Guillain-Barré Syndrome

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Rapidly Progressive Weakness

A 32-year-old man presented to the emergency department with several days of progressive numbness and weakness.

- 3 weeks prior, he had symptoms of a diarrheal illness that resolved without intervention. 5 days prior he noticed low back aching and tingling/numbness in his toes, which spread to involve the arms and legs. 3 days prior he began tripping as he went up stairs and on presentation to the ER he was unable to walk unassisted.

Rapidly Progressive Weakness

A 32-year-old man presented to the emergency department with several days of progressive numbness and weakness.

- Neurologic examination was notable for weakness of eye closure, arm and leg weakness most pronounced in the distal legs, diffuse areflexia and reduced sensation distal to the elbows and groin bilaterally.

- Lumbar puncture:
  - CSF glucose 65 (normal), protein 98 (elevated), RBCs 2, WBCs 0

- Nerve conduction studies:
  - Non-length-dependent neuropathy with features of acquired demyelination.

Guillain-Barré Syndrome

A group of acute immune-mediated disorders of the peripheral nerves and/or nerve roots typically characterized by:

- Acute, areflexic paralysis and sensory changes
- A monophasic course with nadir within 4 weeks of onset[1]
- Cytoalbuminologic dissociation in the cerebrospinal fluid

1. Fokke C et al. Diagnosis of Guillain-Barre syndrome and validation of Brighton criteria. Brain 2014.

Clinical Presentation – Classic GBS

Bilateral, progressive symptoms over hours to days

- Motor: Ascending weakness, facial palsies, respiratory insufficiency
- Sensory: Ascending paresthesias, numbness, limb pain, low back pain
- Reflexes: Generalized hyporeflexia or areflexia
- Autonomic dysfunction: GI dysmotility, arrhythmias and fluctuations in blood pressure

Pathogenesis

- Two-thirds of GBS cases are preceded by infection.

- Associated infectious agents include:
  - *Campylobacter jejuni*
  - *Mycoplasma pneumoniae*
  - Cytomegalovirus
  - Epstein-Barr virus
  - Varicella-Zoster virus
  - Zika virus

- Regarding vaccines:
  - Influenza vaccination may have an overall protective effect in preventing GBS[1]
  - There is no contraindication to vaccination in GBS patients after roughly 3 months[2]

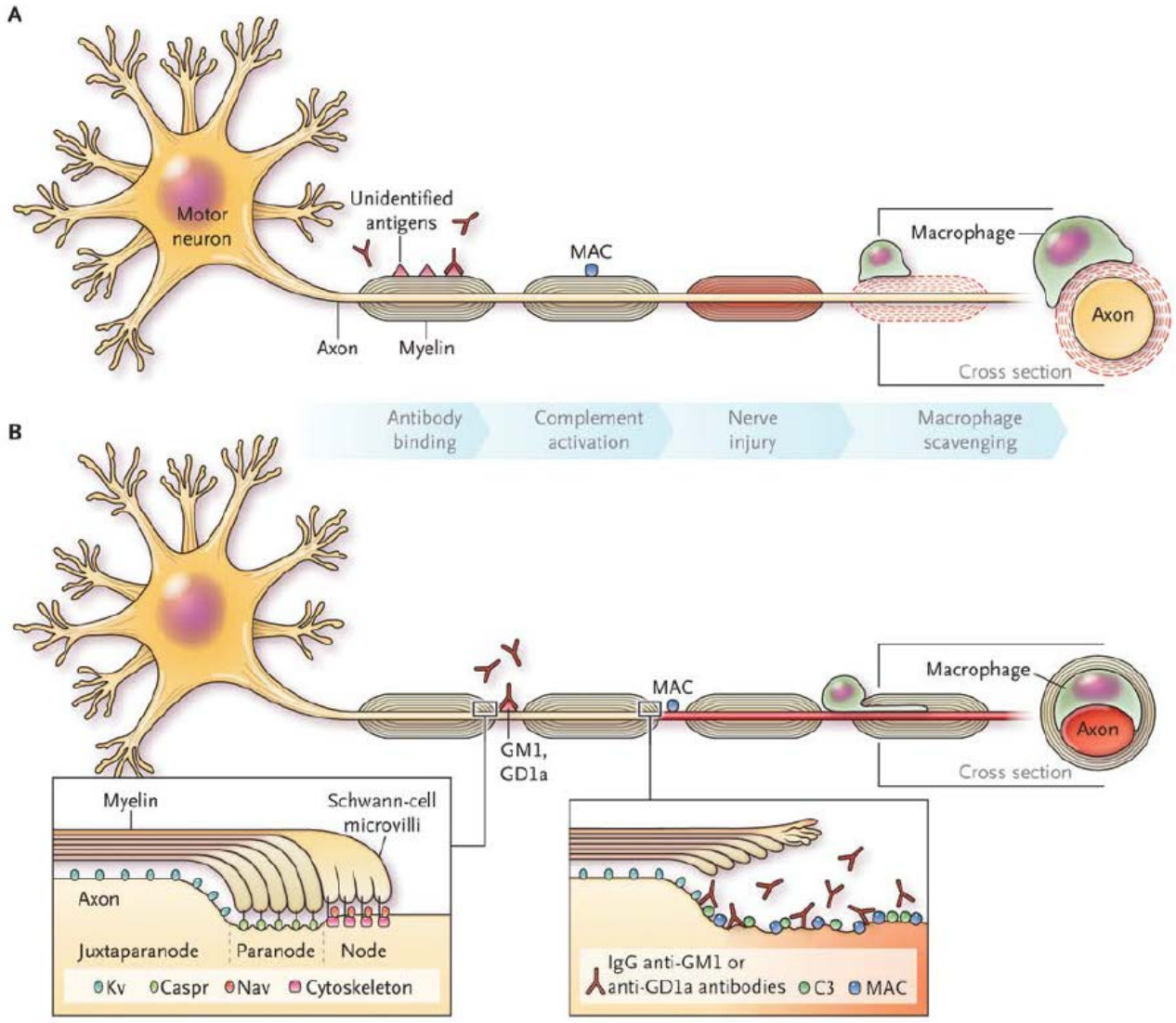
1. Hawkins et al. Simulation study of the effect of influenza and influenza vaccination on risk of acquiring Guillain-Barre Syndrome. Emerg Infect Dis 2015
2. Willison et al. Guillain-Barre syndrome. Lancet 2016.

