LEARNING OBJECTIVES
1. The attendee will be able to describe the latest guidelines for establishing a diagnosis of multiple sclerosis in a child.
2. The attendee will be able to describe what features in children with optic neuritis place them at higher risk for developing future multiple sclerosis.
3. The attendee will be able to explain a potential Pediatric Optic Neuritis Treatment Trial.

CME QUESTIONS
Please indicate whether the following statements are true or false with regard to MS in children:
1. Altered mental status is a criterion for the diagnosis of MS in childhood.
2. White matter lesions on MRI at presentation are predictive of risk of conversion to MS in children with optic neuritis.
3. The risk of conversion to MS after optic neuritis in a child depends on the unilaterality or bilaterality of the optic neuritis.

KEYWORDS
1. Pediatric Optic Neuritis
2. Multiple Sclerosis
3. Pediatric Optic Neuritis Treatment Trial

INTRODUCTION
Optic neuritis is an inflammatory disorder of the optic nerve. Associated with a variety of autoimmune disorders, optic neuritis is most commonly considered a demyelinating disease, and it is often the initial manifestation of multiple sclerosis (MS). The relationship between optic neuritis and multiple sclerosis has been more thoroughly investigated in adults than in children. Clinically, optic neuritis in the pediatric age group is diagnosed by the same criteria used in adults, including sudden or subacute visual loss, central or cecocentral visual field defect, impairment of color vision, afferent pupillary defect, and ocular pain on eye movements. The purpose of this review is to discuss the risk factors for MS in children after optic neuritis.

DIAGNOSIS OF MULTIPLE SCLEROSIS IN CHILDREN
The diagnosis of MS in children is made by demonstration of at least two episodes of CNS demyelination separated in time in space (Krupp et al. 2007).

Dissemination in space can be satisfied by either:
2. Positive MRI by the McDonald (2001) criteria: 3 of 4 of
   i) nine or more white matter lesions or one gadolinium enhancing lesion,
   ii) three or more periventricular lesions,
   iii) one juxtacortical lesion, or
   iv) an infratentorial lesion.
3. Combination of abnormal CSF (oligoclonal bands or an elevated IgG index) and two lesions on MRI, of which one must be in the brain.

Dissemination in time can be demonstrated by either:
2. A new T2 or contrast-enhancing lesion which develops at least 3 months after the initial clinical event.

The events must not satisfy the diagnosis of ADEM (see below), which is a demyelinating or inflammatory event, and includes white or gray matter lesions on MRI, which is i) polysymptomatic and ii) includes encephalopathy (i.e. behavioral or mental status change). Multiple events of this type would be more appropriately termed recurrent or multiphasic ADEM (Krupp et al., 2007).

Neuromyelitis optica (NMO) must be excluded, but it is unclear in children whether the absence of NMO-IgG antibodies excludes the diagnosis.
ACUTE DISSEMINATED ENCEPHALOMYELITIS VS. MULTIPLE SCLEROSIS

Post-infectious neurologic disease is not uncommon in children. For example, acute cerebellar syndrome follows varicella infections, sensorineural hearing loss follows mumps infections, and Sydenham’s chorea is associated with streptococcal infections (Dale et al. 2000). Acute disseminated encephalomyelitis (ADEM) is an autoimmune demyelinating disease that typically follows an illness or vaccination. As opposed to MS, ADEM is typically a monophasic illness that does not require long-term treatment. ADEM is more common in children than adults (Dale et al. 2000). Although patients with ADEM can present with fulminant neurologic signs and symptoms, most patients have an excellent recovery.

The International Pediatric MS Study Group has defined ADEM by its clinical and radiographic features: encephalopathy, multifocal neurologic signs, and large, predominantly white matter, lesions on brain MRI, without alternative explanations (Kelly 2006). When relapses after ADEM occur, such cases are difficult to distinguish from MS. The Study Group has defined ADEM as a single episode lasting up to 3 months. New symptoms may appear during this timeframe. Children who have a second episode involving the same clinical and radiographic areas are diagnosed with recurrent ADEM. If different areas are affected, the child has multiphasic ADEM.

CONVERSION RATE TO MULTIPLE SCLEROSIS AFTER PEDIATRIC OPTIC NEURITIS

According to the ONTT, after acute unilateral optic neuritis, adults have a 50% chance of developing MS within 15 years (Optic Neuritis Study Group 2008).

