Guillain-Barré Syndrome

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Objectives

- Pathophysiology of Guillain Barré Syndrome (GBS)
- Epidemiology
- Signs and symptoms
- Review of GBS subtypes
- Diagnosis, treatment, prognosis
- Outbreaks
Definition

- First described in 1916
- Acute flaccid paralysis, areflexia, ↑protein in CSF
- Flaccid: Voluntary control over muscles has been lost → limp, floppy muscles
- Commonest cause of acute flaccid paralysis
Epidemiology

- 0.9–1.9/100,000 persons

- Incidence differs with age
  - <30 yrs: <1/100,000
  - >75 yrs: >4/100,000

- 20% increase with every 10-year rise in age

- Male to female ratio – 1.2–1.5:1

Sejvar et al, Neuroepidemiology 2011; 36: 123-133
Pathophysiology

[Diagram of a neuron showing dendrites, cell body, axon, myelin sheath, nodes of Ranvier, and synapses.]
Pathophysiology
Pathophysiology

Multiple Sclerosis Trust, UK
Nervous System

- Central nervous system
  - Brain and spinal cord

- Peripheral nervous system
  - Somatic - voluntary
  - Autonomic - involuntary

- GBS affects the 2 components of the peripheral nervous system
Neurology Definitions

- **Paralysis** – loss of voluntary muscle function
  - Partial – affecting one muscle or one limb
  - Total – paralysis of all muscles

- **Plegia** – used to describe paralysis
  - Palsy – not used anymore except for ‘Bell’s palsy’

- **Paresis** – weakness of voluntary movement
Neurology Definitions

- **Hemi** – arm, leg, trunk on the same side of the body
  - Hemiplegia – total paralysis on one side of the body
  - Hemiparesis – weakness on one side of the body

- **Para** – either both arms or both legs

- **Quadri** – all 4 limbs and torso
  - Quadriplegia is the same as tetraplegia

- **Paresthesia** – tingling, burning, numb sensation
Variants

- Autoantibodies (usually IgG) attack gangliosides
  - Part of the cell membrane involved in signal transduction

# Five Variants of GBS

<table>
<thead>
<tr>
<th>Subtypes and variants</th>
<th>IgG autoantibodies to</th>
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<tbody>
<tr>
<td><strong>Guillain–Barré syndrome</strong></td>
<td></td>
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<tr>
<td>Acute inflammatory demyelinating polyneuropathy</td>
<td>None</td>
</tr>
<tr>
<td>Facial variant: Facial diplegia and paresthesia</td>
<td>None</td>
</tr>
<tr>
<td><strong>Acute motor axonal neuropathy</strong></td>
<td>GM1, GD1a</td>
</tr>
<tr>
<td><strong>More and less extensive forms</strong></td>
<td></td>
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<tr>
<td>Acute motor–sensory axonal neuropathy</td>
<td>GM1, GD1a</td>
</tr>
<tr>
<td>Acute motor-conduction-block neuropathy</td>
<td>GM1, GD1a</td>
</tr>
<tr>
<td>Pharyngeal–cervical–brachial weakness</td>
<td>GT1a &gt; GQ1b &gt;&gt; GD1a</td>
</tr>
<tr>
<td><strong>Miller Fisher syndrome</strong></td>
<td></td>
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<tr>
<td><strong>Incomplete forms</strong></td>
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<tr>
<td>Acute ophthalmoparesis (without ataxia)</td>
<td>GQ1b, GT1a</td>
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<tr>
<td>Acute ataxic neuropathy (without ophthalmoplegia)</td>
<td>GQ1b, GT1a</td>
</tr>
<tr>
<td>CNS variant: Bickerstaff’s brain-stem encephalitis</td>
<td>GQ1b, GT1a</td>
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</table>
Geographic Distribution of GBS Subtypes

- **Demyelinating**
  - Autoantibodies attack the myelin sheath

- **Axonal**
  - Autoantibodies attack nerve axon
Geographic Distribution of GBS Subtypes

