Managing GBS and CIDP: Residual Symptoms

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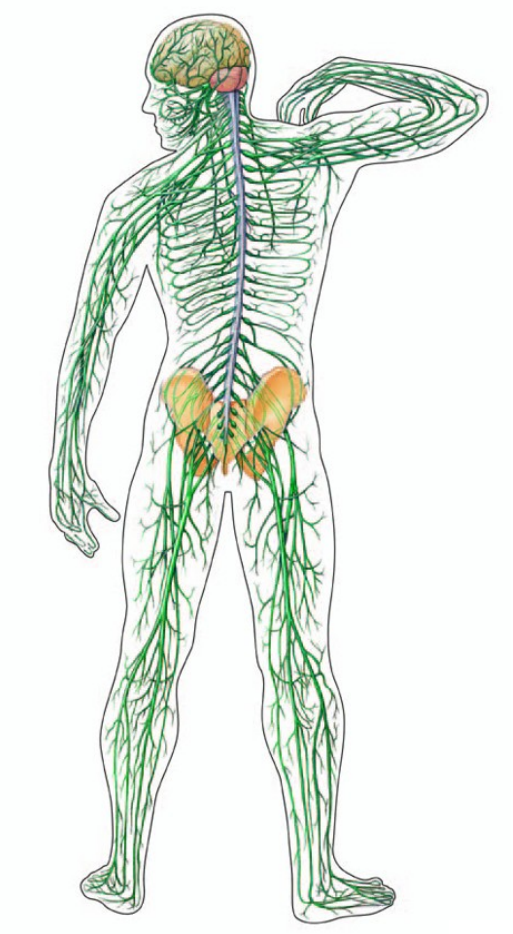
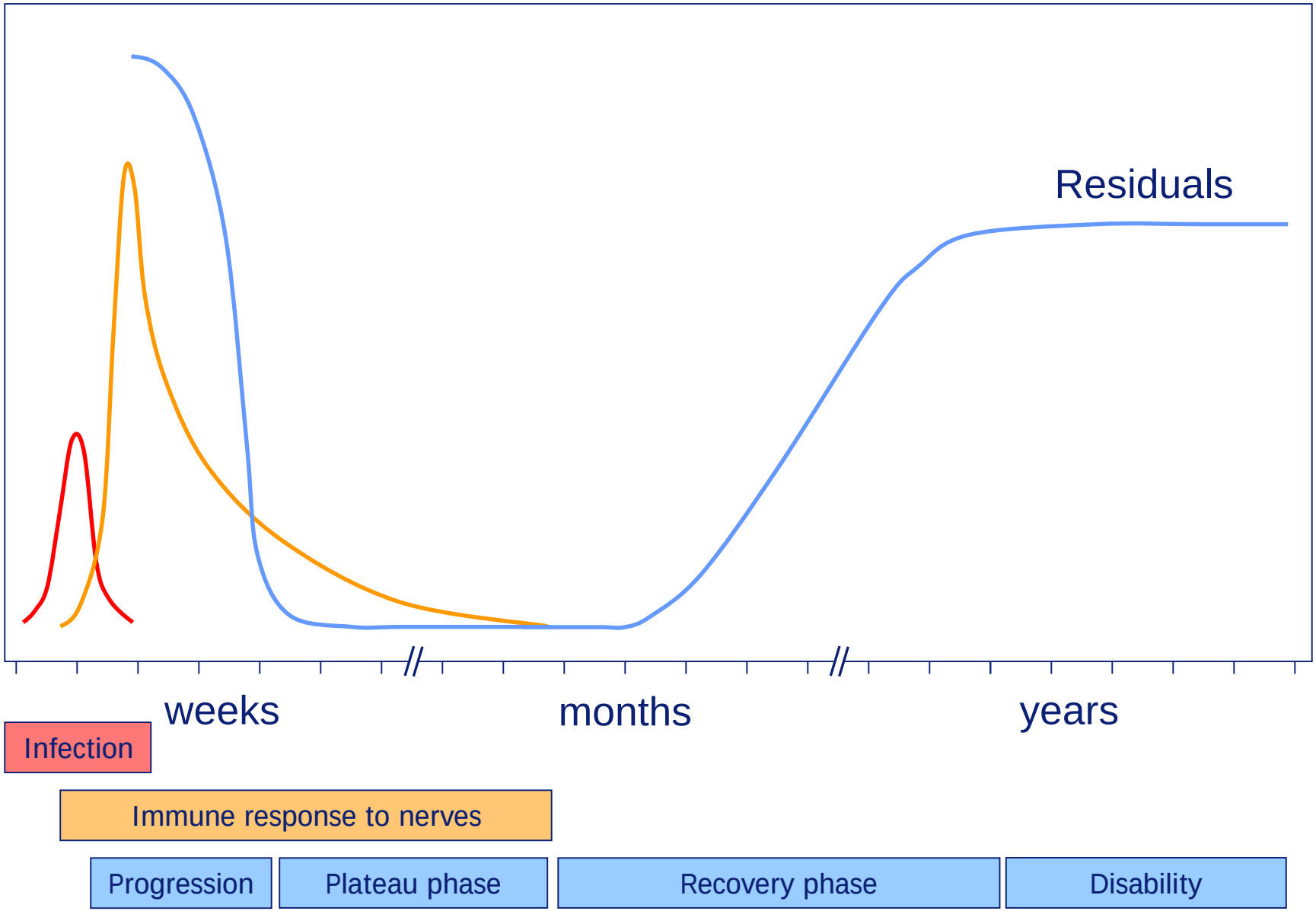


