Chapter 2 Diagnosis

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CHAPTER 2 Diagnosis

2.1 INTRODUCTION

There is no single diagnostic test for multiple sclerosis (MS), but there are diagnostic criteria available to support the neurologist. The clinical diagnosis is heavily dependent on the neurologist in taking and interpreting patients’ medical history, conducting a neurological examination and interpreting magnetic resonance imaging (MRI). Exclusion of other central nervous system (CNS) disorders must also be undertaken. In Ireland, lumbar puncture and evoked potentials tests may also be used to assist in diagnosis. Their results are essential in the exclusion of other alternative diagnosis that may mimic MS (Barnes, 2000). The International Panel on the Diagnosis of MS met in Dublin in May 2010, and here the 2010 revisions were made to the McDonald criteria (Polman et al, 2011). The McDonald criteria are thought to result in earlier diagnosis of MS “with a high degree of both specificity and sensitivity” (Polman et al, 2011). This will be discussed in more detail in this section.

MS presents a number of diagnostic challenges to the physician. There is no single sign or symptom that is specific to MS and, to further complicate matters, there are a variety of presenting symptoms. Moreover, in the early stages of the disease, MS symptoms are usually transitory and therefore not directly observable by the physician.

Planning future care for an MS patient involves the use of a variety of investigations. Liguori (2011) states that “clinical and laboratory predictors of activity and long-term disability are of essential importance in planning patient management”.

A diagnosis of MS evokes an array of emotional responses, such as shock, fear and grief, and the MS nurse has a crucial role in effectively easing patients’ movements through this emotional roller coaster. The role of the MS Nurse Specialist therefore begins at the diagnostic phase.

In this chapter, the diagnosis of MS is discussed and diagnostic criteria are reviewed. Minimum standards that should be met throughout the diagnostic phase are also presented. The role of the nurse during the diagnostic phase is also explored.
2.2 OVERVIEW

This chapter contains the following four sections:

1. History taking and paraclinical testing
2. Diagnostic criteria
3. Standards of healthcare and the role of the nurse in diagnosis
4. Prognostic indicators and survival in MS.

At the end of the chapter, please find a section entitled ‘Progress Check’ – this section tests your knowledge of the information presented in the chapter.

2.3 HISTORY TAKING AND PARACLINICAL TESTING

2.3.1 Introduction and learning objectives

The assessment and diagnosis of the patient with MS begins with a detailed medical and psychosocial history taken by the neurologist. After taking the history, the neurologist will perform a neurological examination including an MRI. According to Wattjes and Barkhof (2009), MRI has been increasingly incorporated into the clinical setting, particularly with regard to neuroimaging.

In this section, strategies for collecting a history from the patient are discussed and various neurological tests are reviewed. Minimum standards of care that should be met throughout the diagnostic phase are also presented.

After completing this section, the reader will be able to:

- Discuss what the neurologist is looking for when he meets a patient suspected of having MS
- Describe the diagnostic work-up of the patient with MS
- Explain the roles of MRI, evoked potentials, and oligoclonal banding in the diagnosis of MS
- Discuss the role of the nurse at diagnosis.

2.3.2 What is the neurologist looking for?

Despite the advancement in technology, the most important aspect of making a diagnosis of MS continues to be the evaluation of patients’ history and clinical presentation by an experienced neurologist (McDonald et al, 2001) The key to diagnosing MS is clinical evidence as identified by the revised 2010 McDonald criteria (see Table 2.3 page 14).
2.3.2.1 Evidence of lesions

A detailed history is essential when diagnosing MS. Certain symptoms and signs are taken as evidence of lesions in specific functional systems of the CNS:

- Visual disturbances, such as unilateral loss or impaired sight and pain behind the eye are evidence of an optic-nerve lesion
- Muscle weakness and paralysis of one or more limbs are termed pyramidal symptoms, and are evidence of a pyramidal tract lesion; abnormal reflexes may also indicate pyramidal tract lesions
- Unsteadiness of gait or poor coordination (cerebellar symptoms) are evidence of a lesion in the cerebellum
- Involuntary eye movements (nystagmus), difficulties in articulating speech, and swallowing problems are evidence of a brain-stem lesion
- Spastic paraparesis (evidence of a spinal lesion)
- Sensory functions (touch, pain, positional sense, etc.)
- Bowel and bladder functions (evidence of spinal lesions)
- Cerebral functions – mood and intellectual capacity.

2.3.3 Paraclinical tests

2.3.3.1 Magnetic resonance imaging (MRI)

MRI images are produced by detecting the differential response of protons of water to strong, pulsed magnetic fields. The major advantage of MRI is that, in contrast to conventional radiography (e.g. computed tomography [CT]), there is no dose of radiation; therefore, the procedure is safe and can be repeated in the same patient many times. MRI is used both for diagnosing (approximately 95% of patients with clinically definite MS have CNS lesions that show up on T2-weighted brain MRI scans [Ormerod et al, 1987]) and monitoring MS, and its use is increasing as MRI technology advances. Wattjes and Barkhof (2009) state that MRI is the most sensitive diagnostic tool in the detection of focal and diffuse changes of MS. Figure 2.1 depicts a typical lesion found using MRI.
Although MRI is a useful supplement to clinical signs and symptoms, it is by no means a conclusive diagnostic test. However, the use of MRI in MS is still developing, and it may become more accurate in the future. MRI applications under development include imaging of the spinal cord and the development of specific measures that reflect various pathological processes, such as degree of demyelination and axonal loss. As observed in a review study of high-field MRI, lesions are frequently found in the spinal cord; however, applications of high-field MRI up to 3T did not demonstrate a higher sensitivity in the detection of spinal cord lesions (Wattajes and Barkhof, 2009).

