Earlier treatment of multiple sclerosis

Towards the end of 2009, the Association of British Neurologists revealed its updated guidelines for MS diagnosis and treatment. This article reviews how they have moved forward from the first edition in 2001 and the impact this now has for the prescriber.

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In 2001 the Association of British Neurologists (ABN) published their first guidance on the use of disease modifying drugs for the treatment of multiple sclerosis (MS). Since then, the management of MS has seen various developments and hurdles, including the well documented, unfavourable, review of disease modifying drugs by NICE, which led to the formation of the risk sharing scheme for patients who met the ABN's criteria.

Knowledge has advanced considerably in the past few years, particularly in relapsing-remitting MS. Several clinical trials have reported results, and several new agents are currently in development that will undoubtedly drive future guideline updates. These advances can only be a good thing for patients who suffer significant disability and reduced life expectancy from this progressive disease.

Since the first 2001 guidelines, revisions have followed in 2007 and now at the end of 2009. These have updated the guidelines to incorporate the new evidence and treatment options. Importantly, the ABN recognises that the 2009 guidance "... aims to represent a national consensus concerning the use of currently approved disease modifying drugs in multiple sclerosis."

One of the most poignant developments in the national consensus on prescribing has been the recognition of the role for the use of disease modifying drugs earlier in the course of the disease.

Beta-Interferon has a consistent effect in reducing relapses (by about one third over two years) in patients with relapsing remitting multiple sclerosis and secondary progressive multiple sclerosis with superimposed relapses. However, the guidelines now recognise that "this may also apply to patients with clinically isolated syndrome in whom abnormal MRI indicates a high probability of subsequent conversion to clinically definite multiple sclerosis and those who subsequently meet the revised McDonald criteria" (Box 1).

The McDonald Criteria[1] for the Diagnosis of MS were developed by an international panel convened under the auspices of the US National Multiple Sclerosis Society and the International Federation of MS Societies. Their remit was to reassess existing diagnostic criteria and to recommend appropriate changes. These were published in 2001 and quickly became recognised by the name of the lead author. The McDonald Criteria were then revised and published again in 2005, with the key recommendations shown in Box 2.

Evidence does show that treating early disease can delay progression into clinically definite multiple sclerosis. A recent review of phase 3 studies of Beta-Interferon in patients with early disease[2] suggests that treatment can delay conversion to clinically definite multiple sclerosis and reduce the risk of new asymptomatic white matter lesions, the authors noting that: "The evidence supports early initiation of treatment."

The inclusion of the now licensed and NICE approved natalizumab into the ABN guidelines is an important addition as it now widens the scope of treatment options in MS. NICE recommended natalizumab for rapidly evolving severe relapsing remitting multiple sclerosis defined by two or more disabling relapses in one year, and one or more gadolinium-enhancing lesions on MRI or a significant increase in T2 lesion load compared with previous MRI.

It is still recommended that disease modifying treatments in the UK are initiated by a consultant neurologist, if possible one with specialist expertise in MS. However, the ABN also recognises the essential role MS nurses have to play in the management of symptoms as well as being an important professional contact for the patient during and between clinic visits; providing additional information and reassurance to those on treatment and their family. The MS Society and MS Trust

Box 1: ABN Guidance for starting disease modifying treatment in relapsing remitting multiple sclerosis

- All eligible patients will normally be ambulant (maximum EDSS 6·5) and aged 18 or more years. No treatments are licensed for use during pregnancy.
- Relapsing remitting multiple sclerosis. Patients with a diagnosis of active multiple sclerosis with relapsing onset; active disease is defined by two clinically significant relapses in the previous two years.
- Neurologists may, in certain other circumstances where the evidence for efficacy is less secure, also consider advising treatment after discussion with the patient concerning the risks and benefits. For example;
  - patients within 12 months of a clinically significant clinically isolated syndrome when MRI evidence predicts a high likelihood of recurrent episodes (ie. development of multiple sclerosis).
  - patients with only a single major relapse in the preceding two years, but combined with MRI evidence of continuing disease activity (ie. meet the revised McDonald criteria for MS)
  - individuals aged less than 18 with relapsing remitting multiple sclerosis.

are also acknowledged as good sources of information for patients, through their helplines and leaflets that are written in suitable lay language for patients and their families.

