Diagnostic Imaging Pathways - Multiple Sclerosis

Summary
This pathway provides guidance on imaging patients with multiple sclerosis.

Date reviewed: July 2014
Date of next review: 2017/2018
Published: October 2014

Quick User Guide
Move the mouse cursor over the PINK text boxes inside the flow chart to bring up a pop up box with salient points. Clicking on the PINK text box will bring up the full text. The relative radiation level (RRL) of each imaging investigation is displayed in the pop up box.

<table>
<thead>
<tr>
<th>SYMBOL</th>
<th>RRL</th>
<th>EFFECTIVE DOSE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Symbol" /></td>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td><img src="image" alt="Symbol" /></td>
<td>Minimal</td>
<td>&lt; 1 millisieverts</td>
</tr>
<tr>
<td><img src="image" alt="Symbol" /></td>
<td>Low</td>
<td>1-5 mSv</td>
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<tr>
<td><img src="image" alt="Symbol" /></td>
<td>Medium</td>
<td>5-10 mSv</td>
</tr>
<tr>
<td><img src="image" alt="Symbol" /></td>
<td>High</td>
<td>&gt;10 mSv</td>
</tr>
</tbody>
</table>

Pathway Diagram
Multiple Sclerosis

32yo M presented with several days of worsening numbness and weakness of his R leg.

1a, 1b: Initial MRI sequence demonstrates multiple periventricular and pericallosal hyperintense lesions. Images shown are T2 weighted turbo spin echo MRI images.

1c: There are also multiple hyperintense lesions in his spinal cord. These satisfy the criteria for dissemination in space.

Follow-up scan

2a, 2b, 2c: Follow-up MRI scan of same patient performed 3 months after
initial MRI. There are multiple new white matter supratentorial lesions demonstrated, predominantly within the right posterior and left temporal lobes, as well as a new spinal cord lesion at the level of C7. These satisfy the criteria for dissemination in time. Additionally, the patient also had oligoclonal bands in his CSF.

Teaching Points

- Multiple sclerosis is an idiopathic inflammatory disease of the central nervous system
- The diagnosis is one of exclusion, as numerous other conditions may mimic it
- Definitive diagnosis of MS is based on the presence of CNS lesions disseminated in time and space (i.e. multiple lesions occurring in different parts of the CNS which evolve over time)
- The MacDonald Criteria for Diagnosis of MS provides MRI criteria for demonstrating dissemination in time and space
- MRI plays a key role in the assessment of MS

Cerebrospinal Fluid (CSF)

- 90% of patients will have raised levels of IgG in their CSF. Upon gel electrophoresis to separate the CSF components, oligoclonal bands will appear, denoting increased concentration of discrete IgG proteins. These are not found in the patient's serum
- However, these findings are not specific to MS patients, and are not diagnostic on their own 1, 2
- A systematic review of diagnostic tests in multiple sclerosis found CSF oligoclonal banding having sensitivities of between 69 percent and 91 percent and specificities of between 59 percent and 94 percent for MS. 3 When combined with MRI sensitivity improved to between 56 percent and 100 percent and specificity between 53 percent and 96 percent

Dissemination in Time and Space

- One of the hallmarks of multiple sclerosis is the development of multiple CNS lesions “scattered in
time and space”. Dissemination in time refers to the development of new lesions in the brain or spine. Dissemination in space refers to the presence of multiple CNS lesions in the brain and/or spinal cord

- The 2010 McDonald MRI criteria for demonstrating dissemination of lesions in time are 4
  - a. A new T2 or gadolinium enhancing lesion on follow-up MRI with reference to the baseline MRI. There is no longer a restriction on the timing of the follow-up MRI
  - b. Concurrent gadolinium enhancing & non-enhancing lesions on a single MRI, at any time

- The 2010 McDonald MRI criteria for demonstrating dissemination in space are based on work by the MAGNIMS research group and has been validated in other centres. 4-6 It requires ?1 T2 lesion in at least 2 of the 4 areas of the CNS
  - Periventricular
  - Juxtacortical
  - Infratentorial
  - Spinal cord