MRI may predict risk of developing MS as well as the future course of the disease. For example, in patients with a single episode of optic neuritis, longitudinal studies have shown that initial MRI lesion number and load correlate strongly with both the risk of developing MS and future disability. If there is any evidence of brain lesions on MRI, patients have a greater than 50% chance of developing MS. If the patient has four or more lesions, they have a greater than 90% chance of developing MS within 5 years. If the patient has a normal MRI scan, their chances of developing MS are less than 20% within 10 years (Thompson, 1994). According to Chard et al (2011), of patients presenting with a clinical isolated syndrome (CIS), 70–80% who had an abnormal MRI will convert to MS (within five years) in contrast to 10% with normal imaging. In their retrospective review study, Okuda et al (2011) found that 21 of 71 subjects with a radiologically isolated syndrome within the cervical spine progressed to a CIS or primary progressive MS.

It is known that normal brain MRI scans are found in 5% of people with multiple sclerosis (PWMS). Palace (2001) state that this is more likely in patients with mild or early relapsing remitting multiple sclerosis (RRMS). In primary progressive multiple sclerosis (PPMS) disease, it is likely that the brain MRI may be normal as the disease predominately affects the spinal cord. Therefore, in some instances, both brain and spinal scans are carried out. In a recent UK longitudinal study, Penny et al (2010) found that early MRI predictors of cognitive impairment in patients with PPMS could be used to identify target populations for suitable therapies.

MRI scans produce valuable information relating to disease activity throughout the illness trajectory. Thompson (1999) states that the appearance of new lesions on MRI correlates reasonably well with relapse activity; however, it is also accepted that MRI scans may detect 10 times more lesions than are apparent through clinical examination (Barkhof, 1997). This is because many lesions can form without causing detectable signs or symptoms. Thompson does go on to say that the relationship of MS lesions with the development of disability or irreversible deficit is poor.
This is particularly evident in people who have PPMS, where there are few lesions seen on MRI, yet there is a steady accumulation of disability. In a recent American retrospective study, Liguori et al (2011) found that using subtraction MRI (sMRI) resulted in a “strikingly more sensitive assessment of MRI activity than contrast enhancement over a 1, 4 or 5-year interval” (Liguori et al, 2011). This study demonstrates the potential utility of sMRI in predicting and monitoring disease activity in MS patients.

In individuals with RRMS and secondary progressive multiple sclerosis (SPMS), a monthly MRI scan will show that lesions appear at a frequency 5 to 10-fold the frequency of clinical relapses, and it is suggested that serial MRI provides a more sensitive marker for disease activity than the logging of relapses or new symptoms (Hartung et al, 1998). In the UK, however, repeated use of MRI scanning during the course of the disease is uncommon (an MRI scan may be performed if a patient with established MS presents with signs and symptoms that are not entirely typical of their disease and there is a need to rule out any other coexisting conditions). The value of MRI scans in the diagnosis of MS, the monitoring of disease activity during clinical trials and as a research tool to track disease activity are undisputed; Gaitan et al (2011) state that MRI has enormous value for detecting and characterising lesions. In a recent study carried out in the Netherlands, comparing effectiveness between MRI and clinical parameters in predicting disease progression, Minneboo et al (2008) found that adding MRI parameters yielded stronger predictive results in disease progression than using a clinical parameter model only. However, Barnes (2000) questions their clinical value in the patient who is experiencing a stable period in their disease trajectory and even those who are developing new, but classic MS symptoms. This is supported by Tenser (2009), who is of the opinion that current data do not support repeated MRI of brains in stable MS patients.

**Types of MRI scans**

The magnetic field in an MRI scanner is pulsed. During the pulse, protons change their alignment in response to the magnetic field. When the pulse ends, the protons switch back to their original position, producing an electric charge. The signal results from the oscillation of the protons as the pulsed magnetic field goes on and off. Therefore, the nature of the signal depends on the timing and strength of the pulses, as well as the composition of the observed tissue.

**T1 and T2-weighted MRI scans**

In a T1-weighted scan, pulses occur every 350 ms. In a T2-weighted scan, pulses occur every 4–5 s. In MS, T1-weighted scans with gadolinium are designed to show new, active lesions; the number and volume of enhancing T1-weighted lesions are generally used as markers of current disease activity.

On the other hand, T2-weighted scans are better for detecting established lesions, both new lesions with active inflammation and old lesions in which inflammation has subsided. The total volume of T2-weighted lesions (the lesion load) is generally used as a measure of overall disease burden.

**Gadolinium enhancement of MRI scans**

MRI scans can be made even more sensitive by using gadolinium–DPTA, an injectable contrast medium that highlights fresh and developing lesions by passing through breaches in the blood–brain barrier, and therefore provides evidence that there is breakdown of the blood–brain barrier. According to Gaitan et al (2011), “gadolinium-enhanced scanning demonstrates the important role of the blood–brain barrier permeability in the development of new lesions” in patients with RRMS and SPMS. Since using this technique often doubles the number of new lesions seen, gadolinium–DPTA is thought to represent one of the first events in lesion evolution (Comi et al, 1998; Koudriavtseva et al, 1996; Koudriavtseva et al, 1997). T1 and T2-weighted scans, including the use of gadolinium–DPTA, are shown in Figure 2.2.
MRI use in clinical trials

In clinical trials, MRI is used in the following ways:

- T1-weighted scans, usually with gadolinium enhancement, are used as markers of current disease activity (since these types of scans indicate breaches in the blood–brain barrier). The endpoints are the number of lesions, the number of new lesions, and the total volume of lesions.

