Chapter 17
Sinusitis in Multiple Sclerosis
and Acinetobacter

17.1 Introduction: The First Descriptions of Upper Respiratory Tract Infections in Multiple Sclerosis

Previous studies have shown that the onset of multiple sclerosis had been associated with the presence of upper respiratory tract infections involving both viral and bacterial agents. The relevance of these reports requires further consideration.

17.2 Tonsillectomy and Multiple Sclerosis

In 1965, an extensive study involving 240 patients with multiple sclerosis was carried by Poskanzer in the Harvard Medical School. The patients came from multiple sclerosis clinics attending the Massachusetts General Hospital and the Tufts New England Medical Center.

In the study, there were 210 patients with a living sibling from whom information was obtained and 190 with a spouse. There were also 167 patients who had both a spouse and sibling.

There were 133 patients (63 %) with a sibling, who had a tonsillectomy versus 77 patients (37 %) who had no tonsillectomy and this difference was statistically significant (p<0.01).

There was no significant difference in siblings who had a tonsillectomy (50.5 %) versus siblings who had not had a tonsillectomy (49.9 %).

There were 121 patients (64 %) with a spouse who had a tonsillectomy versus 69 patients (36 %) who had no tonsillectomy and again this difference was statistically significant (p<0.01).

There was no significant difference between spouses who had a tonsillectomy (49.5 %) versus spouses who had not had a tonsillectomy (50.5 %).
Investigations were carried out to ascertain the frequency of appendicectomy in multiple sclerosis patients and their siblings as well as their spouses. When the multiple sclerosis patients were compared to their nearest siblings, no significant difference in the rate of appendicectomy could be shown. However when multiple sclerosis patients were compared to their spouses, significantly more operations had been carried out in the patients (p<0.05).

The risk of a person acquiring multiple sclerosis was found to be about 1.7 times higher if he or she had had a tonsillectomy than if the subject had not undergone the operation. It was concluded that these operations suggested an exogenous, environmental factor was playing a role in the aetiology of multiple sclerosis (Poskanzer 1965).

### 17.3 Multiple Sclerosis and Infections in Canadian Patients

In 1983, an extensive study was carried out on 251 Canadian multiple sclerosis patients in Quebec. The aim of the investigation was to determine the existence of repeated respiratory tract infections in such patients before the onset of neurological disease.

The 251 multiple sclerosis patients were divided into two groups, those with upper respiratory tract infections before the onset of the disease (group A) and those without a past history of such infections (group B).

The mean number of attacks in the first 5 years of the disease group which suffered from upper respiratory infections was 6.2 attacks compared to 2.9 attacks in the group that had not reported such respiratory infections (p<0.02).

The multiple sclerosis patients with an antecedent respiratory tract infections (group A) when compared to those without such a history (group B), it was found that group A had a significantly higher percentage of visual problems (p<0.01), paresthesiae (p<0.01), pain (p<0.004), motor problems (p<0.016) and sexual dysfunction in males (p<0.02).

These results indicate that upper respiratory tract infections may have a role to play in the onset and progression of the disease in multiple sclerosis patients (Lamoureux et al. 1983).

### 17.4 Multiple Sclerosis Associated with Sinusitis in England

In 1986, the records of 150 multiple sclerosis patients from Essex, Hampshire and Surrey in England, from ten different practices, were examined for possible environmental factors involved in the onset of the disease.

There were 92 patients who had been seen by a consultant neurologist and were diagnosed, according to the McAlpine criteria as “definite” or “probable” multiple sclerosis.

The sample conformed to the classical pattern of multiple sclerosis in that the mean age of first attack was around the age of 30 years (men 32.4 years, women 29.7 years).
These patients were compared to two groups of matched controls who were obtained from practice registers. The first group A consisted of 92 patients matched with the multiple sclerosis patients for age and sex. The second group B were the spouses or cohabitants of the multiple sclerosis patients.

A third group of controls, group C, consisted of 92 patients, who were matched for sex but not for age, who also had a history of recurrent upper respiratory tract allergies, including seasonal rhinitis.