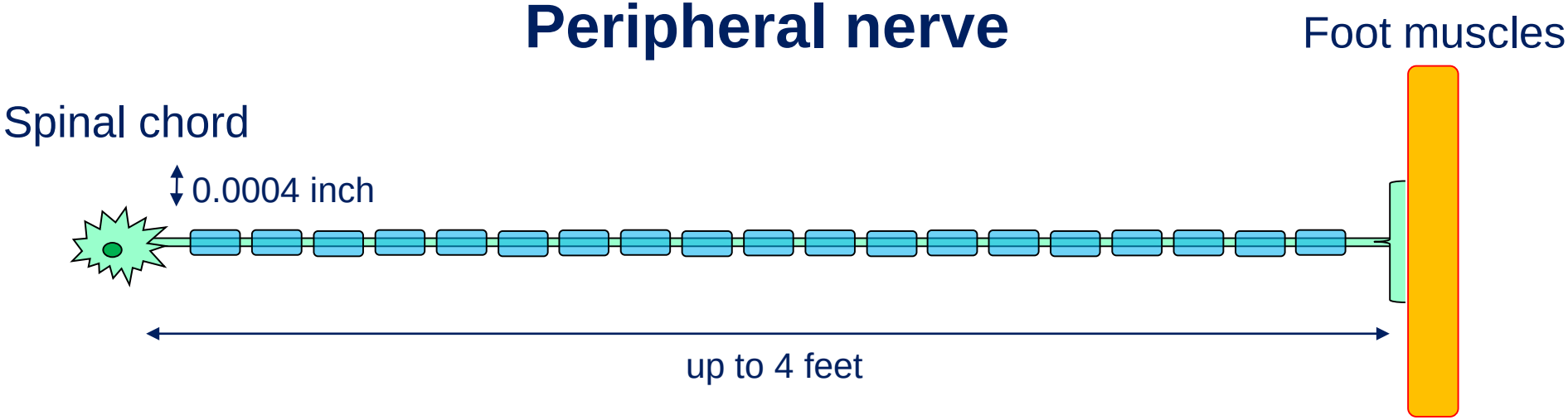
Residuals in GBS, CIDP and Related Immune Neuropathies

- Many patients have residual limitations and complaints.
- May have a major impact on daily activities and quality of life.
- Not caused by ongoing inflammation or disease but by previously damaged and non-regenerating nerves.