In contrast, the conversion rate to MS in children is unclear, perhaps due to the variability in study methodologies in published reports, and because prospective data is lacking. One pediatric study reported a low conversion rate to MS (4%); however, the mean follow-up was 13 months (range 1-41 months) (Lana-Peixoto et al. 2001). Another study calculated the risk of developing MS after childhood optic neuritis using Kaplan-Meyer methods (Lucchinetti et al. 1997) The risk of MS was estimated to be 13% at 10 years, 19% by 20 years, 22% by 30 years, and 26% by 40 years. A different study reported a two-year risk of 36% (Wilejto et al. 2006).

A fourth study reported 16% of their patients with optic neuritis had MS; however, the purpose of that study was to define the presentation and visual prognosis in children, and children with a prior history of demyelinating disease were not excluded (Brady 1999). In our retrospective study (Bonhomme et al. 2009), eighteen patients were followed for more than 24 months, and 3 of the 18 (17%) developed MS.

The results of these and other studies are summarized in Table 1.

WHITE MATTER LesIONS ON MRI ARE PREDICTIVE OF RISK OF MS IN CHILDREN

As established by the Optic Neuritis Treatment Trial, an abnormal baseline brain MRI with white matter lesions is a strong predictor of MS after isolated optic neuritis in adults. Fifteen years after a bout of optic neuritis, 72% of adults with one or more brain MRI lesions at presentation developed MS, in contrast with a 25% conversion rate in those with no lesions (Optic Neuritis Study Group 2008). In children, an abnormal MRI at presentation is likely also predictive.

Mikaeloff et al. (2004) studied 296 patients after a first demyelinating event. Patients were ultimately diagnosed with MS using Poser’s criteria, ADEM (defined as polysymptomatic onset with mental status change, and poorly limited lesions on MRI with thalamus or basal ganglia involvement), or a single focal episode. Similar to the optic neuritis data, there were age differences between the patients with MS (12 years, SD 3.4) and ADEM (7.1, SD 4.3). Twenty-two percent of the patients presented with optic neuritis. Of the patients with optic neuritis at presentation, 86.6% were ultimately diagnosed with MS, whereas as 9% had monophasic ADEM. At the conclusion of the study, 53% of patients met diagnostic criteria for MS. The authors conclude that age of onset greater than 10 years, presence of an optic nerve lesion, and the presence of well-defined periventricular and/or subcortical lesions on MRI were associated with conversion to MS.

In the Wilejto et al. (2006) study, none of the patients with a normal brain MRI at presentation developed MS (although 1 developed NMO). All of the patients who presented with optic neuritis as the first manifestation of MS had at least 1 lesion on their initial MRI of the brain. Four patients with MRI lesions in the brain at presentation did not develop subsequent clinical attacks or further radiographic evidence of MS. Of this subgroup, 2 patients initially met McDonald’s criteria for dissemination in space, and the other 2 patients had multiple lesions (one with 6 lesions and one unavailable to the investigators for further review). None of these patients developed new lesions on subsequent MRI scans. Patients with ADEM were included in this study.

In our study (Bonhomme et al. 2009) we reviewed the medical records of children (<18 years) presenting with optic neuritis between 1993 and 2004 at the Children’s Hospital of Philadelphia. Children with a history of demyelinating disease or prior optic neuritis were excluded. Symptoms, ophthalmologic findings, MRI findings, and clinical outcomes were recorded. We identified 29 consecutive children with idiopathic optic neuritis. Eleven patients (38%) had white matter T2/FLAIR lesions in the brain (not including the optic nerves). Eighteen patients were followed for more than 24 months, and, as stated above, 3 of the 18 (17%) developed MS. All three patients
had an abnormal brain MRI scan at their initial presentation of optic neuritis. None of the patients with a normal brain MRI scan at presentation developed MS over an average follow-up of 88.5 months. Patients with one or more white matter lesions on MRI were more likely to develop MS (3/7 vs. 0/11, \(p=0.04\), Fisher’s exact test). We concluded that children with brain MRI abnormalities at the time of the diagnosis of optic neuritis have an increased risk of MS.

The results of these and other studies are summarized in Table 1. Larger collaborative prospective studies are needed to define better the prognosis for childhood optic neuritis.

**BILATERAL VS. UNILATERAL OPTIC NEURITIS, OR AGE, AS RISK FACTORS**

Compared to adults, bilateral ON is more common in children and is often simultaneous. It has been suggested that unilateral ON carries a greater risk for the development of multiple sclerosis (MS) in children compared to bilateral ON, but age may be a confounder.

