# Guillain-Barré Syndrome (GBS)

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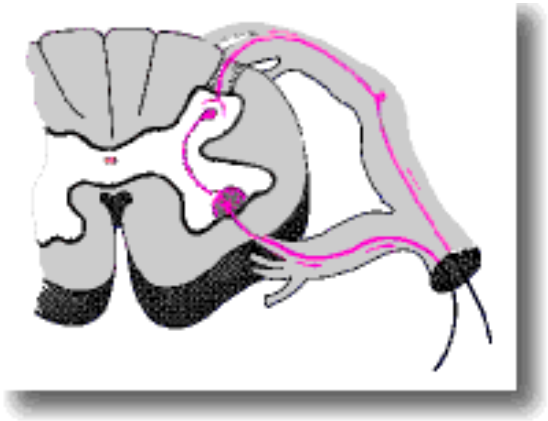


Disorder of spinal roots and peripheral nerves

Most common acquired polyneuropathy in children.

- 1 -2/100,000 general population
- Lifetime likelihood for any individual: 1:1000.
- M/F: may differ between subtypes, 1.4 in our series

Average age 6.3 years old, youngest 3 mo.

Rare neonatal form

Post infectious. No history of infection in 30%.

Common responsible agents: *C.jejuni,* EBV, CMV, HSV, *m.pneumoniae**.

Asymptomatic infection: C. jejuni 50% no GI Sx.
Post-immunisation? Surgery, transplantation.

**Clinically:**

- Walking difficulty 2-3 weeks (mean 12 days) after infection.
- sensory symptoms 20-60% (pain, paresthesia, hypoesthesia), sometimes only Sx.
- Weakness typically ascendent and symmetrical, up to flaccid quadriplegia. Rarely: “locked-in”

However: proximal predominance, non-ascending types too.

Approx. 60-80 % become nonambulatory during the illness.

*Korinthenberg 2007*

# Criteria

- Progressive, relatively symmetrical weakness of two or more limbs because of neuropathy.
- Areflexia.
- Progression < 4 weeks.
- Exclusion of other causes.

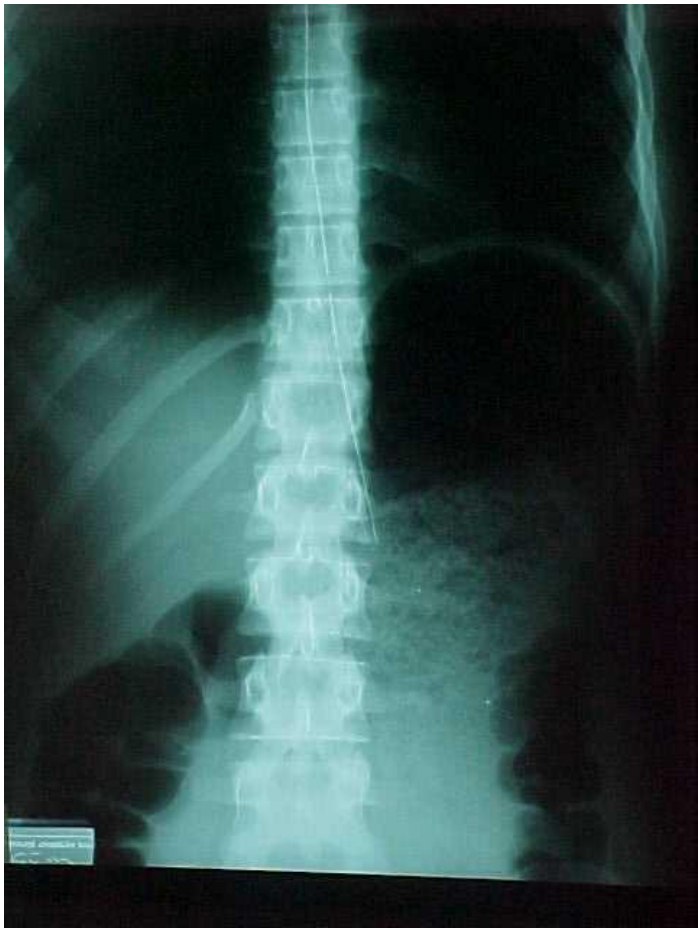
**Supportive**

- Relatively symmetric weakness accompanied by numbness and/or tingling.
- Mild sensory involvement.
- VII or other cranial nerve involvement.
- Absence of fever.
- Typical CSF findings
- Demyelination on ENMG.

- autonomic dysfunction.
- urinary or bowel problems

  <24 hours.
- respiratory failure: 25%.
- bulbar palsy, arm weakness

  esp. in rapid progression



# Neurological examination:

- symmetrical weakness. Persistent asymmetry is rare
- diminished or absent DTR 90%
- sensory deficit stocking- and-glove,
- cranial nerve involvement (**VII,** VIII,III, VI)

Autonomic disturbance: (sympathetic overactivity + parasympathetic underactivity*)

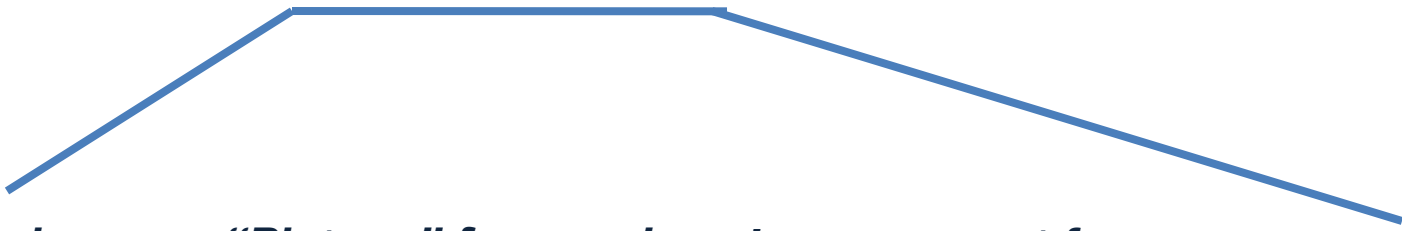
Tachycardia,  life-threatening arrhythmias, hypotension, hypertension

Bladder function, esp. in nonambulatory severe cases.

GI dysmotility*: abdominal distention, pain, cramps, constipation, ileus

*due to autoimmune damage of vagal nerve (stomach, small intestine, and much of the colon) and sacral parasympathetics (distal colon).

# Course



***Progression 1-4 weeks*** ***"Plateau" few weeks*** ***Improvement few mo-yrs***

In general benign, cure expected in 80%. Sequealae 10-20%, mortality 3-10%.

Treatment-related clinical fluctuations: may occur within 8 weeks after starting immunotherapy: still considered monophasic.

Slower progression (> 4 weeks): Subacute form

Progression after 8 weeks from onset or marked deterioration despite appropriate immunotherapy: acute-onset CIDP rather than GBS.

(relatively) negative features for outcome:

Time of onset to admission <7 days.
Inability to cough.
Inability to stand.
Inability to lift the elbows.
Inability to lift the head.
Increases in liver enzyme.

Forced vital capacity < 15-20 ml/kg.
Maximum inspiratory pressure <30 cm $H_2O$.
Maximum expiratory pressure <40 cm $H_2O$.
More than a 30% decrease in either forced vital capacity or maximum inspiratory pressure within 24 h

# Clinical Variants

**Miller-Fisher S**

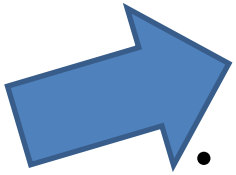
Complaint: Diplopia.

Ataxia.

No weakness.

