

Guillain-Barré Syndrome: A Mechanistic Study

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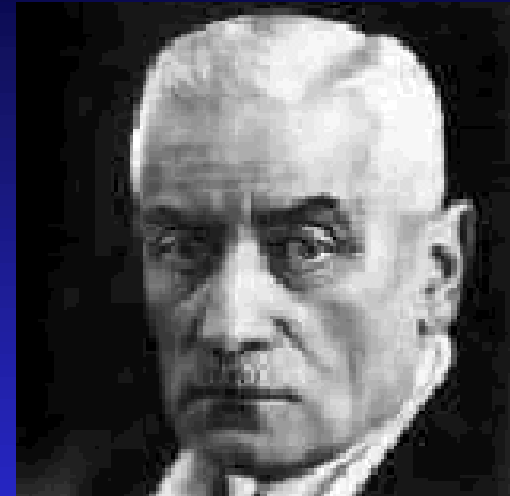
History

- First documented symptoms in 1859 Jean Baptiste Octave Landry de Thezillat (1826-1865)
- Called it Landry's ascending paralysis
- Affects both sensory and motor systems, but the motor system is the most vulnerable



History Cont'

- 1916 – Georges Guillain (top), Jean Alexander Barré (bottom), and Andre Strohl (not shown) documented decreased peripheral reflexes and increased CSF production with normal cell count
- Called it Guillain-Barré Syndrome



What Is Guillain-Barré Syndrome (GBS)

- An autoimmune demyelinating peripheral polyneuropathy
- Also called acute idiopathic polyneuritis
- Symmetric, rapidly progressive weakness which eventually leads to total paralysis, including the respiratory and gastrointestinal systems (in severe cases – 20-30%)
- Patients may develop CNS abnormalities, such as papilledema or extensor plantar responses
- Annual incidence of 0.6-1.9 cases per 100,000 (about 0.001% of the population)

Guillain-Barré Cont'

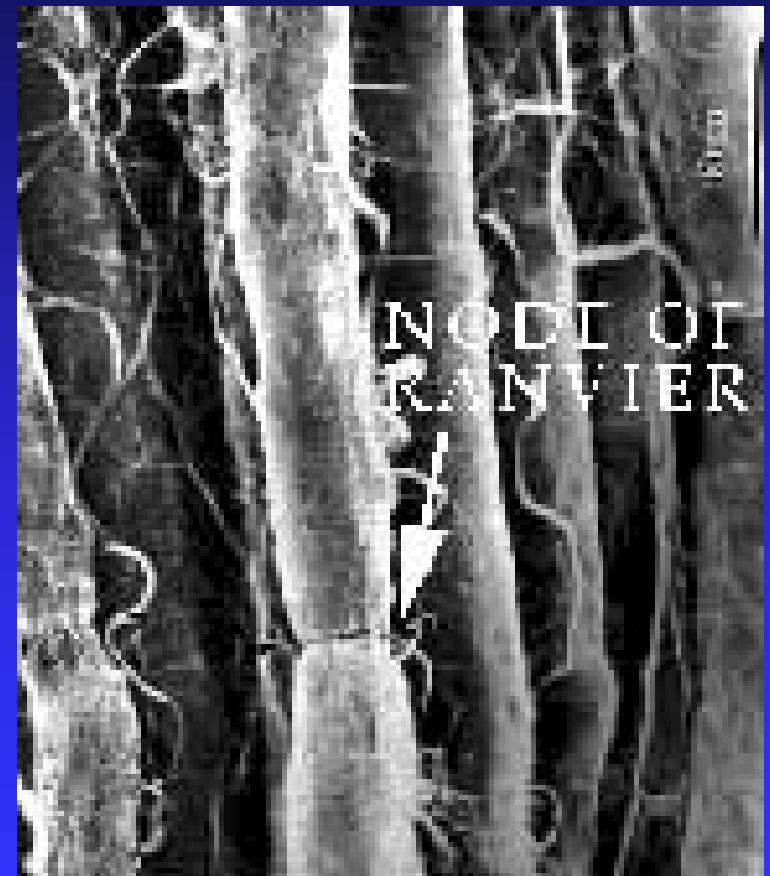
- Most severe stages of disease reached within two to four weeks
- 50% recover completely
- 35% experience permanent neurological damage
- 10% will relapse during recovery
- 2-5% experience recurrence after full recovery
- Death occurs in 5-8% of cases due to sepsis or pulmonary emboli