- T2-weighted scans, which show the overall picture of old and new lesions, are used as markers of disease burden. The endpoint is the total area or volume of lesions, or lesion load/burden.

A UK-based 2009 study, which assessed the relationships between 1) T2 lesion load change and disability change and 2) gadolinium enhancement of MS lesions, found that MRI measures used in clinical trials “add little if anything independently to the clinically relevant relapse and disability outcomes… [the results] reemphasize the importance of validating potential surrogate markers against clinical measures and highlight the need for better MRI markers of disease activity and progression” (Daumer et al, 2009). This study, however, received some rebuttal – Sormani et al (2009) state that the Daumer et al (2009) study has significant flaws in its methodology, which limit the validity of the results.

2.3.3.2 Magnetic resonance spectroscopy (MRS)

Magnetic resonance spectroscopy (MRS) detects the characteristic spectral signature of particular bioactive molecules. Like MRI, MRS uses radiofrequency pulse sequences.

“In MS, proton MRS has been particularly informative by providing evidence of neurodegeneration… in both lesional and non-lesion brain tissue from the earliest stages of the disease”

(De Stefano et al, 2007)

The difference between an imaging sequence and a spectroscopy sequence is that, in spectroscopy, the frequency information is used to identify different chemical compounds. This identification is possible because the resonant
frequency of atoms varies according to the molecular configuration in which they are embedded. The electron cloud is shifted and this variation in electron shielding is identified by MRS.

**2.3.3.3 Evoked potentials (EPs)**

Since demyelination slows the impulses in affected axons, MS affects the speed of nerve transmission. The theory behind evoked potential tests is to use electroencephalography (EEG; the measurement of electrical activity in the brain) to detect this delayed conduction under controlled conditions.

Because the brain is continually active, computer analysis of EEG signals is used to isolate the electrical activity associated with a particular stimulus.

When measuring evoked potentials, the stimulus can be visual (an alternating black and white checkerboard pattern), auditory (rapid clicking) or sensory (mild electric shocks). A 2009 Japanese study of MS patients suggests that multimodality evoked potentials (visual, somatosensory and motor) "are useful tools for detecting clinically overt and silent lesions in the optic nerves and spinal cord" (Watanabe et al, 2009). Of these the visual evoked potentials (VEPs) make the greatest contribution to the diagnosis of MS (Palace, 2001).

VEPs measure conduction speed along the visual pathways. Any delay in the conduction of impulses along them is indicative of demyelination. Abnormal results can supplement information provided by the patient who is suspected of having MS and can provide objective evidence of dissemination of lesions in time and space (McDonald et al, 2001).

**2.3.3.4 Lumbar punctures: cerebrospinal fluid**

Rowland (ed) (2005) states that examination of the cerebrospinal fluid (CSF) often provides supportive information for diagnosis of MS. Abnormal intrathecal antibody production, detected as oligoclonal immunoglobulin, was one of the earliest immune abnormalities identified in MS. More than 90% of patients with clinically definite MS and 50% of patients with new onset MS will have elevated immunoglobulin levels in the CSF (Lumsden, 1972; Rowland [ed], 2005). The introduction of polyacrylamide gels and isoelectric focusing led to this increase in sensitivity. The utility of CSF examination is to corroborate, by the presence of oligoclonal immunoglobulin (oligoclonal bands), that the suspected CNS disease is a chronic inflammatory one. The CSF protein level is usually normal but may be mildly elevated. Interpretation of the meaning of the observed abnormalities depends on the clinical context.

The cells in the brain and CSF are the source for the intra-blood brain synthesis of immunoglobulins. The typical immunoglobulin molecule is a glycoprotein consisting of four polypeptide chains. Although there are five isotopes of immunoglobulin detected in the CSF, the immunoglobulin G (IgG) is the most important one. IgG is synthesised by only one cell in the blood, which is the plasma cell. In healthy individuals there are no plasma cells in the brain and a normal IgG concentration in the CSF is determined by the concentration in the blood, the natural tight junctions of endothelial capillaries in the choroid plexi and by the CSF turnover (Prineas, 1985). An abnormally high concentration of IgG in the CSF may be the result of elevated blood IgG concentrations, a reduced CSF turnover and damage in the choroids plexus epithelial capillary junctions.

Oligoclonal bands (OCBs) result from elevated levels of IgG and myelin basic protein, which is a by-product of demyelination. Increased production of CSF IgG is assessed by calculating the amount of IgG and albumin in serum and in CSF, then evaluating the level of CSF IgG, the CSF IgG index, CSF IgG synthesis rate and CSF IgG:albumin ratio. The albumin index is used to rule out leakage of protein into the CSF from the blood. Leakage of protein from the plasma in to the CSF may cause a false elevation of the IgG index or IgG synthesis rate.
OCBs are detected by electrophoretic separation of CSF where the immunoglobulin molecules migrate in a classical direction and pattern. In normal CSF, the molecules are polyclonal and appear as one diffuse band. In MS the appearance is of two or more bands, reflecting that a few B-cell clones have reached the CSF and proliferated. Patients are considered to be positive for OCBs when there are two or more bands and these are not present in the serum, indicating that IgG is being synthesised within the CNS (Rowland [ed], 2005). A sample of serum is therefore also necessary.

