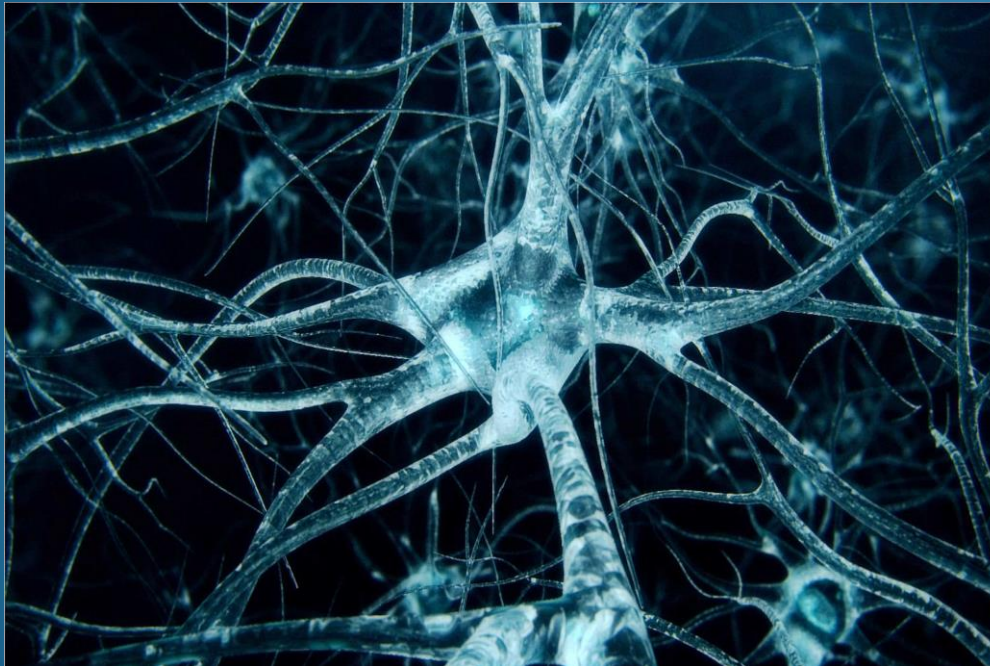


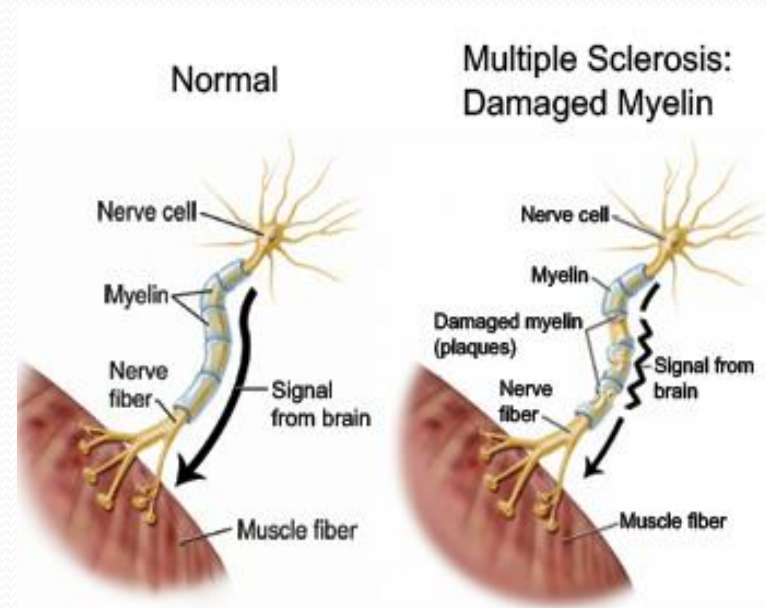
# Analysis of CSF in the diagnosis of Multiple Sclerosis

Kirsty Mc Loughlin  
05/11/15



# Multiple Sclerosis

- ❖ MS is a chronic disease of the central nervous system.
- ❖ Progressive deterioration of various functions of CNS.
- ❖ MS refers to the scars(plaques/lesions) which form in the white matter of the brain over time.
- ❖ Demyelinating disease
  - Myelin sheath around the axons of nerve cells becomes damaged
  - Re-myelination by oligodendrocytes decreases progressively
- ❖ Damage disrupts cell to cell communication resulting in various neurological symptoms including:
  - ❖ physical, mental and sometimes psychiatric problems



# Multiple Sclerosis

- ❖ MS can occur in isolated attacks(relapsing forms) or progressive forms.
- ❖ Relapsing forms- acute attack, disappearing symptoms, some permanent neurological damage.
- ❖ Progressive forms- Symptoms worsen over a long period of time as opposed to acute attacks
- ❖ Onset 20-40yrs.
- ❖ Twice as common in females.
- ❖ Effects 2-2.5million people globally. Apprx 6000 in Ireland.