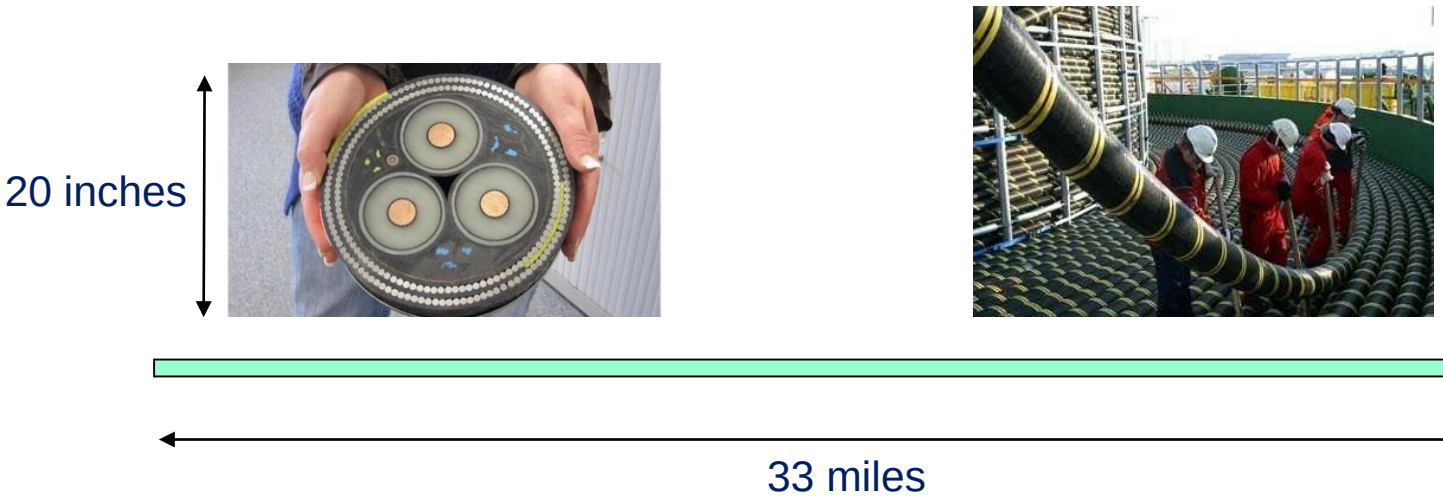
Sequence of events in GBS



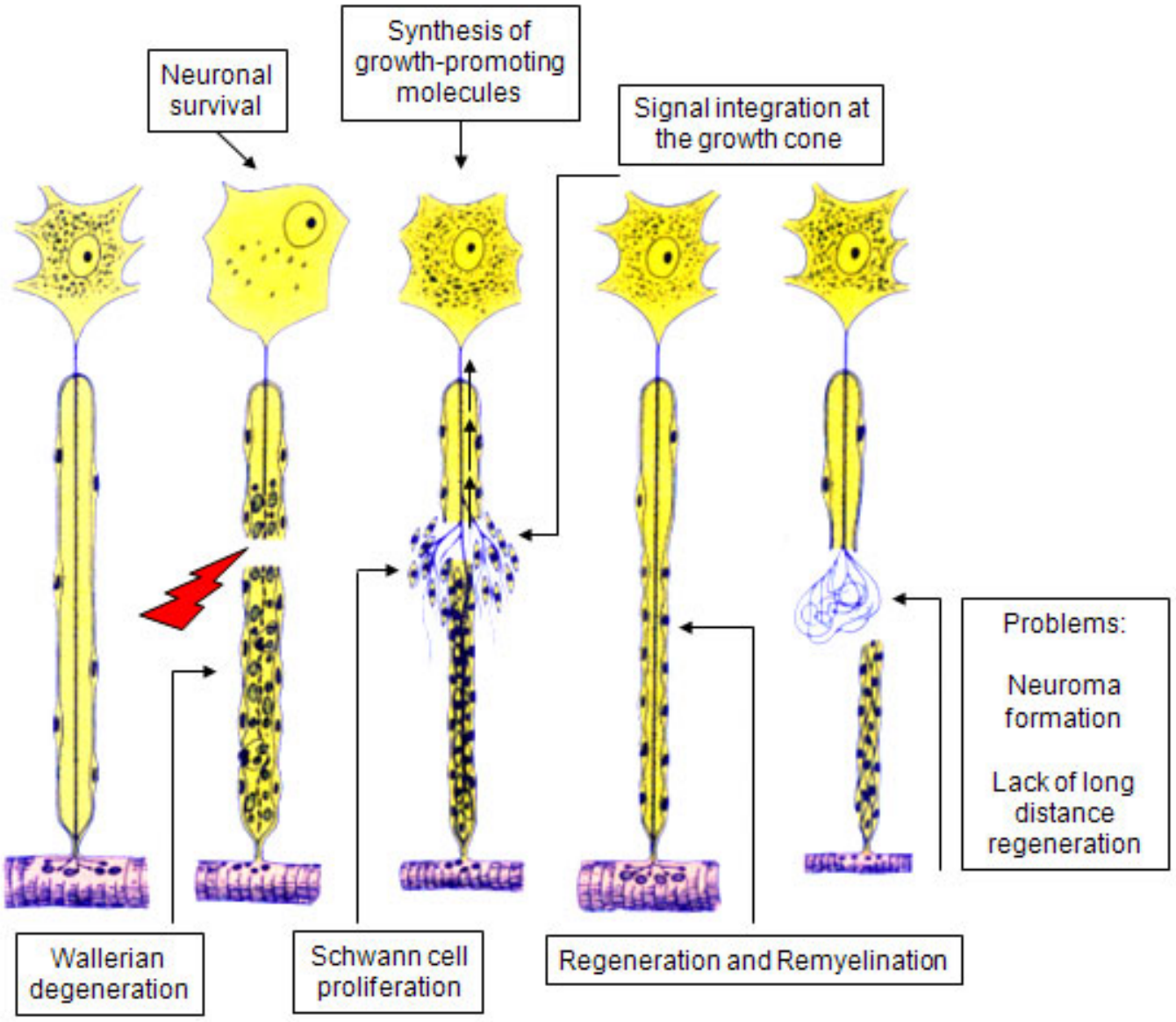
Peripheral nerve



Internet cable



Peripheral nerve regeneration



Why Do Patients Have Residual Deficits?

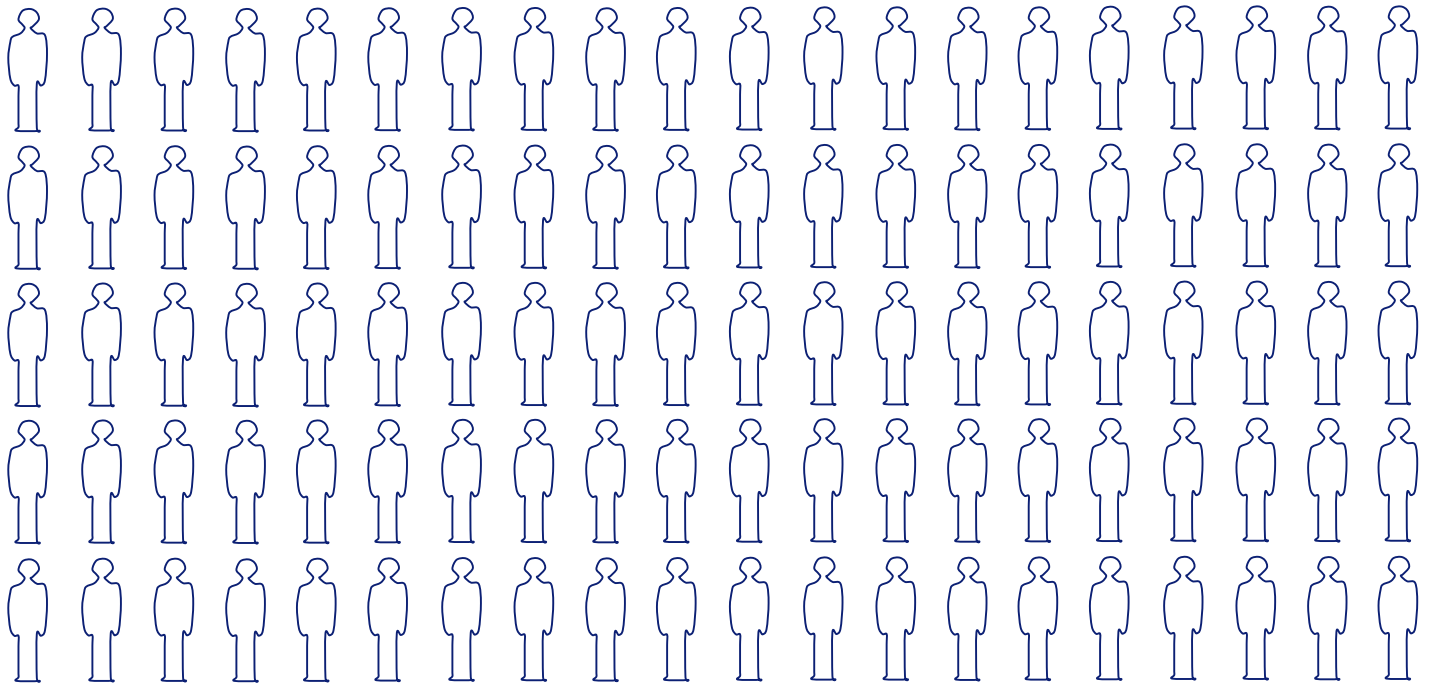
- Related to growth of regenerating peripheral nerves
- About 1 inch per month
- 3 years for a 4 feet long nerve!
- There are no current treatments to grow nerves back

Examples residual deficits/complaints in GBS and CIDP

- Weakness of limbs (10-20%)
  - Problems walking, movements hands, heavy feeling
- Head and face (10-20%)
  - Double vision, weakness face, problem swallowing or speech
- Sensory dysfunction (40-60%)
  - Numbness, changed sensation, tingling, balancing
- Autonomic dysfunction (10-30%)
  - Low blood pressure, constipation, sexual dysfunction
- Pain (50-60%)
- Fatigue (30-70%)

