

# Homework 5: Differential Diagnosis of Multiple Sclerosis

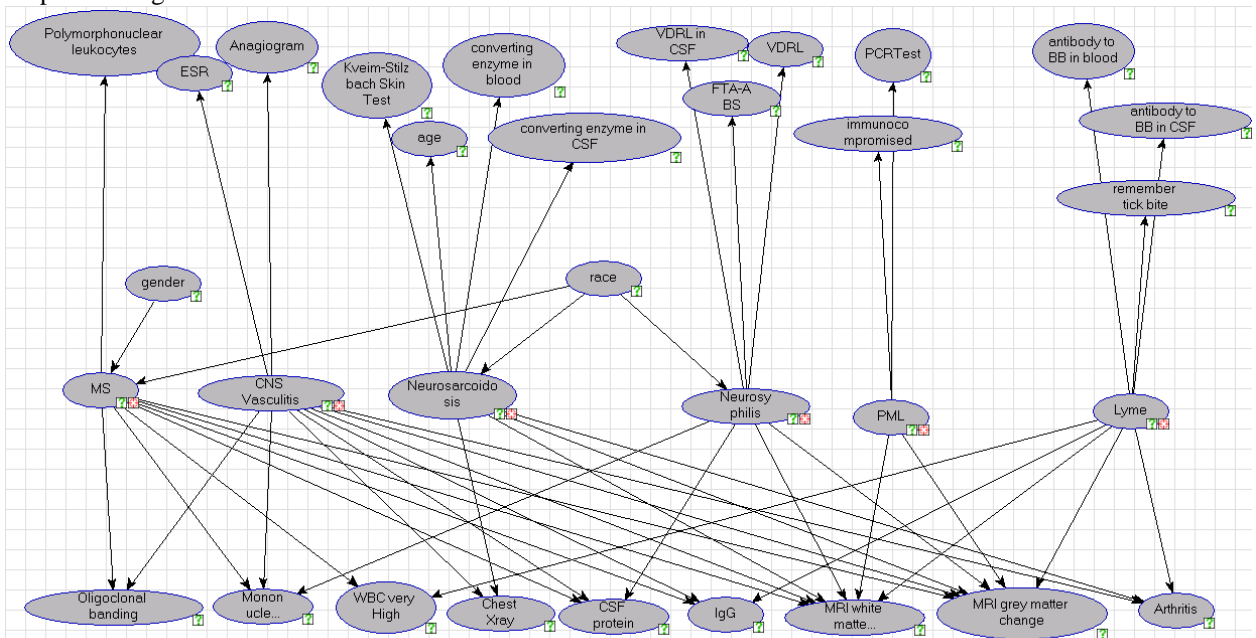
## General comments:

All of the KBs worked fairly well with few bugs. I generally gave almost full credit for the problem set to everyone, taking off a small amount of credit for odd belief network structures or missing influences. Good job!

## Pictures of the knowledge bases.

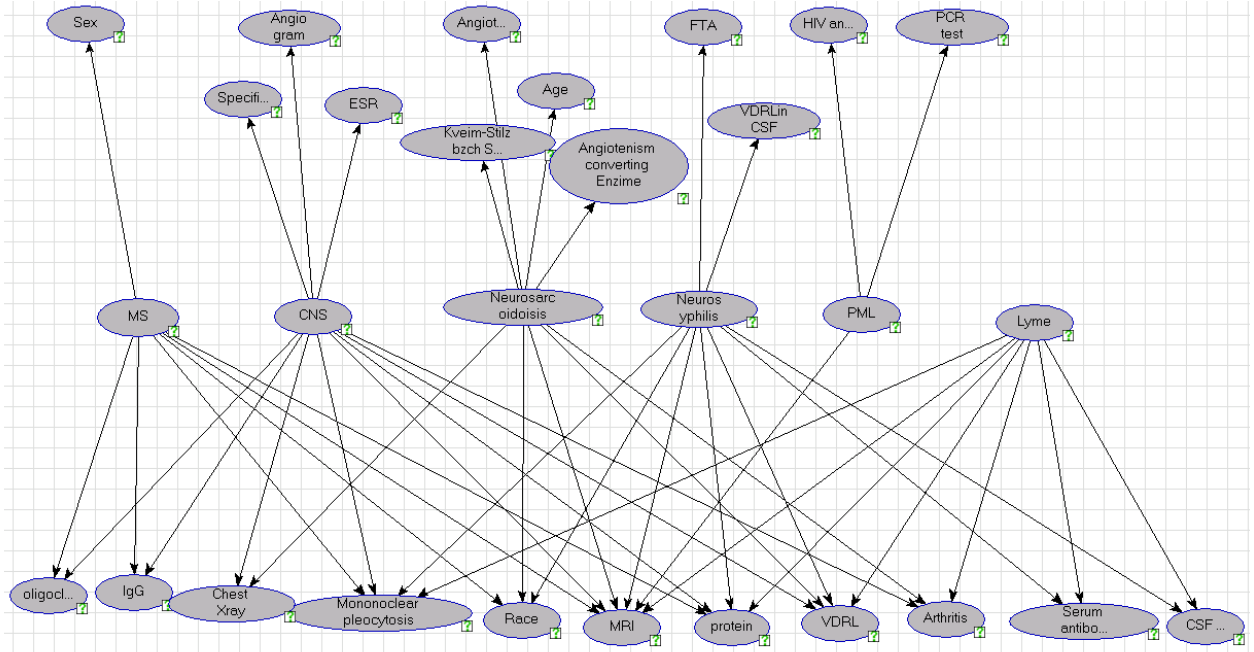
Liang:

Prepared using GeNIe.



