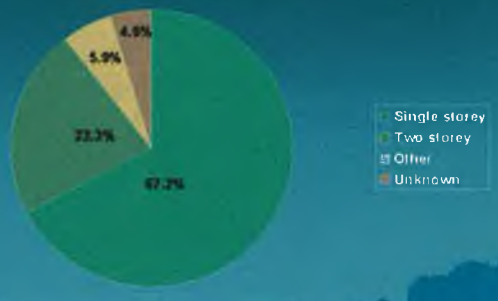
- Profile similar to other studies in male:female ratio and reported prevalence in relatives

Results (contd.)

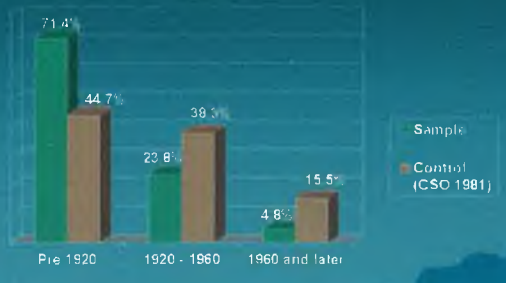
- Most respondants still lived in childhood home or locality

Majority lived in
- one storey, older houses with
- private water supply and
- used open fires for heating

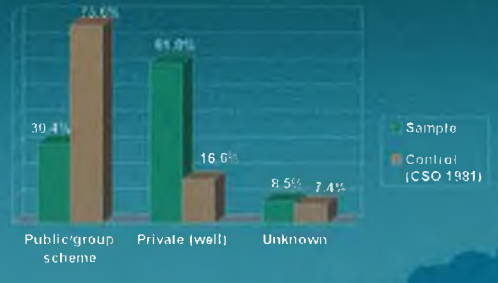
House Type



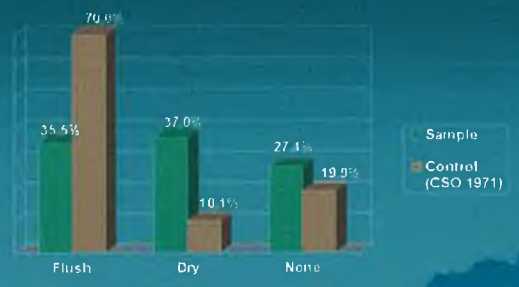
House Age



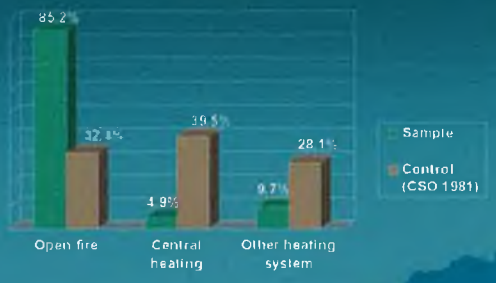
Water



Sanitation



Heating



Discussion

- Radon is nine times heavier than air and therefore accumulates at ground level
- In one storey houses exposure to radon will be greater

Other observations

- Water source from wells may be relevant
- Use of open fires (turf tends to concentrate radioactive elements)
- In this survey, it was not possible to test radon levels

Conclusions

- These pilot studies broadly support hypothesis
- Further work is needed

HYPOTHESIS

- That risk of developing MS (if genetically susceptible) is increased by exposure to natural ionising radiation before age 15 years

Plans

- To test hypothesis with larger cohort

We need to administer questionnaire to as many people with MS as possible

- Can preserve confidentiality if done via consultants
- National MS prevalence rate

IF HYPOTHESIS IS TRUE

- Future research needs will be highlighted
- Anti radon strategies
- Broaden area of study outside Ireland

Long term benefit of MS prevention

Institiúid Teicneolaiochta, Sligeach
INSTITUTE OF TECHNOLOGY, SLIGO
Ballinode, Sligo, Ireland.

Tel: 353 71 91 55222 Fax: 353 71 91 45704

Postal Questionnaire

Dear Reader

I would like to invite you to take part in research into a possible cause of Multiple Sclerosis. I am trying to find out if there is any relationship between developing Multiple Sclerosis and the presence of Radon in the environment. Radon is a naturally occurring gas, which can reach high levels inside buildings.

I am particularly interested in your childhood home(s)/school(s) up to age 15 years.

Results of the survey will be made available to MS News.

As a gesture to acknowledge your participation in this survey, a donation will be made to the Multiple Sclerosis Society of Ireland for each completed questionnaire returned by January 31st 2004.