Pathogenesis

Molecular Mimicry:

- Similarities exist between antigenic molecules on pathogens and molecules found in myelin or nerve axons

- Immune recognition of pathogenic antigens results in an autoimmune reaction against the nerve/myelin



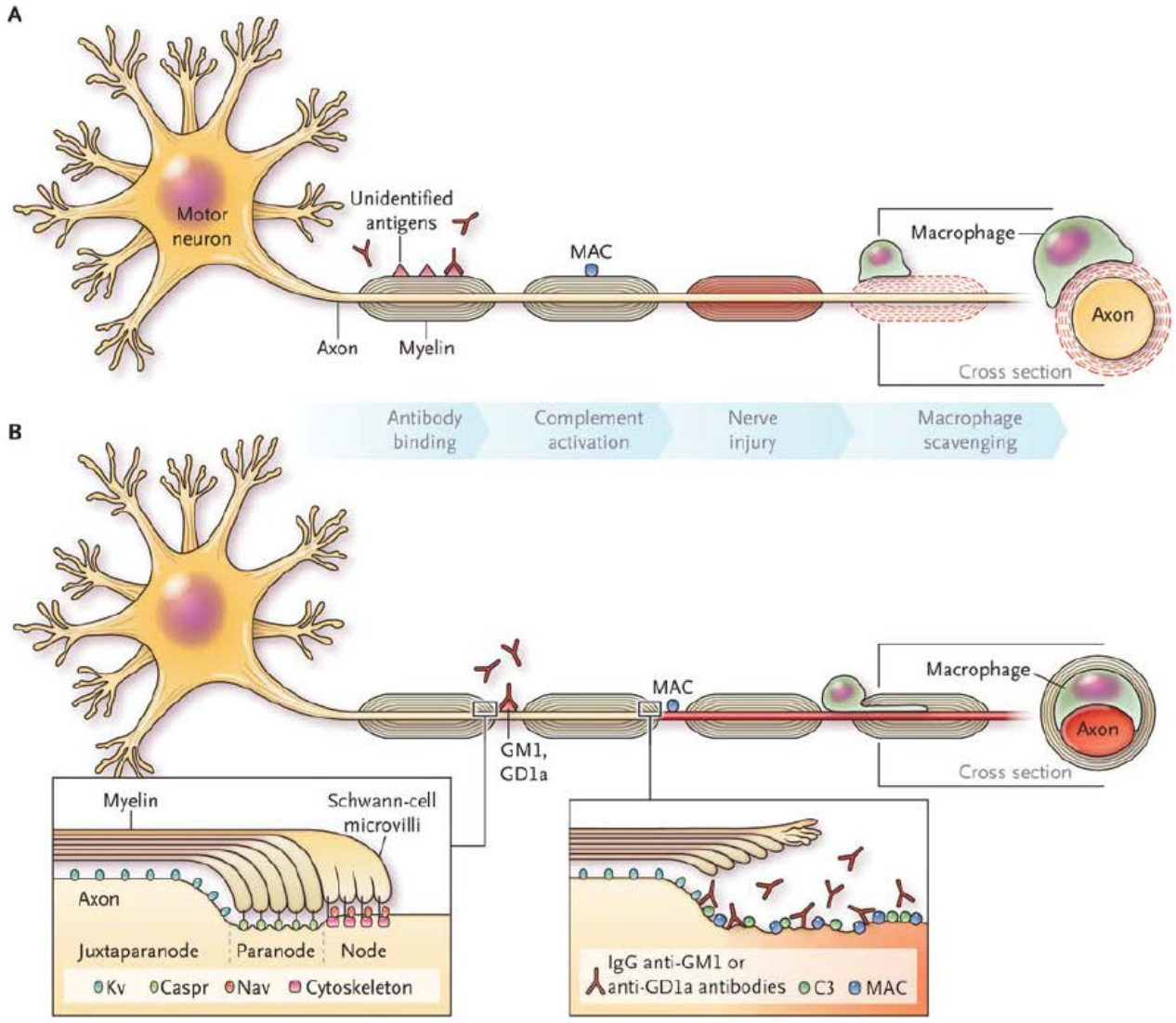
Yuki N, Hartung HP. Guillain-Barre syndrome. N Engl J Med 2012