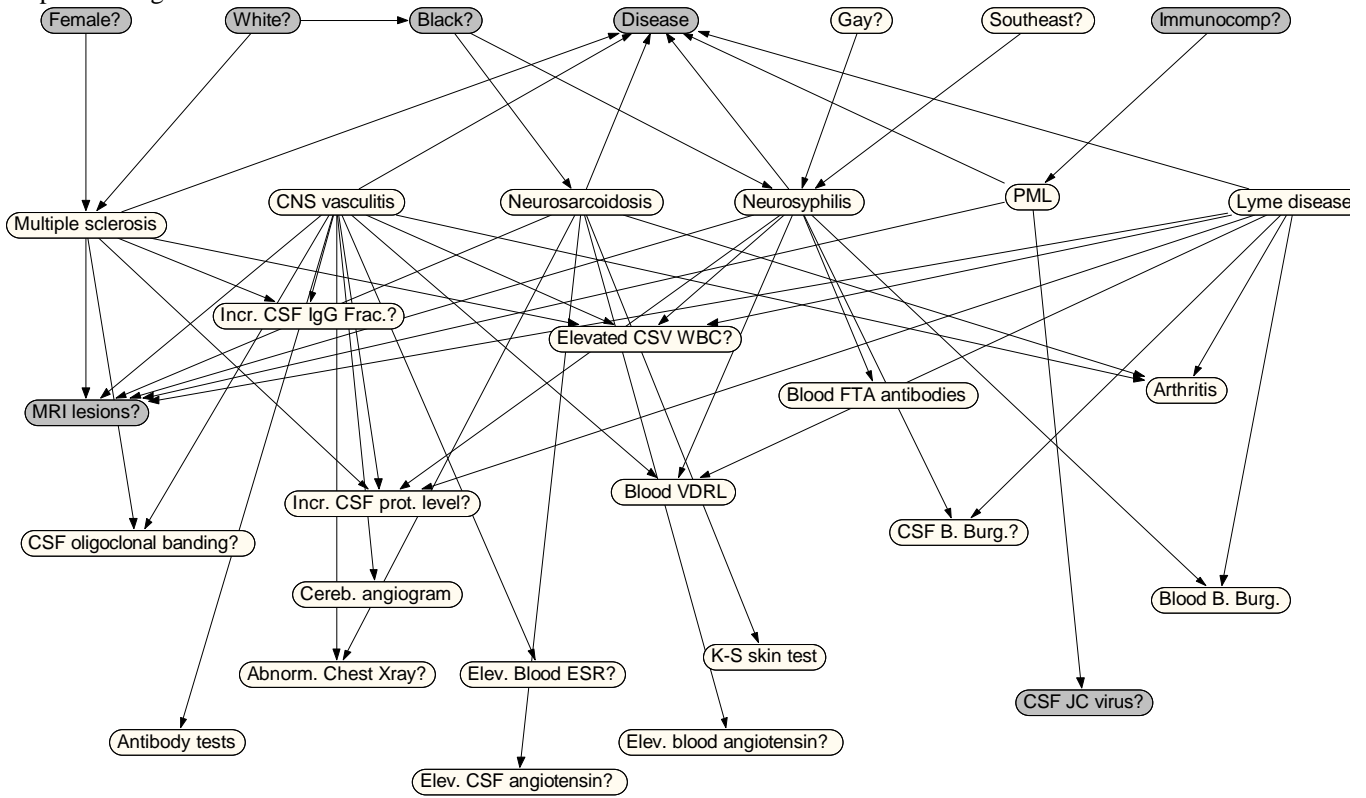
Maria:

Prepared using GeNIe.



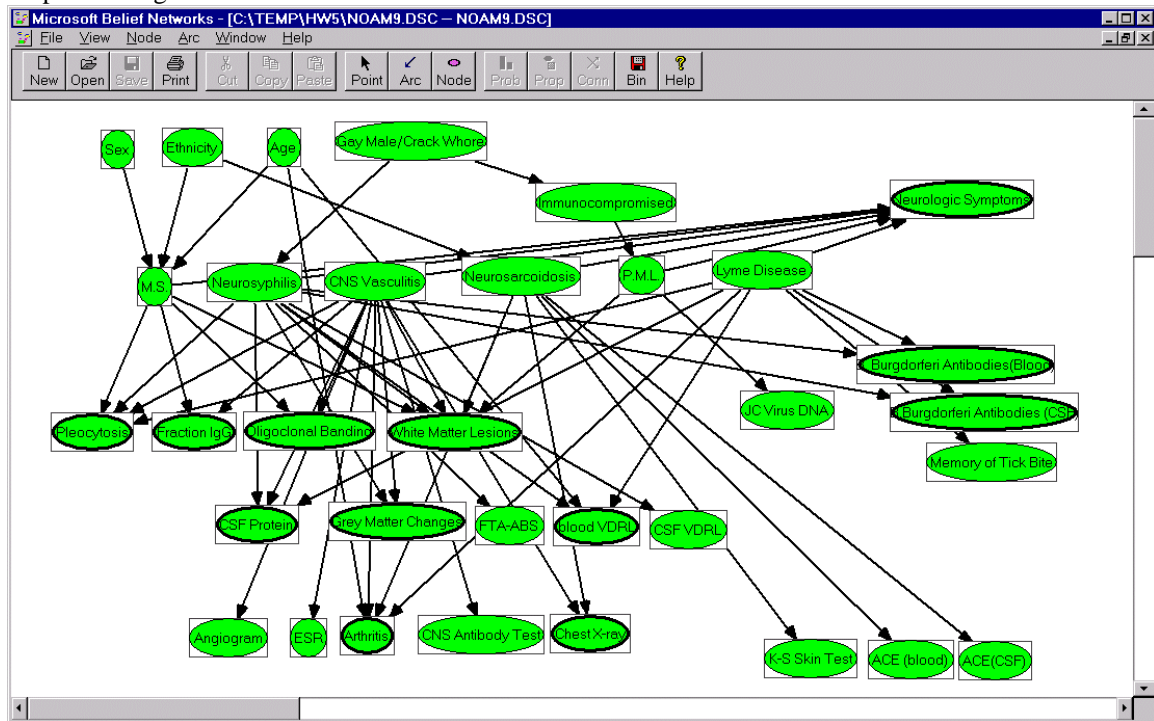
Mark:

Prepared using Netica.



## Noam:

Prepared using MSBN.



## Peot:

Prepared using DXpress. Here is a brief description of some of the features of this KB that may be different from your own.

1. The leak probability for *arthritis* is conditioned on *age* (Noam modeled this effect). This is important: If a young woman has arthritis, you would suspect that it is caused by Lyme or an autoimmune disease. If an elderly woman has arthritis, you might not pursue other diseases because it is very likely that the arthritis is a function of her age.

Example:

$$P\{\text{Lyme or Autoimmune} | \text{Arthritis} = \text{Positive}, \text{Sex} = \text{Female}, \text{Age} = 20\} = 0.30$$

$$P\{\text{Lyme or Autoimmune} | \text{Arthritis} = \text{Positive}, \text{Sex} = \text{Female}, \text{Age} = 70\} = 0.02$$

I modeled extreme age as a cause of arthritis in a noisy-or node.

