MS is primary demyelinating disease of the central nervous system.

MS is considered to be immune mediated, although actual development of MS will depend on many other factors, such as genetic, environmental and others, not yet been determined.
GENETICS

- The risk of developing MS in the general population is approximately 0.1%.
- The risk for a child with one parent who has MS is approximately 2%.
- The risk for a child with two parents who have MS is approximately 12.2%.
- The risk for a dizygotic twin and other siblings is approximately 5%.
- The risk for monozygotic twins is approximately 25%.
- The risk for second-degree and third-degree relatives is approximately 1%.

Onset age 20-45
F:M ratio 2-3:1

25,000 children in U.S.
200 people diagnosed each week
2,300,000 worldwide
All races but with different incidence rates
Preliminary Results of MS Prevalence Study
Estimate Nearly 1 Million Living with MS in the U.S.

October 26, 2017

In a study presented this week at ECTRIMS—the world’s largest MS research meeting—preliminary results from leading experts estimate nearly 1 million people are living with MS in the United States. This is more than twice the previously reported number, which was a result of a 1975 national study and subsequent updates. An important next step in confirming this prevalence number includes anticipated publication in a prominent medical journal.

People affected by MS, health care policy experts and researchers have long expressed the need for understanding how many people live with MS in the U.S. A scientifically sound and up to date prevalence estimate will allow us to better understand and address the needs of people with MS and accelerate our impact through advocacy and research. It can help answer such questions as the economic burden of MS on families and society, while ensuring the National MS Society is able to connect to and support all people affected by MS.

To address the gap in prevalence estimates, the National MS Society launched the MS Prevalence Initiative in 2014 with the goal of determining the best way to develop a scientifically sound and economically feasible estimate of the number of people in the U.S. who have MS. This initiative included leading experts in MS epidemiology, statistics and healthcare, who utilized administrative datasets from a variety of sources including Medicare, Medicaid, Veterans’ Health Administration, and private insurers.

More work is needed to understand all the factors that led to this increase, however the research team leading this study cites evidence that MS prevalence has increased.

Publication of the study is expected in 2018.

Click here for more background on the MS Prevalence Initiative. For more updates from ECTRIMS, click here.

- Inflammatory and neurodegenerative components (?
- Demyelination slows nerve conduction
- Axonal injury associated with permanent neurologic dysfunction
**VARIANTS OF MS**

- relapsing remitting
- secondary progressive
- primary progressive
- progressive-relapsing

**COMMON PRESENTATIONS OF RRMS**

- Optic neuritis
- Numbness, paresthesia, weakness
- Brainstem syndrome (e.g. INO, cerebellar findings, dysarthria)
RADIOLOGIC PROGRESSION OF LESIONS
GAD ENHANCING LESIONS

PERIVENTRICULAR LESIONS
(JUXTA)CORTICAL LESIONS

POSTERIOR FOSA LESIONS
SPINAL CORD LESIONS

DIAGNOSIS OF MULTIPLE SCLEROSIS

- Clinical diagnosis by McDonald criteria
- History
- Exam
- MRI
- CSF: oligoclonal bands, IgG index
- Screening labs
HISTORY OF DIAGNOSTIC MS CRITERIA

- Schumacher 1965
- Posner 1983

Dissemination in time and space remains sine qua non!
1 Clinical Attack

1 Lesion

11/7/2018
RADIOLOGICALLY ISOLATED SYNDROME

PRIMARY PROGRESSIVE MS

1 YEAR OF DISABILITY PROGRESSION INDEPENDENT OF CLINICAL RELAPSES

PLUS 2 OF THE FOLLOWING CRITERIA

1. T₂ HYPERINTENSE LESION (PERIVENTRICULAR, JUXTACORTICAL, OR POSTERIOR FOSSA)

2. SPINAL CORD LESIONS

PRESENCE OF CSF SPECIFIC OLIGOCOLONAL BANDS
Disease activity continues even in the absence of clinical symptoms

Axons are injured as well as myelin

Inflammation is more widespread than visualized on standard MRI

Conclusion: Start treatment early
FDA APPROVED TREATMENTS FOR MULTIPLE SCLEROSIS

- Betaseron 1993 (interferon beta-1b)
- Avonex 1996 (interferon beta-1a)
- Copaxone 1997 (glatiramer acetate)
- Novantrone 2000 (mitoxantrone)
- Rebif 2002 (interferon beta-1a)
- Tysabri 2006 (natalizumab)
- Extavia 2009 (interferon beta-1b)
- Gilenya 2010 (fingolimod)
- Aubagio 2012 (teriflunomide)
- Tecfidera 2013 (dimethyl fumarate)
- Plegridy 2014 (peginterferon beta-1a)
- Lemtrada 2014 (alemtuzumab)
- Glatopa 2015 (generic glatiramer acetate)
- Ocrevus 2017 (ocrelizumab)

FDA APPROVED DMT-S

**Injection:** interferon, copaxone,

**Oral meds:** gilenya, teczidera, aubagio

**Infusions:** tysabri, alemtuzumab, ocrelizumab mitoxantrone
DIFFERENT PHARMACOLOGIC STRATEGIES

1. Switching “bad” => “good” cells (GA)
2. Suppressing “bad” cells (DMF, teriflunomide, IFN-beta)
3. “Hiding” CNS from inflammatory cells (natalizumab, fingolimod)
4. Removing selective arm of immune system (alemtuzumab, ocrelizumab)

<table>
<thead>
<tr>
<th>Time</th>
<th>Preclinical</th>
<th>First Clinical Event</th>
<th>RRMS</th>
<th>SPMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of RRMS</td>
<td>Treatment after a first event</td>
<td>Clinical Threshold</td>
<td>RRMS</td>
<td>SPMS</td>
</tr>
<tr>
<td>Disability</td>
<td>Disability</td>
<td>Disability</td>
<td>Disability</td>
<td>Disability</td>
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</table>
SELECTED SIDE EFFECTS

- PML - tysabri, gilenya, tecfidera, aubagio, ocrelizumab (?)
- lymphopenia - gilenya, tecfidera
- thyroid disease, ITP, anti GBM disease - lemtrada
PML - PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

- “John Cunningham” virus - JCV
- ~ 55% population exposed to virus
- Normally inactive
- Reactivated in immunosuppressed subjects
- AMS, visual symptoms, hemiparesis
- HIV infection, rarely in other conditions lymphoproliferative disorders, transplant recipients
- JCV Ab titer monitoring

DMT-S AND PML

- Natalizumab risk factors:
  - anti-JCV antibody-positive status,
  - have received any prior immunosuppressant therapy of any duration at any time,
  - natalizumab tx. for ≥25 months.

The estimated incidence of PML in this subgroup of patients is 11.1/1000 (or one in 90) patients

- Gilenya risk factors: not known

- Tecfidera risk factors: prolong lymphopenia (<500)
ADDITIONAL UPDATES

- Siponimod had a robust positive effect on disability progression and other relevant outcomes in SPMS.

- Fingolimod showed significant reduction in relapses vs IFN beta 1a IM in pediatric population, and was the first FDA approved treatment in pediatric population.

Thank you!