GBS Subtypes

- Acute Inflammatory Demyelinating Polyneuropathy (AIDP)

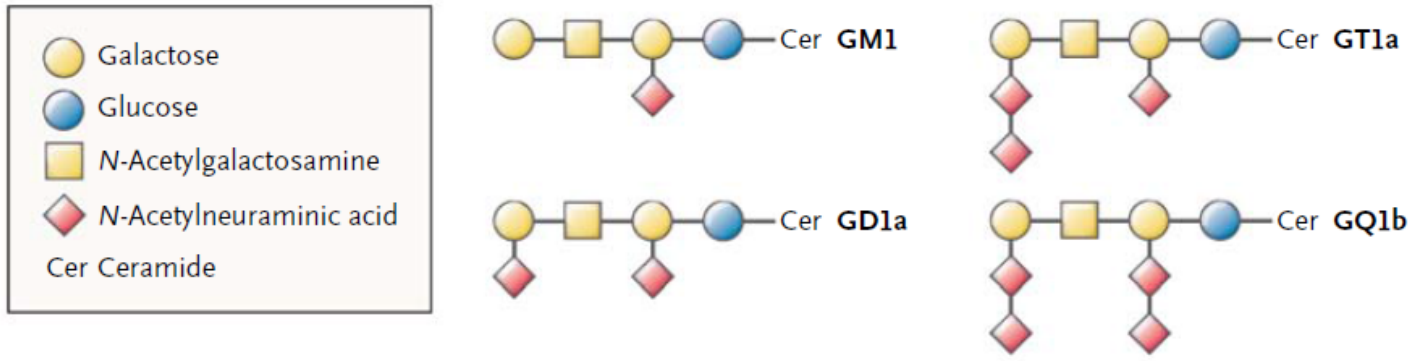
- Axonal Variants
  - Acute Motor Axonal Neuropathy (AMAN)
  - Acute Motor and Sensory Axonal Neuropathy (AMSAN)
  - These variants carry a poorer prognosis for recovery

- Anti-GQ1b-Associated Disorders
  - Miller Fisher Syndrome (MFS): Ataxia, opthalmoplegia and areflexia
  - Bickerstaff encephalitis: Ataxia, opthalmoplegia and encephalitis