It is observed that OCBs may be present in other neurological conditions including sarcoidosis, Guillain–Barre Syndrome and encephalitis. Rowland (ed) (2005) states that OCBs are found in approximately 5% of patients with other non-inflammatory neurological conditions. It is also important to be aware that approximately 10% of patients with clinically confirmed MS are negative for OCBs.

2.3.4 References


2.3.5 Suggested reading


2.4 DIAGNOSTIC CRITERIA

2.4.1 Introduction

It was recognised in 2001 that there was a need to develop a diagnostic criteria to assist in formulating a definitive diagnosis of MS, as no test or clinical feature alone can be ascribed to the disease. Over the last two decades there has been an increase in knowledge of both the disease process and MRI. Therefore, a panel of international MS neurologists came together to revise existing criteria and devise a universal diagnostic criteria. These new criteria were evolved from the Poser criteria in 1983 and it was hoped that these would simplify diagnostic classifications (McDonald et al., 2001). These were updated further in 2005 and again in 2010.

Tables 2.2–2.5 summarise the new, recommended diagnostic criteria for MS developed by an international group of leading MS clinicians (Polman et al., 2011).

At the end of diagnostic work-up for MS, under these new criteria, the patient will either have:

- MS
- Possible MS (the work up has neither confirmed nor excluded MS by these criteria – the diagnostic issue is still open, awaiting evidence of dissemination in time and space)
- Not MS (the work-up has ruled out MS) (Polman et al., 2011).

Table 2.1. McDonald criteria for demonstration of lesion dissemination in space (DIS) (Polman et al., 2011).

<table>
<thead>
<tr>
<th>DIS CAN BE DEMONSTRATED BY ≥1 T2 LESION(^a) IN AT LEAST 2 OF 4 AREAS OF THE CNS:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periventricular</td>
</tr>
<tr>
<td>Juxtacortical</td>
</tr>
<tr>
<td>Infratentorial</td>
</tr>
<tr>
<td>Spinal cord(^b)</td>
</tr>
</tbody>
</table>

\(^a\)Gadolinium enhancement of lesions is not required for DIS.
\(^b\)If a subject has a brainstem or spinal cord syndrome, the symptomatic lesions are excluded from the criteria and do not contribute to lesion count.

Table 2.2. McDonald criteria for demonstration of lesion dissemination in time (DIT) (Polman et al., 2011).

<table>
<thead>
<tr>
<th>DIT CAN BE DEMONSTRATED BY:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, with reference to a baseline scan, irrespective of the timing of the baseline MRI.</td>
</tr>
<tr>
<td>2. Simultaneous presence of asymptomatic gadolinium-enhancing and non-enhancing lesions at any time.</td>
</tr>
</tbody>
</table>
Table 2.3. The 2010 McDonald criteria for diagnosis of MS (Polman *et al.*, 2010).

<table>
<thead>
<tr>
<th>CLINICAL PRESENTATION</th>
<th>ADDITIONAL DATA NEEDED FOR MS DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥2 attacks&lt;sup&gt;a&lt;/sup&gt;; objective clinical evidence of ≥2 lesions or objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack&lt;sup&gt;b&lt;/sup&gt;</td>
<td>None&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>≥2 attacks&lt;sup&gt;a&lt;/sup&gt;; objective clinical evidence of 1 lesion</td>
<td>Dissemination in space, demonstrated by: ≥1 T2 lesion in at least 2 of 4 MS typical regions of the CNS (periventricular, juxtacortical, infratentorial or spinal cord)&lt;sup&gt;d&lt;/sup&gt;; or await a further attack&lt;sup&gt;a&lt;/sup&gt; implicating a different CNS site</td>
</tr>
<tr>
<td>1 attack&lt;sup&gt;a&lt;/sup&gt;; objective clinical evidence of ≥2 lesions</td>
<td>Dissemination in time, demonstrated by:</td>
</tr>
<tr>
<td></td>
<td>· Simultaneous presence of asymptomatic gadolinium-enhancing and non-enhancing lesions at any time; or</td>
</tr>
<tr>
<td></td>
<td>· A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or</td>
</tr>
<tr>
<td></td>
<td>· Await a second clinical attack&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>1 attack&lt;sup&gt;a&lt;/sup&gt;; objective clinical evidence of 1 lesion (clinically isolated syndrome)</td>
<td>Dissemination in space and time, demonstrated by:</td>
</tr>
<tr>
<td></td>
<td>For DIS:</td>
</tr>
<tr>
<td></td>
<td>· 1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial or spinal cord)&lt;sup&gt;d&lt;/sup&gt;; or</td>
</tr>
<tr>
<td></td>
<td>· Await a second attack&lt;sup&gt;a&lt;/sup&gt; implicating a different CNS site; and</td>
</tr>
<tr>
<td></td>
<td>For DIT:</td>
</tr>
<tr>
<td></td>
<td>· Simultaneous presence of asymptomatic gadolinium-enhancing and non-enhancing lesions at any time; or</td>
</tr>
<tr>
<td></td>
<td>· A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or</td>
</tr>
<tr>
<td></td>
<td>· Await a second clinical attack&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Insidious neurological progression suggestive of MS (PPMS)</td>
<td>1 year of disease progression (retrospectively or prospectively determined) plus 2 of 3 of the following criteria&lt;sup&gt;a&lt;/sup&gt;:</td>
</tr>
<tr>
<td></td>
<td>1. Evidence for DIS in the brain based on ≥1 T2 lesions in the MS characteristic (periventricular, juxtacortical or infratentorial) regions</td>
</tr>
<tr>
<td></td>
<td>2. Evidence for DIS in the spinal cord based on ≥2 T2 lesions in the cord</td>
</tr>
<tr>
<td></td>
<td>3. Positive CSF (isoelectrical focusing evidence of OCBs and/or elevated IgG index)</td>
</tr>
</tbody>
</table>

