

# Multiple Sclerosis

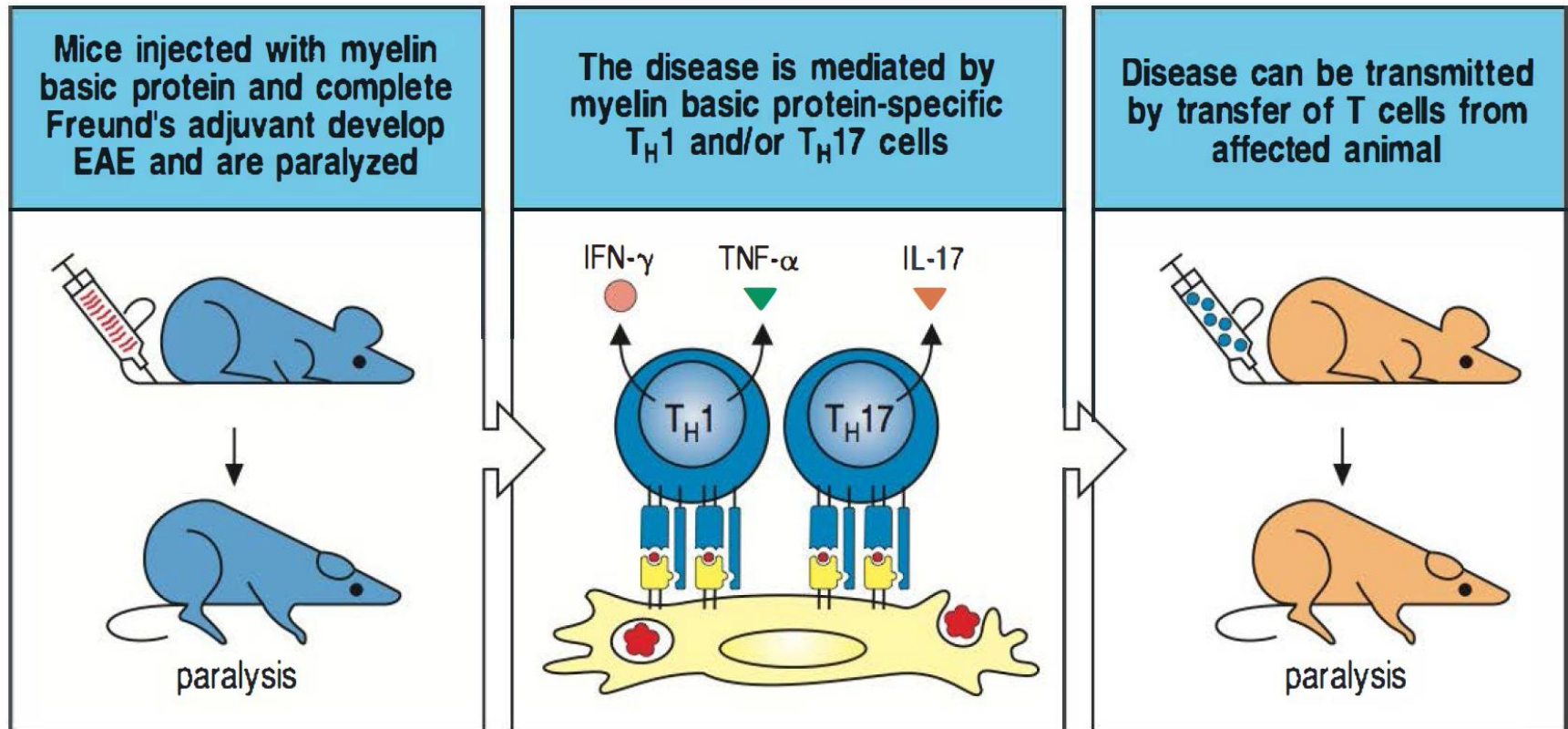
## Case Study

# Multiple