# MS aetiology

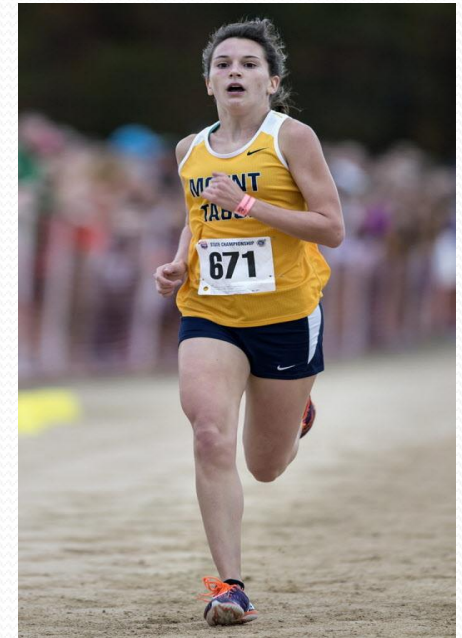
- ❖ Cause is unknown, underlying mechanism- autoimmune destruction of myelin & failure/loss of oligodendrocytes.
- ❖ Some proposed causes include the interaction between an individuals genetics, environmental factors and infections.
- ❖ No known cure
- ❖ Treatments attempt to improve function after an attack and seek to prevent further attacks.
- ❖ However medications are poorly tolerated, adverse side affects occur:
  - ❖ Tachycardia
  - ❖ Fatigue
  - ❖ Low grade fever
  - ❖ chills

# Signs & Symptoms

❖ Almost any neurological sign or symptom can be a feature of MS.

❖ Some symptoms include:

- Loss of sensitivity
- Tingling, pins and needles, numbness
- Muscle weakness/spasms
- Very pronounced reflexes
- Difficulties with coordination and balance
- Difficulties with speech or swallowing
- Visual problems
- Lehermittes sign- an electrical sensation that runs down the back when bending the neck.
- Uhthoffs phenomenon- worsening of symptoms due to exposure to higher than usual temperatures.