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  - 90% of all cases in Europe and North America
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Geographic Distribution of GBS Subtypes

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Guillain Barré Syndrome

- Acute, ascending paralysis
- Decreased or absent reflexes
- Elevated protein in the CSF but normal cell count
- Autoantibodies to myelin sheath or axon of nerve cells
- 5 variants
Acute Inflammatory Demyelinating Polyneuropathy (AIDP)

- Commonest variant of GBS in North America, Europe
- Paresthesias in distal limbs before weakness
- Ascending paralysis, progressive weakness
  - Bilateral, symmetrical
  - At presentation, 60% of patients have weakness in all 4 limbs
  - >60% unable to walk independently when maximum weakness is reached
- Respiratory weakness
  - Presenting symptom in 40% of patients
- Autonomic dysfunction
  - Postural hypotension → syncope
  - Sinus tachycardia
Miller Fisher

- Occurs in 5% of GBS cases
- Classic triad of ophthalmoplegia, ataxia and areflexia
- Presenting complaint usually diplopia
- Elevated CSF protein but less than other types of GBS
Acute Motor Axonal Neuropathy (AMAN)

- Acute/subacute paralysis or paresis without any sensory loss
- Loss of reflexes
- Facial/oropharyngeal muscle weakness
- Associated with *Campylobacter jejuni* gastric enteritis
  - >60% seropositive
Aetiology of GBS: Triggering Event

- >60% of cases preceded by upper respiratory tract infection or diarrhea 3 days–6 weeks prior to symptoms

- Campylobacter jejuni most frequently identified infectious agent (30%)
  - Incidence: 0.25–0.65/1000 cases of C. jejuni

- Cytomegalovirus (10%)

- Epstein-Barr virus, varicella-zoster, Mycoplasma pneumoniae
Immunizations and GBS

- Little evidence to support a causal association with most vaccines

- Older formulations of rabies vaccine cultured in mammalian brain tissue (Semple)

- Swine flu vaccine 1976–77
Time Course

- Pain 2 weeks after triggering event
- Weakness worsens over 2 weeks
- Symptoms plateau at 4 weeks
- Recovery begins
Differential Diagnosis

- **Acute peripheral neuropathies**
  - Toxic: thallium, arsenic, lead, n-hexane, organophosphate
  - Drugs: amiodarone, perhexiline, gold
  - Alcohol
  - Porphyria
  - Systemic vasculitis
  - Poliomyelitis
  - Diphtheria
  - Tick paralysis
Differential Diagnosis

- Disorders of Neuromuscular Transmission
  - Botulism
  - Myasthenia gravis

- Central Nervous System Disorders
  - Basilar artery occlusion
  - Acute cervical transverse myelitis
Diagnosis

- **History**

- **Examination**

- **Lumbar puncture**
  - Elevated CSF protein *without* pleocytosis

- **Nerve and muscle function tests**
  - Electromyography – is muscle weakness due to the muscle itself?
  - Nerve conduction studies
2. Clinical case definitions: Guillain–Barré syndrome (GBS)³,⁴,⁵

**Level 1 of diagnostic certainty**
- Bilateral AND flaccid weakness of the limbs⁶,⁷,⁸
  \[\text{AND}\]
- Decreased or absent deep tendon reflexes in weak limbs⁹
  \[\text{AND}\]
- Monophasic illness pattern¹⁰ AND interval between onset and nadir of weakness between 12 h and 28 days AND subsequent clinical plateau¹¹
  \[\text{AND}\]
- CSF total white cell count <50 cells/µl (with or without CSF protein elevation above laboratory normal value)¹³
  \[\text{OR}\]
- IF CSF not collected or results not available, electrophysiologic studies consistent with GBS¹²
  \[\text{AND}\]
- Absence of identified alternative diagnosis for weakness (see Appendix A.3)³.