This research project ***(A study of the prevalence of Multiple Sclerosis and its relationship with the natural/geological environment in Ireland)*** has been approved by the IT Sligo Research Ethics Committee and your participation is voluntary.

Thank you for your help. Please return the completed questionnaire to me at the address below, or in the envelope provided.

Yours Sincerely

Denis Carroll

DENIS CARROLL B.A.
SCHOOL OF BUSINESS AND HUMANITIES
INSTITUTE OF TECHNOLOGY
BALLINODE
SLIGO
email carroll.denis@itsligo.ie
Phone: 071 91 55307 (direct line)

I would like to acknowledge assistance from the NWHB and IT Sligo for their financial and practical support in this research project.

Any information given will be only be used by the researcher and will not be made available to any other person or institution without the consent of the giver. The results may be published but no individual will be identified. All details will be securely stored.

Section I – Personal

Q 1. Date of Birth _____ M ☐ F ☐

Q 2. When were you diagnosed with Multiple Sclerosis? 19____

Q 3. Has anyone else in your family been diagnosed with Multiple Sclerosis?

Yes ☐a No ☐b Don't know ☐c

If yes, for each blood relative, please describe relationship, e.g. aunt (mother's sister, fathers sister, etc.), for each case.

_____

_____

Did this person(s) live in the same house(s) as you? Yes ☐ No ☐

SECTION II - Accommodation

Please complete the following details for each house (or other accommodation) you have lived in from birth to 15 years of age.

If you have lived in more than one house, please include details on separate sheet if necessary.

Q 4. Address (including townland/district) _____

_____

Q 5. Length of time living there _____

Q 6. When was the house built (approx) – please tick one box

Before 1920	☐	Between 1921 and 1960	☐
Between 1961 and 1980	☐	After 1980	☐
Don't know	☐		

Q 7. Type of House – please tick one box

Single storey	□	Two storey or more	□

Q.8 Was/is there a basement in this house ? Yes□ No□

Q 9. Where was the water supply taken from? – please tick all that apply

Group water scheme	□	Private well	□
Public supply	□	Don't know	□

Q 10. Type of toilet facilities – please tick all that apply

Indoor flush toilet	□	Outhouse flush toilet	□
Dry toilet	□	None	□

Q 11. Heating System – please tick all that apply

Oil fired central heating	□	Gas central heating	□
Electric storage heaters	□	Range /Open fire	□

Q 12. If heating system was range/open fire please indicate type of fuel

Turf □ Coal □ Wood □ Peat Briquettes □

Q 13. Would you describe the house as?

Very draughty	□	A bit draughty	□
Not at all draughty	□	Uncertain	□

Q 14. Types of windows – please tick as appropriate

Wooden sash	□	Wooden – opening out	□
Aluminium	□	uPVC	□
Single glazed	□	Double glazed	□

SECTION III – Schools attended and/or places of work up to age 15

Q 15. Name & address (including townland)_____

_____

For subsequent schools or workplaces please include details on separate sheet if necessary.

Q 16. Length of time spent there – from/to approx _____

Q 17. When was the school built? (approx) – please tick one box

Before 1920	□	Between 1921 and 1960	□
Between 1961 and 1980	□	After 1980	□
Don't know	□		

Q 18. Type of school – please tick one box

Single storey	□	Two storey	□

Q.19 Was/is there a basement in this school? Yes□ No□

Q 20. Where was the water supply taken from? – please tick all that apply

Group water scheme	□	Private well	□
Public supply	□	Don't know	□

Q 21. Type of toilet facilities – please tick all that apply

Indoor flush toilet	□	Outhouse flush toilet	□
Dry toilet	□	None	□

Q 22. Heating System – please tick all that apply

Oil fired central heating	□	Gas central heating	□
Electric storage heaters	□	Range /Open fire	□

Q 23. If heating system was range/open fire please indicate type of fuel

Turf □ Coal □ Wood □ Peat Briquettes □

Q 24. Would you describe the school as?

Very draughty	□	A bit draughty	□
Not at all draughty	□	Uncertain	□

Q 25. Types of windows – please tick as appropriate

Wooden sash	□	Wooden – opening out	□
Aluminium	□	uPVC	□
Single glazed	□	Double glazed	□

Section IV – Optional

If you are still living in your childhood home and the survey shows a strong connection, may we contact you in the future to discuss Radon levels? If yes, please leave your present contact details.

Yes ☐ No ☐

Name_____

Address_____

_____

Thank you for taking the time to complete this questionnaire.

