Autoimmune Testing, Diagnosis, and Treatment in Neurology

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Autoimmune Diseases of the Nervous System

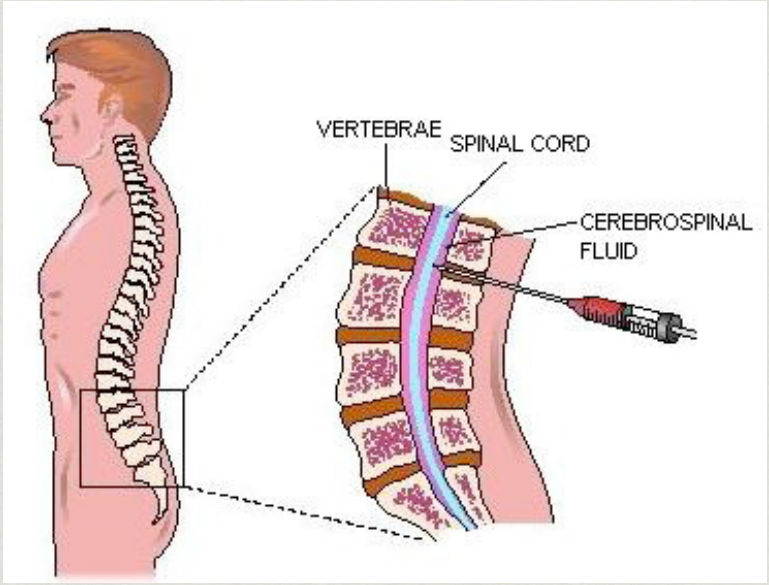
- Guillain-Barre Syndrome
- Inflammatory Myopathy
- Multiple Sclerosis
- Multifocal Motor Neuropathy
- Myasthenia Gravis/LEMS
- NMO
- OMS
- PANDAS
- Paraneoplastic Nervous System Disorders
- Stiffman Syndrome
- Stroke (Antiphospholipid Antibody Syndrome)
- Transverse Myelitis

Guillain-Barre: Features

- Eponym for heterogeneous group of acute immune-mediated PN; multiple variants
- Presentation: Ascending, symmetric paralysis/paresthesias with autonomic dysfxn risk
  - 98% plateau at 4 weeks
- 1-3/100,000 persons annually
- Peaks in young adulthood (C.jejuni and CMV) and elderly (?failing immunosuppressor mechanisms)

Guillain-Barre: Testing

- Physical Exam
- Lumbar puncture
- Electrodiagnostic studies

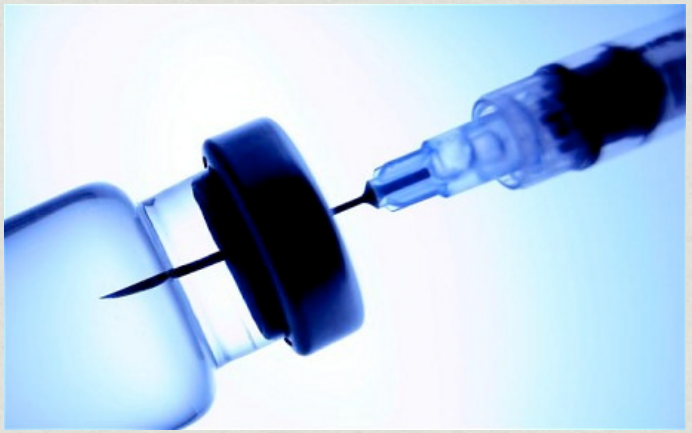


Guillain-Barre: Diagnosis

- Relative symmetry of symptoms
- Mild sensory symptoms or signs
- Cranial nerve involvement, especially bilateral weakness of facial muscles
- Recovery beginning two to four weeks after progression ceases
- Autonomic dysfunction
- Absence of fever at onset
- High concentration of protein in cerebrospinal fluid, with fewer than 10 cells per cubic millimeter
- Typical electrodiagnostic features

- Features excluding diagnosis
- Diagnosis of botulism, myasthenia, poliomyelitis, or toxic neuropathy
- Abnormal porphyrin metabolism
- Recent diphtheria
- Purely sensory syndrome, without weakness

