Epidemiology of Multiple Sclerosis

(The Faroe islands story)
What is multiple sclerosis?

• “Multiple sclerosis is a chronic demyelinating, inflammatory and degenerative disorder of the central nervous system, and is the most common disabling nervous system disease among young adults” - (Pugliatti 2006)

• Etiology (or cause) is not known. Theories are:
  1. Autoimmune disease
  2. Infectious disease
Worldwide prevalence
Patterns in Multiple Sclerosis

- **Age**: Migration studies show that the disease is acquired after the age of 15
- **Sex**: The disease is more common on females
- **Race**: White people are more susceptible
- **Geography**: The further away from the equator, the higher the risk
- **Genetics**: A 35% chance of getting the disease if your monozygotic twin sibling has it.
Forming a theory about disease spread

- Genetics (monozygotic twins)
- Autoimmune disease and hygiene hypothesis (>15 age of susceptibility)
- Epstein-Barr virus and mononucleosis
- Faroe Islands (disease introduced by British troops in WW II)
Epstein-Barr Virus

- 50% of children get infected and do not develop any symptoms.
- If infected in adolescence, probably will develop infectious mononucleosis.
- Mononucleosis highly correlated with MS.
- More than 90% of adults have EBV.
- Infection occurs through saliva (kissing disease).
Faroe Islands

- **Background**: Atlantic islands, part of Denmark
- **WW II**: British troops occupied the island during 1941-1945
- **MS non-existent** prior to occupation
- **MS incidence rate** spikes 1941-1953
- **Today**: one of the highest incidence rates worldwide
Kurtzke’s theory

- Kurtzke studied for several decades the MS epidemic that occurred in the Faroe Islands.
- Kurtzke proposes that the disease is spread through an infective agent.
- PMSA: most infected are asymptomatic, and transmit the disease passively.
Kurtzke’s theory

- **CNMS**: a small proportion develop the clinical symptoms (i.e. MS).
- **Infectives** age: 11-28 (28 is the average disease onset age).
- **Exposure**: two years to become infective.
One Strain with childhood Immunity (Model Assumptions 1)

- Kutzke divides the population into three age groups:
  1. Group 0 with $\text{age} < 11$
  2. Group 1 with $11 < \text{age} < 27$
  3. Group 2 with $27 < \text{age} < 48$.

- Uniform age distribution is assumed.
One Strain with childhood Immunity (Model Assumptions 2)

- **Group 0** when exposed acquire life-long immunity.
- **Group 1** is the only group that has infective individuals.
- **Group 2** can become infected and develop MS.
- MS develops only in a small percentage of the infected individuals.
One Strain Disease Compartments

- **$S_0$**: Susceptible individuals between 0 and 11 years of age
- **$M_0$**: Immune individuals between 0 and 11 years of age
- **$S_1$**: Susceptible individuals between 11 and 28 years of age
- **$M_1$**: Immune individuals between 11 and 28 years of age
- **$E_1$**: Exposed individuals between 11 and 28 years of age
- **$I_1$**: Infective individuals between 11 and 28 years of age
- **$S_2$**: Susceptible individuals between 28 and 48 years of age
- **$M_2$**: Immune individuals between 28 and 48 years of age
- **$R_2$**: Infected individuals between 28 and 48 years of age
# Parameters

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
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<tbody>
<tr>
<td>$N_0$</td>
<td>Population size between 0 and 11 years of age</td>
</tr>
<tr>
<td>$N_1$</td>
<td>Population size between 11 and 28 years of age</td>
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<tr>
<td>$N_2$</td>
<td>Population size between 28 and 48 years of age</td>
</tr>
<tr>
<td>$\beta_1$</td>
<td>Rate of infection in between ages 0 and 11</td>
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<tr>
<td>$\beta_2$</td>
<td>Rate of infection in between ages 11 and 48</td>
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<tr>
<td>$\gamma$</td>
<td>Rate of change from exposed to infective</td>
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One Strain with childhood Immunity