PLEASE RETURN QUESTIONNAIRE BY JAN 31 2004.

Any information given will be only be used by the researcher and will not be made available to any other person or institution without the consent of the giver. The results may be published but no individual will be identified. All details will be securely stored.

Appendix 4

Institiúid Teicneolaiochta, Sligeach
INSTITUTE OF TECHNOLOGY, SLIGO
Ballinode, Sligo, Ireland.

Stiurthoir/Director: Richard Thorn, BA (Mod), MA, PhD, MCIWEM *Tel: 353 71 55222 Fax: 353 71 45704*

Dear

As you are aware, Multiple Sclerosis is considered likely to have an environmental component in addition to a genetic predisposition. My reason for writing to you is, I am carrying out research for a Masters Degree (A study of the prevalence of Multiple Sclerosis and its relationship with the natural/geological environment), under the supervision of

Eamonn Grennan (geologist – School of Science) Institute of Technology, Sligo
and
Margaret Gilmore (medical doctor – Social Studies Department) Institute of Technology, Sligo.

The first objectives of the study are

3. to establish the prevalence of MS in Ireland
4. to establish the natural environmental milieu for the first 15 years of life of people who have MS.

Background Information

The northwest of Ireland appears to have one of the highest prevalence rates of MS in Ireland, but as yet there is no reliable database. The area is one of the highest radon emitting areas in Ireland with Donegal in particular containing some of the most highly uranium enriched granites in the country. This has provided the motivation for the pilot study that was undertaken by E. Grennan and M. Gilmore i.e. an attempt to refine the well known geographical association between MS and temperate climates to a more coherent association between MS and geology. A copy of this pilot survey can be made available on request.

I have written to the country's neurologists and asked them to furnish me with the locations by townland of all their patients. However, this is unlikely to be detailed enough, therefore in order to carry out a survey to achieve the second objective I need your assistance in distributing a questionnaire to all of your members. It would be preferable if I could carry this out myself, but if this is not possible then I am quite happy to carry it out in a mutually acceptable manner. Any information supplied will be treated confidentially and will not be disclosed to anyone else. A copy of the survey results will be sent to you when it is completed.

Should you require any further information, please do no hesitate to contact me at

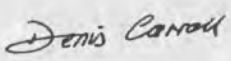
Public Health Department
North Western Health Board
3rd Floor, Bridgewater House
Sligo

Phone – 071 74762 or email – denis.carroll@nwhb.ie

or

Denis Carroll
Department of Business and Humanities
Institute of Technology
Sligo

Kindest Regards
Yours Sincerely



Denis Carroll

SLIGO STUDY LINKS RADON GAS TO MS

The above headline was printed in the Sunday Times on December 15th 2002. It was the result of a study carried out by Eamonn Grennan, a geologist and environmental scientist and Margaret Gilmore, a medical doctor and social studies lecturer, both lecturing at the Sligo Institute of Technology. Perhaps this headline is too dramatic, you may say. Where is the proof? Well, that is where this article and **YOUR** involvement come in.

My name is Denis Carroll and I am a research student, studying at the Institute of Technology, Sligo. I am currently involved in a detailed, nationwide study trying to ascertain whether exposure to indoor Radon can be considered one of the environmental factors that triggers the onset of Multiple Sclerosis, *(it is agreed that genetically susceptible individuals are exposed to some environmental trigger)*. You can help me by completing the enclosed questionnaire, which will contribute to the countrywide picture of Multiple Sclerosis.

Below are the main points from the initial pilot survey. I hope to build on this study with the data obtained from these questionnaires. In the pilot study, the questionnaire was designed to ascertain the environmental milieu of people who have MS. There were questions on house type, house age, types of facilities, i.e. heating, water supply and sanitation.

There is considerable variation in the prevalence of multiple sclerosis around the world and this geographical distribution has been studied in the hope that some clues as to the cause of the disease will be unearthed. The prevalence of Multiple Sclerosis increases with latitude north and south of the equator. There are various theories as to why this might be, too numerous to go into in this article.

There were two studies carried out. The first one examined the membership of MS Society in Ireland and as expected the higher prevalence rates correlated with the general pattern of higher radon emissions as surveyed by the Radiological Institute of Ireland, i.e.

a band of lower prevalence through the country from Kenmare to Drogheda. The second study was via a questionnaire distributed with the help of the Northwest MS Therapy Centre.

RESULTS OF PILOT STUDY

Of the 66 respondents, almost two thirds were female In addition; almost half of female respondents had a relative with MS, as did one fifth of males.