Guillain-Barre: Diagnosis



- Antecedent events in 2/3 pts (CMV, C-jejuni, HIV, EBV, VZV)
- Influenza vaccine - Studies in 1992-1993 and 1993-1994 flu seasons; CDC Vaccine Adverse Event Reporting System - 2003 surveillance summary “the risk of developing vaccine-assoc GBS is less than the risk of severe influenza”

Guillain-Barre: Diagnosis

- **The following groups should not receive the flu shot (TIV):**

- People who have ever had a severe allergic reaction to influenza vaccine.
- People with a history of Guillain-Barré Syndrome (a severe paralytic illness, also called GBS) that occurred after receiving influenza vaccine and who are not at risk for severe illness from influenza should generally not receive vaccine. Tell your doctor if you ever had Guillain-Barré Syndrome. Your doctor will help you decide whether the vaccine is recommended for you.

Guillain-Barre: Treatment

- Early intubation: hypoxia, weak cough, aspiration, FVC < 15mL/kg or reduction of >30% of FVC
  - 30% of pts (Hahn AF, Lancet 1998).
- Autonomic monitoring: HR/BP/Arrythmias - atropine, short-acting agents (nitroprusside); IV fluids and supine positioning, temporary pacing the 2nd/3rd degree heart block
- DVT prophylaxis
- ICU admit: labile dysautonomia, FVC < 20mL/kg, severe bulbar palsy (Hughes RA, Arch Neurology, Aug 2005)

Guillain-Barre: Treatment

- Only two therapies proven effective (Hughes RA, et al. Neurology. 2003).
  - PE - 5 PE over 5-10 days
  - IVIG - 400mg/kg/day for 5 days; start w/in 4 wks of sx onset
- Thought to dec autoantibody production/increase solubilization/removal of immune complexes
- Shorted recovery time by 50%
- Combining neither improves outcome/shortens duration (Hughes, et al. Neurology, Sept 2003)

Guillain-Barre: Treatment

Evidence-based guideline: Intravenous immunoglobulin in the treatment of neuromuscular disorders

Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology

Recommendations. There is insufficient evidence to support or refute the effectiveness of IVIg in children with GBS (Level U). IVIg should be offered to treat GBS in adults (Level A). IVIg combined with plasmapheresis should not be considered for treating GBS (Level B). Evidence is insufficient to recommend MP in combination with IVIg (Level U).

Clinical context. Many experts consider it reasonable treatment to use IVIg for GBS in children given its effectiveness in the same disease in adults.

Evidence-based guideline update: Plasmapheresis in neurologic disorders

Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology

Recommendations. Plasmapheresis should be offered in the treatment of AIDP/GBS severe enough to impair independent walking or to require mechanical ventilation (Level A). Plasmapheresis should be considered in the treatment of milder clinical presentations of AIDP/GBS (Level B).

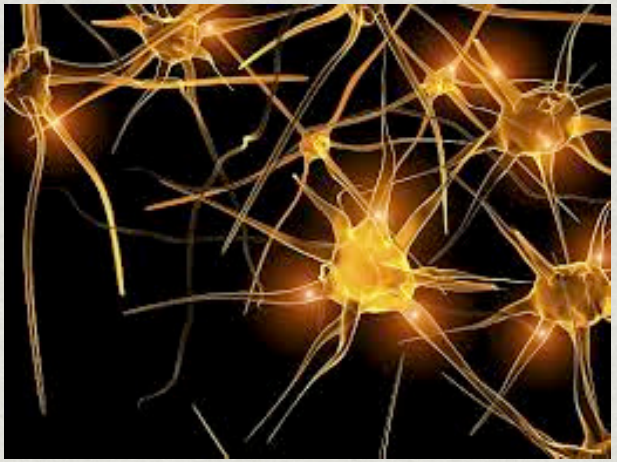
Clinical context. IV immunoglobulin (IVIg) is an alternative treatment used in patients with AIDP/GBS. There is insufficient evidence to demonstrate the superiority of one treatment over the other.[6-9]