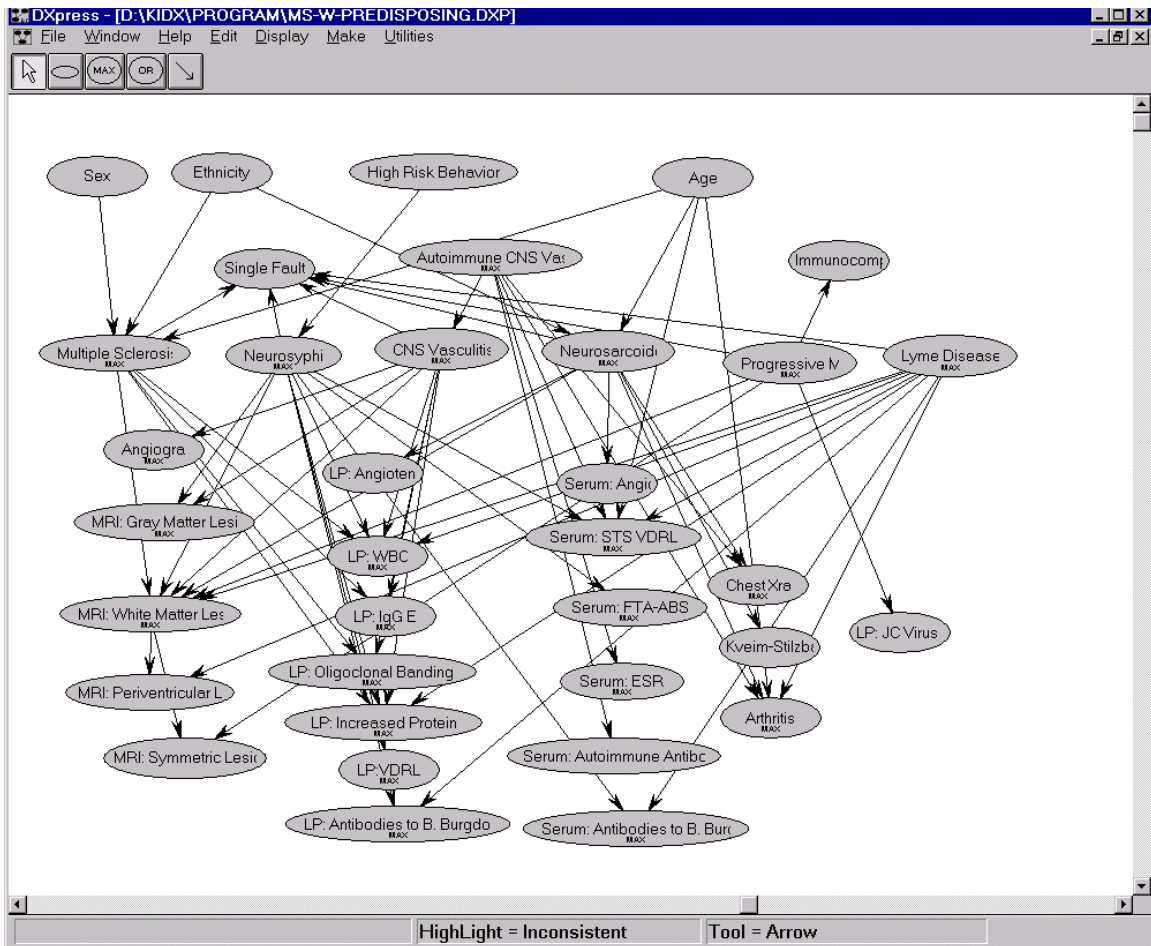
2. CNS vasculitis is split into two "classes." *CNS Vasculitis* represents vasculitis cases that are not caused by an autoimmune disorder. *Autoimmune CNS Vasculitis* is a kind of *CNS Vasculitis*. If *Autoimmune CNS Vasculitis* is true, then *CNS Vasculitis* is true with probability 1. This allows *Autoimmune CNS Vasculitis* to "inherit" the symptoms of *CNS Vasculitis*.
3. If someone is manifesting neurological symptoms commensurate with MS, it is very likely that they have one of the diseases listed in the homework. Since all of these diseases are rare, it is very unlikely that a patient will have more than one of them at the same time. I enforced this single fault condition using a **single fault** node that is true if and only if exactly one disease is present. The Peot/Single Fault results reported later in this report are compiled with *single fault* set to true. The Peot/Multiple Fault results are compiled with *single fault* unobserved. Noam and Mark used similar structures to force a higher prior probability distribution and to force additional mutual exclusion between diseases.
4. I boosted all of my prior probabilities to reflect the fact that it is more likely that the patient will have one of the diseases if they exhibit neurological symptoms. The priors are boosted in Noam's KB using

a noisy-or node "neurological symptoms" that has a link probability of 0.1 for each disease and a leak probability that is 0.01. This node boosts the prior probabilities by 10-100 times and forces the diseases to be almost mutually exclusive. Mark uses an "or" node named *diseases*. When this is true, at least one of the five diseases must be present.

One of the results of boosting the prior probabilities in my knowledge base is that multiple faults are much more likely. This is a bit of a bug: when single fault is turned off, the "explaining away" effect of the noisy-or is insufficient to eliminate diseases that compete with the primary disease.

5. The node *High Risk Behavior* is used to condition neurosyphilis so that I would not have to derive a complicated probability distribution that captured the effect of drug use, race, sexual preference, etc, on the incidence of venereal disease.
6. I used several noisy-max nodes in the knowledge base (same as noisy-or, except you can have more than two states). The nodes with noisy-max distributions are *LP: WBC*, and *LP: Oligoclonal Banding*. If we use a noisy-max node, we need to define a total order on the states: the noisy-max node takes the "maximum" of the effect caused by each disease that is present. For *LP: WBC*, this total order is ( $< 5$  cells /  $\mu$ L, 5-75 cells /  $\mu$ L, 75+ cells /  $\mu$ L) and for *LP: Oligoclonal Banding* the total order is (no bands, 1 band, 2+ bands).

If one disease causes a WBC of 80 and another causes a WBC of 30, the noisy-max effect selects the maximum (80) as the number of cells in the WBC count.



7. The hardest node to define in the entire system is the prior probability of multiple sclerosis given age, ethnicity, and sex. In retrospect, I should compute the probabilities in a spreadsheet (using facts such as "the incidence rate for women is twice that of men") and use these probabilities in a full conditional probability table. I modeled multiple sclerosis using a noisy-or node. The link probability for MS given Age is zero for the elderly and is slightly increased for people close to 35 years of age. The link probability for MS given Race is zero for African Americans and Asian Americans and is higher for Caucasians. The link probability for MS given Sex is 0.015 for women and zero for men. The problem with this approach: the prior probability of MS for women should be roughly twice that of men for all combinations of the other factors. This is not possible to engineer exactly using a Noisy-Or.

