INTERNATIONAL PANEL UPDATES DIAGNOSTIC CRITERIA FOR MS

An international panel has updated the criteria used to diagnose multiple sclerosis, incorporating new data which should speed the diagnosis without compromising accuracy. The International Panel on Diagnosis of MS, organized and supported by the National Multiple Sclerosis Society, with additional financial support from the MS International Federation, developed new diagnostic criteria for MS in 2001 which have been extensively tested and used since then. These have now been updated based on an assessment of new data and new consensus by the Panel, chaired by Dr. Chris Polman of the Free University of Amsterdam. Commentary and tables attached here describe the original “McDonald Criteria” and their 2005 Revisions. Full details can be obtained from the Panel’s publication in the December 2005 issue of *Annals of Neurology* (58: 840-846).

Determining if an individual with neurological symptoms and signs has MS, an unpredictable neurological disease, has always been difficult because there is no single test that can accurately determine an MS diagnosis. Traditionally, the process of diagnosis has involved obtaining evidence from patient history, clinical examination and a variety of laboratory tests, all intended to rule out other possible causes of disease and to gather data consistent with a diagnosis of MS. Magnetic resonance imaging (MRI) studies have become important as a tool to help confirm an MS diagnosis, but it was not until 2001 that the International Panel on MS Diagnosis presented new diagnostic criteria that focused specifically on the use of MRI as an aid to diagnosis.

The resulting McDonald Criteria for Diagnosis of MS have been used worldwide since their appearance in a publication in the *Annals of Neurology* in 2001, and have been the subject of extensive debate and testing. As a consequence, a significant body
of new information about the utility of the Criteria has been published. The International Panel reconvened in March 2005 in Amsterdam to consider these new data and to recommend appropriate revisions to the original McDonald Criteria. These recommendations – termed the 2005 Revisions to the McDonald Diagnostic Criteria for MS – will make confirmation of an MS diagnosis more secure and rapid.

“A key goal is to speed the diagnosis of MS without compromising accuracy,” stated John R. Richert, MD, Vice President of Research and Clinical Programs at the National MS Society. “These updated criteria appear to achieve this goal.”

The 2005 Revisions

What has not changed:

1. The core of an MS diagnosis is the objective (i.e., by physician exam) demonstration of dissemination of typical disease signs and symptoms in time and space. These overriding concepts remain central to the diagnosis process and are retained in the 2005 Revisions.

2. It remains the case that no single test can provide adequate information to support an MS diagnosis. Therefore, supportive and confirmatory paraclinical examinations – including analysis of lesions by MRI, of cerebrospinal fluid (CSF), and sometimes of evoked potentials – are still important in helping to confirm an MS diagnosis.

3. It has always been the case that, while use of paraclinical and laboratory examination can speed an MS diagnosis, a solid diagnosis can be made on clinical grounds alone. This is important particularly in geographical areas around the world where quality paraclinical testing may not be available or may not be standardized sufficiently to provide the necessary information.

4. There must be no better explanation than MS for the clinical and laboratory findings – other possible diagnoses must be eliminated.

What has changed:

1. In the original McDonald Criteria, specific guidelines were presented for using MRI to demonstrate dissemination of disease in time. These focused primarily on contrast enhancing lesions, and it was more difficult to use non-enhancing T2 lesions for this demonstration. Based on data collected since then, the 2005
Revisions indicate that an MRI scan that shows a new T2 lesion, compared with a reference scan performed at least 30 days after the initial clinical event, can now be used to demonstrate dissemination in time (see Table 1).

2. In the original McDonald Criteria, specific guidance was provided on how MRI can be used to demonstrate abnormality consistent with MS and used to demonstrate dissemination of disease in space. While this focused on brain MRI and brain lesions, spinal cord lesions can also be useful. The 2005 Revisions amplify on how spinal cord lesions can more specifically contribute to the determination of an MRI abnormality consistent with MS (see Table 2).

3. The original McDonald criteria pointed to the difficulty of making a diagnosis of primary progressive MS and required finding an abnormality in CSF analysis to make such a diagnosis. Data collected since suggest that a reasonable proportion of individuals with true primary progressive disease may have normal CSF findings. The 2005 Revisions indicate that positive CSF findings can be useful in making such a diagnosis, but with appropriate MRI findings in the brain and spinal cord, CSF abnormalities are not required for a definitive diagnosis (Table 3).