If the criteria are fulfilled and there is no better explanation for the clinical presentation, the diagnosis is ‘MS’; if suspicious, but the criteria are not completely met, the diagnosis is ‘possible MS’; if another diagnosis arises during the evaluation that better explains the clinical presentation, then the diagnosis is ‘not MS’.

<sup>a</sup>An attack (relapse; exacerbation) is defined as patient-reported or objectively observed events typical of an acute inflammatory demyelinating event in the CNS, current or historical, with duration of at least 24 hours, in the...
absence of fever or infection. It should be documented by contemporaneous neurological examination, but some historical events with symptoms and evolution characteristic for MS, but for which no objective neurological findings are documented, can provide reasonable evidence of a prior demyelinating event. Reports of paroxysmal symptoms (historical or current) should, however, consist of multiple episodes occurring over not less than 24 hours. Before a definite diagnosis of MS can be made, at least 1 attack must be corroborated by findings on neurological examination, visual evoked potential response in patients reporting prior visual disturbance, or MRI consistent with demyelination in the area of the CNS implicated in the historical report of neurological symptoms.

Clinical diagnosis based on objective clinical findings for 2 attacks is most secure. Reasonable historical evidence for 1 past attack, in the absence of documented objective neurological findings, can include historical events with symptoms and evolution characteristics for a prior inflammatory demyelinating event; at least 1 attack, however, must be supported by objective findings.

No additional tests are required. However, it is desirable that any diagnosis of MS be made with access to imaging based on these criteria. If imaging or other tests (for instance, CSF) are undertaken and are negative, extreme caution needs to be taken before making a diagnosis of MS, and alternative diagnoses must be considered. There must be no better explanation for the clinical presentation, and objective evidence must be present to support a diagnosis of MS.

Gadolinium-enhancing lesions are not required; symptomatic lesions are excluded from consideration in subjects with brainstem or spinal cord syndromes. CNS = central nervous system; CSF = cerebrospinal fluid; DIS = dissemination in space; DIT = dissemination in time; IgG = immunoglobulin G; MRI = magnetic resonance imaging; MS = multiple sclerosis; PPMS = primary progressive multiple sclerosis.

2.4.2 Diagnosing PPMS

The diagnosis in patients presenting with progressive disease takes considerable time and should only be made after a variety of other causes are ruled out, in particular spinal cord compression (Palace, 2001). The very fact that a delay occurs in the diagnosis of this particular pattern of the disease generally results in a clear picture of progressive deterioration. As already stated, the patient tends to be in the more mature age range (over 40) and will generally have signs and symptoms correlating to spinal disease. Because of the need to rule out other diagnosis, this group of patients are also more likely to have had a lumbar puncture (LP) and visual evoked potentials (VEPs).

In 2010, the International Panel on the Diagnosis of MS revised the McDonald criteria for diagnosing PPMS to include evidence of 1 year of disease progression as well as two of the following: positive MRI brain, positive MRI spinal cord or positive CSF. These revised criteria are considered to reflect the important roles of CSF examination and spinal cord MRI in diagnosing PPMS (Polman et al, 2011).
Table 2.4. 2010 McDonald Criteria for diagnosis of MS in disease with progression from onset (Polman et al, 2011).

<table>
<thead>
<tr>
<th>PPMS MAY BE DIAGNOSED IN SUBJECTS WITH:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 1 year of disease progression (retrospectively or prospectively determined)</td>
</tr>
<tr>
<td>2. Plus 2 of the 3 following criteria:</td>
</tr>
<tr>
<td>a. Evidence for DIS in the brain based on &gt;1 T2(b) lesions in at least 1 area characteristic for MS (periventricular, juxtacortical, or infratentorial)</td>
</tr>
<tr>
<td>b. Evidence for DIS in the spinal cord based on &gt;2 T2\textsuperscript{b} lesions in the cord</td>
</tr>
<tr>
<td>c. Positive CSF (isoelectric focusing evidence of OCBs and/or elevated IgG index)</td>
</tr>
</tbody>
</table>

\textsuperscript{a}If a subject has a brainstem or spinal cord syndrome, all symptomatic lesions are excluded from the criteria.

\textsuperscript{b}Gadolinium enhancement of lesions is not required.

CSF = cerebrospinal fluid; DIS dissemination in space; IgG = immunoglobulin G; MS = multiple sclerosis; PPMS = primary progressive multiple sclerosis.

Tables 2.1-2.4 reproduced with permission from the author and publisher of Polman et al (2011).