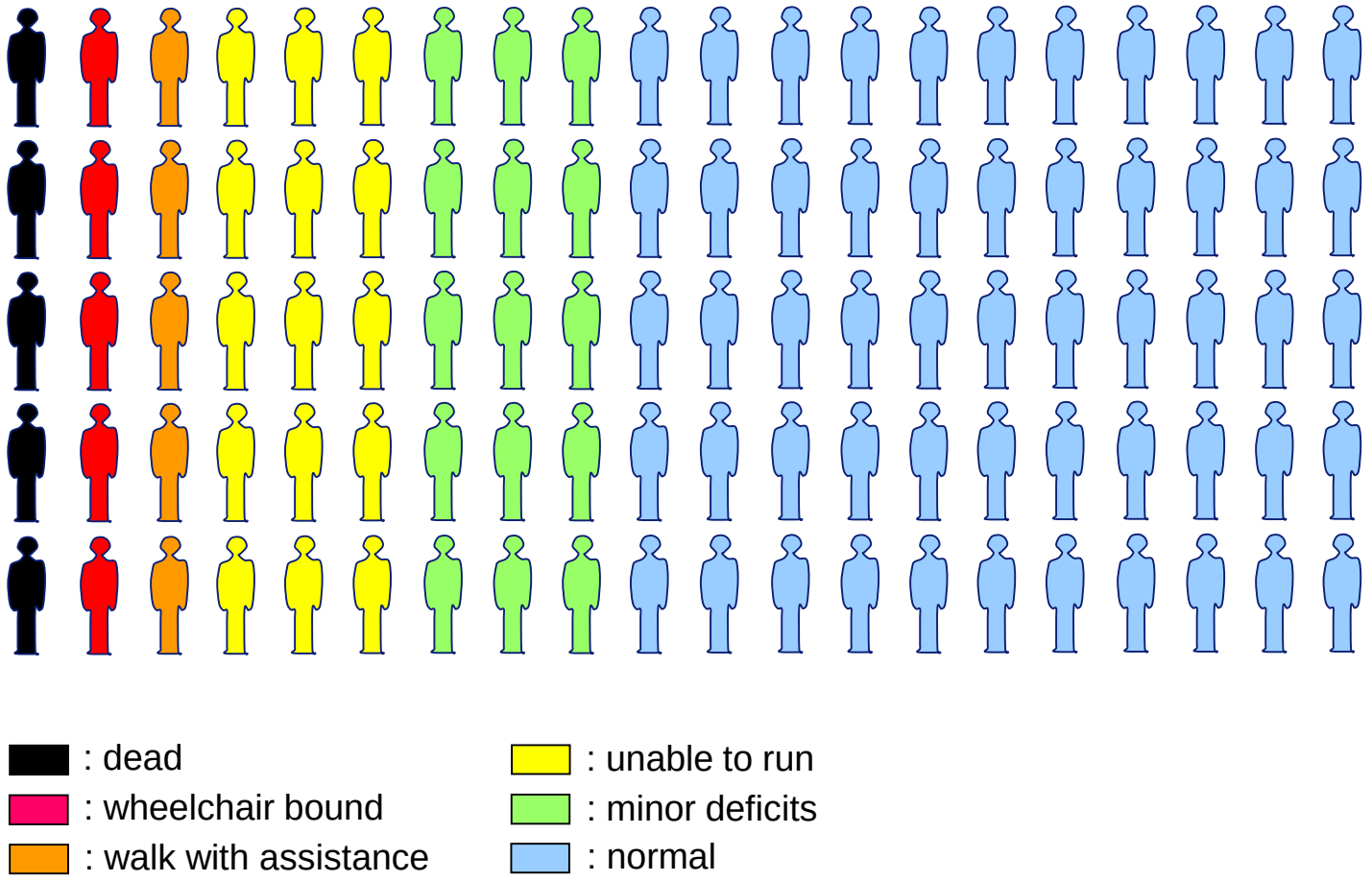
Who will get residuals after GBS and who not?

Long term disability in 100 persons after GBS

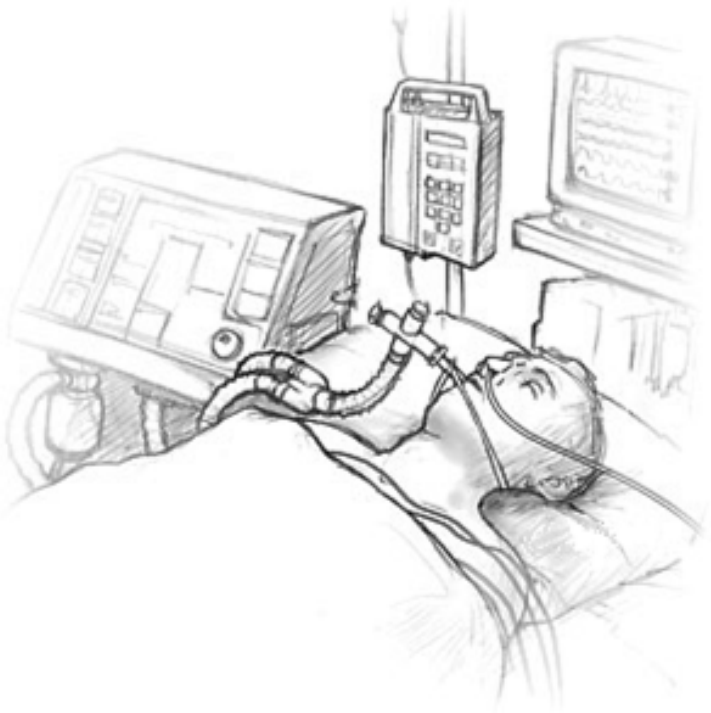


: dead
: wheelchair bound
: walk with assistance
: unable to run
: minor deficits
: normal

Long term disability in 100 persons after GBS



How long after diagnosis improvement is still possible?