Finally, a further group D of 92 patients, matched for sex and as closely as possible for age were interviewed and their clinical records examined.

The authors stated that “To our surprise it became clear early in the analysis that multiple sclerosis patients had a very much higher recorded rate of chronic and relapsing nasopharyngeal infections than their controls” (Gay et al. 1986).

The mean of recorded sinusitis in the multiple sclerosis group was 69.5 % whilst in control group A it was 17.4 % and in control group B it was 16.3 %. The overall rate of recorded sinusitis in the multiple sclerosis group was over four times that found in control group A and control group B and this difference was highly significant (p < 0.0001).

A high rate of recorded sinus infection was found in the allergic group C (45.6 %) but even that rate was significantly lower than the rate found in the multiple sclerosis patients (p < 0.0001).

Direct questioning of group D patients gave a rate of 38.0 % which was still lower than the rate found in the multiple sclerosis patients.

The mean age (±standard deviation) of first attack of multiple sclerosis was 30.4 ± 9.9 years and for attacks of sinusitis was 32.5 ± 10.7 years. It is interesting to note the similarity in ages of the first attack in sinusitis and multiple sclerosis. Whether this implies a link between these two conditions awaits further studies.

The authors pointed out that “If the infectious hypothesis has any validity we would expect to find seasonal fluctuations in multiple sclerosis patients. We found significant seasonal fluctuations in both first attacks and exacerbations of multiple sclerosis”.

When the seasonal behaviour of multiple sclerosis and sinusitis were compared, it appeared that sinusitis preceded multiple sclerosis by approximately 1 month.

A similar association of frequency between multiple sclerosis and sinusitis appeared to be present in all the ten GP practices that were examined in this study.

The authors concluded that “a commensal bacterium with growth favoured by the conditions in a diseased sinus might elicit an immune reaction against central nervous system antigens due to cross-reacting antigenic groups”.

17.5 Sinusitis in Scottish Multiple Sclerosis Patients

In 1986, a study involving 32 multiple sclerosis patients from the county of Angus in Scotland was carried out for attacks of sinusitis. As controls an equal number of spouses or cohabitants were examined and assessed from the case notes.

No cases of radiologically confirmed sinusitis were found in the controls but 6 were noted in the multiple sclerosis patients (19 %). Furthermore, 22 multiple
sclerosis patients (69%) were recorded to have had sinusitis whilst sinusitis was also recorded in five controls (16%) and this difference was statistically significant (p < 0.0001).

The mean age of the first attacks in the Scottish investigation were similar to the English study: The mean age of first attack of multiple sclerosis was 29.7 years and the mean age of first attack of sinusitis was 25.6 years. Overall the mean age during which attacks of sinusitis occurred in the multiple sclerosis patients was 29.2 years. It would appear that sinusitis and multiple sclerosis are correlated, at least in these Scottish patients (Callaghan 1986).

### 17.6 Reversible Optic Neuritis Following Paranasal Sinusitis

In 1989, three patients were described in whom optic neuritis, a disease which precedes overt multiple sclerosis was presumably caused by concurrent sinus infection. Aggressive treatment of the underlying sinus condition led to prompt visual improvement.

The three patients were seen in the Tucson Veterans Administration Medical Center in Arizona. The antibiotic treatment in two patients was oral ampicillin whilst the third patient received trimethoprim and methoxazole.

In two patients the maxillary sinus was drained and bacteriological cultures of the drained fluid grew *Haemophilis influenzae*. Since the maxillary sinus does not have a contiguous physical relationship with the optic nerve, it was inferred that autoimmune demyelination was the most likely mechanism for the onset of optic neuritis (Awerbuch et al. 1989).

### 17.7 Incidence of Sinusitis in Multiple Sclerosis as Measured by Magnetic Resonance Imaging

In 1997, a retrospective study was carried out on the incidence of sinus disease in multiple sclerosis patients attending the City Hospital in Birmingham, UK.

Magnetic resonance imaging was carried out on 108 multiple sclerosis patients (71 females and 37 males) with an age range of 22–67 years (Mean age: 39.7 years).