2.4.3 The Kurtzke Expanded Disability Status Scale (EDSS)

The Expanded Disability Status Scale (EDSS; please see Chapter 4, mobility section for scale) has become the most widely used assessment tool for measuring impairment and disability in MS. It was developed specifically for MS by Kurtzke in 1955, and updated some years later (Kurtzke, 1983). It is a 20-step ordinal scale that ranges from 0 (normal status) to 10 (death due to MS). Scores of 0–3.5 mainly rely on the functional systems; 4–7.5 rely on ambulation; 8–8.5 will indicate upper arm function; and 9–9.5 indicate bulbar involvement. The assessment is made by a neurologist who, after performing a neurological examination, grades patients according to a set of 8 functional system scales, combining these with ambulatory function. An example of this scale is given in Appendix 1.

2.4.3.1 Uses and limitations of the EDSS

The EDSS is the most widely used assessment scale in MS (especially in clinical trials). This tool is commonly used by neurologists all over the world and provides a commonly accepted language between them when discussing MS. However, it is not generally regarded as an assessment tool that is appropriate to nursing practice. It can be seen by looking at the scale that it only provides a snapshot view of a patient at the precise moment in time that they are being examined. It is heavily dependent on walking ability and does not reflect many of the symptoms that are so distressing to people, such as fatigue, pain, cognition and continence, nor does it take into account the psychosocial problems that patients are facing.
2.4.3.2 Advantages of the measure

- Familiar and widespread scale providing a common language amongst neurologists
- Easy to perform and is based on a neurological examination
- Language is understandable
- Scoring system is relatively straightforward
- Evidence is available to support its reliability.

2.4.3.3 Limitations of the EDSS

- Heavily based on ambulation
- Does not examine fatigue or cognition
- The average time spent at each EDSS varies greatly (see Figure 2.3). This means that an outcome measure, such as time to progress one point on the EDSS means something different depending on which EDSS stage was the starting point.
- The EDSS is not a linear scale; degree of disability when moving from 0 to 1 is quite trivial when compared to moving from 5 to 6 (the difference between 5 and 6 is walking unaided and walking with assistance).
- Can be very subjective – the ambulation distance tends to be estimated and this can be inaccurate (Sharrack and Hughes, 2000).
- There are difficulties if the patient scores high on functional system but has normal ambulation.
- Blumhardt et al (ed) (2004) point out that there are several limitations to this scale found in the literature, including lack of precision, low reliability, uneven distribution and low responsiveness. The authors also state that the EDSS is not only a disability scale as it measures impairment in the range < 3.5.

Figure 2.3. Average time spent at each EDSS stage.
2.4.4 Other disability scores

Although the EDSS is the most commonly used disability scale in MS, others include:

2.4.4.1 The MS Functional Composite Score (Rudick et al, 1996)

A task force developed recommendations for a new multi-dimensional assessment tool based on the use of quantitative measures, which include:

- Arm function in the form of the 9-hole peg test
- Ambulation in the form of a timed 25-metre walk
- Cognitive function in the form of the PASSAT (Paced Auditory Serial addition Test) (Ratchford et al, 2010).

This has the advantage of addressing a more global deficit than other existing scales but is basically unfamiliar and only has a use in patients with a degree of ambulation. It is, however, reliable and valid in measuring impairment and it also has low cost implications.

2.4.4.2 The MS Impact Scale (MSIS-29) (Hobart et al, 2001)

This is a relatively new scale examining the physical and psychological impact of MS from patients’ perspective; it measures 20 physical items and 9 psychological items. This scale is disease specific, combining psychometric testing and quality of life issues. A 2007 Irish study that looked at the effectiveness of this scale describes it as “a psychometrically designed patient-reported measure of the effect of MS on activities of daily living” (Costelloe et al, 2007). This study found that the MSIS-29 performs well over time and has few limitations (Costelloe et al, 2007).

Other disability scores include:

- Scripps Neurological Rating Scale (Sipe et al, 1984)
- The Ambulation Index (Hauser et al, 1983)
- The Functional Independence Measure (Keith et al, 1987)
- Modified Fatigue Impact Scale (MFIS).

2.4.5 References


### 2.4.6 Suggested reading


2.5 ROLE OF THE NURSE IN THE DIAGNOSIS OF MS

A diagnosis of MS is a life-altering and uncertain time for PWMS. The role of the nurse has evolved from that of supportive caregiver to include educator, researcher, patient advocate and consultant (Halper, 2002). According to Burgess (2010), the MS Clinical Nurse Specialist (CNSp) is in a position to build a therapeutic relationship with the patient and family at or soon after diagnosis. The nurse should provide clear, accurate evidence-based information, relating it to individual patients and assist the patients in making informed decisions relating to their disease and treatment options. Forbes et al (2006), cited in Burgess (2010), show that information provision was improved for patients who were referred to the MS nurse. Nurses further expand the role by addressing issues such as psychosocial impact, sexuality, family planning and other issues, which may arise as a result of an MS diagnosis. The ultimate goal of the nurse at the diagnostic stage is to provide the highest quality of care to the PWMS and their families in order to enhance patients’ quality of life at the time of diagnosis and throughout the disease continuum. It may be appropriate for the MS CNSp to provide the patient with time to absorb the diagnosis before providing detail information, and following this arrange to meet the patient and their family.

The nurse is in a key position to provide support and education for people at the time of diagnosis, which can have a real impact on how the person manages their disease (Johnson, 1997). The MS nurse is a highly valued point of contact (Forbes et al, 2006, cited in Burgess, 2010).