Recovery in GBS Patients with Prolonged Mechanical Ventilation (MV)

- 526 GBS patients analysed from 4 prior studies (1985- 2008)
  - 111 MV < 2 months; 33 MV > 2 months (6% of cohort)
- Questionnaires via Dutch patient organization

- Confirmed diagnosis and history

- Follow-up of mean 11 years (range 4-20 years)

Van den Berg B et al. JNNP 2018

Recovery in GBS Patients with Prolonged Mechanical Ventilation (MV): Clinical Features

Patients with prolonged (> 2 months) MV had:

More severe bulbar (speech and swallowing) weakness

Greater limb weakness at entry and peak deficit (nadir)

More often had “inexcitable” nerves on EMG

18% recovered to walk at 6 months (vs. 76% in non-prolonged MV pts)

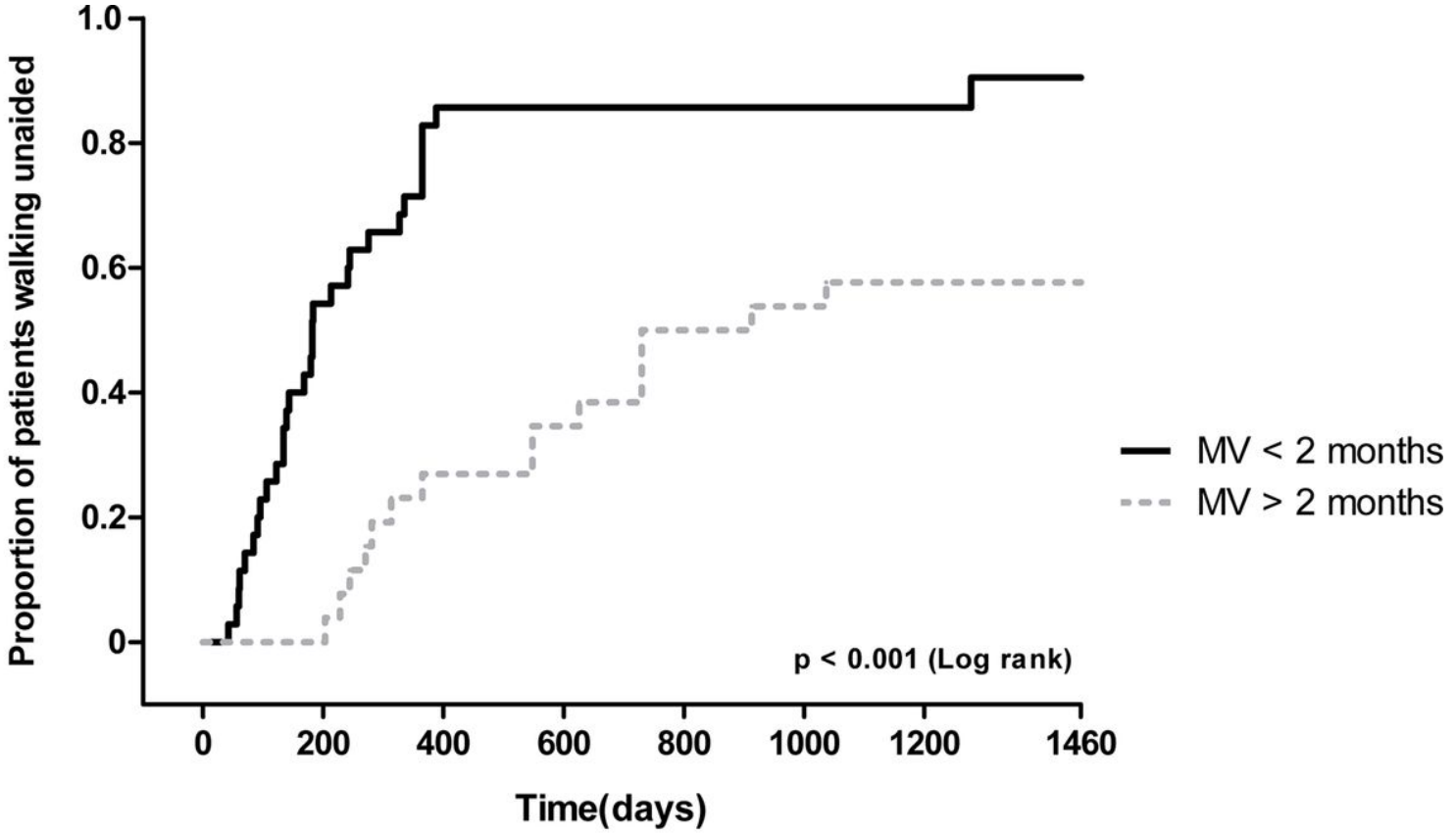
Time to walk 154 days (vs. 70 days in non-prolonged MV pts)

More severe residual limb weakness at 6 month follow-up

Continuous recovery > 1-2 years occurred in 31%

Van den Berg B et al. JNNP 2018

Kaplan-Meier analysis of the time until patients regained independent ambulation after short and prolonged mechanical ventilation (MV).



Number at risk

MV < 2 months	35	17	6	6	6	6	3	2
MV > 2 months	26	26	19	17	13	12	12	11

Bianca van den Berg et al. J Neurol Neurosurg Psychiatry 2018;89:949-954

Prognosis of GBS patients with prolonged ventilation (Long-term via Questionnaire)

- 58% were eventually able to walk without help
- 62% were able to live independently
  - 38% with adaptive changes to home
- 71% altered, adjusted or stopped employment
- 95% residual deficits or complaints (esp. leg mobility)
- However: results influenced by selection of patients
- Survey based on who responds, not a predefined cohort

Residual Symptoms Common to GBS, CIDP and Related Disorders

- Residual disability
  - Weakness, imbalance, trouble walking
    - Impaired ADLs
- Pain
- Fatigue
- Sleep disorders
- Mood disorders

Some general remarks

- Prevention of nerve damage in the acute stage is much more effective than treatment of residuals in the chronic stage.

- Very few studies have investigated residual symptoms in GBS and CIDP, and unfortunately even less studies on therapeutic interventions.

- Management should be personalized.

- Treatment response difficult to predict in individual patients.

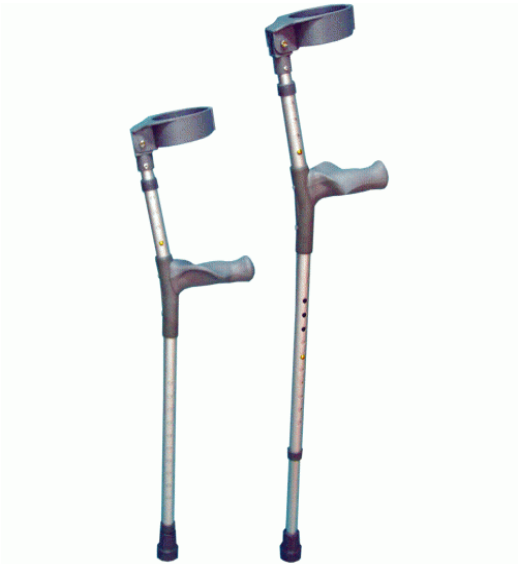
- Treatment of residual symptoms does not affect nerve recovery itself.