**Level 2 of diagnostic certainty**
- Bilateral AND flaccid weakness of the limbs⁶,⁷,⁸
  \[\text{AND}\]
- Decreased or absent deep tendon reflexes in weak limbs⁹
  \[\text{AND}\]
- Absence of an identified alternative diagnosis for weakness (see Appendix A.3)³.
Nerve Conduction Tests

- Motor and sensory nerves

- Nerve conduction velocity is measured
  - Conduction slowing
  - Conduction block

- F waves and H reflexes
  - Prolonged or absent
Treatment

- **Supportive care**
  - Intubation
  - Occupational therapy
  - Physiotherapy
  - Speech and language therapy

- **Specific therapy**
  - Intravenous immunoglobulins
  - Plasmapheresis
Prognosis

- Recovery starts at ~2–4 weeks after symptom onset
- Months to years
  - 20% unable to walk 6 months after symptom onset
- Time to recovery depends on many factors
  - Age
  - Severity
  - Delay in receiving treatment
- Various prognostic scales
  - Patient’s age, presence/absence of antecedent diarrhea, severity
  - Time between weakness onset and admission, facial weakness
- Complications of intubation
  - Pneumonia, sepsis, PE in 60%
Prognosis Depends on Subtype

- **AIDP**
  - 5% mortality
  - >75% of patients have complete/near-complete recovery, no deficits or with mild residual fatigue and distal weakness

- **Miller Fisher**
  - Improvement begins at a median of 2 weeks
  - Full recovery takes a median of 1-3 months

- **AMAN**
  - Recovery time similar to or quicker than AIDP
GBS Surveillance

- **1976 influenza**
  - 40 million doses of influenza vaccine administered in US
  - Cluster of GBS cases noted
  - Vaccine associated with small, but statistically significant increased risk of GBS in 6 weeks post-vaccination

- **CDC Emerging Infections Program (EIP) 2009–10**
  - Active, population-based surveillance
  - Connecticut, Maryland, New Mexico, Tennessee, New York, Minnesota
  - Metropolitan areas in Georgia, Oregon, California, Colorado
Key Points

- **GBS characterised by:**
  - Muscle weakness or paralysis
  - Loss of reflexes
  - High protein in the CSF but a normal cell count

- **Not a single disease but a group of immune-mediated neuropathies**

- **Autoantibodies against cell membrane gangliosides**

- **Clusters are rare**
Simultaneous Outbreaks of Guillain-Barré Syndrome and Bell's Palsy in Hawaii in 1981

Jonathan E. Kaplan, MD; Joel R. Greenspan, MD; Mona Bomgaars, MD; Ned Wiebenga, MD; Robert D. Bart, Jr, MD; Kenneth Robbins, MD; Robert Wiebe, MD; Frank Tabrah, MD; John Stewart, MD; Lawrence B. Schonberger, MD

In early January, 1976, an outbreak of gastroenteritis caused by contamination of the water supply system occurred in Salt, Jordan. This
Association study between an outbreak of Guillain-Barre syndrome in Jilin, China, and preceding Campylobacter jejuni infection.


Department of Diagnosis, National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China.

Abstract
From June to July 2007, 36 cases of Guillain-Barre syndrome (GBS) occurred in a township in north China. Serological study and bacteria culture were performed to investigate the association between preceding Campylobacter jejuni infection and this GBS outbreak. Anti-C. jejuni antibodies were found in significantly higher numbers of GBS patients (IgM 84%, IgG 87.5%) than in healthy inspection cases in early January, 1970, an outbreak of gastroenteritis caused by contamination of the water supply system occurred in Salt, Jordan. This
Outbreaks

Guillain-Barre Syndrome Strikes AZ-Mexico Border

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
EXTRA SLIDES
Risk Factors

- Older age
- Male
- Recent gastrointestinal or respiratory infection
- Recent surgery
- History of lymphoma, lupus, AIDS