The nurse needs to be aware of patients’ adjustment to their diagnosis. This can be affected by a variety of aspects of patients’ lives. The literature suggests that MS patients have poorer adjustment outcomes than those with other chronic conditions (Pakenham and Flemming, 2011). Reasons for this include the uncertain and unstable course of the disease, the onset of disease during the reproductive years, (Motl and McAuley, 2009, cited in Pakenham and Flemming, 2011) and impact on employment and relationships (Pakenham and Flemming, 2011). It can be suggested that acceptance is an important factor in disease adjustment due to the challenging changes associated with MS (Pakenham and Flemming, 2011).

There is an increasing amount of literature available that discusses the role of the nurse at the time of diagnosis (Brechin and Burgees, 2001; Halper, 1999). Work carried out by Halper (1999) confirms that a newly diagnosed person will have a multitude of needs including living with an uncertain future, experience a wide symptomatic variability and needing emotional, spiritual and psychological support. She suggests a model of care that indicates to the nurse what a patient and their family need throughout this disconcerting time:

\[E = \text{Education (about the disease, its course, symptomatic management and psychosocial implications)}\]

\[A = \text{Adaptation (adjustment, modifying lifestyle, setting priorities and promoting self-care)}\]

\[S = \text{Support (counselling, providing information on support groups and help in obtaining entitlements)}\]

\[E = \text{Enhancement (self-care, improvement of coping skills and facilitation of communication about needs and concerns)}\]
Following diagnosis, the MS CNSp is made aware of the patient either verbally or in writing by the neurology team as soon as possible.

Following review by the MS CNSp, each patient is provided with a list of relevant contact telephone numbers and support network.

Relevant literature on MS is offered.

Appropriate referrals to the multidisciplinary team are initiated if necessary.

Flow Chart for breaking bad news (adapted from University College London Hospital, 2006).

- Do I have all the facts/information?
- Has the patient had the opportunity to have another person present?
- Is a quiet room available? If not, maximise privacy
- Have I asked “What do you understand about your condition so far?”
- Give information slowly and gently, avoiding medical terminology
- Ask if further information is wanted at this time
- Encourage patients to express their feelings and any concerns
- Summarise and plan follow-up. Future availability is essential
- Communicate with other team members and document in notes
2.5.1 References


University College London Hospital. Breaking bad news to adults. 2006.

2.5.2 Suggested reading

2.6 PROGNOSTIC INDICATORS AND SURVIVAL IN MS

2.6.1 Introduction and learning objectives

At diagnosis, PWMS often ask whether there is information available that can forecast what life is going to be like for them in the future. This is a difficult area to discuss. Predicting the long-term outcome of an individual diagnosed with MS at the onset of symptoms, or during the early course of the disease, remains a problem and is not, as yet, one that can be fully answered.

A survival rate in MS is also an area that is constantly changing. It used to be thought that MS reduced life expectancy considerably, but the work carried out in a series of studies by Weinshenker et al, the latest of which was in 1998, produced interesting data. The results, which provide the information that we are currently using, estimate that life expectancy is reduced by 5–7 years. More recent data revealed that the life expectancy for the MS population is approximately 10 years less than the general population. The most common causes of death in the MS population were complications to severe disability, such as infections (Bronnum–Hansen et al, 2004).

After completing this section, the reader will be able to:

- List the clinical indicators that are current when discussing the prognosis of MS
- Discuss the mortality issues associated with MS.

2.6.2 Prognostic indicators in MS

MS is a disease of uncertainty and unpredictability. Many questions that people ask concerning their future are generally left unanswered or are approached in a vague manner. Ebers (1998) says we tend to err on the optimistic side when conducting conversations regarding long-term outcome of living with MS, especially with the newly diagnosed people, but as the illness progresses, it is appropriate to use the prognostic guidelines that are available. It does, of course, have to be emphasised that any clinical indicators available are not, as yet, completely reliable. Instead, Ebers goes on to say that it is reasonable to offer an individual prognosis on the experience of the first 5–10 years of the illness. There are some factors that may predict long-term outcome in MS. These are commonly accepted as:

2.6.2.1 Positive predictors

- Younger age at onset
- Female gender
- Normal MRI on presentation
- Complete recovery following first relapse
- Low relapse rate
- Long interval to second relapse
- Low disability at 2 and 4 years.
2.6.2.2 Unfavourable predictors

- Older age at onset
- Male sex
- High lesion load on presentation
- Lack of recovery from first relapse
- High relapse rate
- Early cerebellar involvement
- Short interval to second relapse
- Early development of disability
- Insidious motor onset.


2.6.3 Survival in MS

There are many studies published that examine the mortality rates associated with MS. Many of the results of these studies differ, probably due to the widely variable study design, patient sample type and size, methods of ascertainment and completeness of follow-up (Koch-Henriksen and Brønnum-Hansen, 1999). However, much of today’s current thinking is centred around the studies of Weinshenker *et al*, the latest of which was performed in 1998. He and his team followed 1,000 PWMS and examined their natural data over a 25-year period. He admits that there are limitations with the data collected, but he clearly states that although life expectancy in MS is shortened overall, it is little affected in Western countries. MS patients live an average of 5–7 years less than the general population. Severe MS disability, as measured by an EDSS of 7.5 or higher, is a major risk factor for death (Pryse-Phillips and Costello, 2001)

2.6.4 References


2.7 PROGRESS CHECK

1. MRI usually detects ________ times more lesions than are apparent through clinical examination.

2. Distinguish between T1- and T2-weighted MRI.

______________________________________________________________________________________________________
______________________________________________________________________________________________________
______________________________________________________________________________________________________
______________________________________________________________________________________________________

3. List two major weaknesses of evoked potential tests.
   a. __________________________________________________________________________________________
   b. __________________________________________________________________________________________
4. Complete the table below.