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### Dissemination in Time

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- A recent study comparing the 2010 and 2005 McDonald MRI criteria for dissemination in time found in classic multiple sclerosis the newer criteria overall performed better 7

### History and Examination

- Clinical assessment is an essential part of the diagnostic work up of MS 4
- Symptoms and signs can be classified as either monofocal (indicative of a single lesion) or multifocal (indicative of more than one lesion). These clinical findings can be used to indicate dissemination in space and/or time
- A purely clinical diagnosis remains appropriate when MRI and other investigations are not possible
Clinical features suggestive of an MS attack may include:
- Sensory disturbances
- Unilateral optic neuritis
- Diplopia
- Limb weakness
- Clumsiness
- Gait ataxia
- Lhermitte's sign

Suspected Multiple Sclerosis (Summary)

- Multiple sclerosis (MS) is an idiopathic inflammatory disease of the central nervous system, characterised pathologically by demyelination and axonal damage.
- Clinically, it can present as relapsing-remitting MS (RRMS) which is characterised by acute episodic periods of worsening neurological symptoms (“attacks”) followed by (partial or full) recovery. MS may also present as primary progressive MS (PPMS) which is characterised by gradual progressive deterioration. Other forms can also include secondary-progressive multiple sclerosis (SPMS), progressive-relapsing multiple sclerosis (PRMS) and clinically-isolated syndrome (CIS).
  - RRMS affects the majority of MS patients (80%), typically presenting in the second/third decades of life, and more commonly affecting women (by 2:1). A large proportion (70%) of these patients will go on to develop symptoms that progressively worsen (secondary progressive MS). A small proportion of RRMS patients will have a relatively benign course following their initial attack.
  - PPMS affects 20% of patients, but has no sexual predominance. It typically presents as a slowly evolving upper neuron syndrome of the legs.
  - Secondary-progressive Multiple Sclerosis (SPMS) follows the initial relapsing-remitting course which then follows onto a progressive course with or without occasional relapses. Approximately half of the patients with RRMS will convert to SPMS at the ten year mark and ninety percent at the twenty five year mark.
  - PRMS presents as progressive disease from the onset of symptoms, with distinct acute relapses, which may or may not involve full recovery. Between periods of relapses there is continuing progression. It is recognised that PRMS may present as a subtype of PPMS.
- Other MS subtypes include:
  - Radiologically isolated syndrome (RIS): In this syndrome there is no evidence of clinical disease but an incidental finding of typical MS lesions on MRI. There is emerging data that those identified with RIS go onto develop clinical symptoms.
  - Clinically isolated syndrome (CIS): a first clinical episode which is suggestive of MS.
  - Malignant MS where the disease has a rapid and progressive course leading to significant disability and marked neurological dysfunction or death.
  - Single-attack progressive MS: generally described as a rarer variant and thought to be a subtype of SPMS. Characterised by single initial attack followed by progressive phase.
- In Australia, there are an estimated 20,000 MS sufferers. Tasmania has one of the highest rates of MS in the world with an incidence of 75 per 100,000. This is also substantially higher than other parts of Australia.
- The diagnosis of MS is one of exclusion, as there are numerous conditions that may mimic it:
  - CNS infections (e.g. syphilis, encephalitis)
  - CNS inflammation (e.g. sarcoidosis, SLE)
  - CNS microvascular disease (e.g. vasculitis, ischaemic stroke)
Genetic disorders (e.g. cerebral autosomal-dominant arteriopathy with subcortical infarcts and leucoencephalopathy)

- Vitamin B12 deficiency

- Definitive diagnosis of MS is based on the presence of CNS lesions disseminated in time and space. That is, multiple lesions occurring in different parts of the CNS which evolve over time.

- This can be demonstrated clinically, such as when the patient experiences episodic “attacks”. These periods of neurologic impairment should last longer than 24 hours and should not be attributable to another cause (e.g. encephalitis). The neurologic impairment may take weeks to recover to baseline and sometimes there is only a partial recovery.