sclerosis

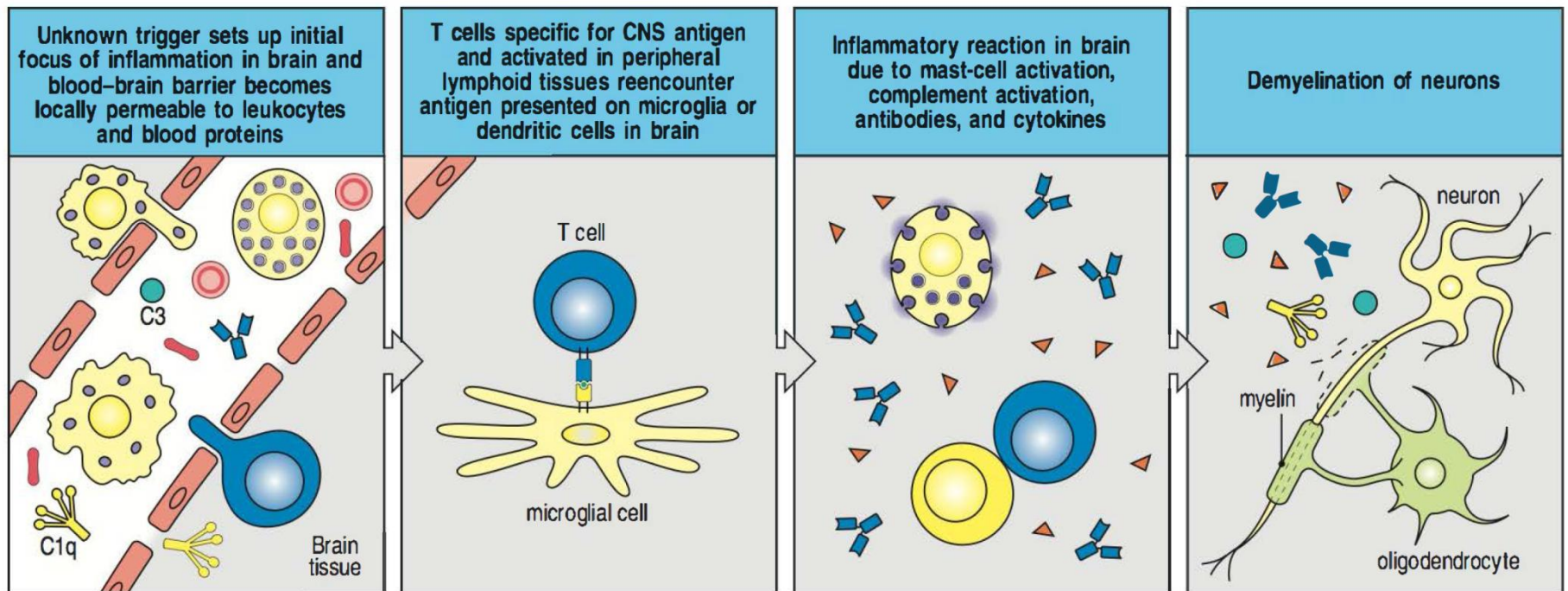
Type IV T cell-mediated autoimmune disease.