**New, Recommended Diagnostic Criteria for MS.**

<table>
<thead>
<tr>
<th>CLINICAL PRESENTATION</th>
<th>ADDITIONAL DATA NEEDED FOR MS DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
</tr>
</tbody>
</table>
| ≥2 attacks; objective clinical evidence of 1 lesion | Dissemination in time, demonstrated by:  
  - Simultaneous presence of asymptomatic gadolinium-enhancing and non-enhancing lesions at any time; or  
  - A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or  
  - Await a second clinical attack |
| 1 attack; objective clinical evidence of 1 lesion (clinically isolated syndrome) | |

5. List four reasons why the EDSS is not a perfect assessment tool.

a.  

b.  

c.  

d.  

2.8 PROGRESS CHECK ANSWERS

1. MRI usually detects 10 times more lesions than are apparent through clinical examination.

2. Distinguish between T1 and T2-weighted MRI.

   In a T1-weighted scan, pulses occur every 350 ms. In a T2-weighted scan, pulses occur every 4–5 s. In MS, the number and volume of T1-weighted lesions are generally used as markers of disease activity. T2-weighted scans are better for detecting established lesions. The total volume of T2-weighted lesions (the lesion load) is generally used as a measure of overall disease burden.

3. List two major weaknesses of evoked potential tests.
   a. Tests are not standardised between centres
   b. There is no consensus about what constitutes a normal response

4. Complete the table below.

New, Recommended Diagnostic Criteria for MS.

<table>
<thead>
<tr>
<th>CLINICAL PRESENTATION</th>
<th>ADDITIONAL DATA NEEDED FOR MS DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥2 attacks; objective clinical evidence of ≥2 lesions or</td>
<td>None</td>
</tr>
<tr>
<td>objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack</td>
<td></td>
</tr>
<tr>
<td>≥2 attacks; objective clinical evidence of 1 lesion</td>
<td>Dissemination in space, demonstrated by ≥1 T2 lesion in at least 2 of 4 MS typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord); or await a further attack implicating a different CNS site</td>
</tr>
<tr>
<td>1 attack; objective clinical evidence of &gt;2 lesions</td>
<td>Dissemination in time, demonstrated by:</td>
</tr>
<tr>
<td></td>
<td>• Simultaneous presence of asymptomatic gadolinium-enhancing and non-enhancing lesions at any time; or</td>
</tr>
<tr>
<td></td>
<td>• A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or</td>
</tr>
<tr>
<td></td>
<td>• Await a second clinical attack</td>
</tr>
<tr>
<td>1 attack; objective clinical evidence of 1 lesion (clinically isolated syndrome)</td>
<td>1 year of disease progression (retrospectively or prospectively determined) plus 2 of 3 of the following criteria:</td>
</tr>
<tr>
<td></td>
<td>1. Evidence for DIS in the brain based on &gt;1 T2 lesions in the MS characteristic (periventricular, juxtacortical or infratentorial) regions</td>
</tr>
<tr>
<td></td>
<td>2. Evidence for DIS in the spinal cord based on &gt;2 T2 lesions in the cord</td>
</tr>
<tr>
<td></td>
<td>3. Positive CSF (isoelectrical focusing evidence of OCBs and/or elevated IgG index)</td>
</tr>
</tbody>
</table>
5. List four reasons why the EDSS is not a perfect assessment tool.
   a. Inter-rater variability can be large
   b. The EDSS is not a linear scale
   c. The average time spent at each EDSS stage varies greatly and, therefore, an outcome measure such as time to progress one EDSS stage means something different depending on which EDSS was the starting point
   d. EDSS depends heavily on walking ability; upper limb function and cognitive function are underrepresented
## 2.9 GLOSSARY

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>CIS</td>
<td>Clinically isolated syndrome</td>
</tr>
<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>CNSp</td>
<td>Clinical nurse specialist</td>
</tr>
<tr>
<td>CSF</td>
<td>Cerebrospinal fluid</td>
</tr>
<tr>
<td>DIS</td>
<td>Dissemination in space</td>
</tr>
<tr>
<td>DIT</td>
<td>Dissemination in time</td>
</tr>
<tr>
<td>EDSS</td>
<td>Expanded disability status scale</td>
</tr>
<tr>
<td>EEG</td>
<td>Electroencephalography</td>
</tr>
<tr>
<td>IgG</td>
<td>Immunoglobulin G</td>
</tr>
<tr>
<td>LP</td>
<td>Lumbar puncture</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>MRS</td>
<td>Magnetic resonance spectroscopy</td>
</tr>
<tr>
<td>MS</td>
<td>Multiple Sclerosis</td>
</tr>
<tr>
<td>OCBs</td>
<td>Oligoclonal bands</td>
</tr>
<tr>
<td>PPMS</td>
<td>Primary progressive multiple sclerosis</td>
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<tr>
<td>PWMS</td>
<td>People with multiple sclerosis</td>
</tr>
<tr>
<td>RRMS</td>
<td>Relapsing remitting multiple sclerosis</td>
</tr>
<tr>
<td>sMRI</td>
<td>Subtraction magnetic resonance imaging</td>
</tr>
<tr>
<td>SPMS</td>
<td>Secondary progressive multiple sclerosis</td>
</tr>
<tr>
<td>VEPs</td>
<td>Visual evoked potentials</td>
</tr>
</tbody>
</table>