We therefore performed a meta-analysis of published series to determine if age is a risk factor for unilateral vs. bilateral simultaneous optic neuritis and establish the risk of multiple sclerosis in children after unilateral vs. bilateral optic neuritis (Waldman et al. 2009). A MEDLINE search (1950 to May, 2010) was performed to identify published studies containing individual patient data of children (<18 years) with ON. References were scanned to identify additional pediatric studies. Patient age at onset of ON, laterality (unilateral vs. bilateral simultaneous ON), presence of brain MRI abnormalities outside the visual system (if available), and outcome (the development of MS) were recorded. Logistic regression was used to determine the risk of MS after unilateral vs. bilateral ON, adjusting for age and MRI abnormalities. Sixteen studies met the inclusion criteria, and 227 patients were analyzed. After unilateral ON as a first demyelinating event compared to bilateral ON, children were perhaps more likely to develop MS (OR 2.0, \(p=0.07\)). However, unilateral ON occurred more frequently in older children (OR 1.26, \(p<0.0001\)). After adjusting for age, the risk of MS after unilateral vs. bilateral ON was not significant (OR=1.67, \(p=0.2\)). For every 1 year increase in age, the risk of MS increases by 32% (\(p=0.006\)). After adjusting for age, the risk of MS significantly increases in children with abnormal brain MRI scans at presentation (OR 30.0, \(p<0.001\). Thus, the relation between unilateral vs. bilateral ON and the development of MS is dependent upon age. Unilateral ON is more common in older children; this population may be at greater risk for MS, especially in those children with brain MRI abnormalities at presentation.

**RECURRENT OPTIC NEURITIS**

In our study of pediatric optic neuritis (Bonhomme et al. 2009), nine patients (31%) had relapses of optic neuritis during the study period and 5 had more than one relapse. The pattern and location of the recurrent episodes showed no specific pattern. For example, 3 patients who initially presented with bilateral optic neuritis had subsequent unilateral relapses. In contrast, the remaining 6 patients presented with unilateral optic neuritis, half of whom ultimately met criteria for bilateral sequential optic neuritis and the other half for recurrent optic neuritis. Of the nine patients with recurrent optic neuritis, two patients developed MS. The relative risk of developing MS among patients with optic neuritis recurrence was 4.0 (\(p=0.25\)). It is unclear whether this would be confirmed in larger cohorts. Patients with bilateral simultaneous or sequential optic neuritis did not have a greater risk of MS compared to patients presenting with unilateral disease (\(p=0.53\)).

**A POSSIBLE PEDIATRIC OPTIC NEURITIS TREATMENT TRIAL**

In order to resolve the controversy concerning the benefit of corticosteroids for pediatric optic neuritis and to establish appropriate treatment guidelines, a multi-center Pediatric Optic Neuritis Treatment Trial (PONTT) is needed.

In such a trial, patients can be randomly assigned to one of three treatment groups, consisting of two corticosteroid groups and a placebo group:

1. IV methylprednisolone group: 1,000 mg/day or 30 mg/kg/day (depending upon the child’s weight) for 3 days, followed by a 15 day prednisone taper (starting at 1 mg/kg).
2. Oral methylprednisolone group: 1,136 mg/day or 34 mg/kg/day (depending upon the child’s weight) for 3 days, followed by 15 day prednisone taper (starting at 1 mg/kg).
3. Oral placebo: inert substance given using the same schedule as the oral placebo group.

Primary end points will be related to visual function and OCT measurements, but secondary outcome measures will be related to conversion to multiple sclerosis.

