MULTIPLE SCLEROSIS **MEDICAL APPENDIX**

DEFINITIONS

1. **Multiple Sclerosis (MS)** is the commonest of the **demyelinating diseases**. It is characterised pathologically by the widespread occurrence in the central nervous system of patches of demyelination.

2. **Demyelination** is the term applied to the disappearance of the **myelin sheath** which surrounds nerve tissue.

CLINICAL MANIFESTATIONS

3. Multiple sclerosis affects 30-80 people per 100,000 of the population in the United Kingdom. The incidence of the disease rises throughout the second decade of life and is highest in the 30s. It is rare in people over 65. More women than men are affected. in a ratio of 2:1.

4. The principal manifestations of MS are weakness of one or more limbs, spasticity, muscle fatigue, unsteadiness of gait and difficulties with speech. Loss of sensation may occur. Difficulty in bladder control is common and there may be urinary incontinence. As the disease progresses walking may become increasingly difficult, and the patient may ultimately become chair or bed-bound. Mood swings and short term memory defects are features of the more advanced stages of MS.

5. Visual disturbances are a major feature of MS, and blurred or double vision may be an initial presenting symptom. Progressive visual impairment may ensue, as may visual field defects.

6. The course and effects of MS vary widely from patient to patient and are unpredictable. Spontaneous remissions of varying length are common, particularly in the earlier stages of the disease. The most common pattern is of frequently recurring relapses spread over many years, leading to chronic disability and dependency.

AETIOLOGY

7. The aetiology of MS is unknown. Current theory is that it involves an **interplay between genetic and environmental factors**, resulting in an immunologically-mediated inflammatory response within the central nervous system. The evidence for genetic susceptibility to MS is direct and convincing, whereas the findings with respect to environmental initiators or triggers are suggestive but less compelling.

8. Immunological abnormalities have been repeatedly documented. The tissue response in MS has features of an immunopathologic process and other evidence indicates a likely immunological basis. Some authorities go so far to regard MS as an autoimmune disease.

Epidemiology

9. Multiple sclerosis is a disease of Northern Europeans and occurs less frequently in other racial groups. The highest rates are in Scandinavia, Northern Germany and the United Kingdom; within the British Isles prevalence is highest in north east Scotland, and the Orkneys and Shetlands. In various parts of Europe the frequency of MS has been shown to differ between geographically integrated but ethnically distinct populations. These patterns suggest that racial susceptibility affects the distribution of the disease.

10. The geographical distribution of MS cannot however be explained solely on the basis of population genetics. Migration studies have shown that in white South Africans and in Australia, prevalence rates are half those documented for many parts of Northern Europe, and there is a gradient in frequency in Australia which does not follow genetic origins. This indicates that racially determined differences in risk for MS are modified by environment. Epidemics of MS reported in a number of islands make it likely that fluctuating environmental factors play a part.

Genetics

11. Evidence of genetic susceptibility to MS is provided by epidemiological studies within ethnic groups. About 15% of patients have an affected relative. Three recent studies have shown a concordance rate for MS of 25% in monozygotic twins and 3% for dizygotic twins.

12. The precise genetic basis of susceptibility to MS cannot yet be defined but it is likely that several interacting genes are involved. Alleles encoded within the major histocompatability complex (MHC) on chromosome 6 have been confirmed in recent studies as susceptibility genes; other genes encoded within the MHC may also contribute.

Priming factors in childhood

13. Several studies have associated **exposure to viral illness in late childhood** with the ultimate development of clinical MS. The explanation proposed is that the risk of MS is increased for individuals who develop a variety of common viral disorders comparatively late in childhood (early teens); the viruses concerned are measles, mumps, rubella or Epstein-Barr virus. This exposure is thought to alter immune responsiveness, sensitising genetically predisposed individuals to develop clinical MS later in life if they encounter one of a variety of precipitants.

Factors leading to clinical disease onset

14. The nature and mode of operation of these precipitating factors is not precisely known. In many patients the initial clinical manifestations appear to occur spontaneously.

15. Respiratory infections, particularly adenoviruses, can bring about onset or relapse of symptoms: 9% of presumed viral infections occurring in patients with MS are followed by a clinical relapse, and 27% of new episodes are related to infection. The incidence of relapse is increased in the puerperium.

16. Exposure to heat, or immersion in hot water, may bring about a temporary worsening of symptoms; several studies have demonstrated that relapses are more frequent in the spring or early summer.

17. Recent controlled studies have found significant associations between **stressful life events** and the onset of symptoms or relapse, in MS. Using the internationally recognised Life Events and Difficulties Schedule (LEDS), stressful life events were divided into two categories: **severely threatening events**, such as loss of job by patient or spouse; and **marked difficulties**, such as ongoing conflict with spouse or close relative, or major health changes affecting these. One such study found that 75% of recent clinical onset MS patients had such an event or difficulty in their life during the 6 months prior to clinical onset.

18. **Physical trauma** has not been shown to be a cause of MS; some studies have suggested that physical trauma may precipitate the onset of the disease or provoke a relapse, although other studies have not found any such association. The overall consensus is that no correlation between trauma and MS has been demonstrated.

CONCLUSION

19. Multiple Sclerosis is a disease of the central nervous system which involves demyelination, with a resultant varied clinical presentation. The aetiology is unknown. Current evidence suggests that the disease arises in genetically susceptible individuals further primed as a result of a viral infection in late childhood. The initial clinical manifestations follow a precipitating event or exposure.

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