Guillain-Barré Cont'

- Often preceded by a viral/bacterial respiratory or gastrointestinal infection by 1-3 weeks
- Can also be associated with *Campylobacter jejuni* infection (most common), hepatitis, infectious mononucleosis, *Mycoplasma pneumoniae*, cytomegalovirus, vaccination, surgery, lymphoma, pregnancy, HIV, or SLE
- Lymphocytic infiltration of spinal roots and peripheral nerves
- Macrophage-mediated demyelination and secondary axonal degeneration

Guillain-Barré Cont'

- The first area of the nervous system appears to be at the Node of Ranvier
- During recovery, this is also the area that seems the remyelinate the slowest, dragging out the symptoms

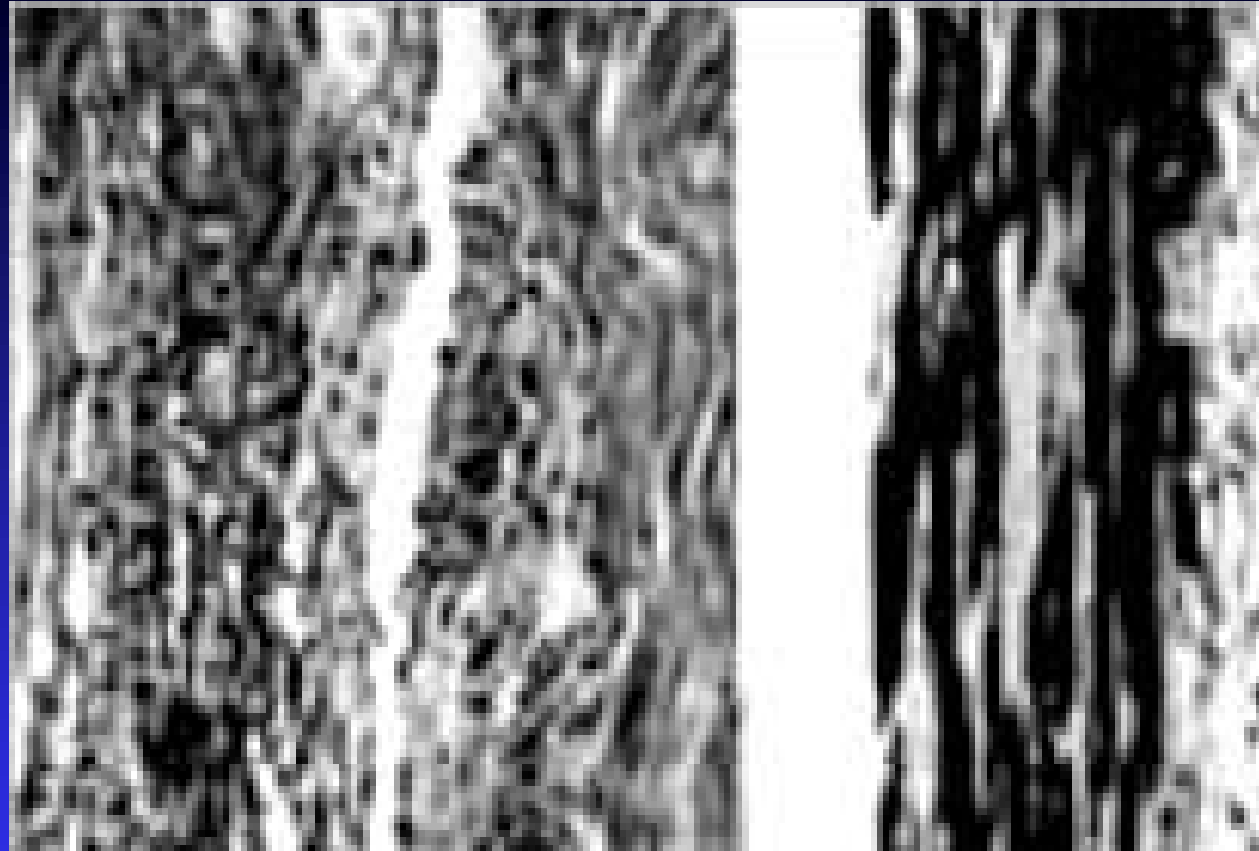


Symptoms (listed in order of syndrome progression)

- Numbness, tingling, and other sensations in distal extremities
- Complete paralysis of limbs
- Paralysis of breathing muscles
- Paralysis of swallowing mechanism
- Blood pressure and heart rate are also affected
- → Characteristic of familial dysautonomia and hypophosphataemia

Pathogenesis

- Mechanism is unclear, but believed to be immunologic
- In animals, caused by inoculation with myelin P-2 and GM antigens eliciting both a cell-mediated and humoral response
- Immune response to infecting organisms cross-reacts with neural tissues leading to the symptoms of GBS



These are microscopic views of peripheral nerves showing lymphocytic infiltration on the LEFT and fragmentation of myelin on the RIGHT.

Diagnosis

- Diagnosis very difficult due to its varied symptoms
- Spinal Tap to check for increased cytoalbumin dissociation
- Electromyogram (EMG) to test muscle activity and nerve conduction
- Nerve conduction Velocity Test (NVC) to test nerve impulse speeds

Treatment

- **High-dosage immunoglobulin therapy (IV IgG)**
- Intravenous injection of the proteins that, in small quantities, the immune system uses naturally to attack invading organisms
- 0.4 g/kg daily for 5 days
- Derived from a pool of thousands of normal donors, but supply is limited at this time
- Costly procedure
- Some renal impairment due to osmotic effect of sucrose in the solution