Ptosis, pupillary reflex: III.

**Bickerstaff's brainstem encephalitis**



- **Bickerstaff** reported 8 patients: acute ophthalmoplegia, ataxia **+ drowsiness**
- **extensor plantar responses** (40%)**, hyperreflexia, or hemisensory loss.**

92% had an antecedent illness.

- **Flaccid symmetrical tetraparesis 60%** "overlapping GBS"
- facial diplegia (45%)
- bulbar palsy (34%)
- ENMG: motor axonal degeneration
- Serum **anti-GQ1b IgG** antibody 66%

**MRI** in MFS: cranial n. enhancement

in BBE: cranial n. enhancement and posterior fossa, white matter, thalamic lesions 30%

# BBE, MFS and GBS are within the same spectrum

# Other variants of GBS

Pharyngeal-cervical-brachial form

Oropharyngeal form

Isolated forms: Pure sensory *

Pure autonomic

Regional or asymmetric distribution

DTR normal or brisk (10%) *(antiGM1 or antiGD1a, AMAN)*

**Notturno 2008: pure acute sensory ataxic neuropathy with anti-GQ1b and anti-GD1b*

*2/3:recent C. jejuni infection. Anti-GD1b, -GQ1b -GD1b,-GT1a.*

*Motor nerve conduction: normal.*

*Sensory nerves: reduced amplitude or absent action potentials.*

*All recovered in 2 months and ENMG: in 3-5 months*

# MFS or acute ataxic neuropathy?

Acute sensory ataxic neuropathy : profound sensory ataxia

no ophthalmoplegia

Romberg sign +

ataxic GBS?

| | acute sensory ataxic neuropathy | ataxic GBS |
|---|---|---|
| AntiGQ1b antibodies | 18% | 65% |
| AntiGD1b IgG antibodies | 35% | 14% |

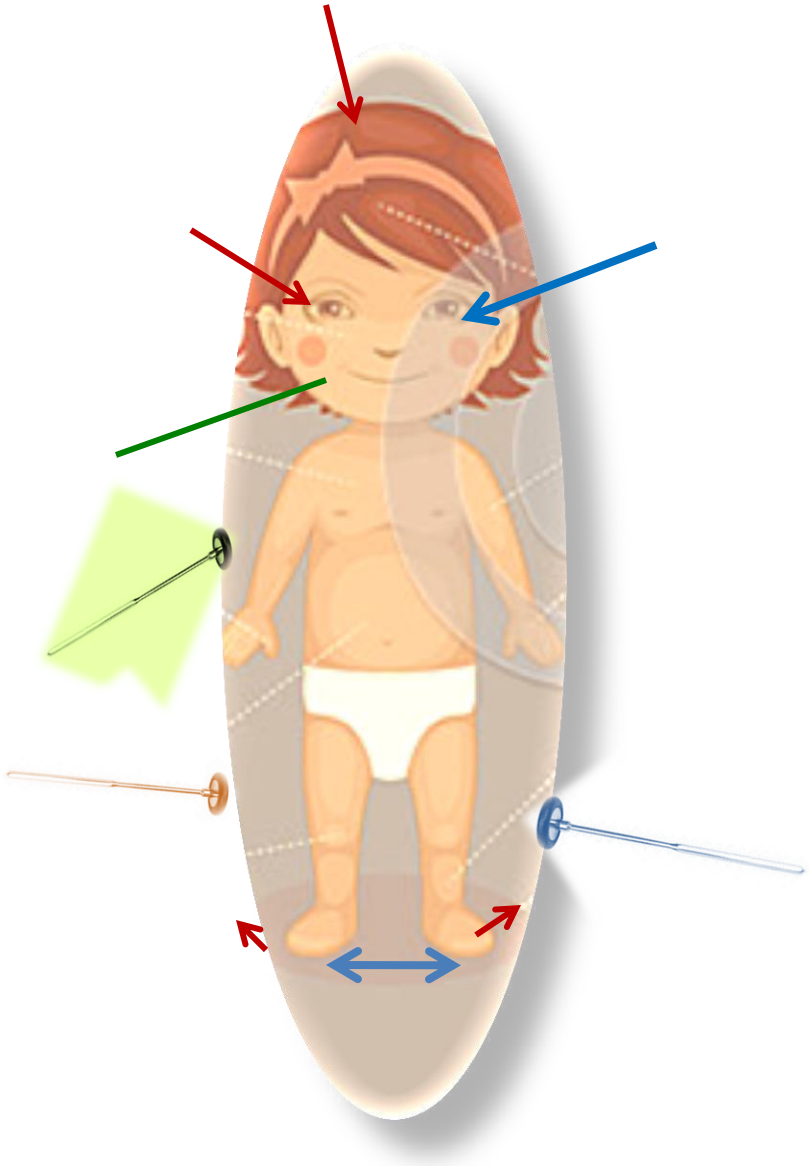
variants within a continuous spectrum

# overlapping

- **MFS** (1/3 original patients drowsiness)
- **Brainstem encephalitis** who develop limb weakness can overlap with GBS. BBE can have absence of H reflex. Bickerstaff ’s patients: 50% hypo/areflexia

- **GBS pharyngeal-cervical-brachial variant** overlaps with BBE, MFS

- Overlap between: GBS-ADEM, GBS-myelitis



## Electrophysiological-pathological-geographical subtypes:

- A. inflammatory demyelinating polyradiculoneuropathy (AIDP),
- A. motor and sensory axonal neuropathy (AMAN/AMSAN),

AMSAN: adults<children, not geographic. Abrupt onset, rapid progression. Mechanical ventilation: freq. Outcome: usually residual disability

Certain types are related to geography and season.

In Western Europe, N.America, Australia, 80- 90% of GBS in children: AIDP

In Northern China, S.America and Japan, 50 -70% of GBS in children: AMAN.

In Turkey: 50% AIDP,
40% AMAN.

- Axonal forms also associated with antiganglioside antibodies
- All GBS patients might show promptly reversible nerve conduction failure or axonal degeneration.

This suggests **a common pathogenetic mechanism** of Ab-mediated dysfunction or disruption at the nodes of Ranvier, resulting in a continuum of nerve pathologies from

transitory conduction failure to axonal degeneration.

In ≈ 40% of patients, nerve conduction studies within 1st week may suggest neuropathy without showing criteria for electrophysiological subtype.
ENMG results later change in 24–38% of patients: accurate classification depends on timing?

"Rather than broadly categorizing each subtype as an axonal or demyelinating neuropathy, we propose new diagnostic criteria based on an inclusive set of clinical features"

Wakerley, *Uncini, Yuki for the GBS Classification Group*
*Nat. Rev. Neurol*. 10, 537–544 (2014)

# Differential diagnosis

- Acute myelopathy: inflammation (myelitis), compression, ischemia.
- Brainstem encephalitis (Bickerstaff's)
- Acute anterior poliomyelitis: polio, also non-polio enterovirus

Hyperreflexia, Babinski (corticospinal findings may be absent early).

enterovirus 71: acute flaccid paraparesis. Australia,Cambodia. Prodromal diarrhoea, lethargy, irritability, nuchal rigidity. Then acute flaccid paraparesis up to 20%. West Nile virus (WNV): poliomyelitis syndrome, asymmetric paralysis: monoparesis-quadriparesis. Enterovi 68 ? Five cases.

- **Chronic** inflam. demyelinating p.n.pathy (CIDP) may start acutely, progress rapidly (< 4 weeks).

  Clinical or ENG evidence of ongoing demyelination. Usually more proximal, usually no antecedent inf.