**CONCLUSION**

Prospective studies in adults such as the ONTT have provided important, useful data regarding the prognosis of optic neuritis with regards to conversion to MS. There are now several good retrospective studies in pediatric optic neuritis and the risk of MS, particularly those studying the role of an abnormal MRI at presentation. We are sorely in need of a prospective, multi-center study in children to supply data comparable to the adult ONTT for the pediatric age group.
<table>
<thead>
<tr>
<th>Study</th>
<th>No.</th>
<th>F:M (ratio)</th>
<th>Age (years)</th>
<th>Mean f/u (years)</th>
<th>Bilateral BS or BSeq</th>
<th>Unilateral (CIS)</th>
<th>Recurrent ON</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkin 1984</td>
<td>19</td>
<td>13:6 (2.2:1)</td>
<td>5.5-12 (8.0)</td>
<td>18 (0.5-30)</td>
<td>All*</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Riikonen 1988</td>
<td>21</td>
<td>16:5 (3.2:1)</td>
<td>4-14 (9.9)</td>
<td>6.7 (0.8-13)</td>
<td>13 (62%) BS vs Bseq*</td>
<td>8 (38%)</td>
<td>9 (all pts w/ MS developed a 2nd attack of ON within 1 year)</td>
</tr>
<tr>
<td>Kriss 1988</td>
<td>39</td>
<td>29:10 (2.9:1)</td>
<td>3-15 (8.6)</td>
<td>8.8 (0.25-29)</td>
<td>29 (74%) BS 4 Bseq</td>
<td>10 (26%)</td>
<td></td>
</tr>
<tr>
<td>Brady 1999</td>
<td>25</td>
<td>13:12 (1.1:1)</td>
<td>1.75-18 (9.4)</td>
<td>0.92 (0.04-4.7)</td>
<td>14^^^ (56%) (6/7 under 6 years, 85%) (8/18 over 7 years, 44%) B/L Simul: 11/14 B/L Recurrent: 3/14</td>
<td>11 (44%) (1/7 &lt;6 yrs, 15%) (10/18 &gt;7 yrs, 56%)</td>
<td>B/L Recurrent 3^^^</td>
</tr>
<tr>
<td>Lana-Peixoto 2001 BRAZIL</td>
<td>27</td>
<td>12:15 (1:1.25)</td>
<td>3-16 (10.9)</td>
<td>10 (37%) BS 2 Bseq16%</td>
<td>17 (63%)</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

* This is a follow-up study for patients with bilateral optic neuritis only.
^ Patient was originally classified at probable MS in 1959; upon further review, diagnosed with ADEM
© Defined bilateral as involvement of both eyes within one month or less between attacks
# excluded possible MS
+ Other diagnoses: Encephalitis (parotitis), ALL, encephalomyeloradiculitis after autoimmune reaction to sulphafurazole, post-vaccinal reaction, Leigh’s disease
^^ Other diagnoses: Encephalomyelitis (5), Meningitis (1), Pyramidal involvement (3)
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<th>Family History of MS/ON</th>
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<th>LP Abnormalities at time of ON</th>
<th>ADEM</th>
<th>MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>1^</td>
<td>1 (5%) Female, EP/L MS</td>
</tr>
<tr>
<td>3 (14%)</td>
<td>57% Performed in 14/21 Abnormal: 8/14 (57%) 2 w/ mono-symptomatic ON 5 w/ MS 1 w/ encephalo-myeloradiculitis</td>
<td>57-92% Performed in 12/21 --Abnl WBC in 12 (57%) WBC 6-76 (mean 14 cells/mm³) --OCB 2/4 at onset of ON**** --IgG 11/12 (92%) at onset --Viral Ab 2/4</td>
<td>5/9 (56%) children w/ MS had a URI or vaccine prior to ON 5 w/ s/s of disseminated dz at 1st attack, 2 prior to 1st attack</td>
<td>9 (43%) CDMS# 9/16 (56%) Subgroups 8/9 Female (7/8 with unilateral 2/13 with bilateral) 1/9 w/ Devic 7 (34%) possible MS 5 w/ other diagnoses*</td>
</tr>
<tr>
<td>N/A</td>
<td>N/A</td>
<td>47.6% Performed in 21/39 (10 abnl) --3 w/ modest WBC and protein --5 w/ WBC --2 w/ protein</td>
<td>46% w/ febrile prodome 9 (23%) other s/s during or within 6 weeks of onset of ON^^ Of these, 1/9 developed MS</td>
<td>6 (15%) Subgroups 2 w/ CDMS 4 probable MS (3 w/ b/l simult 3 w/ seq or unilateral) 5/30 without neuro s/s developed MS</td>
</tr>
<tr>
<td>N/A</td>
<td>13/23 (56.7%) Performed in 23/25 Brain Abnl: 12 SC Abnl: 1 B/L ON: 11 Uni ON: 2</td>
<td>9/21 (43%) Performed in 21/25 Abnl 9/21 ↓ prot 7/9 OCB none</td>
<td>8 patients w/ documented viral prodome B/L: 4 Unil: 4</td>
<td>4 (16%)## B/L 3</td>
</tr>
<tr>
<td>N/A</td>
<td>16.7% Performed in 6/27 Abnl: 1 (16.7%)</td>
<td>0% Performed in 12/27 All WNL</td>
<td>1 (4%) --Male, Unilateral</td>
<td></td>
</tr>
</tbody>
</table>