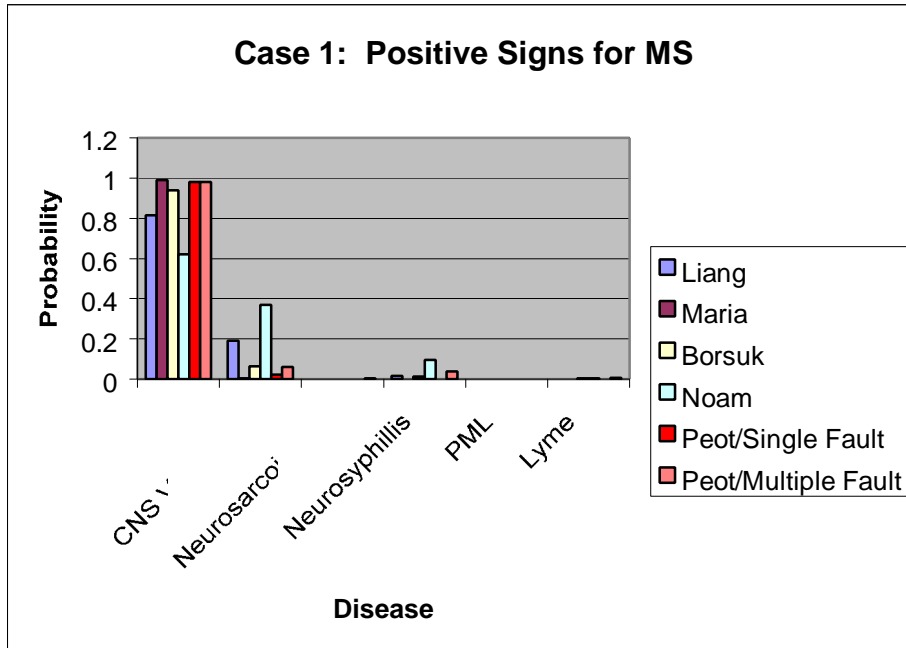
## Features Included in each of the Knowledge Bases

Features	Liang	Maria	Mark	Noam	Peot
<b>Miscellaneous</b>					
Mutual exclusion node			✓	✓	✓
Used nonzero leak terms		✓	✓	✓	✓
Dependence of arthritis leak term on age.				✓	✓
<b>Multiple Sclerosis</b>					
History: Twice as common in women	✓	Reversed	✓	✓	✓
History: Dependence on race	✓	Reversed	Black and white not mutually exclusive	✓	✓
History: Dependence on age		Reversed		✓	✓
CSF: Increased WBC in CSF	Two nodes	Multiple states	Binary	Multiple states	Multiple states
CSF: IgG in CSF	✓	✓	✓	✓	✓
CSF: Mild increase in protein level	✓	✓	✓	✓	✓
CSF: Oligoclonal banding	✓	✓	✓	✓	✓
MRI: White matter (log odds of 12 to 1)	✓	Non-specific	Non-specific	✓	✓
<b>Neurosyphilis</b>					
History: Sexual preference			✓	✓	"High Risk Behavior"
History: Gender				✓	
History: Race	✓	Reversed	✓		
History: Southeast			✓		
History: Crack cocaine				✓	"High Risk Behavior"
Serum: VDRL	✓	✓	✓	✓	✓
Serum: VDRL dependence on age				✓	✓
Serum: VDRL dependence on autoimmune			Modelled via CNS vasculitis		✓
Serum: VDRL dependence on Lyme Disease	✓	✓	✓	✓	✓
Serum: FTA-ABS	✓	✓	✓	✓	✓
CSF: Increased protein	✓	✓	✓	✓	✓
CSF: VDRL	✓	✓	✓	✓	✓
MRI: Gray matter changes	✓		Non-	✓	✓

			specific		
MRI: White matter changes	✓	Gray and white are mutually exclusive	Non-specific	✓	✓
<b>CNS Vasculitis</b>					
Misc: Distinction between autoimmune and nonspecific forms of the disease.		In write up, but not net.			✓
CSF: Increased protein	✓	✓	✓	✓	✓
CSF: Increased WBC	✓	✓	✓	✓	✓
CSF: Oligoclonal banding	✓	✓	✓	✓	✓
CSF: Increased IgG	✓	✓		✓	✓
Angiogram: Positive for vasculitis	✓	✓		✓	✓
MRI: Changes		Gray and white are mutually exclusive	Non-specific		
MRI: Gray matter	✓			✓	✓
MRI: White matter	✓			✓	✓
Serum: ESR	✓	✓	✓	✓	Via autoimmune node
History: Arthritis	✓	✓	✓	✓	Via autoimmune node
Chest X ray	✓	✓	✓	✓	Via autoimmune node
Serum: Autoimmune Antibodies		✓	✓	✓	Via autoimmune node
<b>Neurosarcoidosis</b>					
History: Racial dependence	✓	✓	✓	✓	✓
History: Age dependence		Reversed			✓
MRI: White matter	✓	✓	Non-specific	✓	✓
Chest X ray	✓	✓	✓	✓	✓
Misc: Kveim-Stilzbach skin test	✓	✓	✓	✓	✓
Serum: Elevated ACE	✓	✓	✓	✓	✓
CSF: Elevated ACE	✓	✓	✓	✓	✓
History: Arthritis	✓	✓	✓	✓	✓
<b>Progressive Multifocal Leukoencephalopathy</b>					
History: Immunocompromised	✓	✓	✓	✓	✓
MRI: White matter lesions	✓	✓	Non-specific	✓	✓
MRI: Lesions are symmetric					✓
<b>Lyme Disease</b>					
History: Memory of a tick bite	✓			✓	
History: Arthritis	✓	✓	✓	✓	✓
CSF: Increased protein		✓	✓	✓	✓
CSF: Highly elevated WBC	Two nodes:	Numeric WBC	Binary WBC	Numeric WBC	Numeric WBC

	one for high counts, one for increase	node	node	node	node
CSF: Antibodies to <i>B. Burgdorferi</i>	✓	✓	✓	✓	✓
CSF: False positive for <i>B. Burgdorferi</i> with syphilis		✓	✓	✓	✓
Serum: Antibodies to <i>B. Burgdorferi</i>	✓	✓	✓	✓	✓
Serum: False positive for <i>B. Burgdorferi</i> with syphilis		✓	✓	✓	✓
MRI: White matter changes	✓	✓	Non-specific	✓	✓
MRI: Ventricular changes					✓