- CNS infection: GBS can present with meningismus and IICP
- Polymyositis:

  Bilateral proximal weakness over weeks-months. Patient ill, myalgia, fever, muscles tenderness.

  (GBS also: poorly localized pain on the back, buttocks, legs, muscle pain -irritability, and dysesthesia as many as 50% at presentation).

- **Neuromuscular transm. disorders**: myasthenia (no sensory symptoms). Botulism (infantile) nausea, vomiting, constipation, ophthalmoplegia, ptosis, dilated pupils, blurred vision, dysphagia, dysarthria, urinary retention. No cranial involvement rules out botulism.
- **Periodic paralyses** with hypo K, hypo P
- **Pseudoparalysis** (trauma, JIA, ARF).
- **Other polyneuropathies:**
  - ✓ **CMV** in immunosuppressed patients
  - ✓ **toxic** (axonal).
  - ✓ **metabolic**: Leigh S, vit B1/B12 def.
  - ✓ **critical illness**,
  - ✓ **vasculitic,**
  - ✓ **Lyme** (endemic area, season; tick bite, CSF pleocytosis. Axonal)
  - ✓ **porphyria** Usually more asymmetric. Axonal. In 50% weakness starts in the arms -- may be confused with pharyngeal-cervical-brachial GBS. Severe abdominal pain, psychiatric symptoms or seizures.

# *Diagnostic delays and errors in young children:*

*Roodbol et al. 2011*

| | 23 preschool | 32 older |
|---|---|---|
| initially misdiagnosed | **68%** | **21%** |
| delay until going to pediatrician | **5 days** | **5 days** |
| Delay until GBS Dx | **3 days** | **0 days** |
| Common Sx | refusal to walk<br>leg pain | weakness,<br>paresthesia |

myopathy, tonsillitis, meningitis, rheumatoid disorders, coxitis, discitis

# Laboratory: may be normal in the first days. Diagnosis essentially clinical

**CSF protein**

Increased in 50% on day 1, in 90% day 15.

pleocytosis: think infectious (HIV, CMV, Lyme), sarcoid, Leu/lymphoma

**ENMG** abnormal after 2nd week: features of *acquired* demyelination.

temporal dispersion,

prolonged distal and F-wave latencies,

non-uniform slowing conduction velocities, conduction block.

In 1.week: 50-70% "sural-sparing" pattern in sensory n.

***normal in sural + abnormal in upper* extremities (ulnar or median)**

- Frequent, less specific: absent H-reflexes, low motor CMAP amplitudes on distal stimulation, prolonged F-wave responses.
- Related to prognosis: very low CMAPs on distal stimulation at initial testing: probability of poor outcome.
- Often non-diagnostic in the first week. Do not delay treatment, if GBS likely

Required for Diagnosis:

- Progressive weakness in two or more limbs.
- Areflexia

(distal areflexia + proximal hyporeflexia enough if other features are consistent).

Strongly Supportive of Diagnosis:

Progression <4 weeks

50% by 2 wks,

80% by 3 wks,

90% by 4 wks.

Relative symmetry, seldom absolute

Mild sensory symptoms or signs.

Cranial nerve **VII ~**50 %, freq.bilateral.

Autonomic dysfunction.

Recovery begins 2-4 weeks after progression stops.

Absence of fever at onset of neurologic symptoms.

# THESE SUGGEST VARIANT CLINICAL FORMS:

1. Fever at onset of neuropathy
2. Severe sensory loss with pain
3. Progression >4 wks.
4. Cessation of progression- no recovery, or major residual deficit
5. Sphincter dysfunction (usually bladder only transiently)
6. CNS involvement (occasional patients: extensor plantar responses and ill-defined sensory levels)
7. Transient neck and back stiffness early in the course, resolution within days.

# Cast doubt on the diagnosis

Marked, persistent asymmetry

Bladder or bowel dysfunction at onset.

Persistent bladder or bowel dysfunction.

Sharp sensory level.

CSF: >50 mononuclear leukocytes or any polymorphonuclear leukocytes

No CSF protein rise in 1-10 weeks after onset (rare).

# Is autoimmune serology helpful in the diagnosis?

- 50-60% of acute-phase sera: Ab against at least one ganglioside
- Titers decrease with clinical improvement: cause, not a result, of nerve damage
- Anti-GQ1b and GT1a: Miller Fisher syndrome and GBS with ophthalmoplegia.

- Anti-GQ1b in ~95% of patients with acute MFS and approx. 2/3 of BBE. **the "anti-GQ1b antibody syndrome".**
- anti-GT1a: pharyngeal-cervical-brachial variant
- anti- GM1 and GM1b: AMAN

**BUT many centres test only for anti-GM1 and anti-GQ1b and results are often delayed.**

# Gangliosides:

Each ganglioside has particular distribution in the peripheral nervous system

Biochemical analysis of extracts: GQ1b is present in cranial n. and spinal nerve roots (ventral and dorsal):