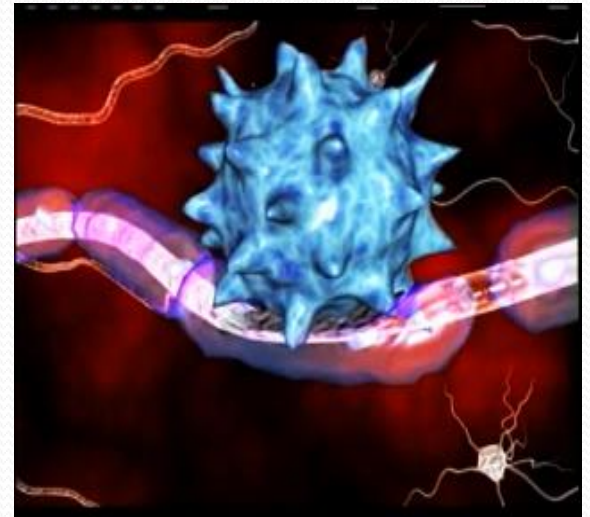
# Three main characteristics of MS

1. Inflammation
2. Destruction of myelin sheath
3. Formation of lesions in white matter



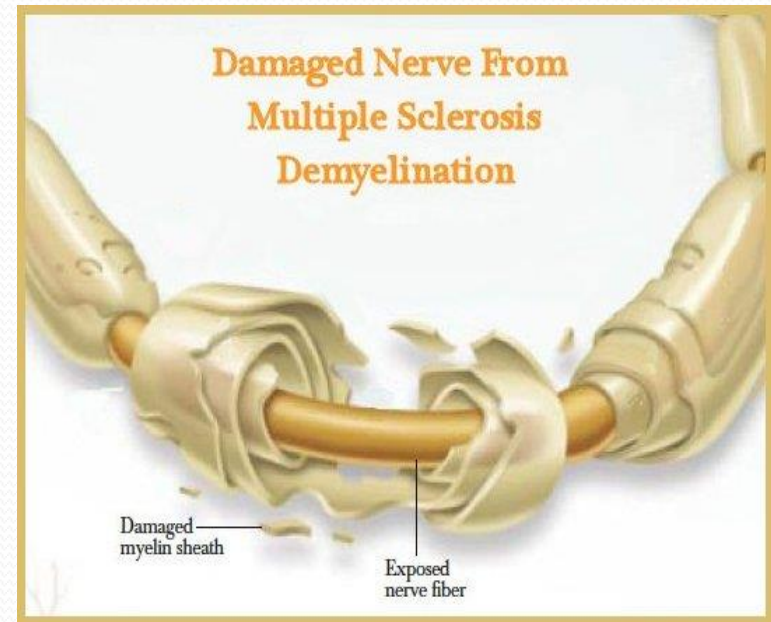
# Inflammation

- **The blood brain barrier-** a capillary system, prevents entry of T-cells into the CNS. It may become permeable to these types of cells secondary to an infection by a virus or bacteria.
- T-cells gain entry to the brain via disruptions in the blood brain barrier.
- Recognises myelin as foreign and attacks it.
- Attack of myelin starts an inflammatory process
- Cytokines and antibodies(IgG) are produced
- Other immune cells are recruited to the site
- Further breakdown of the blood brain barrier, progression of disease.



# Destruction of the Myelin sheath

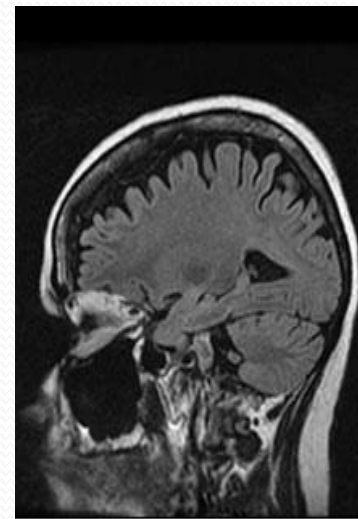
- Oligodendrocytes are the cells responsible for creating and maintaining the fatty layer known as the myelin sheath.
- ODs are targets of immune attack in MS, gradual loss.
- Thinning/complete loss of myelin sheath and as the disease progresses the breakdown of the axons of neurons.
- Reduced remyelination & repeated attack means a scar like plaque is built.





# Formation of Lesions

- The lesions most commonly effect the cells of the white matter.
- optic nerve, brain stem, spinal cord, basal ganglia.
- White matter cells carry signals between grey matter areas- where processing is done.
- The rest of the body, the peripheral nervous system is rarely effected.



Healthy brain



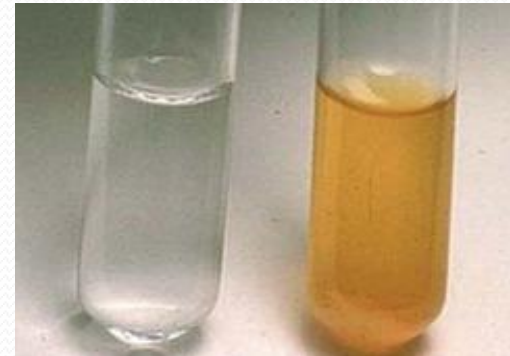
Brain with damage (lesions or plaques) caused by MS

# Diagnosis of MS

- Typically diagnosed based on the presenting signs and symptoms with supporting medical imaging and laboratory testing.
- Most commonly used diagnostics tools:
  - Neuroimaging- MRI to detect lesions in CNS
  - Evoked potentials- is an electrical potential recorded from the nervous system following presentation of a stimulusAnalysis of
  - CSF analysis for the presence of Oligoclonal bands

# CSF/Serum analysis

- CSF analysis for the diagnosis of MS is considered the gold standard with a sensitivity and specificity of >95%
- A paired CSF and serum sample are required.
- Must be collected within two weeks of each other.
- Half life of IgG in serum- 23 days.
- We are looking for the presence/absence of protein bands in the CSF/serum.