Fifty seven patients (53%) had evidence of disease, the most common sinus involved was the maxillary, followed by the ethmoid, frontal and sphenoid. Three patients had fluid levels and four patients had retention cysts.

The authors concluded that incidence of sinus disease in multiple sclerosis is higher compared to studies of normal populations (Jones et al. 1997).
17.8 Viral and Bacterial Infections Associated with Onset of Multiple Sclerosis

In 1998, a study from Nottingham involving 41 patients with definite multiple sclerosis (28 women and 13 men) (Median age 35 years; range 21–50 years) was carried out. The multiple sclerosis patients consisted of 21 having relapsing-remitting and 20 were labelled as having secondary-progressive disease. They were investigated for the relation between symptomatic and serologically confirmed upper respiratory tract infections (URTI) and neurological disease which was monitored by magnetic resonance imaging (Edwards et al. 1998).

A total of 114 “upper respiratory tract infections” (URTI’s) were reported by 34 of 41 patients (83 %) during the 15 month period of observation, giving an average annual infection rate of 2.4 respiratory tract infections or episodes per patient.

In 8 out of 64 (12.5 %) clinical “upper respiratory tract infections” were accompanied by a rise in antibody titre to 1 of 2 viruses, namely influenza B.

Many viruses have been suggested to be implicated in the pathogenesis of multiple sclerosis, including measles, parainfluenza, canine distemper, Epstein-Barr viruses, corona viruses, adenoviruses, herpes simplex and reoviruses. However no single virus has been consistently linked to multiple sclerosis. This implies that there may not be a specific viral multiple sclerosis agent.

However many upper respiratory viral infections are followed by secondary bacterial infections especially by common and ubiquitous microbes such as Acinetobacter or Pseudomonas which could be involved in the onset of neurological disease.

17.9 Inflammatory Changes in Acute Optic Neuritis Associated with Paranasal Changes

In 2000, magnetic resonance imaging studies were carried out on 23 patients with acute onset optic neuritis attending the University of New Mexico Hospital and the Veterans Medical Center in Albuquerque (New Mexico) and compared to 48 control subjects.

Optic neuritis is an acute, sporadic inflammatory neuropathy where patients experience impairment of vision as a result of demyelinating inflammation of the optic nerves. Optic neuritis is a common presenting feature of multiple sclerosis. Long-term follow-up studies have indicated that multiple sclerosis develops in as many as 75 % of patients who initially have optic neuritis.

It was found that 83 % of patients had paranasal sinus inflammatory changes compared to a frequency of 54 % in controls.

The distribution of paranasal inflammatory changes was highest in the maxillary sinuses (83 % versus 52 % in controls). The inflammatory changes in the ethmoid
was 4% versus 2%, in the frontal sinuses it was 9% versus 14% and in the sphenoid it was 4% versus 10%.

In the maxillary sinuses there was thickened mucosal lining and mucous retention cysts. A higher prevalence of bilateral sinus inflammatory changes was seen in patients with optic neuritis.

The authors concluded that optic neuritis may be associated with sinus inflammatory changes (Rupp et al. 2000).

17.10 Infections and Multiple Sclerosis in Italy

In 2002, in a wide ranging review of the prevalence of multiple sclerosis it was shown that the mountainous island of Sardinia in Italy has one of the highest prevalence rates of the disease in the world.

The authors speculated that it could be due to distant genetic links to the Samis of northern Europe. However the possibility that the physical geography of the island with increased episodes of winter sinusitis, may have been involved in an environmental predisposition to the disease was not considered (Pugliatti et al. 2002).

17.11 Prospective Studies in Dutch Multiple Sclerosis Patients

In 2002, a longitudinal study involving 73 multiple sclerosis patients (56 women and 17 men) aged between 18 and 55 years was carried out in the Netherlands. The patients participated in the “Rotterdam Study on Exacerbations” (ROSE) in multiple sclerosis.

Multiple sclerosis starts in 80–85% of patients usually with a relapsing-remitting course and exacerbations are affected by clinically manifest infections.