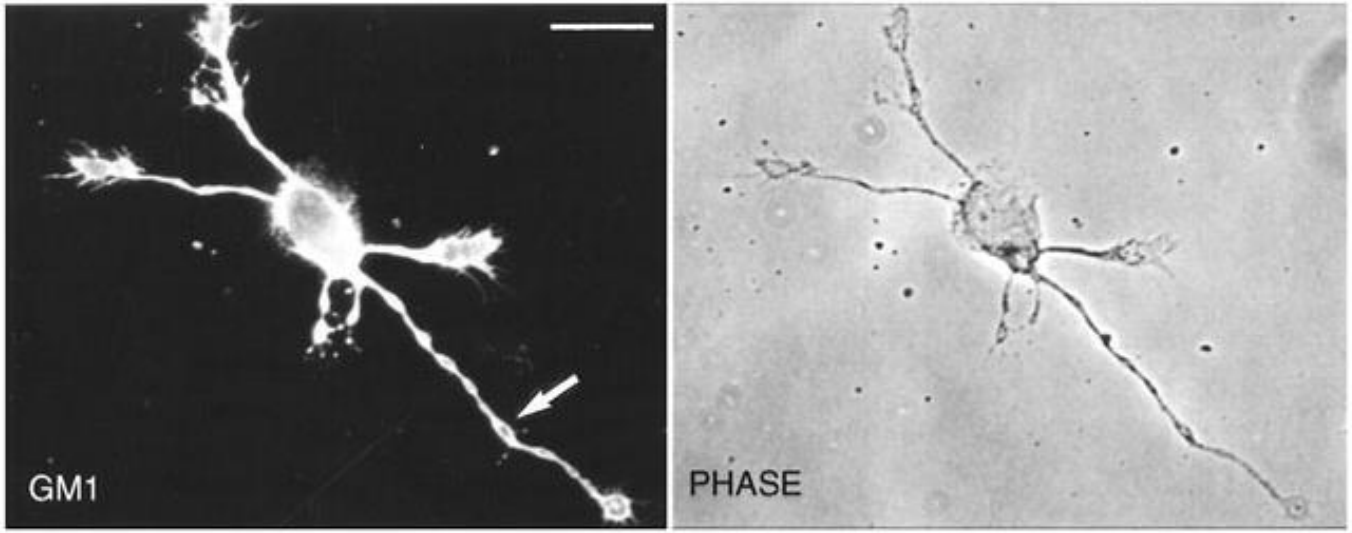
III, IV, VI have higher content GQ1b

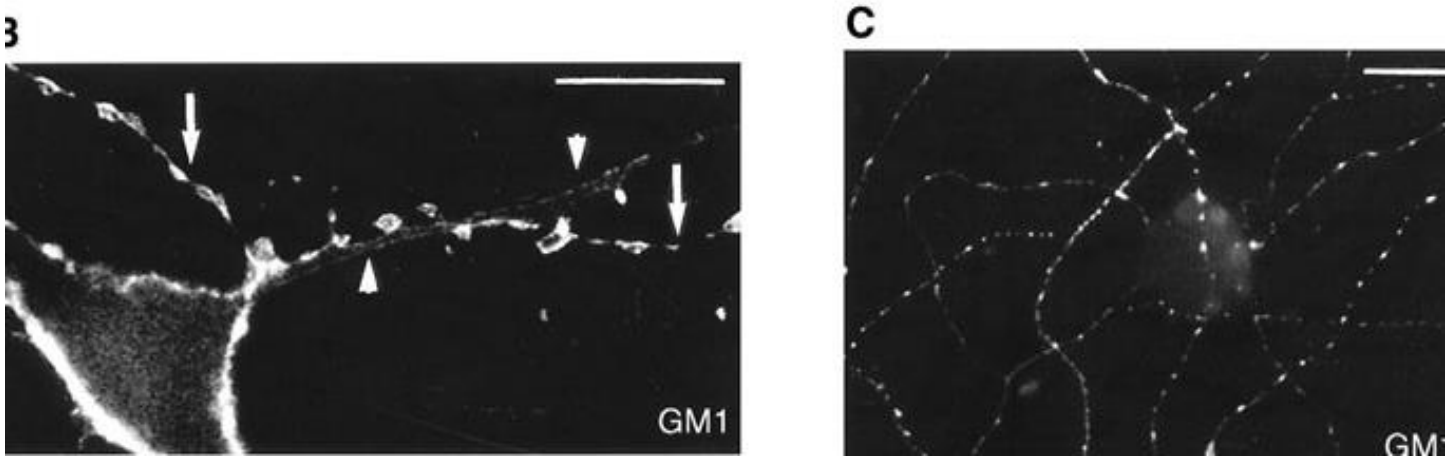
interact with receptors or signal transducers;

Abs may affect the function of the axon or Schwann cell—impair nerve conduction

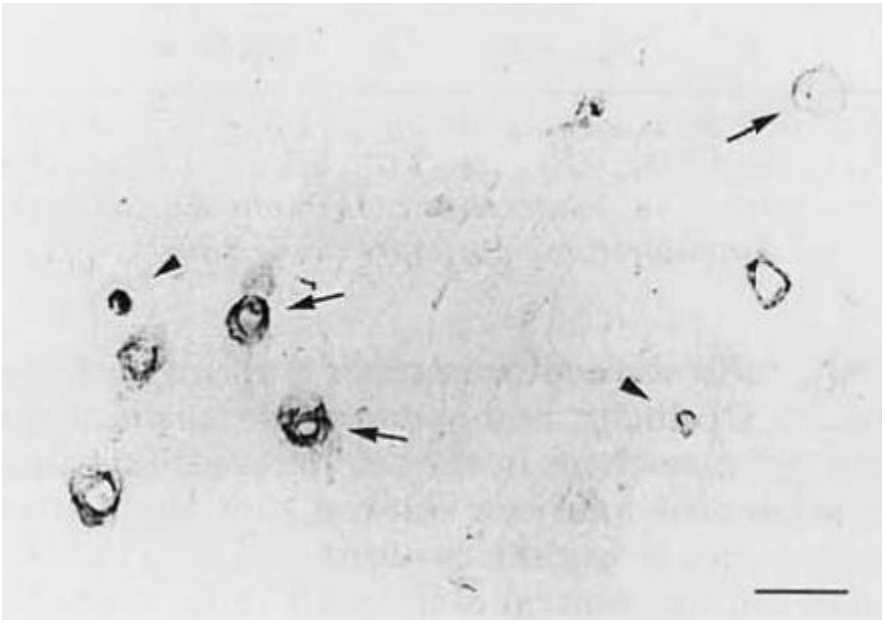
*Kusunoki 1999*

GM1 on the surface of both axon (arrow) and dendrites of stage 3 neurons




Stage 5 neuron: dendrite (arrowheads) is devoid of GM1 staining. *Ledesma et al 1999*



*Oculomotor nerve immunostained with anti-GQ monoclonal Ab.*

*unstained axoplasm surrounded by a stained portion.*

*Chiba, Neurology 1993*

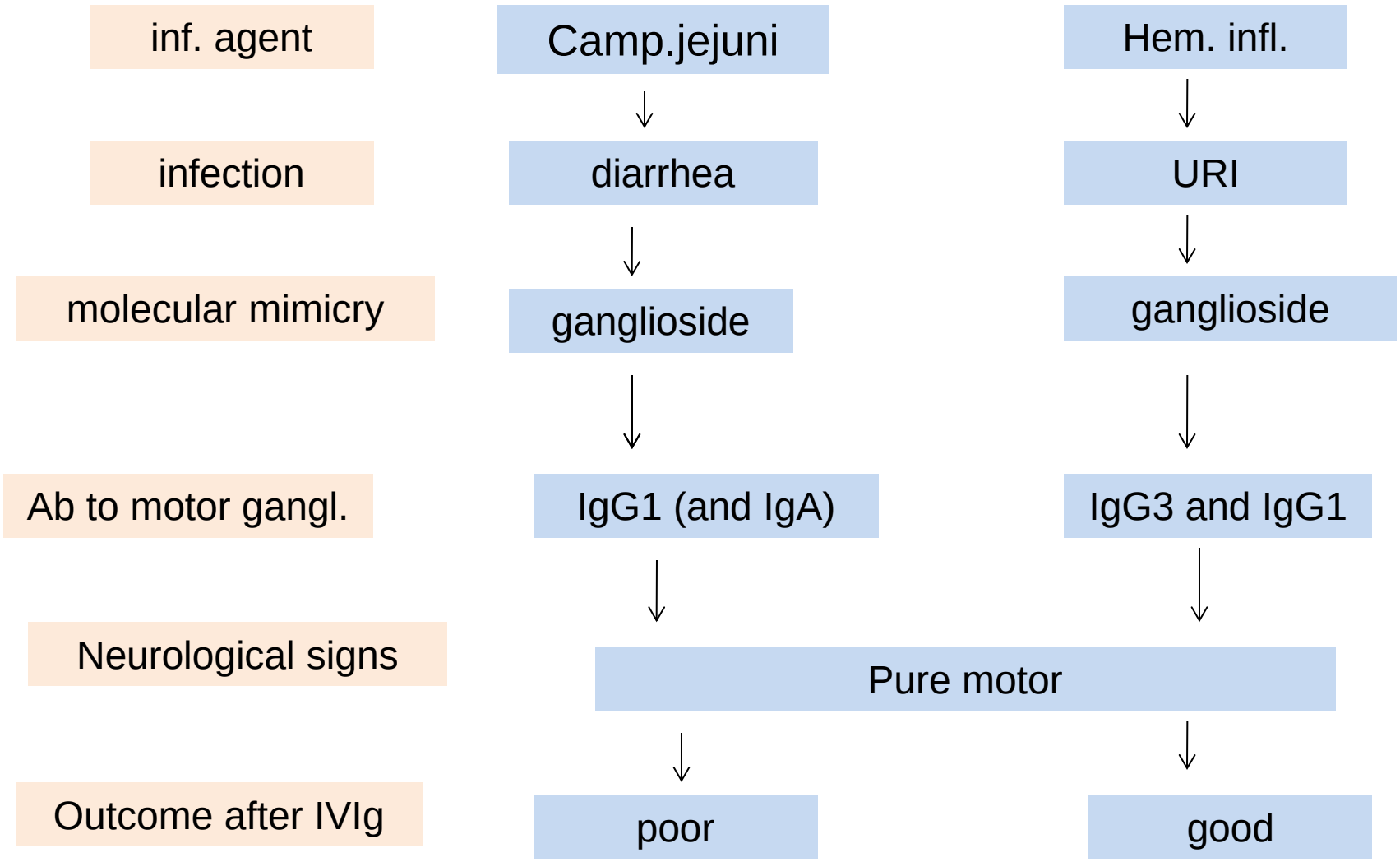
# Some Abs may be related to prognosis:

Response to plasmapheresis may vary with the IgG subclass of the Ab

Anti-ganglioside Abs are highly variable in specificity, avidity, titer and subclass.