Guillain-Barre: Treatment

- Corticosteroids - ineffective alone/ with IVIG may hasten recovery without impact on long-term (Hughes, Cochrane, Apr 2006).
- IV eculizumab (prevents reps paralysis in animals) (Pritchard J, Neurology, Nov 2003) ▪
- Mycophenolate mofetil with IVIG - no benefit (Garssen MP, J Neurol Neurosurg Psychiatry. Sep 2007) ▪

Guillain-Barre: Treatment

- Pain management: gabapentin, carbmazepine, TCAs, tramadol; avoid narcotics (ileus)
- Manage psychologic stress

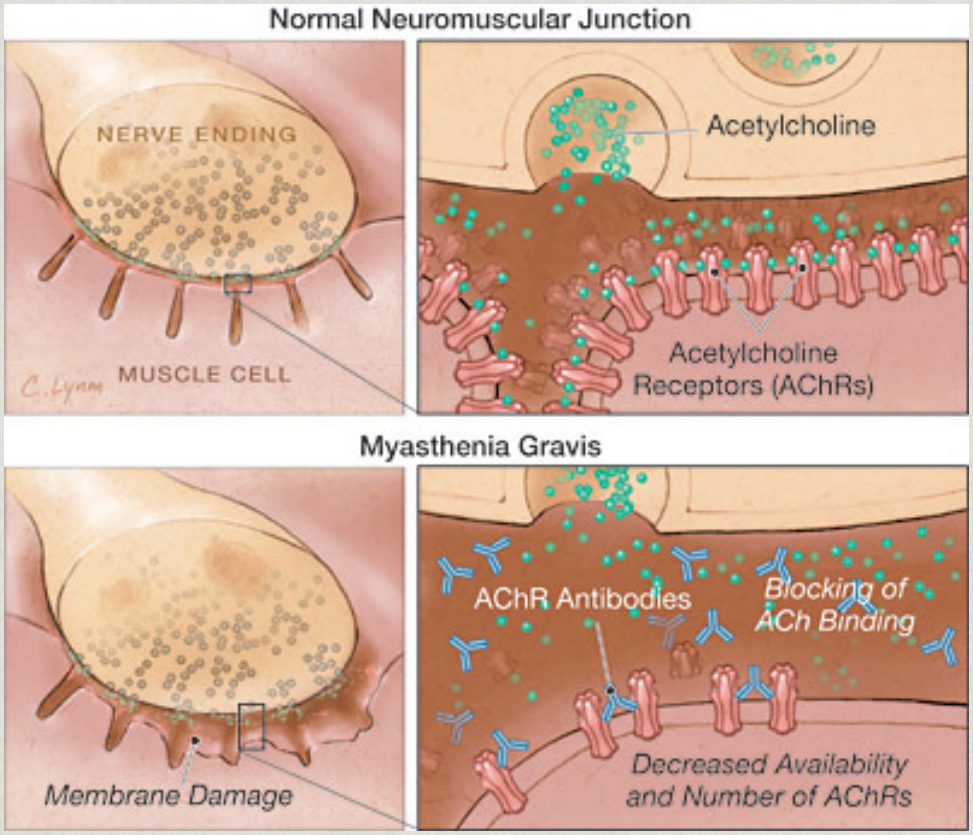


Guillain-Barre: Prognosis

- Prolonged intubation/ICU management;
- 2-12% mortality (Bersano A, J Neurol. 2006)
- Long-term residual PN (medium-/large-sized myelinated fibers) (Dornonville de la Cour C, Neurology. Jan 2005)
- Poorer prognosis: female, >57yo, LOS > 11dys, ICU tx, D/C to rehab (Khan, et al. J. Neurol. Jul 2010)
- Not correlative with severity at onset
- 85% pts full/fxnal recovery in 6-12 mos.; maximal at 18 mos

Myasthenia Gravis: Features

- Autoimmune d/o of ab formation against Ach nicotinic postsynaptic receptors at the NMJxn of skeletal mm
- Ocular/generalized
  - EOM 50% initially; 90% during the course
  - Increased by exertion/alleviated by rest
  - 87% have generalized dz within 13 months after onset
- 20/100,000 individuals