Yuki N, Hartung HP. Guillain-Barre syndrome. N Engl J Med 2012

Subtypes and variants	IgG autoantibodies to
Guillain–Barré syndrome	
Acute inflammatory demyelinating polyneuropathy	None
Facial variant: Facial diplegia and paresthesia	None
Acute motor axonal neuropathy	GM1, GD1a
More and less extensive forms	
Acute motor–sensory axonal neuropathy	GM1, GD1a
Acute motor-conduction-block neuropathy	GM1, GD1a
Pharyngeal–cervical–brachial weakness	GT1a > GQ1b >> GD1a
Miller Fisher syndrome	GQ1b, GT1a
Incomplete forms	
Acute ophthalmoparesis (without ataxia)	GQ1b, GT1a
Acute ataxic neuropathy (without ophthalmoplegia)	GQ1b, GT1a
CNS variant: Bickerstaff's brain-stem encephalitis	GQ1b, GT1a



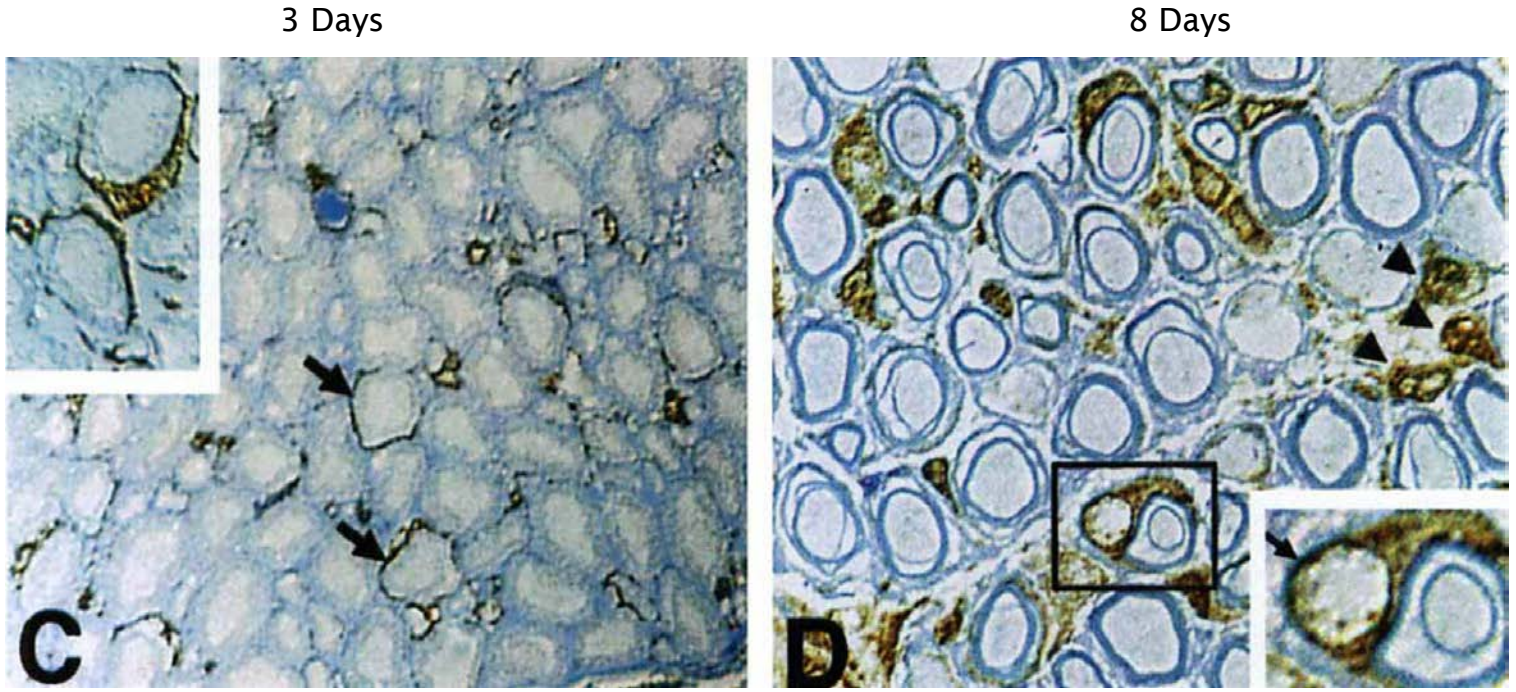
Yuki N, Hartung HP. Guillain-Barre syndrome. N Engl J Med 2012

Epidemiology

- 1-2 cases per 100,000 person-years in the US and Europe[1]
- AIDP accounts for up to 90% of cases in the North America[2]
- Axonal variants are more common in Northern China[3]