- *C. jejuni* …. GM1, GM1b, GD1a, GalNAc-GD1a and pure motor or axonal variants
- *C. jejuni* …. also GQ1b and GT1a and oculomotor weakness
- GM1, GM1b, GD1a, GalNAc-GD1a : **diarrhea.** Patients with preceding diarrhea --poor recovery after IVIg.
- Preceding **URTI** and negative *C. jejuni* serology…. IgG3 and IgG1-better recovery after IVIg.
- *H. influenzae* IOS: …. GM1
- CMV …… IgM against GM2, severe motor-sensory, frequent VII. nerve

*Yuki 2012*


inf. agent
Camp.jejuni
Hem. infl.
infection
diarrhea
URI
molecular mimicry
ganglioside
ganglioside
Ab to motor gangl.
IgG1 (and IgA)
IgG3 and IgG1
Neurological signs
Pure motor
Outcome after IVIg
poor
good

| **Polyclonal antibodies against** | **Neurological disease** |
|---|---|
| GA1 | GBS, MMN,lower motor neuron dis., motor neuropathy, CIDP |
| GM1 | GBS, AMAN, MMN, lower motor neuron dis, ALS, motor neuropathy CIDP |
| GM1 | GBS |
| GM1b | GBS |
| GM2 | GBS , motor-sensory neuropathy |
| GD1a | AMAN, MMN, motor neuropathy |
| GalNAc-GD1a | GBS AMAN, motor neuropathy |
| GD1b | GBS ataxic GBS MMN CIDP, ataxic sensory neuropathy, Chr. ataxic sensory neuropathy w.ophthalmoplegia |
| GD2 | Chr. ataxic sensory neuropathy w.ophthalmoplegia |
| GD3 | Chr. ataxic sensory neuropathy w.ophthalmoplegia |
| GT1a | Oropharyngeal GBS, MFS, BBE, acute ophtalmoparesis |
| GT1b | Chr. ataxic sensory neuropathy w.ophthalmoplegia |
| GQ1b | MFS, BBE,acute ophtalmoparesis, Chr. ataxic sensory neuropathy w.ophthalmoplegia |

# How Are Abs Synthesized?

- Both T-cell dependent and T-independent response against glycans

- Anti-GM1 antibodies in GBS: $IgG_1$ or $IgG_3$ subclass are T-cell-dependent
- T-cell-independent anti-GM1 IgM found at low level in normal individuals, but higher titers in neuropathy patients.

- Immunogenicity of GM1 in humans:

bovine brain gangliosides and purified

GM1 were applied for treatment of various diseases

a few patients developed GBS

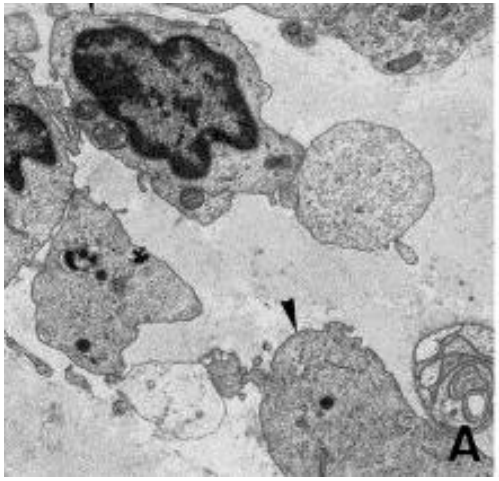
with antiGM1 antibodies

The New York Times 2008

# Molecular mimicry or “better fit” hypothesis?

- B-lymphocytes undergo mutation of their V genes and modification of their binding sites.
- Some of these mutations produce a better “fit” in the IgM antibody/GM1 contact area,
- allowing new binding points (binding site expansion) that increase affinity for GM1.
  - ❑ In most normal individuals, high-affinity B-lymphocytes are absent and there is no immune response to GM1.
  - ❑ In GBS, the antibody response has class-switched from IgM to complement-fixing IgG1 and IgG3 isotypes.
- Control mechanism for drift: normal plasma contains Abs that block binding of pathogenic anti-GM1 antibodies
- IVIG may do the same

# Effector mechanisms




- Nerve terminal damage after Ab and C binding:
- Demyelination earliest at proximal nerve roots and distal IM nerve twigs **where the blood-nerve barriers are weak**: the perisynaptic Schwann cell can be damaged by antiganglioside Ab.
- Activation of C pathway-- membrane attack complex --terminal axon cytoskeleton , mitochondria damage

AIDP: demyelination, lymphocytic infiltration, macrophage-mediated clearance of myelin

Axonal form:

- Target epitopes are likely the constituents of the axolemma of motor fibers.
- *Macrophages* attracted to Ranvier by C products dissect into the internodal periaxonal spaces, displace axons from inner Schwann cell plasmalemma, and cause axonal degeneration: more protracted course and incomplete recovery.
- *Ab binding* may alter Na+ *channel function*, causing conduction block: rapid improvement.

# Genetic predisposition?

- A patient with severe tetraparesis, bulbar syndrome, and ophthalmoparesis. The nadir was reached within 1 day, requiring mechanical ventilation.
- Molecular analysis revealed a duplication at chromosome 17p11.2-12, the genetic cause of Charcot-Marie-Tooth disease type 1A (CMT1A).

*(Munch et al 08)*

Treatment: only supportive treatment reduces mortality.

SPECIFIC Treatment:

Admit to hospital

Close follow-up during progressive phase (ventilation bag, tracheotomy set bedside).

**Intravenous immunoglobulin** (IVIg) in the first 2-4 weeks of symptoms

**Plasmapheresis** (PE) (1 plasma vol.50 mL/kg with 5% alb.)

PE done after 7 days ,

IVIg given after 2 weeks …… benefit questionable.

Mild GBS: IVIg (2 PE for adults). Moderate/Severe GBS, bulbar GBS, BBE overlapping GBS: PE, IVIg (4 PE for adults). MFS:? Outcome good

IVIG after PE: not significantly better than PE alone

Pediatric trial comparing 2 g/kg IVIG over 2 days vs. 5 days: no difference in recovery. Two-day group: more early relapses.

**In children:**

moderate/severe GBS , IVIG the first-line drug

protracted cases: IV steroids added to IVIG **may** hasten independent walking.

If such therapy fails: PE

Oral corticosteroids? combined with IVIg, *may* hasten recovery.

*Hughes et al Brain, 2007*

Complications of IVIg:

Certain do not respond, or ***even worsen after***

Expensive and not free of side effects

- Acute tubular necrosis: products with high sucrose.
- Anaphylactic reaction due to the IgA in patients with common variable immunodeficiency

Immunoadsorption removes Ig from circulation, fewer side effects.