Regular follow-up is advised on initiation of treatment with a schedule suggested of month one and three initially, then three month intervals for the first year and six monthly thereafter. Despite the frequent use of MRI to follow disease activity by specialists in the USA and parts of Europe, the guidelines are slightly less specific on the role of MRI in the UK, probably due to the cost associated and the variability in the ease of availability. However, they do recognise that MRI "... may be occasionally useful when decisions need to be made concerning the termination of treatments."

Guidance on this sometimes difficult decision to discontinue treatment has also been revised in the 2009 edition. This now highlights the importance of patient choice, advising that patients should be fully informed of all the relevant facts and uncertainties before any decision is made in discussion with their treating neurologist.

Up to about 100,000 people in the UK have MS, the majority of which is relapsing remitting multiple sclerosis. Obviously, some patients may benefit more than others from early treatment, and healthcare professionals must use their limited resources wisely. However, recent data show that the majority of costs are outside of the healthcare system. Those who treat MS know that, above all else, it is a human condition with the burden being on those with the disease and those around them. People with MS are often young, have a family, a job and are an established part of society when MS strikes.

The 2009 revisions certainly seem to have addressed the growing evidence base for MS treatment in the UK and have been welcomed by healthcare professionals and patients. Laura Weir, Head of Policy and Campaigns for the MS Society, confirmed that "The revised guidelines are far clearer and move towards encouraging earlier treatment. Yet despite this shift in emphasis from the ABN, it is worth noting that NICE has placed both its appraisal on medicines to treat clinically isolated syndrome and the MS clinical guideline on the static list. It is crucial that clinical guidelines are updated to reflect the most up to date evidence. This is one of the reasons the MS Society is urging NICE to review its clinical guidelines on MS as a matter of urgency."

This article reviewed the Association of British Neurologists Revised (November 2009) Guidelines for Prescribing in Multiple Sclerosis, which can be found at: http://theabn.org/abn/userfiles/file/ABN_MS_Guidelines_2009_Final(1).pdf.

Box 2: McDonald criteria.[1] The 2005 Revisions to the McDonald Diagnostic Criteria for MS aimed to simplify and speed diagnosis.

Clinical presentation	Additional data needed for MS diagnosis
Two or more attacks; objective clinical evidence of two or more lesions	None
Two or more attacks; objective clinical evidence of one lesion	Dissemination in space, demonstrated by: MRI or Two or more MRI-detected lesions consistent with MS + positive CSF or Await further clinical attack implicating a different site
One attack; objective clinical evidence of two or more lesions	Dissemination in time, demonstrated by: MRI or Second clinical attack
One attack; objective clinical evidence of one lesion (monosymptomatic presentation; clinically isolated syndrome)	Dissemination in space, demonstrated by: MRI or Two or more MRI-detected lesions consistent with MS + positive CSF and Dissemination in time, demonstrated by: MRI or Second clinical attack
Insidious neurological progression suggestive of MS	One year of disease progression (retrospectively or prospectively determined) and Two of the following: a. Positive brain MRI (nine T2 lesions or four or more T2 lesions with positive VEP) b. Positive spinal cord MRI (two focal T2 lesions) c. Positive CSF

Clinicians should refer to the full publication for additional information

References

1. Polman CH, Reingold SC, Edan G, et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria". *Ann Neurol* 2005; **58**(6): 840–46
2. Kremenchutzky M, Kinkel P. The Efficacy of Interferon Beta in Delaying Conversion to Clinically Definite Multiple Sclerosis. *Int J MS Care* 2010; **12**: 42–50.