Diagram:
- **S0** connects to **M0** with rate $\frac{B}{N_0}$ and from **M0** to **S0** with rate $\frac{\beta_1 I_1}{N_0}$.
- **S1** connects to **E1** with rate $\frac{\beta_2 I_1}{N_1}$ and from **E1** to **S1** with rate $\gamma$.
- **E1** connects to **I1** with rate $\frac{B}{N_1}$ and from **I1** to **E1** with rate $\frac{B}{N_1}$.
- **I1** connects to **M1** with rate $\frac{B}{N_1}$ and from **M1** to **I1** with rate $\frac{B}{N_1}$.
- **M1** connects to **M0** with rate $\frac{B}{N_0}$.
- **S3** connects to **R3** with rate $\frac{B}{N_2}$ and from **R3** to **S3** with rate $\frac{\beta_2 I_1}{N_2}$.
- **R3** connects to **M3** with rate $\frac{B}{N_2}$ and from **M3** to **R3** with rate $\frac{B}{N_2}$.
Faroe Islands MS incidence rate 41-93 (Kurtzke 2001)
Absence of immunity

Calendar Year (Starting 1940)

Percentage of population

I1 + R2
Ib
M
Immunity acquired in childhood

[Graph showing percentage of population over calendar years, starting from 1940.]
Problems with this model

• Poul Joensen reports in 2011 the following MS incidence rates from 1943-1952, in Faroe islands, with two peaks:

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<tbody>
<tr>
<td>Mean Age</td>
<td>32</td>
<td>27</td>
<td>26</td>
<td>34</td>
<td>33</td>
<td>37</td>
<td>38</td>
<td>30</td>
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<tr>
<td>Incidence Rate per 100,000</td>
<td>5.9</td>
<td>2.8</td>
<td>0.7</td>
<td>0.5</td>
<td>4.3</td>
<td>4.9</td>
<td>2.4</td>
<td>2.7</td>
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</table>
Poul Joensen MS Incidence Rates in Faroe Islands 1943-2007

Calendar Year (Starting 1940)
Two Strains Theory

• There are two strains of the transmissible agent.
• One strain has a higher infectivity than the other, and a shorter period of infection.
• Both strains induce cross immunity on infecting children (age < 11), and on recovery.
• There are only two age cohorts: (group 0 of age < 11, and group 1 of age > 11)
Two Strains Disease Compartments

\( S_0 \)  Susceptible individuals between 0 and 11 years of age

\( M_0 \)  Immune individuals between 0 and 11 years of age

\( S_1 \)  Susceptible individuals older than 11 years of age

\( M_1 \)  Immune individuals older than 11 years of age

\( E_{11} \)  Strain 1 exposed individuals older than 11 years of age

\( I_{11} \)  Strain 1 infective individuals older than 11 years of age

\( E_{12} \)  Strain 2 exposed individuals older than 11 years of age

\( I_{12} \)  Strain 2 infective individuals older than 11 years of age

\( R_2 \)  Recovered individuals older than 11 years of age
Two Strains Parameters

$N_0$  Population size between 0 and 11 years of age

$N_1$  Population size between 11 and 48 years of age

$N$    Population size between 0 and 48 years of age

$\beta_{11}$  Rate of infection with strain 1 for age < 11

$\beta_{21}$  Rate of infection with strain 1 for age > 11

$\gamma_1$  Rate of change from strain 1 exposed to strain 1 infective

$\beta_{12}$  Rate of infection with strain 2 for age < 11

$\beta_{22}$  Rate of infection with strain 2 for age > 11

$\gamma_2$  Rate of change from strain 2 exposed to strain 2 infective
Two Strains Parameters

$\alpha_1$ Rate of recovery from infection with strain 1

$\alpha_2$ Rate of recovery from infection with strain 2

$B$ Birth Rate
Two Strains with Cross Immunity
Infected and at risk of developing MS

[Graph showing the percentage of population infected over calendar years starting from 1940, with lines for different categories labeled I11, I12, and I11+I12.]
All compartments

Calendar Year (Starting 1940)
Infected and at risk of developing MS (The future)
Infected and at risk of developing MS (The future)
Discussion

• The two strain model does capture the general features of the disease:
  1. The sharp initial increase (1943-1953)
  2. The sharp decline to small values (1953-1983)
  3. The second peak
Future Work

• Study the age structure of incidence rates offered by the two strain hypothesis
• Try to fit the model to other available data in the literature
References

• Multiple sclerosis in the Faroe Islands: an epitome (Kurtzke and Heltberg-2001)
• Multiple sclerosis: variation of incidence of onset over time in the Faroe Islands (Poel Joensen-2011)
• Environmental Risk Factors for Multiple Sclerosis Part I: The Role of Infection (Ascherio and Munger-2007)