Conclusions: The 2005 Revisions to the McDonald Diagnostic Criteria for MS should speed and make more certain the diagnosis of MS (Table 4). As with the original Criteria, these need prospective study and it is expected that new data in the future will result in further refinements. The 2005 Revisions continue to emphasize objective clinical, imaging and laboratory evidence, the diagnosis of MS remains a partly subjective process. The diagnosis is best made by an expert who is familiar with the disease and who can interpret imaging and laboratory evidence that can supplement the clinical diagnostic process.
Table 1 – Magnetic Resonance Imaging Criteria to Demonstrate Dissemination of Lesions in Time (DIT)

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<th>ORIGINAL MCDONALD CRITERION</th>
<th>THE 2005 REVISIONS</th>
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| 1. If a first scan occurs 3 months or more after the onset of the clinical event, the presence of a gadolinium-enhancing lesion is sufficient to demonstrate dissemination in time, provided that it is not at the site implicated in the original clinical event. If there is no enhancing lesion at this time, a follow-up scan is required. The timing of this follow-up scan is not crucial but 3 months is recommended. A new T2- or gadolinium-enhancing lesion at this time then fulfills the criterion for dissemination in time. | 1. There are two ways to show DIT using imaging:  
   a. Detecting gadolinium enhancement at least 3 months after the onset of the initial clinical event, if not at the site corresponding to the initial event.  
   b. Detecting a NEW T2 lesion if it appears at any time compared to a reference scan done at least 30 days after the onset of the initial clinical event. |
| 2. If the first scan is performed less than 3 months after the onset of the clinical event, a second scan done 3 months or more after the clinical event showing a new gadolinium-enhancing lesion provides sufficient evidence for dissemination in time. However, if no enhancing lesion is seen at this second scan, a further scan not less than 3 months after the first scan that shows a new T2 lesion or an enhancing lesion will suffice. |
Table 2 – Magnetic Resonance Imaging Criteria to Demonstrate Brain Abnormality and Demonstration of Dissemination in Space (DIS)

<table>
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<tr>
<th>ORIGINAL MCDONALD CRITERIA</th>
<th>THE 2005 REVISIONS</th>
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<tr>
<td>Three out of four of the following:</td>
<td>Three out of four of the following:</td>
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<td>1. One gadolinium enhancing lesion or nine T2 hyperintense lesions if there is no gadolinium enhancing lesion</td>
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<tr>
<td>2. At least one infratentorial lesion</td>
<td>2. At least one infratentorial lesion</td>
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<tr>
<td>3. At least one juxtacortical lesion</td>
<td>3. At least one juxtacortical lesion</td>
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<tr>
<td>4. At least three periventricular lesions</td>
<td>4. At least three periventricular lesions</td>
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NOTE: One spinal cord lesion can substitute for one brain lesion

NOTE: A spinal cord lesion can be considered equivalent to a brain infratentorial lesion: an enhancing spinal cord lesion is considered to be equivalent to an enhancing brain lesion, and individual spinal cord lesions can contribute along with individual brain lesions to reach the required number of T2 lesions.
Table 3 – Diagnosis of MS in Disease with Progression from Onset

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<th>ORIGINAL MCDONALD CRITERIA</th>
<th>THE 2005 REVISIONS</th>
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<td>1. Positive CSF <strong>AND</strong></td>
<td>1. One year of disease progression (retrospectively or prospectively determined)</td>
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| 2. Dissemination in space by MRI evidence of 9 or more T2 brain lesions **Or** 2 or more cord lesions **Or** 4-8 brain lesions and 1 cord lesion **Or** positive VEP with 4-8 MRI lesions **Or** positive VEP with less than 4 brain lesions plus 1 cord lesion **AND** 3. Dissemination in time by MRI **Or** continued progression for 1 Year | 2. **PLUS** 2 out of the following 3:  
   a. Positive brain MRI (9 T2 lesions or 4 or more T2 lesions with +VEP)  
   b. Positive spinal cord MRI (2 focal T2 lesions)  
   c. Positive CSF (isoelectric focusing evidence of OCB and/or elevated IgG index) |
Table 4 – The 2005 Revisions to the McDonald Diagnostic Criteria for MS

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<th>CLINICAL PRESENTATION</th>
<th>ADDITIONAL DATA NEEDED FOR MS DIAGNOSIS</th>
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<td>2 or more attacks; objective clinical evidence of 2 or more lesions</td>
<td>• None</td>
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| 2 or more attacks; objective clinical evidence of 1 lesion                              | • Dissemination in space, demonstrated by:  
  ➔ MRI  
  OR  
  ➔ 2 or more MRI detected lesions consistent with MS plus positive CSF  
  OR  
  ➔ Await further clinical attack implicating a different site |
| 1 attack; objective clinical evidence of 2 or more lesions                              | • Dissemination in time, demonstrated by:  
  ➔ MRI  
  OR  
  ➔ Second clinical attack                                                                                                  |
| 1 attack; objective clinical evidence of 1 lesion (monosymptomatic presentation; clinically isolated syndrome) | • Dissemination in space, demonstrated by:  
  ➔ MRI  
  OR  
  ➔ 2 or more MRI-detected lesions consistent with MS plus 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 out of three of the following:  
    a. Positive brain MRI (9 T2 lesions or 4 or more T2 lesions with positive visual evoked potentials;  
    b. Positive spinal cord MRI (two or more focal T2 lesions);  
    c. Positive CSF                                                                                                         |