# SYMPTOMATIC TREATMENT

Monitoring and management for Respiratory and Airway Compromise

Respiratory failure requiring mechanical ventilation: 20-30% of adults, 9% in our series

Monitor signs of respiratory insufficiency:

- anxiety,
- pallor,
- restlessness,
- tachypnea,
- use of accessory muscles,
- asynchronous chest and abdomen movements,
- tachycardia

At risk for mechanical ventilation:

time from onset to admission <1 week,

facial weakness,

inability to cough,

inability to lift head off pillow,

atelectasis on chest X-ray

demyelinating –axonal?

Sometimes mechanical ventilation is indicated because of severe bulbar dysfunction: secretions, risk of aspiration.

*(Burns, 2008)*

# Complications of mechanical ventilation:

pneumonia, pulmonary embolus, bacteremia.

Tracheostomy-when?

2 weeks following intubation, but if pulmonary function tests and strength are improving at 2 weeks, allow 1 more week

Early tracheotomy improves patient comfort, airway safety, weaning.

but complications: hemorrhage, infection, dislodgement of the tube

# Autonomic Dysfunction: take care during patient care

Severe dysautonomia most likely at clinical nadir (such as intensive care patient) but can also occur early in the disease

Cardiac and hemodynamic disturbances:

tachycardia , hypertension*, postural hypotension * --identify patients at risk for severe bradycardia, heart block, and asystole.

Endotracheal suction and pharmacological agents may provoke bradycardia and asystole: hyperoxygenate before suction to minimize the effects of severe bradycardia.

*labile; can be followed by hypotension. Do not leave patients at risk upright.

Blood pressure and heart rate monitoring until clinical improvement

*Disturbances of heart rate and blood pressure can also be due to:

pulmonary embolus, sepsis, dehydration, pain, and electrolyte disturbance

- Do: routine abdominal auscultation.
- Tx: Interrupt enteral feeding, nasogastric suctioning, and erythromycin. If possible, avoid narcotics
- Parenteral nutrition if > a few days.

Quadriplegic patients should not be left unattended in the sitting position without assessment of orthostatic hypotension.

Intravascular volume should be maintained, particularly during positive-pressure ventilation.

Drugs with hypotensive side effects should be avoided

Arrhythmias frequently occur during suctioning.

Succinylcholine should be avoided.

Plasma exchange can cause hypotension and electrolyte disturbances.

# Pain Management

- Back and extremity pain
- Not correlated with degree of disability.

1. try acetaminophen or nonsteroidal anti-inflammatory agents
2. as for neuropathic pain: GBP, CBZ, Amitriptylline

prevention of complications (bed sores, urinary infections, pulmonary complications or renal calculi due to immobilization) by:

positioning, physical therapy and rehabilitation as soon as patient stable

exercise regimen

range-of-motion exercises to prevent shortening of weak muscles, joint contractures

strength exercises, but avoid overworking muscles

orthotics

sensory reintegration techn., repetitive exercises for proprioceptive loss and ataxia

Persistent fatigue is a common problem due to permanent axon loss

# PROGNOSIS and OUTCOME

- Most of the recovery  in first year, but even during 2-6 years
- Persistent disability in 20-30% of adults, much less in children
- more common with axonal, severe, mechanically ventilated patients
- rapid progression associated with long-term prognosis.
- In some studies, axonal involvement at initial ENMG also related to poorer outcome.
- GBS disability score at 2 weeks after admission,
- diarrhea
- age

# Guillain-Barré Syndrome Disability Score

0 = healthy state

1 = minor symptoms and capable of running

2 = able to walk >10 m without assistance,unable to run

3 = able to walk 10 m across an open space with help

4 = bedridden or chairbound

5 = req.assisted ventilation for at least part of the day

6 = dead

# Future Immunisations

- Withhold 1 year, then continue routine immunization
- Influenza, tetanus, and typhoid: associated with relapse
- Influenza vaccination: 1-2 additional GBS cases/$10^6$ doses. Weigh risk/benefit
- British GBS patients: 11/311 (3.5%) reported symptoms within 6 weeks of immunization
- No patient needed hospitalization or treatment.

## Clinical Characteristics of Guillain-Barre Syndrome

Çetin Okuyaz, Semra Kurul, and *the Turkish Guillain-Barre Study Group

M:F 1.3

Age 6.7 ± 4.2 years (6.2)

ENMG: 48% demyelinating, 38% axonal .

Axonal-demyelinating: only difference in severity **score: axonal worse at onset (p<0.022)**

- CSF protein 13-384 mg/dl, elevated in 82%. **Clinical score (weakness) at onset and discharge: less in patients with increased CSF protein** (demyelination rather than axonal, or timing of LP: milder cases admitted and investigated later, therefore protein higher )

**Patients weaker at onset require ventilation, stay longer, and are weaker 6-12 months after discharge.**

| | All Cases | Electrophysiological subtypes | | p |
|---|---|---|---|---|
| | | Demyelinating | Axonal | |
| **Age (y)** | 6.74 ± 4.28 | 7.46 ± 4.0 | 6.20 ± 4.34 y | >0.05 |
| **Sex** | 130 M, 96 F | 42 M, 38 F | 49 M, 30 F | >0.05 |
| **Duration (d) weakness** | 7.93 ± 7.96 | 7.58 ± 6.94 | 8.41 ± 8.84 | >0.05 |
| **Duration (d) hospitalization** | 14.79 ± 19.02 | 13.41 ± 8.26 | 16.07 ± 21.97 | >0.05 |
| **CSF protein** mg/dl | 96.56 ± 63.81 | 94.03 ± 59.0 | 96.34 ± 61.64 d | >0.05 |
| **Distribution weakness %** | Parap. (53.4)<br>Tetrap. (31.7)<br>Tetrap.+ bulbar (14.9) | Parap. (54.4)<br>Tetrap. (34.2)<br>Tetrap.+ bulbar (11.4) | Parap. (43.0)<br>Tetrap. (38.0)<br>Tetrap.+ bulbar (19.0) | >0.05 |
| **Sensory %** | 23.9 | 25.3 | 15.4 | >0.05 |
| **Sphincter %** | 2.3 | 3.8 | 0 | >0.05 |
| **Cranial n.%** | 16 | 19 | 19.7 | >0.05 |
| **Ventilation requirement %** | 9.2 | 8.8 | 11.8 | >0.05 |
| **Treatment %** | None (24.8)<br>IVIg (0.8)<br>Plasmaph. (10.4) | None (28.3)<br>IVIg (56.3)<br>IVIg+Plasmaph.(15.0) | None (26.6)<br>IVIg (58.2)<br>Plasmaph.(12.7) | >0.05 |

# Case:

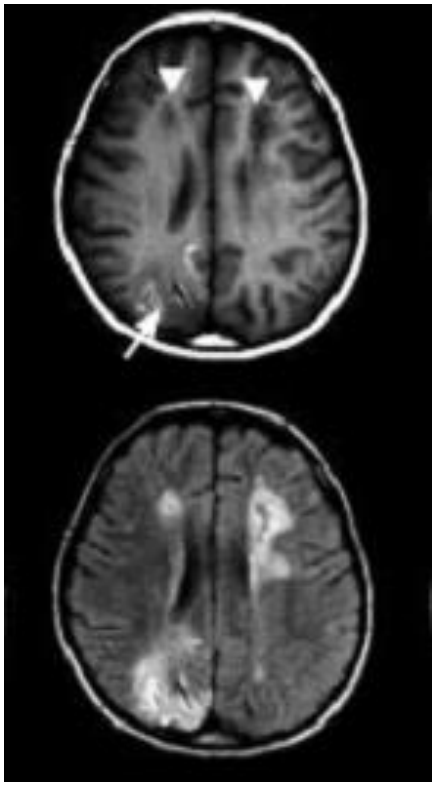
9 year old girl admitted for progressive ascending weakness for 5 days.