# CSF Isoelectric focusing

- CSF and serum samples are ran simultaneously by means of isoelectric focusing.
- It is the most sensitive method for the detection of OBS in CSF/serum.
- Principle:
  - The separation of proteins in paired patient serum and CSF using agarose gel electrophoresis followed by passive transfer onto a nitrocellulose membrane. The separated IgG's are then detected directly by horseradish peroxidase labelled anti-human antibodies.
- The patterns on the gel are then visualised and interpreted.

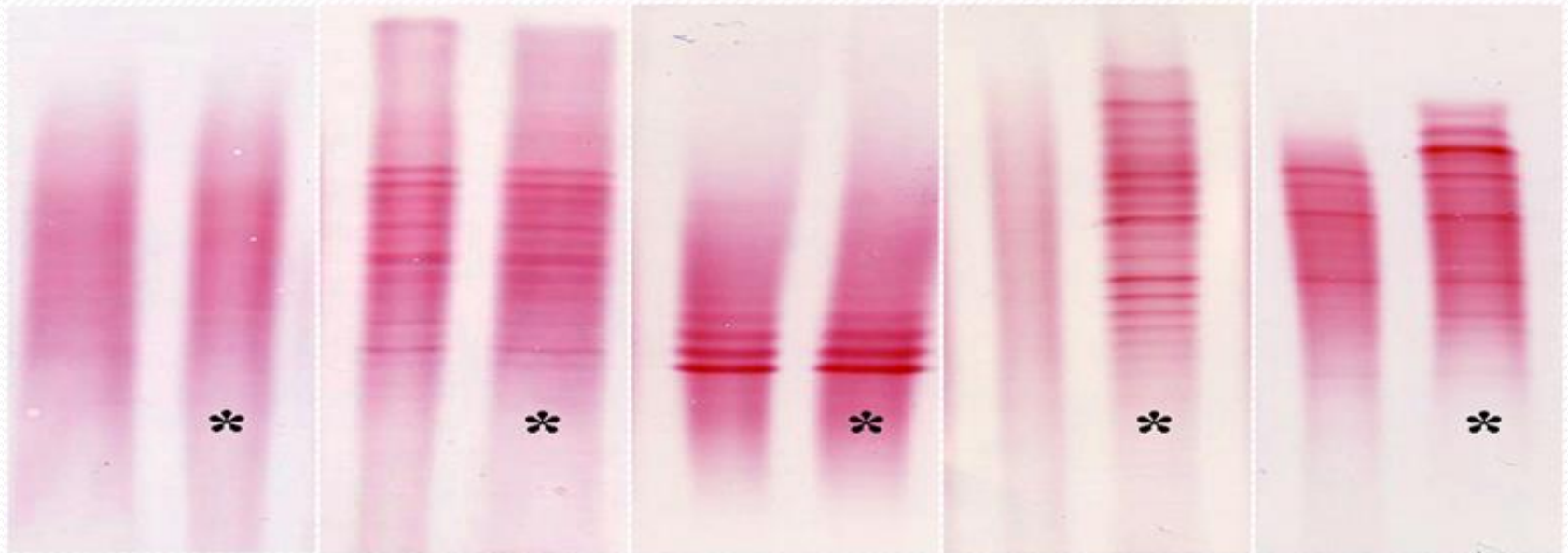
# Oligoclonal IgG

- Once T-cells gain entry to CNS, become auto-reactive or begin to secrete cytokines.
- Cytokines and other immune cells including B-cells are recruited to the site of inflammation.
- Intrathecal oligoclonal IgG is then produced by B-cells.
- When analysing CSF in the lab, intrathecally produced IgG is the protein of interest.
- OBS can be produced in the CSF in many other disease states.
- It is the pattern of OBS in comparison with serum OBS which determines a MS diagnosis.

# OBS interpretation

- Five Patterns

## Oligoclonal Band pattern



**Pattern:** No bands

**Normal**

**Pattern:** Identical pattern

**Infection/inflammation**

**Pattern:** Identical pattern

**Monoclonal protein**

**Pattern:** CSF pattern.

**Seen MS**

**Pattern:** extra CSF bands.

**Also seen in MS**





# Thanks Girls....

- Questions?