1. Sejvar et al. Population incidence of Guillain-Barre syndrome: a systematic review and meta-analysis. Neuroepidemiology 2011
2. Hadden et al. Electrophysiological classification of Guillain-Barre syndrome: clinical associations and outcome. Ann Neurol 1998
3. McKhann et al. Acute motor axonal neuropathy: a frequent cause of acute flaccid paralysis in China. Ann Neurol 1993

Complement Deposition in Early AIDP



Hafer-Macko et al. (1996)

Diagnostics

Careful Physical Examination

- Cranial Nerves
- Sensation
- Strength
- Reflexes

1. Fokke et al. Diagnosis of Guillain-Barre syndrome and validation of Brighton criteria. Brain 2014
2. Wong et al. Cytoalbuminologic dissociation in Asian patients with Guillain-Barre and Miller Fisher syndromes. J Peripher Nerv Syst 2015

Diagnostics

Nerve Conduction Studies (NCS):

- NCS can be normal early and develop over weeks[1]
- Serial NCS are often done, but may not change the subtyping of GBS[2]

1. Hadden et al. Electrophysiological classification of Guillain-Barre syndrome: clinical associations and outcome. Ann Neurol 1998
2. VanDenBergh et al. Guillain-Barre syndrome subtype diagnosis: A prospective Multicentre European Study. Muscle Nerve 2018

AIDP Electrodiagnostic Features

Motor NCS

- Increased distal latencies
- Conduction block
- Temporal dispersion
- Slowing of nerve conduction velocities (usually not seen until the third or fourth week)

AIDP Electrodiagnostic Features

Sensory NCS

- "Sural Sparing" pattern – in AIDP or axonal variants
- Absent responses or slowed conduction velocities.

Late Responses (earliest feature in AIDP)

- Prolonged or absent F waves
- Absent H reflexes

Needle EMG

- Reduced recruitment in weak muscles.
- Fibs/PSWs after weeks IF there has been axon loss.

Axonal Variant EDx Features

AMSAN:

- No demyelination
- Motor and sensory responses severely reduced or absent
- F waves may be absent (not significantly prolonged)
- Denervation on needle study after weeks

AMAN:

- No sensory nerve involvement or demyelination
- Motor amplitudes may be reduced
- F waves may be absent (not significantly prolonged)
- Denervation in needle study after weeks

Proposed GBS EDx Criteria

Definite	Probable	Possible
2 abnormal motor nerves* AND the sural-sparing pattern**	2 abnormal motor nerves* AND either normal SNAP or a diffuse (non sural-sparing) decrease in SNAP** OR	1 abnormal motor nerve* with or without sensory nerve abnormalities OR
	1 abnormal motor nerve* AND the sural-sparing pattern	Normal motor nerve NCS with SNAP decrease** (either diffuse or in sural-sparing pattern)
	SNAP changes cannot be isolated to the sural nerve	

- Decreased CMAP amplitude
- Prolonged distal motor latency
- Decreased motor conduction velocity
- Temporal dispersion (increased duration of more than 30% compared to the distal)
- Conduction block (decrease of more than 50% in proximal CMAP compared to distal without an increase on duration of more than 30%)
- Prolonged F latency

Umapathi et al, A Simplified, Graded, Electrodiagnostic Criterion for Guillain-Barré Syndrome That Incorporates Sensory Nerve Conduction Studies. Scientific Reports. 2019

Diagnostics

Lumbar Puncture

- CSF cytoalbuminologic dissociation = elevated protein with normal white blood cells
- Cytoalbuminologic dissociation is present in 50% of GBS patients in the first week after onset, but 70-90% 2 weeks after onset [1,2]
- CSF Pleocytosis may indicate disease mimics: lymphoma, sarcoidosis, Lyme, West Nile Virus
- CSF Pleocytosis is also present in some GBS patients with HIV

Consider MRI:

- Assess for cauda equina syndrome or other compressive lesion of the spinal nerve roots

Consider serum antibodies:

- Particularly to GQ1b in suspected MFS and Bickerstaff

Management – Respiratory

GBS patient require admission for close monitoring of respiratory status

- Roughly 30% of GBS patients require mechanical ventilation[1]
- Elective intubation is preferred over emergent intubation
- Hypoxemia and hypercarbia are late signs of neuromuscular respiratory weakness