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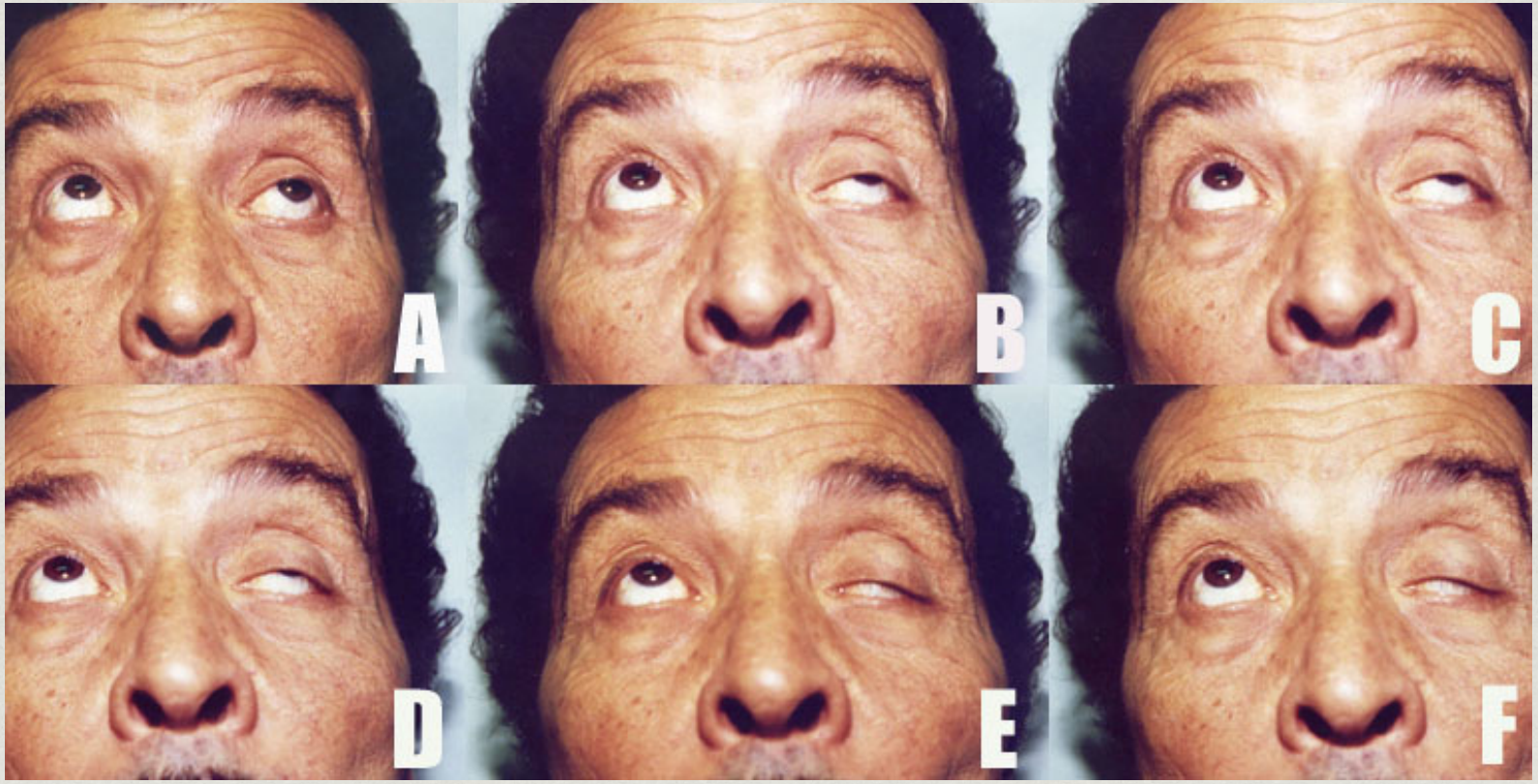
Myasthenia Gravis: Testing

- Labs: 67% positive (generalized), 44% (ocular)
  - False positives: thymoma, LEMS, small cell lung CA, RA with penicillamine, 1-3% of pop >70 yo
- Chest CT/XR for thymoma; MRI for ocular MG; Electrodx studies
- Ice test
- Tensilon test