NE: can not stand up. DTR absent

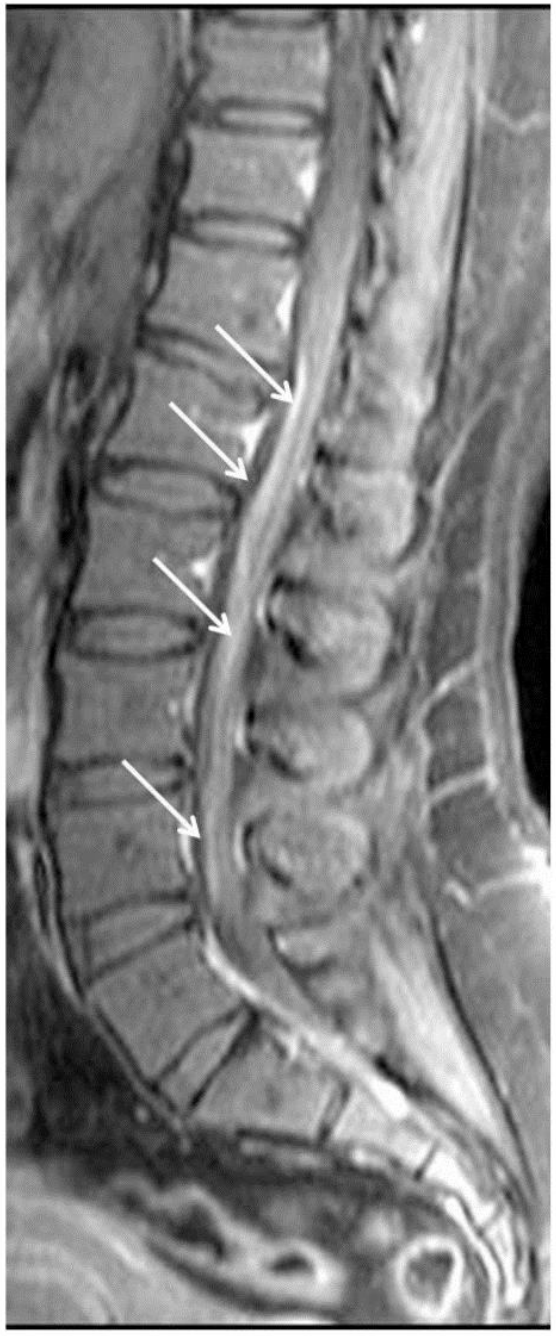
CSF cell count of $1\times10^9$/l and 89 mg/dl protein.

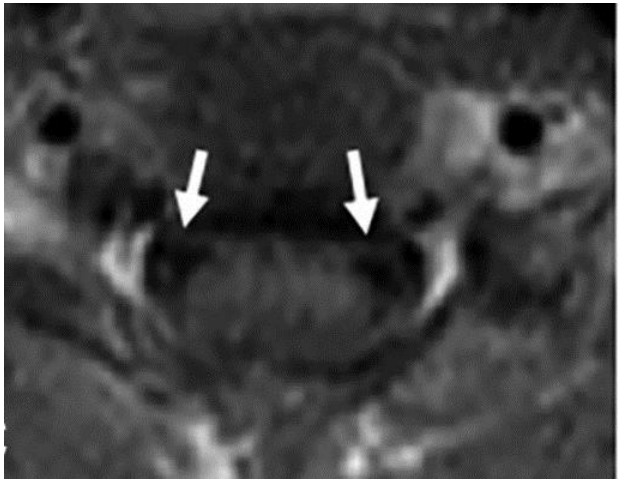
NCV decreased.

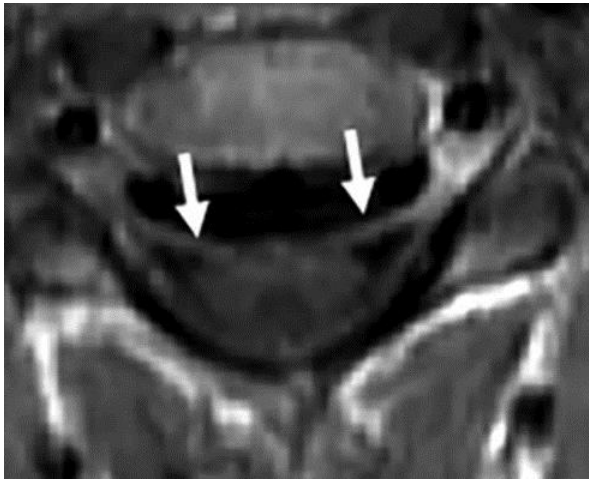
IVIg 5 days no improvement. Headache, meningism on day 4 of IVIg

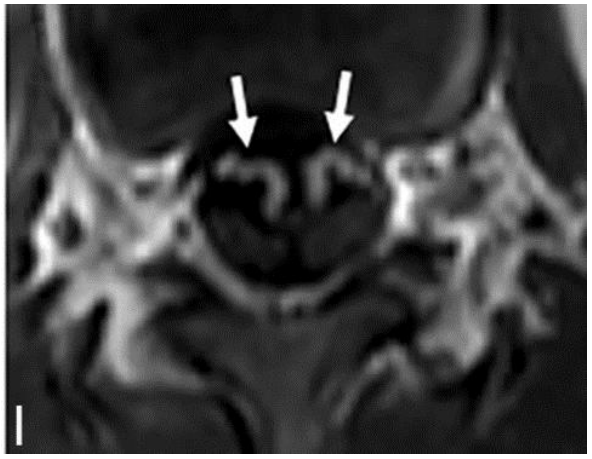


CNS lesions can be silent









Alkan et al 2009

# Case: 9 y.o. girl *Lacroix et al 2010*

fever for 10 days, productive cough, colicky abdominal pain, vomiting.

Clarithromycin for interstitial pneumonia on chest X-ray.

Also headache, diffuse leg pain, weakness

PE: respiratory rate 30 breaths/min, pulse 100 /min. Retractions, nasal flaring, abdominal breathing. Oxygen saturation 88%.

Hypoventilation of the right lung, wheezing, diffuse crackles.

Blood pressure high (165/105 mm Hg).

NE: Neck pain and stiffness on anterior flexion.

DTR absent – spinal cord CT normal

Had to be intubated

**CSF normal**

A second lumbar puncture on day 6: marked increase of protein

# Case

- 2-year-old girl transferred with lethargy, anorexia, and inability to walk for 1 day.
- Muscle tone decreased in all four extremities; able to sit briefly, unable to stand.
  CSF:  Normal
- Worsens in 24 h: no movements in extremities
- 36 h: lethargic and difficult to arouse, unable to follow commands, no verbal output.
  small reactive pupils , eye movements intact.
- Motor examination, truncal hypotonia, poor head control, unable to sit w/o support.

  minimal spontaneous movements in extremities; briefly able to elevate upper and lower extremities against gravity.
- Feels noxious stimuli applied to all four extremities.
- DTR  2+ in biceps and triceps , absent in patella, and 1+ in Achilles. plantar responses  flexor
- Neurological consultation. GBS?

# Important part of PE

Burke et al 2014

- removal of the tick,
- lethargy significantly improved within hours
- Next day:  strength  near normal.