1. Sharshar T, Chevret S, Bourdain F et al. Early predictors of mechanical ventilation in Guillain-Barre syndrome. Crit Care Med 2003

Management – Respiratory

Frequently Check:

- Vital Capacity (VC)
- Maximal Inspiratory Pressure (MIP), also know as Negative Inspiratory Force (NIF)
- Maximal Expiratory Pressure (MEP)

"20/30/40 rule", intubate when[1]:

- Vital Capacity is <20ml/kg (i.e. <1.4L in a 70kg person)
- MIP/NIF is less negative than -30cm H_2O
- MEP is <40cm H_2O
- >30% decline in any of these parameters

1. Lawn et al. Anticipating mechanical ventilation in Guillain-Barre syndrome. Arch Neurol 2001

Management – Respiratory

Single Breath Count (SBC)[1]

- Each 10 digits counted on a single breath corresponds with ~1L VC
- Demonstrated in patients with myasthenia gravis
- Useful when formal VC/MIP/MEP aren't available

1. Elsheikh et al. Correlation of single-breath count test and neck flexor muscle strength with spirometry in myasthenia gravis. Muscle Nerve 2016

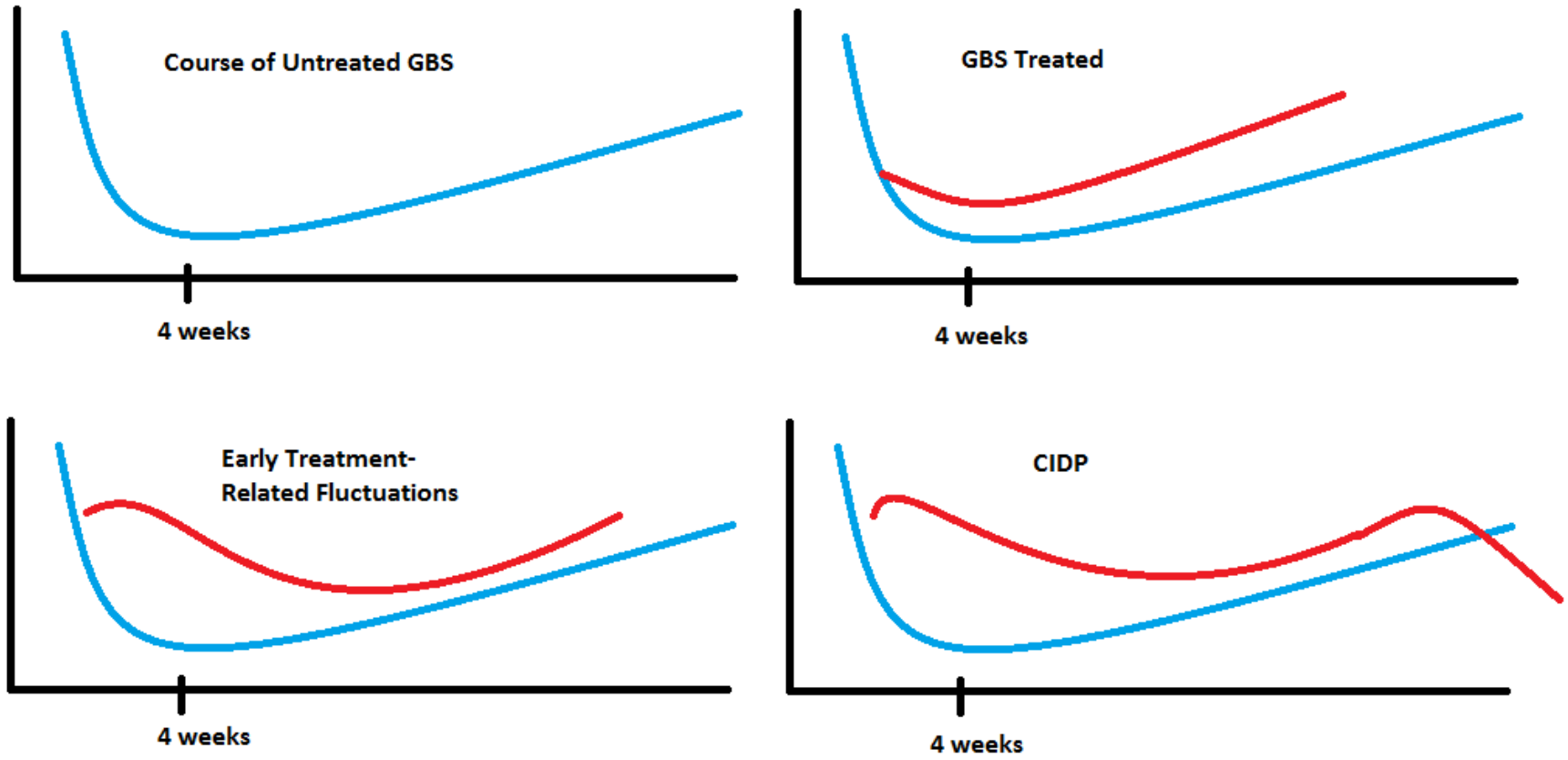
Therapies

Patients with GBS should be treated with Intravenous Immunoglobulin (IVIG) or plasmapheresis (PLEX)

- IVIG and PLEX are equally effective in GBS[1,2]
- Choice of IVIG 2gm/kg over 5 days v. PLEX 4-6 exchanges over 8-10 days
- Treatment should be initiated as soon as there is a clinical diagnosis
- IVIG v. PLEX depends on: institutional availability and patient comorbidities
  - Avoid IVIG in: renal failure, hypercoagulable states, IgA deficiency
  - Avoid PLEX in: sepsis due to hemodynamic changes and bacterial colonization of catheter

1. Chevret et al. Plasma exchange for Guillain-Barre syndrome. Cochrane Database Syst Rev 2017
2. Hughes et al. Intravenous immunoglobulin for Guillain-Barre syndrome. Cochrane Database Syst Rev 2014

Treatment-Related Fluctuation v. CIDP



When does AIDP become CIDP?

Consider Maintenance Treatment for CIDP (corticosteroids, chronic IVIG) When:

- There is clinical deterioration after 8 weeks from onset
- When deterioration occurs 3 times or more.

Suggestive features of CIDP:

- Patient remains able to walk independently
- Patient has no cranial nerve dysfunction
- Electrophysiologic features likely to be compatible with CIDP

Ancillary Supportive Care

- Monitor/Treat Dysautonomia:
  - Cardiac monitoring for arrhythmias
  - Blood pressure management
  - GI dysmotility and urinary retention

- Proactively Address Immobility and Associated Comorbidities
  - Early physical and occupational therapy
  - DVT Prophylaxis
  - Carful skin care to avoid decubitus ulcers

- Pain Management
  - Neuropathic agents (gabapentin, pregabalin, low dose tricyclic antidepressants)
  - Avoid long-term opioid use

Prognosis

- Mortality in Europe and North America is 3-7%, often due to respiratory complications or autonomic dysfunction[1]
- Nearly 90% experience full recovery or only minor residual deficits[2], though recovery may be slow and 20% remain unable to walk unassisted at 6 months[3]
- Axonal variants may have a more protracted course and slower, incomplete improvement[4]

1. Willison et al. Guillain-Barre syndrome. Lancet 2016.
2. Gonzalez-Suarez et al. Guillain-Barre syndrome: natural history and prognostic factors: a retrospective review of 106 cases. BMC Neurol 2013
3. Yuki N, Hartung HP. Guillain-Barre syndrome. N Engl J Med 2012
4. Griffin et al. Pathology of the motor-sensory axonal Guillain-Barre syndrome. Ann Neurol 1996

Follow Up on Our Case

A 32-year-old man with several days of progressive numbness and weakness. Areflexia, weakness and numbness on exam. Cytoalbuminologic dissociation in CSF. Acquired, demyelinating neuropathy on NCS.

- Diagnosed with AIDP
- Treated with 5 days of IVIG (0.4gm/kg daily for 5 days)
- Treated with gabapentin for burning leg pain
- Respiratory function was closely monitored and was stable over a week
- Transferred to rehab after 10 days
- On evaluation 3 months later, he had regained most of his strength and returned to work
- He continue to experience mild, intermittent tingling in the feet

Summary

- Guillain-Barré Syndrome refers to a group of monophasic, immune-mediated polyneuropathies/polyradiculoneuropathies, typically characterized by rapidly progressive areflexic paralysis and sensory symptoms.
- Key diagnostic tests include NCS and lumbar puncture for cytoalbuminologic dissociation.
- Management includes treatment with IVIG or PLEX and close respiratory function monitoring.
- Prognosis is good in most patients.

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