## Inference Results for Several Cases



### Case 1: Positive signs for MS. No other symptoms.

Patient: caucasian female

Lumbar puncture:

Mononuclear pleocytosis: 20/uL

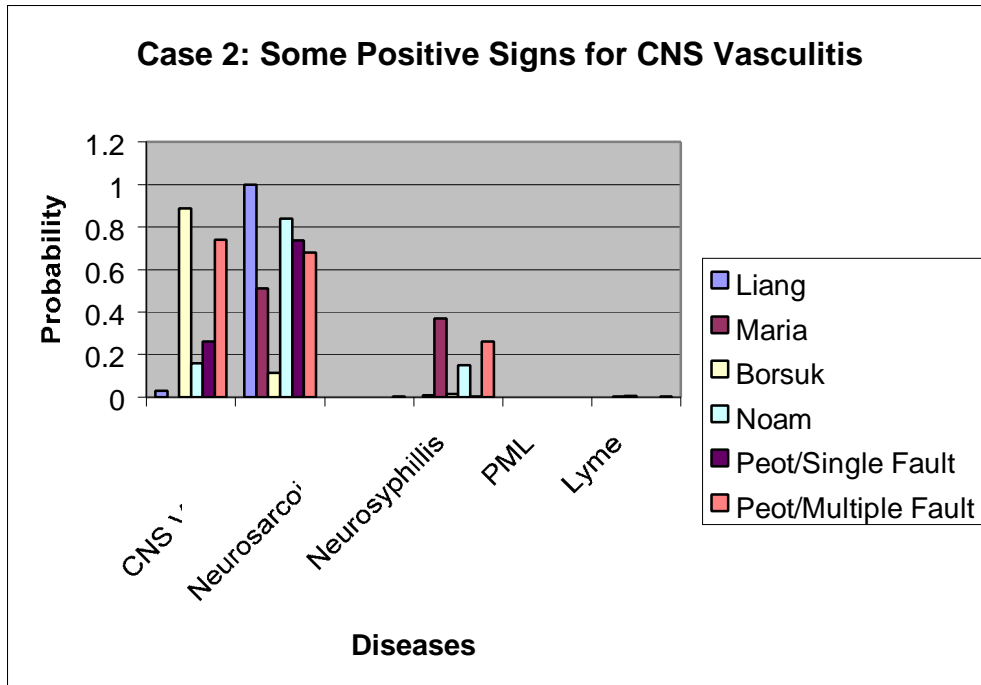
IgG: Increased

CSF Protein: Mild increase.

Oligoclonal banding: Two or more bands.

MRI: White matter.

These symptoms are consistent with CNS vasculitis except for the MRI lesions (white, only, for MS).



**Case 2: Some positive signs for Nonspecific CNS Vasculitis**

Patient: Caucasian Female

Lumbar puncture

Increased CSF protein

Moderate increase in WBC in lumbar puncture

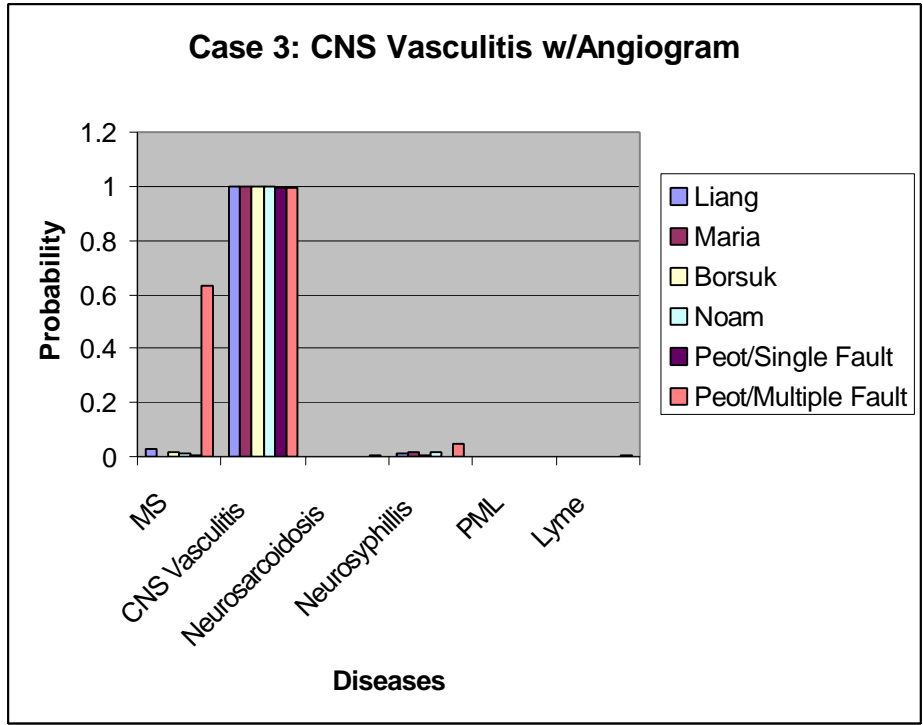
2+ Oligoclonal bands

Increased IgG

MRI: lesions in white and gray matter.

Blood Test: ESR elevated.

Notice how Peot/Single performs with respect to Peot/Multiple. I believe that Peot/Multiple can explain the data using several common faults (neurosyphilis and MS are more prevalent than neurosarcoidosis in my knowledge base). When single fault is engaged, the probability of MS and neurosyphilis drops significantly.