Th1 cells attacking Myelin Basic Protein (MBP) in CNS

# Experimental Autoimmune Encephalomyelitis (EAE)



# Multiple Sclerosis mode of action



# Case of Vivie Warren

29 year-old Oboe player

Sudden loss of vision in one eye

Family history of MS, brain MRI ordered

Lesions in white matter seen, Gadolinium-enhanced MRI ordered

Short IV corticosteroid therapy given, vision restored

3 years later, weakness on facial muscles on one side, lumbar puncture and PEP

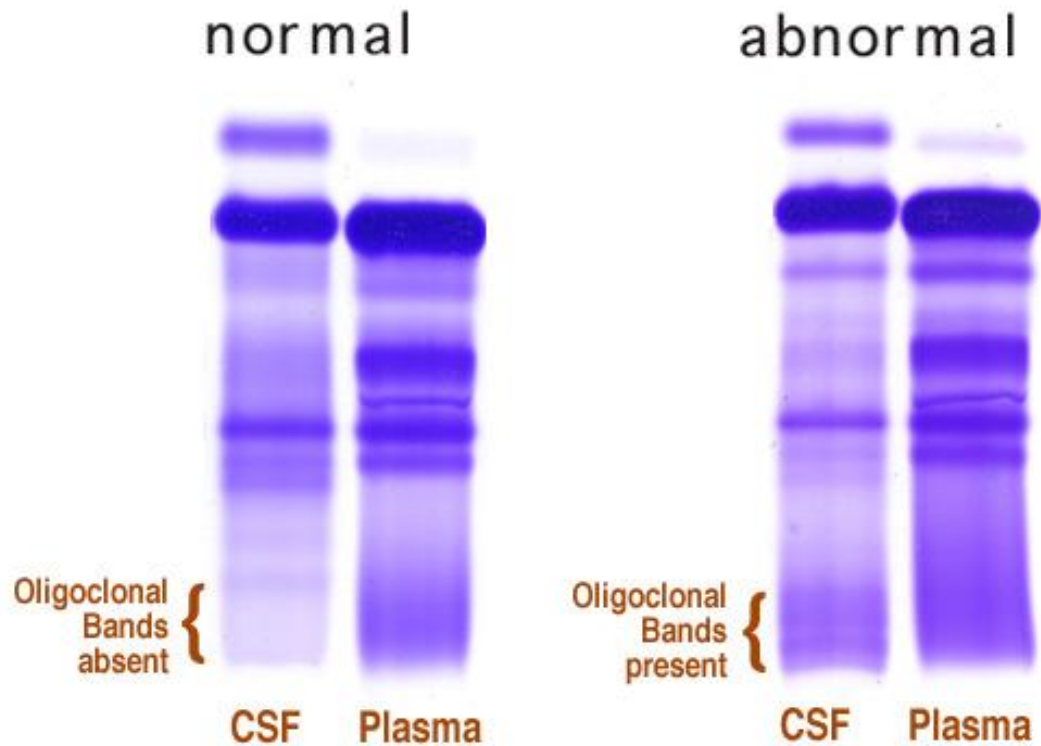
Lymphocyte infiltrate in CSF, high IgG content, PEP reveals clonal expansion of B cells in CSF. Steroids plus weekly injections of IFN- $\beta$  were administered.

3 years later, weakness in left leg and hand. Nystagmus and Ataxia and slurring.