*** Defined bilateral simult as both eyes affected within 1 month of each other, and bilateral recurrent disease as 1 or both eyes affected more than once
## It is unclear whether these patients were known to have MS at the time of diagnosis. Conclusions about the risk of developing MS after ON cannot be drawn from this study.
* Weakly associated with developing MS (hazard ratio 2.99, p 0.071, 95% CI 0.91-9.86)
** Recent infection within 2 weeks before onset of ON decreased risk of developing MS (hazard ratio 0.24, p 0.060, 95% CI 0.05-1.06)
*** All 13 patients had abnormal brain MRI
**** Performed by agarose electrophoresis
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<th>Recurrent ON</th>
</tr>
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<tbody>
<tr>
<td>Morales 2000</td>
<td>15</td>
<td>9:6 (1.5:1)</td>
<td>4-15 (9.8)</td>
<td>1.5 years (17.5 months)</td>
<td>10 (67%) (BS)</td>
<td>5 (33%)</td>
<td>4</td>
</tr>
<tr>
<td>Lucchinetti 1997</td>
<td>94</td>
<td>58:36 (1.6:1)</td>
<td>2-16 (Median: 11)</td>
<td>22 (2.7-43.2)</td>
<td>54 (57%)</td>
<td>40 BS 14 Bseq</td>
<td>37 (39%)</td>
</tr>
<tr>
<td>Wijelto 2006</td>
<td>36</td>
<td>21:15 (1.6:1)</td>
<td>2.2-17.8 (12.2)</td>
<td>2.4 years (0.3-8.3)</td>
<td>42% (13/36=36%????)</td>
<td>58% (64%)</td>
<td>?3</td>
</tr>
</tbody>
</table>

* This is a follow-up study for patients with bilateral optic neuritis only.

^[^] Patient was originally classified at probable MS in 1959; upon further review, diagnosed with ADEM

^[^] Defined bilateral as involvement of both eyes within one month or less between attacks

^[#] excluded possible MS

^[+] Other diagnoses: Encephalitis (parotitis), ALL, encephalomyeloradiculitis after autoimmune reaction to sulphafurazole, post-vaccinal reaction, Leigh's disease

^[^^] Other diagnoses: Encephalomyelitis (5), Meningitis (1), Pyramidal involvement (3)
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<th>MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 (20%)</td>
<td>3/9</td>
<td>7/9 Mild pleocytosis 2 w/ +Lyme</td>
<td>10/15 w/ antecedent viral illness within 2 weeks of visual sx</td>
<td>4 (26%)</td>
</tr>
<tr>
<td>Not statistically significant. Details not reported.</td>
<td>N/A</td>
<td>47%</td>
<td>43 (46%) w/ neurologic signs and symptoms Subgroup 10 w/ myelitis 9 w/ seizures 9 w/ encephalopathy 8 w/ meningismus Infection**</td>
<td>15 (19%) Subgroups 8 Female, 7 Male 13/15 (87%) CDMS 4/13 w/ Devic Dz 12/15 w/ bilateral (5/12 BS, 7/12 Bseq) Devic subgroup 3/4 BS 1/4 Bseq 2/15 Unilateral 1/15 Recurrent ON 2/15 (13%) LSDM</td>
</tr>
<tr>
<td>6 (16.7%)</td>
<td>35 studied 54% brain abnl (17/35=49%?) 11 McDonald + 4 &gt;/=2 lesions 2 only 1 lesion</td>
<td>21 12/21 WBC&gt;6 2/12 also had Inc protein</td>
<td>1 diplopia 9 other neuro sx 10 viral prodome 2 immunization 11 Abnl exam Subgroups Without MS --3/22 =abnl exam --12/22=prodrome With MS --9/13 =abnl exam --7/13 prodrome NMO --0/1 abnl exam --0/1 prodome</td>
<td>13 (36)** 1 Devic</td>
</tr>
</tbody>
</table>

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**^[3]** Defined bilateral simult as both eyes affected within 1 month of each other, and bilateral recurrent disease as 1 or both eyes affected more than once

**^[4]** It is unclear whether these patients were known to have MS at the time of diagnosis. Conclusions about the risk of developing MS after ON cannot be drawn from this study.