Myasthenia Gravis: Diagnosis



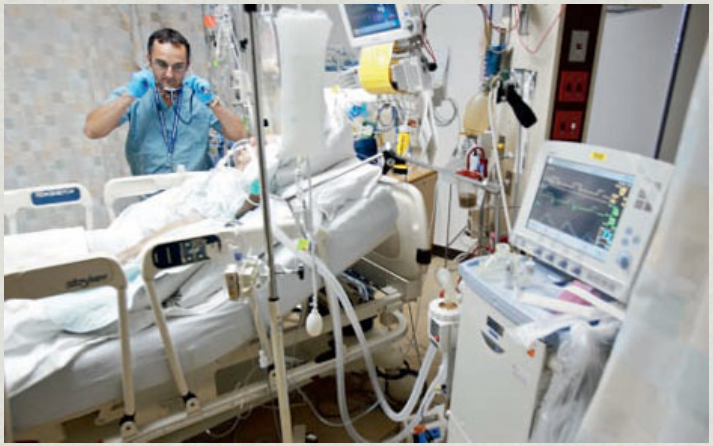
- http://emedicine.medscape.com/article/1171206-overview

Myasthenia Gravis: Diagnosis

- No formal diagnostic criteria established
- Classification System
  - Class I - ocular
  - Class II - Mild weakness other than ocular
  - Class III - Mod weakness other than ocular
  - Class IV - Severe weakness
  - Class V - Intubation

Myasthenia Gravis: Treatment

- Monitor for rapid resp decline
  - Hypoxemia; CO_2 retention; poor resp effort
- Monitor for initial deterioration



Myasthenia Gravis: Treatment

- AchE inhibitors - initial tx for mild MG
- Immunomodulating agents - Corticosteroids, azathioprine, cyclosporine A, methotrexate/cyclophosphamide
- IVIg - moderate/severe MG worsening into crisis; elderly; complex comorbid dz
- PE - myasthenic crisis; prep for sx; improvement in couple days, doesn't last for more than 2 months
- Thymectomy - all pts with thymoma and pt's age 10-55 without thymoma but with gen MG; delay in ocular

Myasthenia Gravis: Treatment

Practice parameter: The medical treatment of ocular myasthenia (an evidence-based review)

Report of the Quality Standards Subcommittee of the American Academy of Neurology

Recommendations. For patients with ocular myasthenia, the evidence does not support or refute the use of corticosteroids and/or azathioprine to reduce the risk of progression to generalized MG (Level U). The decision to use such agents should be weighed against the potential for harmful side effects of these medications. Furthermore, it is not possible to make any evidence-based recommendations with regard to the question of whether cholinesterase inhibitors have any effect in reducing the risk of progression to generalized MG. Recommendations cannot be made because of an absence of evidence.

Myasthenia gravis: Treatment

Evidence-based guideline: Intravenous immunoglobulin in the treatment of neuromuscular disorders

Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology

Recommendation. IVIg should be considered in the treatment of MG (Level B).

Evidence-based guideline update: Plasmapheresis in neurologic disorders

Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology

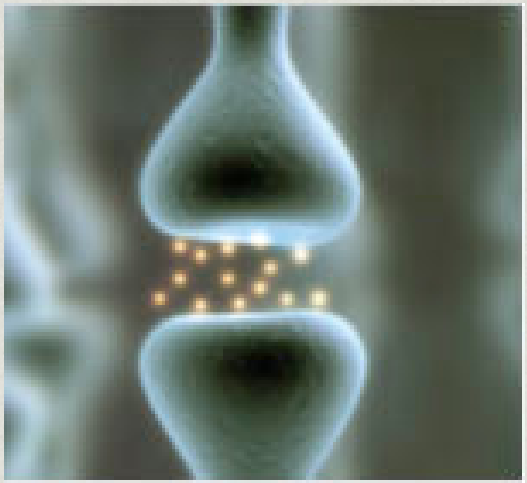
Recommendation. Because of the lack of randomized controlled studies with masked outcomes, there is insufficient evidence to support or refute the efficacy of plasmapheresis in the treatment of myasthenic crisis (Level U) or MG prethymectomy (Level U).

Clinical context. Despite the fact that the use of plasmapheresis in myasthenic crisis and MG prethymectomy receives a Level U recommendation, plasmapheresis is used at many medical centers for these indications.