The average age of onset for males was 27.9 years, while the average age at diagnosis was 35 years, whereas for females the average age of onset was higher at 33.4 years with average age at diagnosis 38.3 years. The average time span from onset to diagnosis for males was 7 years with the longest spell being 26 years, while for females the average was lower at 5 years with the longest spell being 16 years.

Over two thirds of respondents lived in single storey houses and the majority spent their early years in houses built prior to 1960. Over half had a private water supply, (*Radon is found in water*). Almost three quarters had an open fire (probably burning turf).

DISCUSSION

As there were no actual radon measurements carried out in any of the respondents' homes it cannot be said with any degree of certainty that exposure to indoor radon during the first fifteen years of life has been a contributing factor. However, most authorities on MS agree that exposure to some environmental agent in genetically pre-disposed individuals up to the age 15, may result in development of MS.

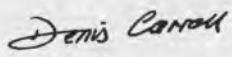
Over half of respondents spent the first 15 years of their lives in the counties Donegal, Sligo and Mayo. To assist in identifying areas at greatest risk of high indoor radon levels, the Radiological Protection Institute of Ireland, which has responsibility for the detection and measurement of radon gas in Ireland, initiated a national geographically based radon survey in 1992.The county with the largest proportion of high radon houses measured was County Sligo where 20% of the houses exceeded the Reference Level. This and the fact that over two thirds of respondents spent the early years of their lives in single storey, older type houses could also point to radon being one of the environmental

triggers. Radon gas can become trapped in buildings, especially older type buildings that have had no radon extraction works carried out, and is nine times heavier than air. It can become trapped in homes especially during the night when there is little airflow in bedrooms. This exposure over a long period can have health implications. For the first time, researchers have found direct evidence that the occurrence of radon in people's homes may account for 1 in 20 cases of lung cancer in the UK. Radon is also known to be soluble in fat. Myelin is a fatty substance that insulates the nerves and it is the breakdown and subsequent scarring of this tissue that is responsible for the distortion or even blocking of messages from the brain that lead to the symptoms of MS.

CONCLUSION

Given what is known about Radon and its distribution throughout Ireland, it is clear that it could be one of the environmental factors that trigger MS in genetically susceptible individuals. The fact that over half of the respondents spent the first 15 years of their lives in homes located in areas known to have higher than average indoor radon levels and over two thirds lived in single storey homes, it seems logical to suggest that indoor Radon can be considered to be one of the environmental triggers. However, a nationwide study, mapping the incidence of the disease would shed even more light on the mystery surrounding this debilitating disease and if the hypothesis is proven, we could take preventative action to lessen the number of future cases.

This current study aims to do just that, via a refined questionnaire, which is included in this issue of MS News. It has been over twenty-five years since anyone has tried to establish the national prevalence rate and this study aims to rectify that situation while trying to correlate it with Radon exposure. The more that is known about a disease, the more likely a cause, or a cure can be identified.



Denis Carroll
Research Assistant
Institute of Technology, Ballinode, Sligo

Appendix 6

Report on breakdown of Multiple Sclerosis Patients as at June 2003-10-02

GMS(P) Board September 2003

Health Board	Population	No. of Patients on Interferon	County/City
ERHA HB		467	Dublin City
	1,122,821	165	Dublin County
	163,994	61	Kildare
	114,676	47	Wicklow
		963	*Unallocated
Total		1703	
Midland HB			
	58,774	29	Laois
	31,068	25	Longford
	63,663	25	Offaly
	71,858	35	Westmeath
Total		114	
Midwestern HB			
	103,277	54	Clare
	175,304	69	Limerick City
		66	Limerick County
		32	Tipperary N.R
Total		221	
North Eastern HB			
	56,546	27	Cavan
	101,821	70	Louth
	134,005	71	Meath
	52,593	30	Monaghan
		2	Carrickmacross
Total		200	
North Western HB			

	137,575	144	Donegal
	25,799	41	Leitrim
	58,200	62	Sligo
Total		247	
South Eastern HB			
	46,014	35	Carlow
	80,339	40	Kilkenny
	140,131	40	Tipperary S.R.
		11	Waterford City
	101,546	27	Waterford County
	116,596	85	Wexford
Total		238	
Southern HB			
	447,829	201	Cork City
		160	North Cork
	132,527	88	Kerry
		4	South Cork
Total:		453	
Western HB			
	209,077	170	Galway
	117,446	55	Mayo
	53,774	21	Roscommon
Total		246	
Total:		**3,422**	