Treatment Cont'

- **Therapeutic plasma exchange (TPE) (aka plasmapheresis)**
- Five 50 mL/kg exchanges over 8-13 days
- Seems to reduce the severity and duration
- Appears to work better in children than adults

Treatment Cont'

- OTC analgesics, Valium for muscle spasms, and Gabapentin, a tricyclic antidepressant to treat lingering sensation problems
- Physiotherapy
- Hydrotherapy
- Note: Combination therapy does not appear to provide an additional benefit to recovery
- Corticosteroids have not shown to be of any benefit, except...

GBS Variations

→ Miller-Fisher Syndrome

- Acute disseminated encephalomyeloradiculopathy
- Very rare
- minimal motor weakness, gait ataxia, areflexia, and diplopia (ophthalmoparesis), facial sagging, and slurred speech (indicates all cranial nerves, esp. VII, but not I or II)
- More sensory based with no known cause
- Increased CSF protein
- Can be treated with corticosteroids such as methyl-prednisolone

GBS Variations

→ CIDP

- Chronic Inflammatory Demyelinating Polyradicalneuropathy
- Attacks the epitopes contained in the axonal membrane
- Less common than GBS
- Evolves more slowly – months to years
- Continuous periods of worsening and improvement
- Very depressing and debilitating
- Similar treatment methods

GBS Variations

→ GBS Axonal Form

- Nearly identical to demyelination except...
- Attack directly to the axon itself in the form of an acute toxic peripheral polyneuropathy
- Extremely debilitating
- Recovery rarely more than 40-50%
- Very poor prognosis

Continuing Research

- Find new treatments and refine existing ones
- Determine which immune cells are responsible
- Figure out why GBS usually results from viral and bacterial infections and their actions in the inappropriate immune response
- Come up with better preventative care

Final Comments

- Very devastating and potentially life-threatening illness
- Significant advances in treatment have been made that affect the disease course and outcome.
- Treatment requires a team approach
- Personal experience

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