In this carefully controlled study, a total of 167 infections were recorded in 86% of patients: 77% were described as upper respiratory tract infections, 16% were characterized by gastrointestinal symptoms and 7% by urinary tract symptoms. In 25% of the infections patients reported fever at some point during the course of the illness (Buljevac et al. 2002).

It would appear that upper respiratory tract infections are associated with exacerbations, at least in these Dutch multiple sclerosis patients.

17.12 The Latitude Problem in Multiple Sclerosis and Sinusitis

Multiple sclerosis is distributed throughout the world within three zones of high, medium and low frequency (Kurtzke 1993).

The high frequency countries comprise northern and central Europe, northern USA, Canada, New Zealand and south-eastern Australia.
In the U.K. there is more multiple sclerosis in northern Ireland and Scotland compared to England.

In general, the higher the latitude, the greater the prevalence of multiple sclerosis and the reverse occurs in the southern hemisphere. There is seven times more multiple sclerosis in the southern island of New Zealand and Tasmania compared to Queensland in populations coming from Anglo-Celtic stock.

The clear question arises, if sinusitis is commoner in cold countries then this could explain the latitude prevalence observed in multiple sclerosis.

Another possible explanation for the latitude effect that has been proposed is that decreased exposure to sunlight leads to decreased vitamin D production (Ascherio et al. 2010). However it is not clear how vitamin D exerts its protective effect in multiple sclerosis.

### 17.13 Acinetobacter Microbes in Nasal Sinuses and Multiple Sclerosis

These extensive and wide ranging studies from many different parts of the world indicate that an upper respiratory tract infection is associated with the onset and continuation of clinical disease in multiple sclerosis patients.

The main site of an upper respiratory tract infection are the tonsils and the nasal sinuses where the disease is known as simply “rhino-sinusitis”.

This raises the question of which microbes or viruses are linked to these anatomical areas.

*Acinetobacter* species form part of the bacterial flora of skin and can be grown from the oral cavity and respiratory tract of some healthy adults.

*Acinetobacter baumannii* causes 90% of clinical infections and is also present in soil.  
*Acinetobacter calcoaceticus* is present in soil and is occasionally associated with clinical infections.

The diagnosis and treatment of bacterial rhino-sinusitis is a challenge to the oto-laryngologist. A computer tomography (CT) scan is usually performed and this may show mucoperiosteal thickening and air fluid levels especially in the maxillary sinus.

An “antral tap” has some disadvantages in that it can result in trauma such as bleeding within the maxillary sinus or in the soft tissues of the cheek.

A prospective study of 20 patients with acute rhino-sinusitis admitted to the Trauma Intensive Care Unit of the Jackson Memorial Hospital, University of Miami (Florida) was carried to compare two methods of examining microbial cultures of nasal sinuses over a period of 18 months.

The mean age of the patients was 40 years (Range: 23–77 years and 17 (85%) were men).

The two methods of comparison were: “Endoscopically directed tissue culture” (ETC) which is easily performed with a nasal telescope and “antral tap” which is usually carried out under local anaesthesia.

A positive culture was defined as greater than $10^3$ organisms per ml of fluid.
All patients showed mucoperiosteal thickening and variable degrees of opacification in the osteo-meatal complex. Furthermore, they all had muco-periosteal thickening in the maxillary, frontal, and sphenoid sinuses.

The total number of micro-organisms cultured was not significantly different between the two methods: 49 organisms in “antral tap” with 52 microorganisms in “endoscopically directed tissue culture”.

Gram negative bacteria represented almost 60% of the organisms. The most common microbe identified was *Acinetobacter baumannii*.

The second most common microbes were *Pseudomonas aeruginosa* and the Gram positive microbe *Staphylococcus aureus*.

*Acinetobacter* species accounted for 37% of Gram-negative bacteria in the “antral tap” cultures and 33% of the Gram-negative bacteria from the “endoscopically directed tissue culture” (Casiano et al. 2001).

It is clear that *Acinetobacter* species can be readily grown from nasal sinuses.

It would appear that examination of the nasal sinuses during onset and exacerbations in multiple sclerosis patients may require further neurological and otolaryngological attention.

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