Management of Residual Functional Disability

- Education to improve understanding of the process, expectations for recovery
- Continued PT, OT, Speech therapy
- Assistive Devices
  - Help with writing, utensils, buttons, zippers,
- Home Assessment
  - Ramps, chairlifts, handle bars, raised toilet seats, pop-up seats
- Walking devices
  - Canes, crutches, walkers, wheelchairs and scooters
- Bracing

Ankle Foot Orthotics

Walking Assist Devices



Wheelchairs and Scooters

Upper limb splints

ADL Devices

Zipper pull

Button hook

ADL Devices

Pain in GBS and CIDP

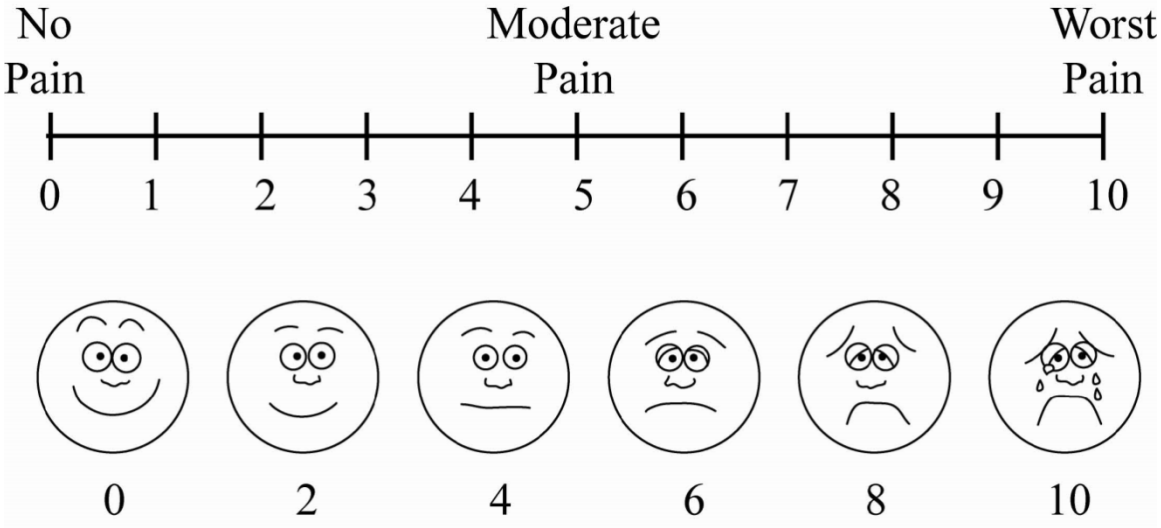
- High frequency of pain in patients with GBS (50-60%)
  - May occur at all stages of GBS
  - May be the first symptom, even before weakness starts
  - Also in patients with pure motor GBS or Miller Fisher syndrome
  - More predominant in children and in patients with sensory deficits or severe weakness

- Various types of pain:
  - Neuropathic pain: nerve damage
    - Peripheral nerves: painful tingling/touch of feet and hands
    - Nerve roots: lancinating pain in back radiating to limbs
  - Muscle pain and cramps
  - Nociceptive pain: tissue damage (joints and muscles)

Pain

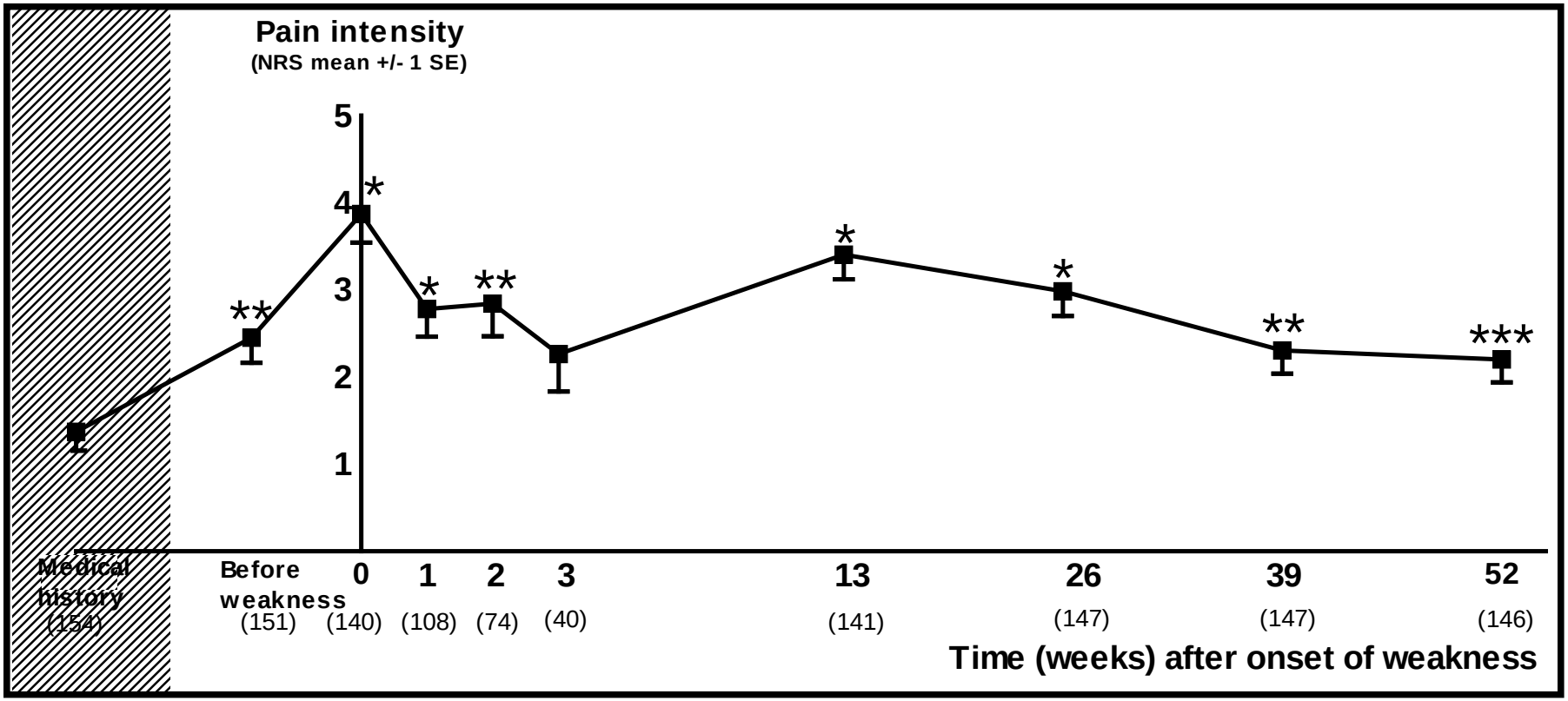
Important to quantify the intensity of the pain:

- Visual analogue scale (adults)
- Smiley scale (children)



Intensity of pain during 1 year follow-up in GBS patients

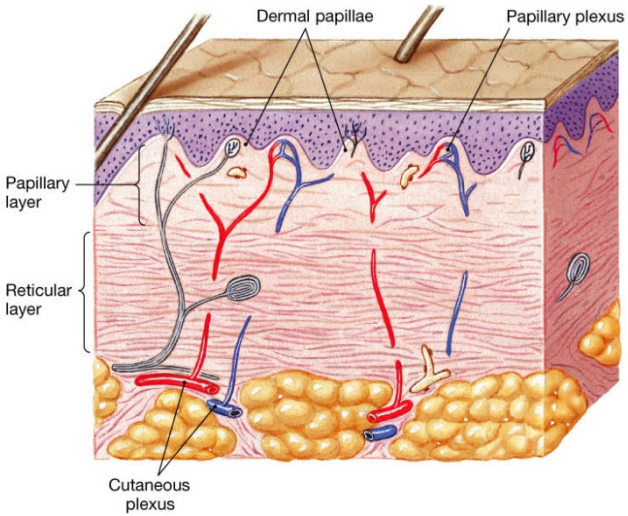
Ruts et al. Neurology 2010

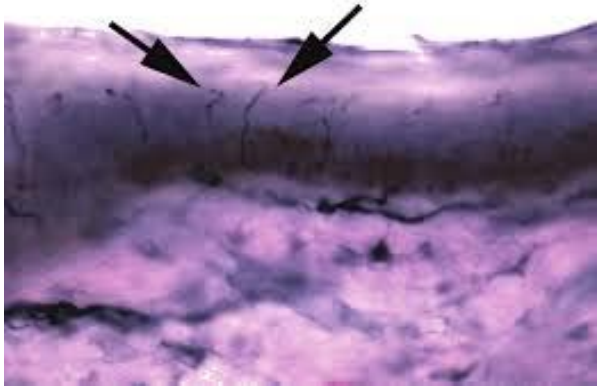


Pain related to loss of dermal nerve fibers

Ruts et al. Pain 2012

- Nerves in skin biopsies from 32 GBS patients





- Number of nerve fibers in skin:
  - is reduced in patients with GBS
  - in acute phase associated with severity of pain

Management of Pain: Basic Concepts

- For nociceptive pain we use the ‘WHO pain ladder’
  - Acetaminophen, Ibuprofen and other NSAID, Opioids.
  - Topical ointments and patches
  - PT/OT
  - Appropriate rest and pacing activities
- For neuropathic pain:
  - Anti-depressants or anti-convulsants are effective
  - Start one drug, low dose, titration to benefit or side effects
  - If inadequate response, start a new drug, or add a 2nd drug
  - Advantages of few side effects, sustained benefit, no tolerance
  - Examples: gabapentin, pregabalin, duloxetine, nortriptyline
  - Set expectations, this is trial and error
- Consult multidisciplinary pain teams
  - Nerve blocks; dorsal column stimulators
  - Alternative approaches: acupuncture, meditation, CBD, etc.

Fatigue in GBS and CIDP

- Most frequent residual complaint
  - GBS (60%) and MFS (27%) (in healthy controls 12%)
  - More frequent in female and elderly patients
  - Both mild and severe cases
  - Also in persons with otherwise full motor recovery

- Severe fatigue has considerable impact on daily life
  - 37% changed work and 44% hobbies because fatigue

Management of Fatigue: Exclude Other Medical Conditions First

- Non-restorative sleep
  - Sleep apnea, RLS, nocturia, noctural pain, anxiety/depression (EMA)
  - Menopausal symptoms
  - Chronic insomnia from other causes
- Medical disorders
  - Cardiac, pulmonary conditions
  - Hypothyroidism
  - Anemia
  - Medications (blood pressure, pain medications)
  - Low testosterone (men and women)
- Primary Mood disorders = **DEPRESSION**
  - Especially relevant when fatigue is out of proportion to functional disability (severe fatigue, no disability)

Management of fatigue

- Things the patient can do:
  - Fix sleep dysfunction
  - Adequate hydration
  - Good nutrition (avoid sugar)
  - Some form of regular exercise
  - Pace yourself, plan your day, build in proper rest periods, naps

- Physical training
  - Two studies conducted in GBS/CIDP patients

    (Garssen et al. Neurology 2004, Graham et al. J Neurol 2007)

Management of Fatigue: Medications

- Amantadine is proven ineffective to treat fatigue in GBS *(Garssen et al. J Neurol Neurosurg Psych 2007).*
- Other drugs only case studies and small series
- Energizing anti-depressants (not for depression)
  - Bupropion, desipramine, venlaflaxine
- Stimulants (not for ADD)
  - Caffeine
  - Modafinil, Armodafinil
  - Methylphenidate, amphetamines