**Case 3: Positive signs for Nonspecific CNS Vasculitis w/Angiogram**

Patient: Caucasian Female

Lumbar puncture

- Increased CSF protein

- Moderate increase in WBC in lumbar puncture

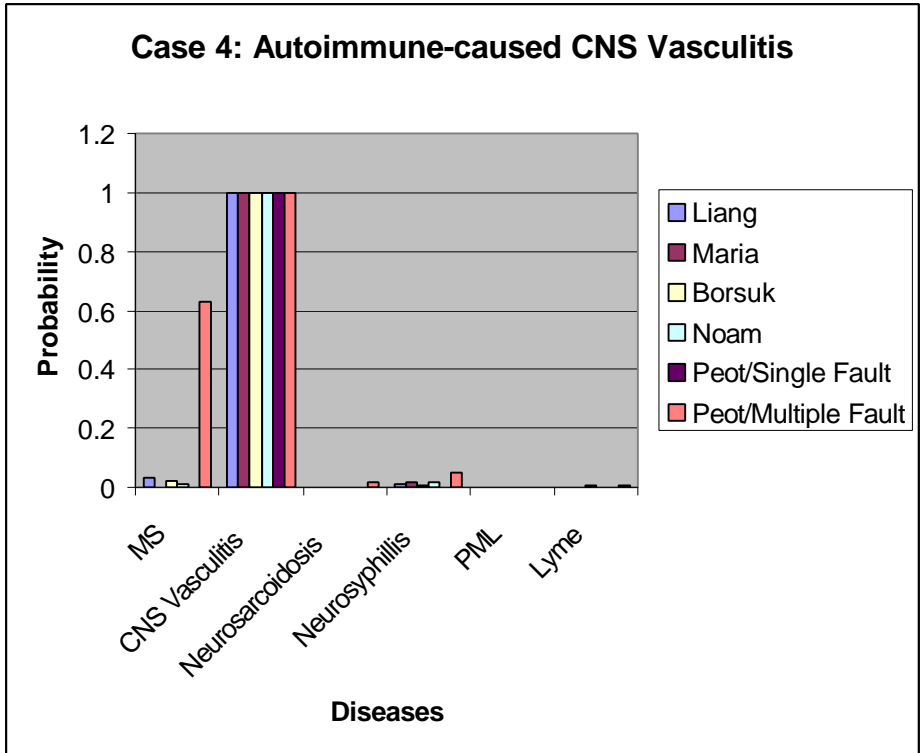
- 2+ Oligoclonal bands

- Increased IgG

MRI: lesions in white and gray matter.

Blood Test: ESR elevated.

Angiogram: Positive for vasculitis



**Case 4: Positive signs for CNS Vasculitis due to an autoimmune disorder**

Patient: Caucasian Female

Lumbar puncture

- Increased CSF protein

- Moderate increase in WBC in lumbar puncture

- 2+ Oligoclonal bands

- Increased IgG

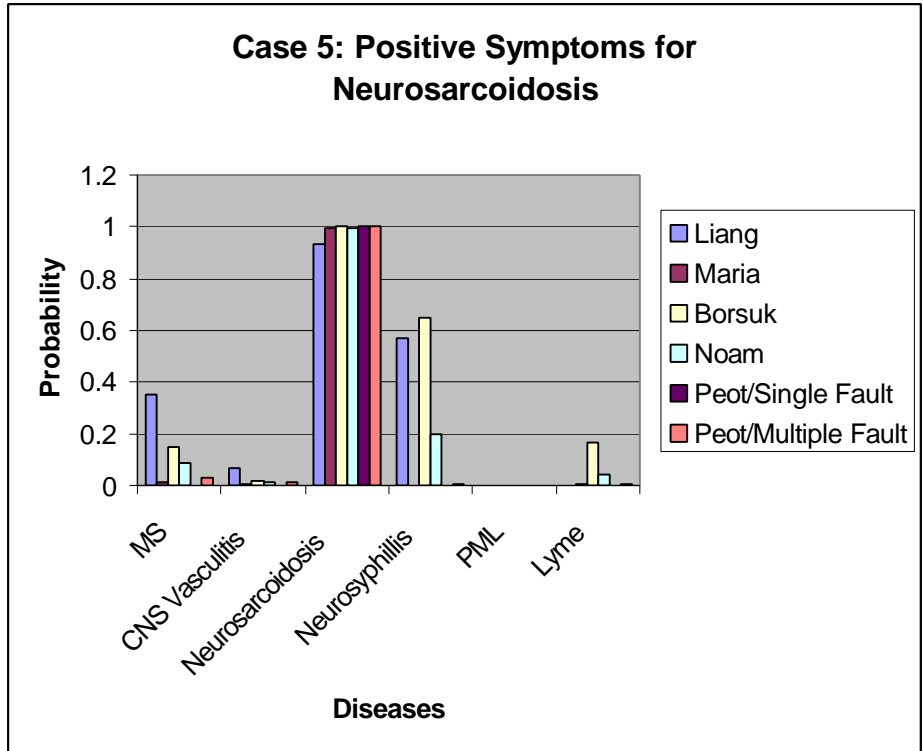
MRI: lesions in white and gray matter.

Blood Test:

- ESR elevated.

- Autoimmune specific antibodies

Chest X-ray: Abnormal



**Case 5: Positive signs for Neurosarcoidosis**

Patient: Black female

Lumbar puncture

Increased angiotensin converting enzyme

Increased WBC (false positive) 20/uL

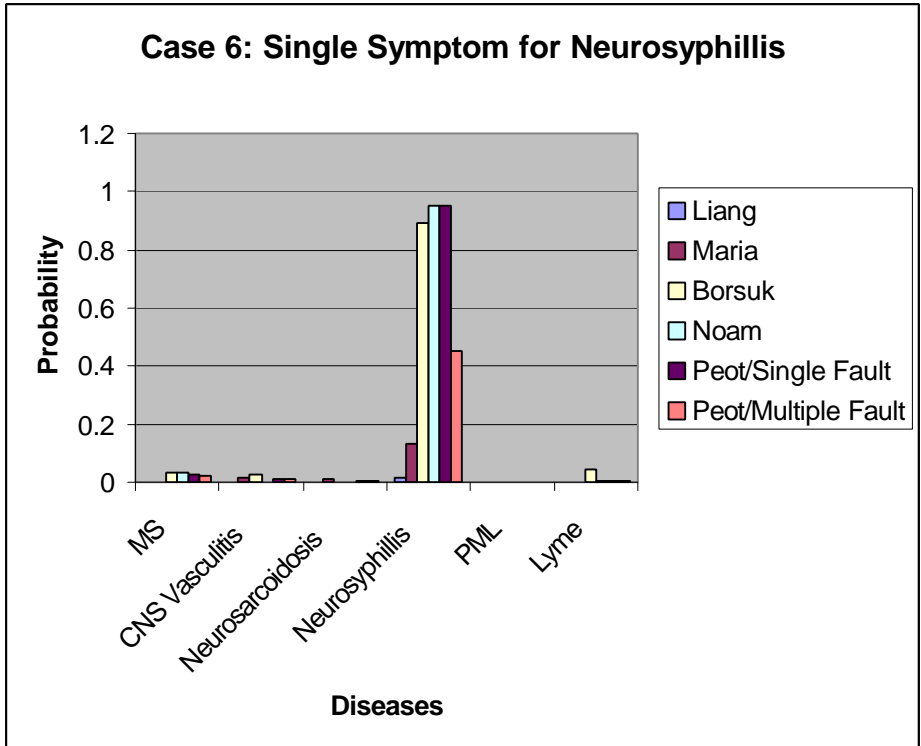
MRI: lesions in white matter. No gray matter lesions.