Myasthenia Gravis: Prognosis

- 3-4% mortality (aspiration - pneumonia, falls, med complications)
- Risk factors: age >40, thymoma, short history of progressive disease

LEMS



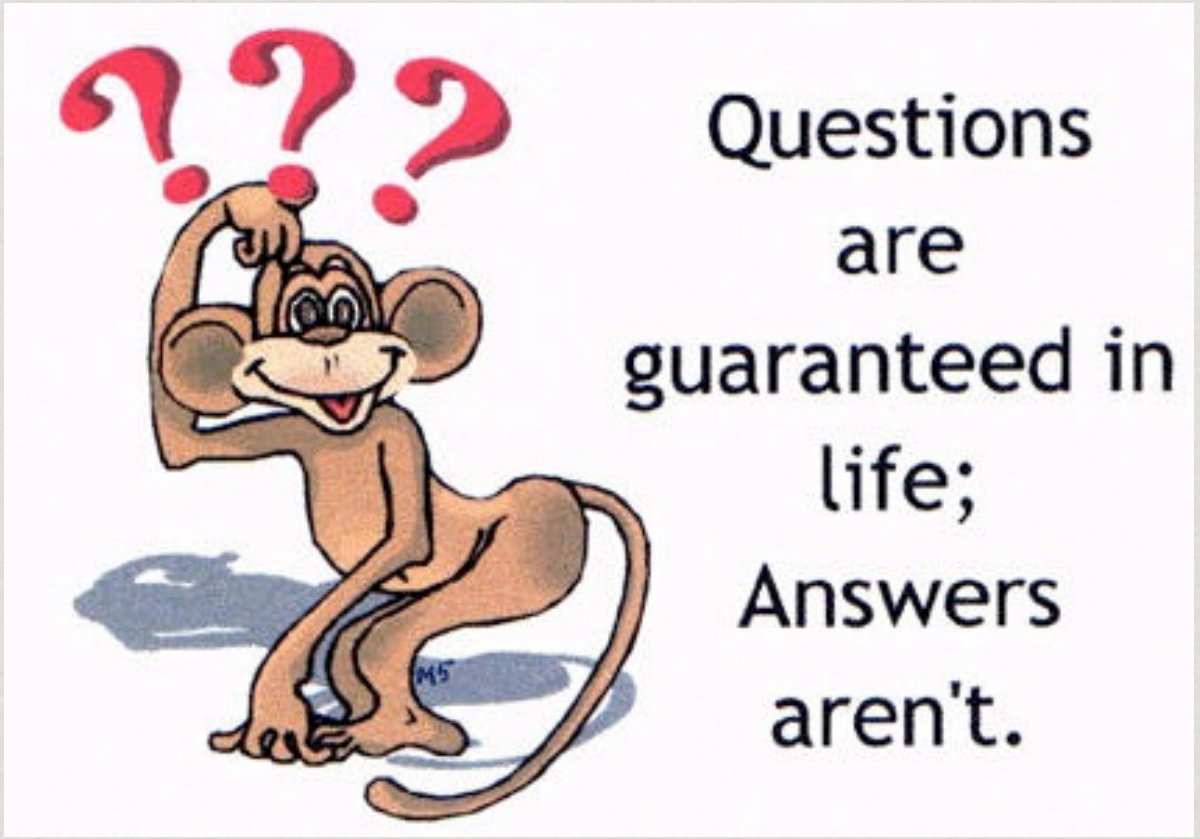
- Pre-synaptic disorder
- Autoimmune response against the VGCCs on the pre-synaptic motor nerve terminal
- Associated SCLC - 1%

Other Paraneoplastic Syndromes

- Subacute cerebellar ataxia
- Limbic encephalitis
- Opsoclonus-myoclonus
- Stiff-Person syndrome

The End

Questions?



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References

- Saguil, Aaron. "Evaluation of the Patient with Muscle Weakness." American Family Physician. 2005 Apr 1: 71 (7): 1327-1336.
- Newswanger, Dana, et al. "Guillain-Barre Syndrome" American Family Physician. 2004 May 15; 69 (10): 2405-2410.