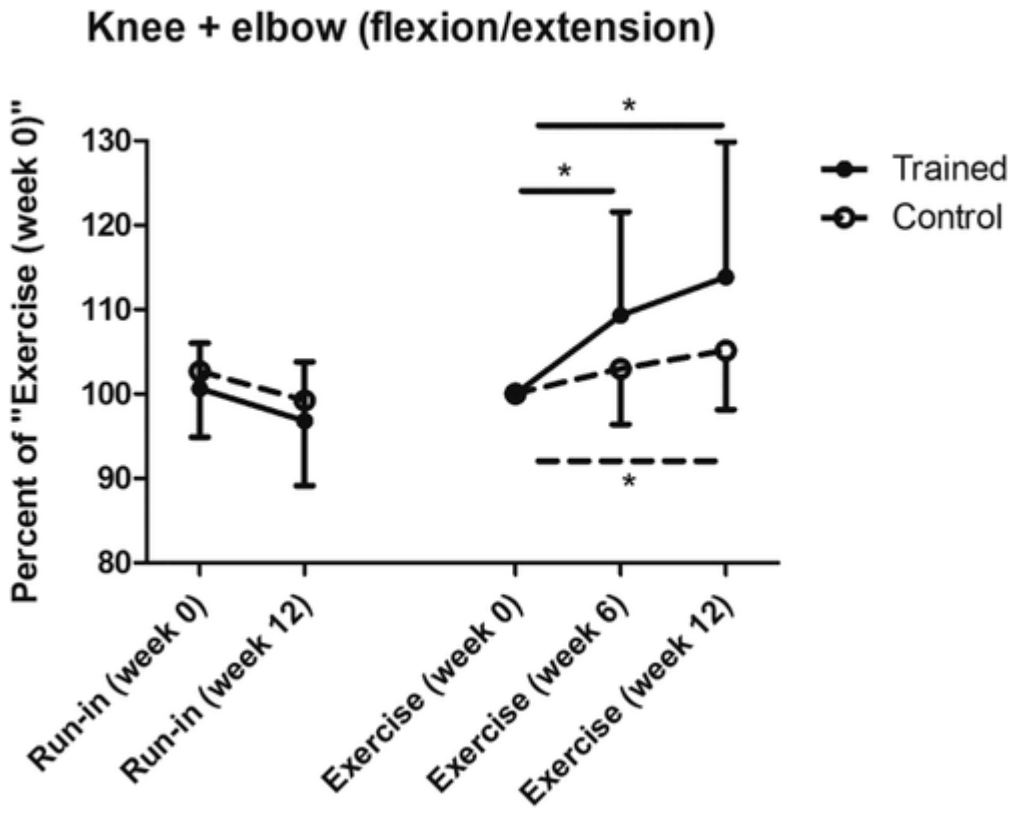
Is physical training also helpful to increase muscle strength in GBS and CIDP?

Physical Training in GBS and CIDP

- Effects unknown and again very few studies conducted in GBS or CIDP.
- Acute progressive and plateau phase of GBS:
  - Starting training too early may cause deterioration
  - Aim should not be to increase muscle strength
  - Should not lead to increase in pain or fatigue

- Late recovery phase and long-term phase of GBS
  - Studies on effect on fatigue showed that physical training is safe with heart rate up to 65%-90% (Garssen 2004, Graham 2007, Markvardsen 2018)
  - Personalised and professional guidance
  - No obvious contraindications but unknown

Resistance training and aerobic training improve muscle strength and aerobic capacity in CIDP



Resistance training and aerobic training improve muscle strength and aerobic capacity in chronic inflammatory demyelinating polyneuropathy, Volume: 57, Issue: 1, Pages: 70-76, First published: 27 March 2017, DOI: (10.1002/mus.25652)

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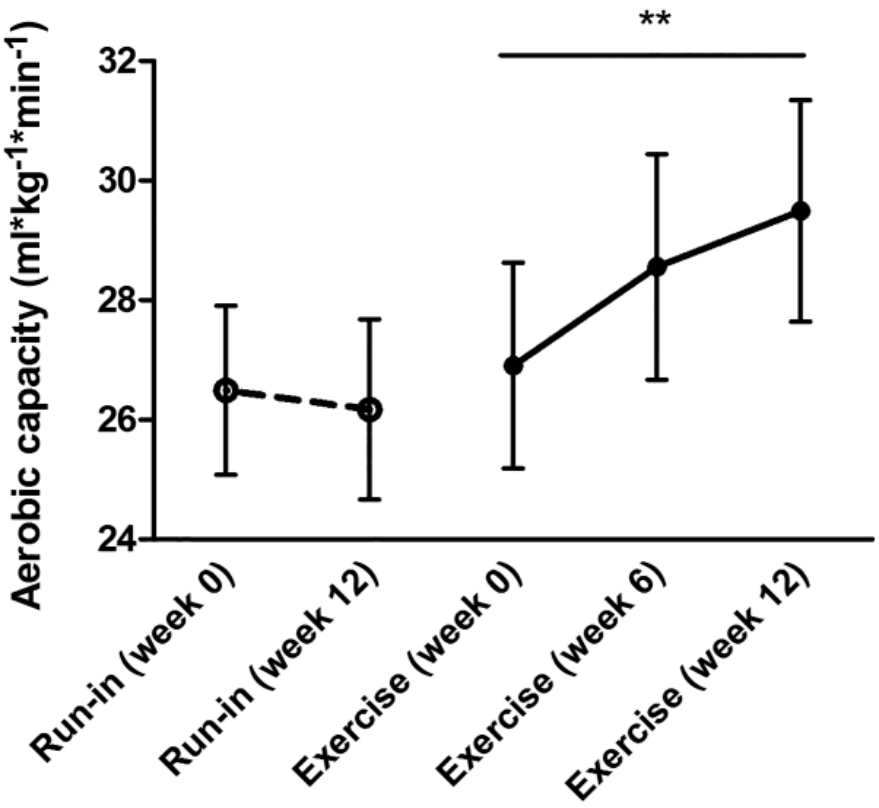

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Conclusions

- GBS, CIDP, Variants, and related immune neuropathies (MMN, paraproteinemic neuropathies) may cause considerable long term effects interfering with daily function and quality of life

- Residual symptoms are caused by previously damaged nerves, NOT by ongoing inflammation or active disease: more immune therapy does not help
- Residual symptoms are treatable in the majority of patients and can improve function and quality of life

- PLEASE: Talk to your doctor, focus on issues that may be treatable, seek another opinion if appropriate