- Magnetic Resonance Imaging (MRI) is one the main investigations for MS, and has become a vital part of the diagnostic process. The McDonald Criteria for Diagnosis of MS make extensive use of MRI for detecting lesions. MRI can be used to demonstrate both dissemination in space (e.g. multiple lesions present on one MRI scan) and dissemination in time (e.g. old and new lesions present on one MRI scan, or new lesions seen on repeat MRI). MS lesions appear as discrete T2 lesions in typical areas of the brain. T2 lesions are hyperintense areas on T2 weighted MRI scans, and indicate areas of oedema and pathology.

- A systematic review of diagnostic tests in multiple sclerosis found the sensitivity of MRI criteria for MS ranged from 35 percent to 100 percent and specificity of 36 percent to 92 percent.

- Information for consumers on Magnetic Resonance Imaging (MRI) InsideRadiology

The 2010 McDonald Criteria for Diagnosis of Multiple Sclerosis

<table>
<thead>
<tr>
<th>Attacks</th>
<th>Clinical Lesions</th>
<th>Additional requirements for MS Diagnosis</th>
</tr>
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<tbody>
<tr>
<td>2 or more</td>
<td>2 or more</td>
<td>None (however, MRI imaging is recommended).</td>
</tr>
<tr>
<td>2 or more</td>
<td>1 lesion</td>
<td>Dissemination in space:</td>
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<tr>
<td></td>
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<td>- MRI (brain, spine) showing</td>
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<tr>
<td></td>
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<td>?1 T2 lesion in at least 2</td>
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<td></td>
<td></td>
<td>of 4 typical areas for MS; or</td>
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<tr>
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<td></td>
<td>- Await second clinical</td>
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<tr>
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<td></td>
<td>attack implicating a different site.</td>
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<tr>
<td>1 attack</td>
<td>2 lesions</td>
<td>Dissemination in time:</td>
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<tr>
<td></td>
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<td>- Single MRI demonstrating</td>
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<td></td>
<td>simultaneous gadolinium</td>
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<td></td>
<td></td>
<td>enhancing &amp; non-enhancing lesions; or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Repeat MRI demonstrating new lesions</td>
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<tr>
<td></td>
<td></td>
<td>(T2 or gad. enhancing); or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Second clinical attack.</td>
</tr>
<tr>
<td>1 attack</td>
<td>1 lesion</td>
<td>Dissemination in space &amp; time:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- MRI (brain, spine) showing</td>
</tr>
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<td></td>
<td></td>
<td>?1 T2 lesion in at least 2</td>
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</tbody>
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of 4 typical areas for MS; or
- Await second clinical attack implicating a different site; and
- MRI demonstrating simultaneous gadolinium enhancing & non-enhancing lesions; or
- Repeat MRI demonstrating new lesions (T2 or gad. enhancing); or
- Await second clinical attack implicating a different site.

<table>
<thead>
<tr>
<th>0 attacks (insidious symptoms)</th>
<th>1 year of disease progression &amp; 2 of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• MRI brain shows dissemination in space</td>
</tr>
<tr>
<td></td>
<td>• MRI spinal cord shows dissemination in space</td>
</tr>
<tr>
<td></td>
<td>• Positive CSF</td>
</tr>
</tbody>
</table>

**Primary Progressive Multiple Sclerosis**

- Around 20% patients with multiple sclerosis have a gradually progressive course, known as primary progressive multiple sclerosis (PPMS)
- The McDonald criteria for diagnosis of primary progressive multiple sclerosis require 1
  1. One year of disease progression and
  2. Two of the following
     a. Positive brain MRI demonstrating dissemination in space
     b. Positive spinal cord MRI demonstrating dissemination in space
     c. Positive CSF (isoelectric focusing evidence of oligoclonal IgG bands and/or increased IgG index)

**References**

**Date of literature search: June 2014**

The search methodology is available on request. [Email](mailto:)

References are graded from Level I to V according to the Oxford Centre for Evidence-Based Medicine, Levels of Evidence. [Download the document](#)


Information for Consumers

| Information from this website | Information from the Royal |


Consent to Procedure or Treatment
Radiation Risks of X-rays and Scans
Magnetic Resonance Imaging (MRI)

Gadolinium Contrast Medium
Magnetic Resonance Imaging (MRI)

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