* **^[5]** Weakly associated with developing MS (hazard ratio 2.99, p 0.071, 95% CI 0.91-9.86)

**^[6]** Recent infection within 2 weeks before onset of ON decreased risk of developing MS (hazard ratio 0.24, p 0.060, 95% CI 0.05-1.06)

*** **^[7]** All 13 patients had abnormal brain MRI

**** **^[8]** Performed by agarose electrophoresis
### ADDITIONAL STUDIES

<table>
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<tr>
<th>Study</th>
<th>No.</th>
<th>F:M (ratio)</th>
<th>Age (years)</th>
<th>Mean f/u (years)</th>
<th>Bilateral BS or BSeq</th>
<th>Unilateral (CIS)</th>
<th>Recurrent ON</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mikaeloff 2004</td>
<td>296</td>
<td>169:127 (1.3:1)</td>
<td>0.7-16 (9.9)</td>
<td>2.9 (0.5-14.9) Med 1.9</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Dale 2000</td>
<td>48</td>
<td>22:26 (0.85:1)</td>
<td>3-15 (8)</td>
<td>9</td>
<td>ADEM 0^</td>
<td>ADEM 0^</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADEM 13:15 (0.87:1)</td>
<td>ADEM 28 Mean 7.3 Med 5.5 Mode 3.5</td>
<td>ADEM 1-15.4 (5.78)</td>
<td>ADEM 5^</td>
<td>ADEM 0^</td>
<td>ADEM 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MDEM 3:4 (0.75:1)</td>
<td>MDEM 7 Mean 8 Med 7 Mode 4</td>
<td>MDEM 1.5-14.4 (5.3)</td>
<td>MDEM 3^</td>
<td>MDEM 0^</td>
<td>MDEM 2 w/ B/L recurrent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MS 6:7 (0.86:1)</td>
<td>MS 13 Mean 9.4 Med 11 Mode 10.3</td>
<td>MS 1.25-11 (5.3)</td>
<td>MS 1^</td>
<td>MS 3^</td>
<td>MS 5 (including UON and BON dz)</td>
</tr>
</tbody>
</table>

* MRI was performed in all patients, but stratified by type of lesion (suggestive of MS, suggestive of ADEM, subtentorial, thalamus, BG, ON, etc). MRI was suggestive of MS if there were well-limited multiple lesions with periventricular and/or subcortical locations.

^ In the ADEM group, 5 patients had bilateral optic neuritis as part of their initial presentation. In the MDEM group, 3 patients had bilateral optic neuritis as part of their initial presentation. One patient in the MDEM group had unilateral optic neuritis during a relapse but did not have visual symptoms at initial presentation. In the MS group, 4 patients presented with ON (3 unilateral, 1 bilateral); however, 9 of the 13 patients had optic neuritis (including bilateral, unilateral, and recurrent) at some point during their disease.
<table>
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<tr>
<th>Family History of MS/ON</th>
<th>Lesion on MRI excluding orbits at time of ON</th>
<th>LP Abnormalities at time of ON</th>
<th>ADEM</th>
<th>MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 (5%)</td>
<td>N/A*</td>
<td>Cells &gt;= 10: 118 (40%)</td>
<td>85/296 (29%)</td>
<td>168/296 (57%)</td>
</tr>
<tr>
<td></td>
<td>MRI suggestive of MS*: 96 patients</td>
<td>Protein &gt;= 0.5 71 (24%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Final dx of MS: 96</td>
<td>OCB 72 (24%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>48 (100%)</td>
<td>ADEM/MDEM 33 tested 75% w/ either pleocytosis or inc protein</td>
<td>31</td>
<td>13 (27%)</td>
</tr>
<tr>
<td>ADEM</td>
<td>ADEM/MDEM 32 available for review 91% had subcortical or deep white matter lesions 44% had PV lesions</td>
<td>Pleocytosis 64% Inc protein 60% OCB: 6/21 (29%)</td>
<td>ADEM/MDEM: 26 had a preceding illness in month before presentation</td>
<td></td>
</tr>
<tr>
<td>MDEM</td>
<td>MS 12 available for review 92% had subcortical or deep white matter lesions AND 92% had PV lesions</td>
<td>MS 12 tested 58% w/ either pleocytosis or inc protein Pleocytosis 5 42% Inc protein 4 33% OCB: 7/11 (64%) Repeat 9/11 (82%)</td>
<td>MS: 5 had a preceding illness in month before presentation</td>
<td></td>
</tr>
<tr>
<td>MS</td>
<td>15 (5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CME ANSWERS

1. False
2. True
3. False

REFERENCES