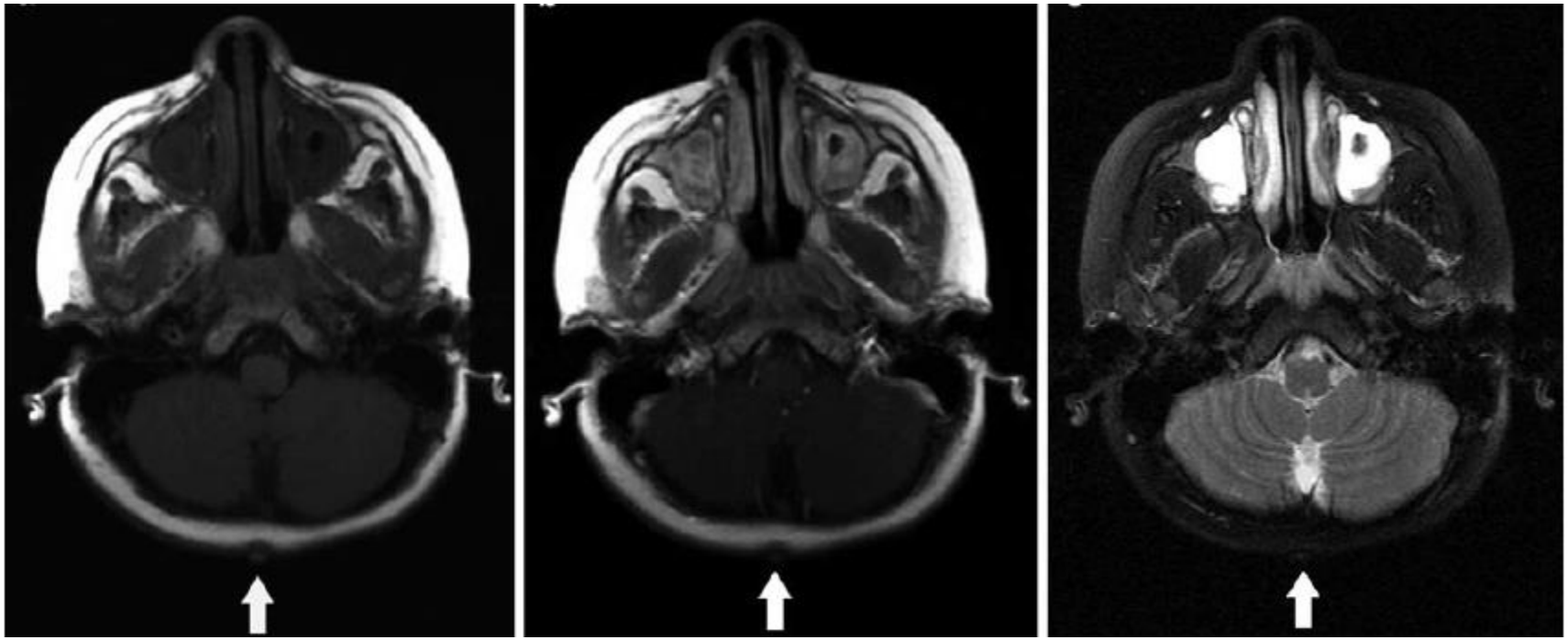
  (+) patellar reflex, but Achilles, biceps, and triceps reflexes absent

  able to walk and run without assistance

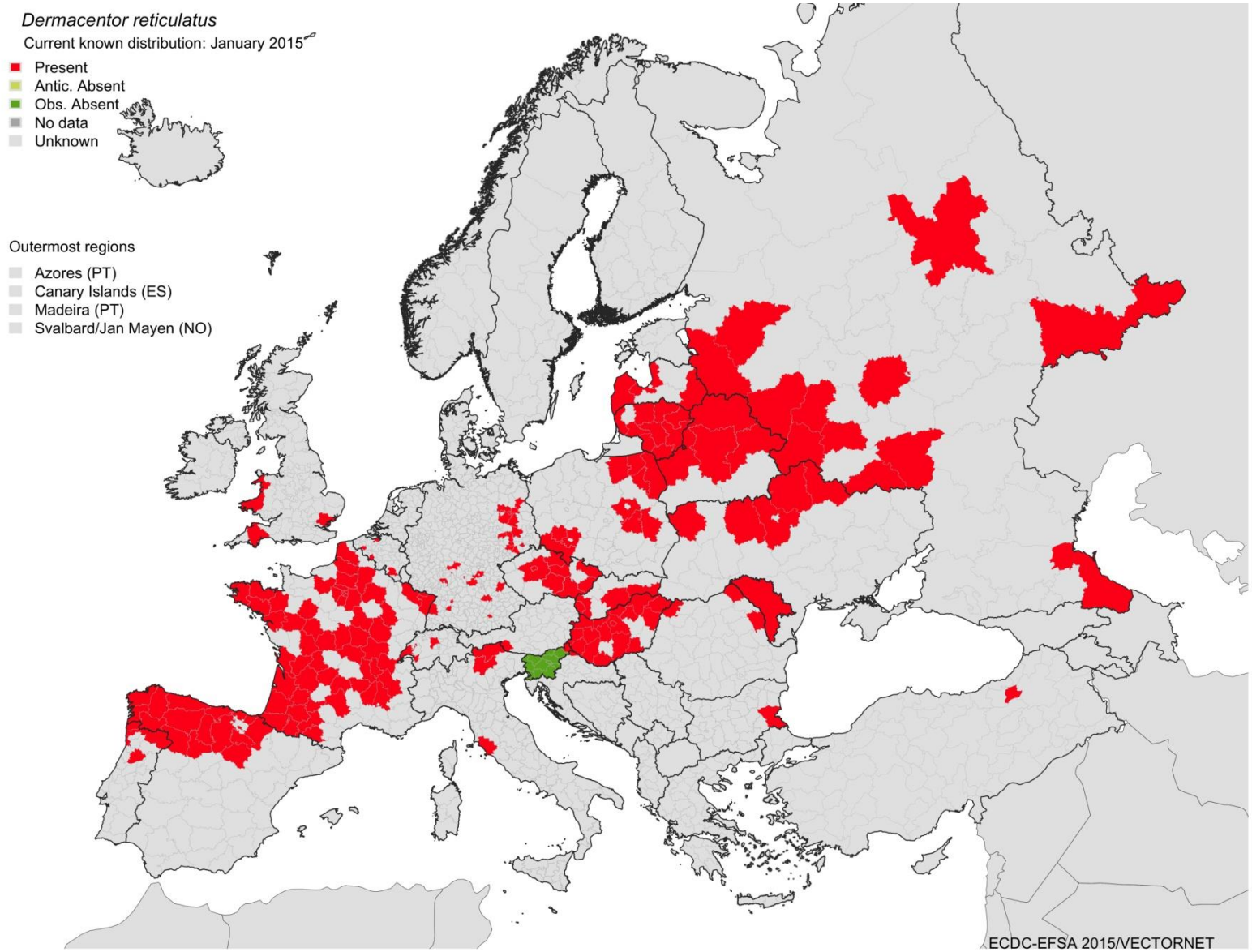
  2 weeks: N

- the most frequent attachment site retroauricular skin.
  The pathophysiology of tick paralysis by ixobotoxin, the neurotoxin released by Dermacentor species, involves reduction of muscle action potential with sparing of neuromuscular transmission.

- nonspecific lethargy and weakness, acute ataxia, symmetric flaccid paralysis with areflexia.



Burke et al 2005


*Dermacentor reticulatus*
Current known distribution: January 2015
Present
Antic. Absent
Obs. Absent
No data
Unknown
Outermost regions
Azores (PT)
Canary Islands (ES)
Madeira (PT)
Svalbard/Jan Mayen (NO)
ECDC-EFSA 2015/VECTORNET