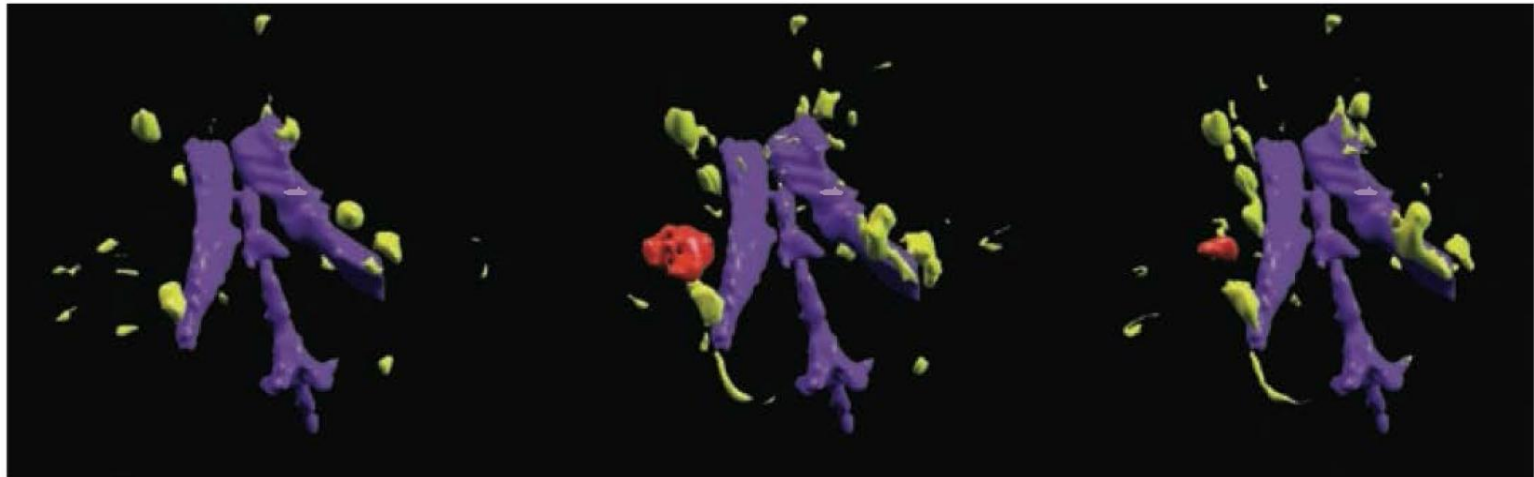
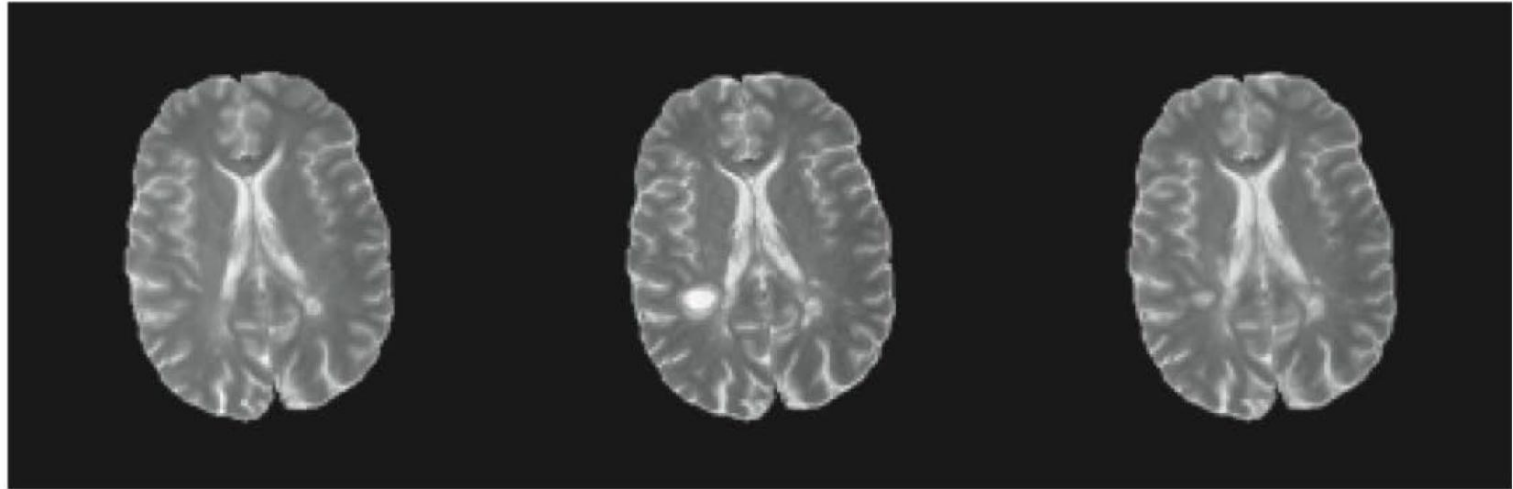
Placed on corticosteroid and cyclophosphamide injections. (Aggressive therapy)

# Protein Electrophoresis and MS diagnosis

## Oligoclonal Bands in CSF



# MRI in MS diagnosis



How do you explain Oligoclonal bands in PEP?

Limited number of B cells clone breaking BB barrier into CNS receiving T cell help.

How do corticosteroids, cyclophosphamide, and IFN- $\beta$  work?

Corticosteroids and Cyclophosphamide (Powerful cytotoxic drug) inhibit T cell proliferation= less pro-inflammatory cytokines. IFN- $\beta$  mechanism unknown.

A trial was proposed to treat MS with IFN- $\gamma$ ? Predictions?

Trial done. Patients got dramatically worse.

What is the rationale behind feeding MBP to mice to prevent EAE?

Peripheral immune response is usually suppressed to oral antigens. Lack of co-stimulation in GALT, Development of Tregs inhibiting Th1 response.



Can we induce EAE in CD28 KO and CTLA-4 KO mice?

CD28 KO = NO

CTLA-4 KO= Yes (Worse disease course than WT)