Blood Test:

Increased angiotensin converting enzyme

Kveim-Stilzbach Skin Test

Chest X-ray: Abnormal

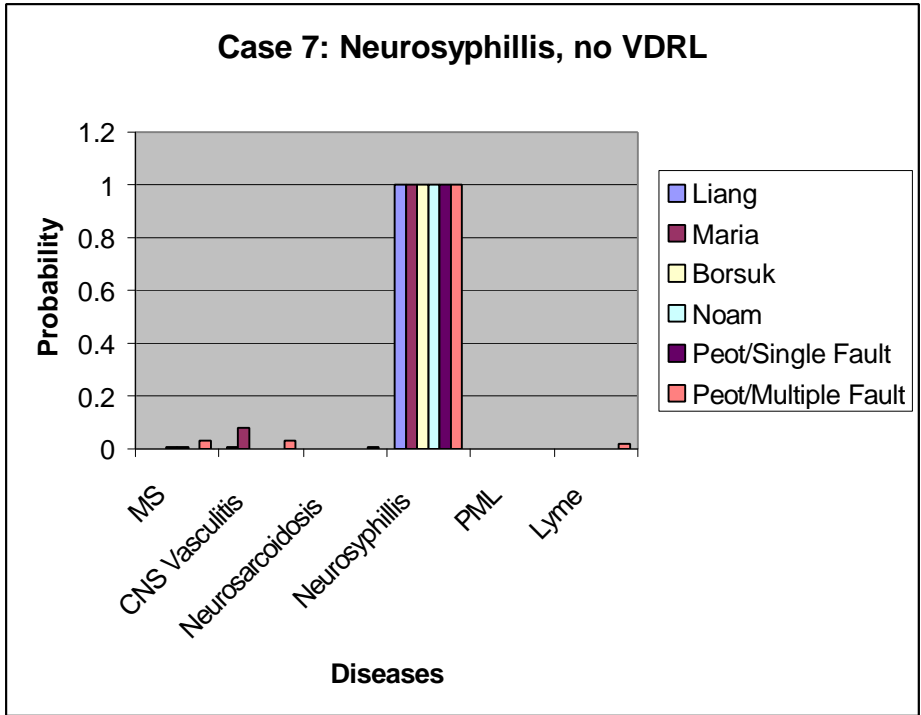


**Case 6: Single specific positive sign for Neurosyphilis**

Patient: White male

Lumbar puncture

VDRL positive (highly specific)



**Case 7: Neurosyphilis, no CSF VDRL.**

Patient: White male

Blood:

VDRL positive

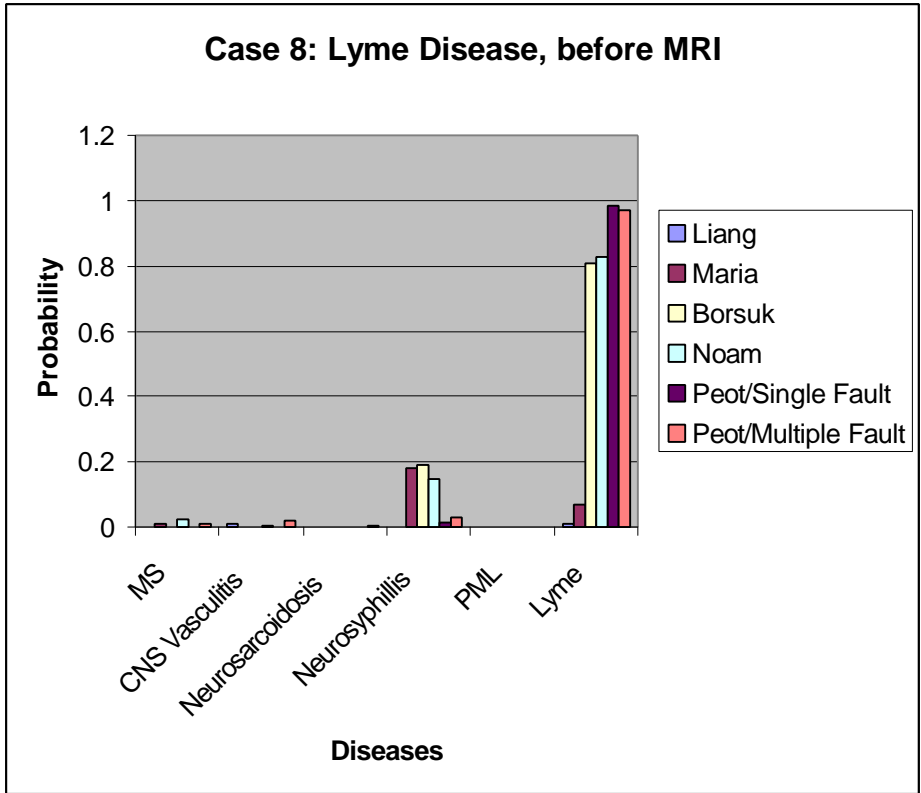
FTA-ABS positive

Lumbar puncture:

Increased protein

Increased WBC (80/uL)

MRI: White and gray matter changes.



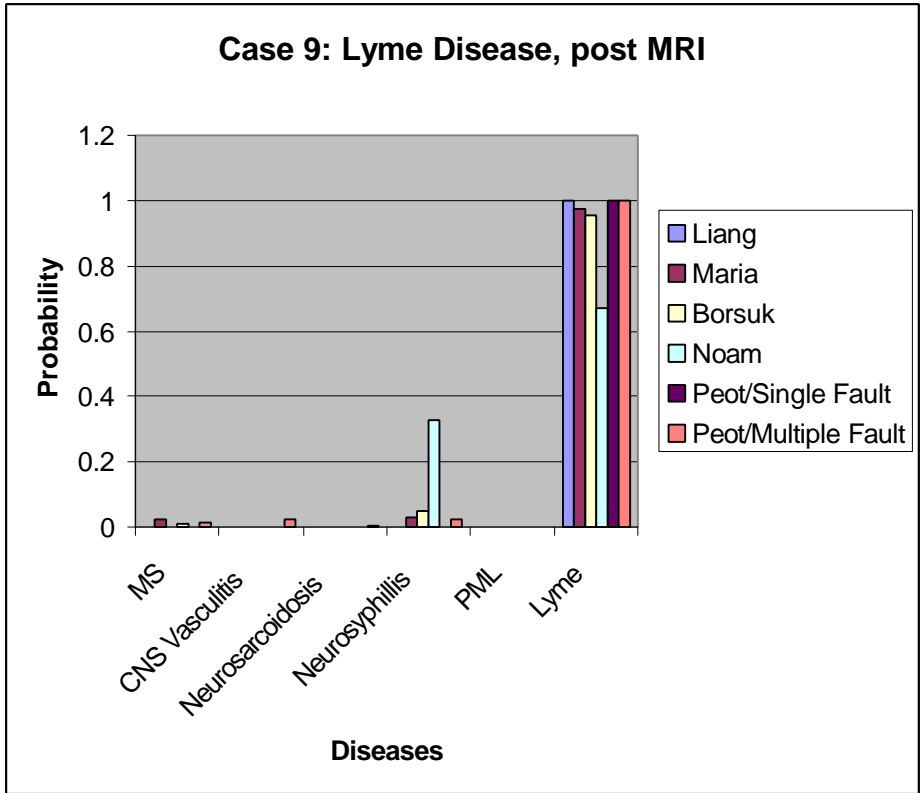
**Case 8: Lyme disease (pre MRI)**

Patient: Asian male, 16 years old, no memory of tick bite.

Arthritis: Positive

Blood:

Antibodies to B. Burgdorferi present.



**Case 9: Lyme disease (post MRI)**

Patient: Asian male, 16 years old, no memory of tick bite.

Arthritis: Positive

Lumbar puncture:

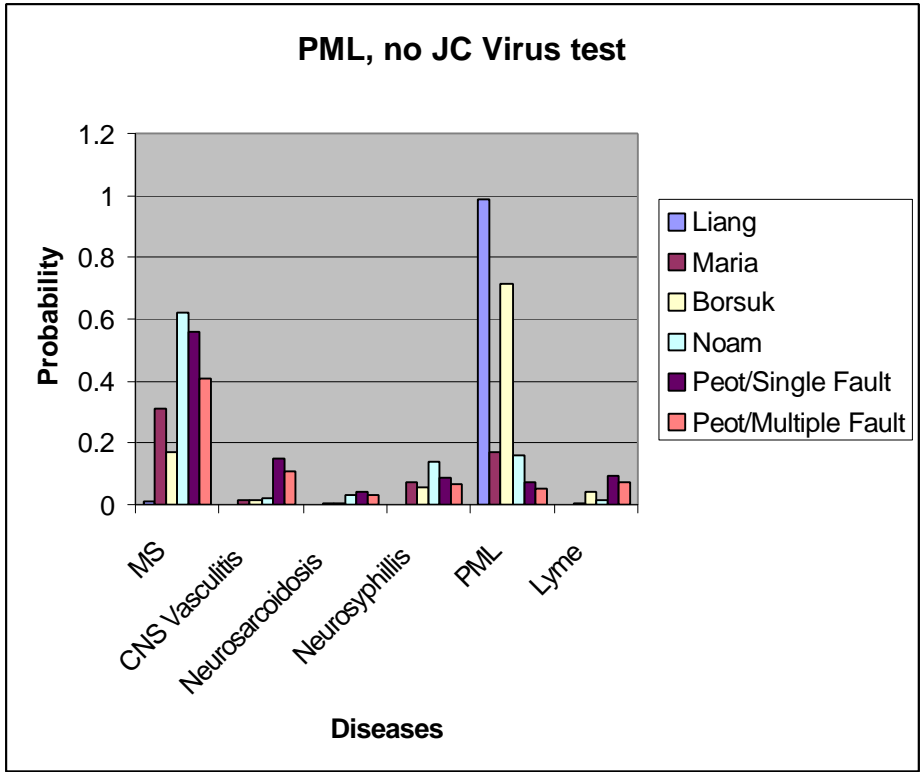
Antibodies to B. Burgdorferi: Present

WBC: > 100/uL

Blood:

Antibodies to B. Burgdorferi: Present.

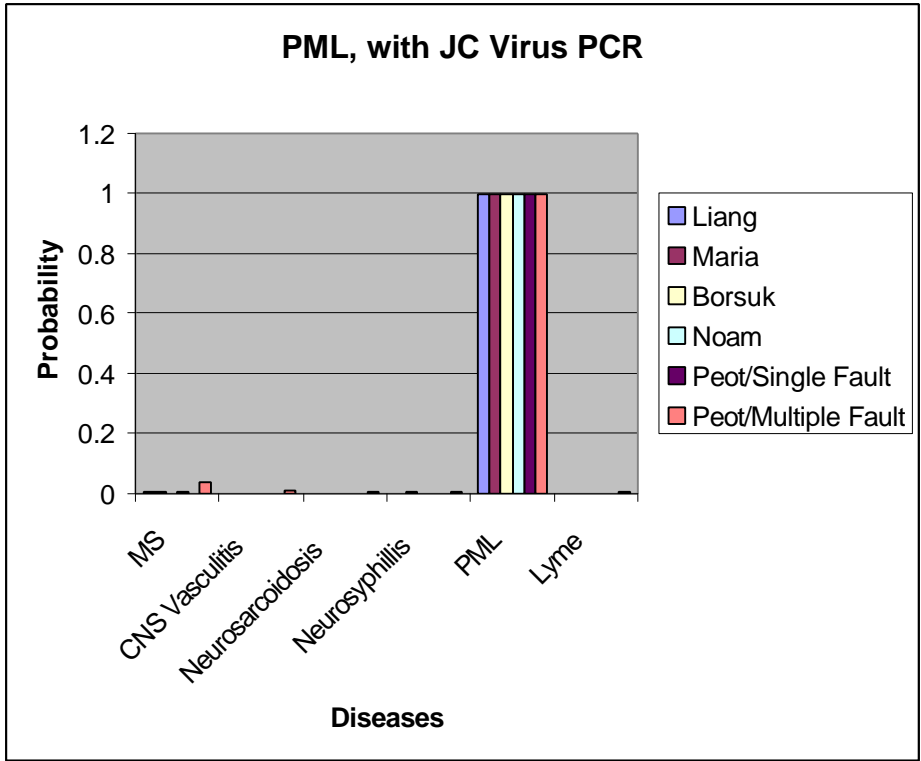
MRI: Changes in the white matter around the ventricles. Gray matter lesions absent.



**Case 10: PML (without JC virus)**

Patient: HIV positive White female.

MRI: Symmetric lesions in the brain. No gray matter involvement



**Case 11: PML (with JC virus)**

Patient: HIV positive White female.

MRI: Symmetric lesions in the brain. No gray matter involvement

Lumbar puncture: Antibodies to the JC virus present.