Guillain–Barré syndrome and it looks like

นพ.นฤพัชร สวนประเสริฐ

สถาบันประสาทวิทยา

Guillain, Barré and Strohl (1916)

Jean Baptiste Octave Landry
1850

II.

TRAVAUX ORIGINAUX.

NOTE SUR LA PARALYSIE ASCENDANTE AIGUE,
par le docteur O. LANDRY.

L'objet de cette note est de signaler un état morbide assez rare et généralement inconnu, mais qui mérite de figurer parmi les affections les plus remarquables des cadres pathologiques.

Dans un assez grand nombre de paralysies, auxquelles convient la qualification générique d'*extenso-progressives*, les troubles fonctionnels, d'abord restreints à une partie limitée du corps, s'irradient graduellement plus ou moins loin de leur point de départ. Cette propagation s'effectue tantôt de proche en proche, et d'après un ordre bien déterminé; tantôt, au contraire, sans régularité et comme au hasard. On peut appeler les paralysies de ce dernier groupe : *extenso-progressives irrégulières*, et à celles du premier, bien plus importantes à connaître, donner le nom d'*extenso-progressives ascendantes*, ou, plus simplement, de *paralysies ascendantes* ou *centripètes*. Dans ces affections, en effet, les symptômes

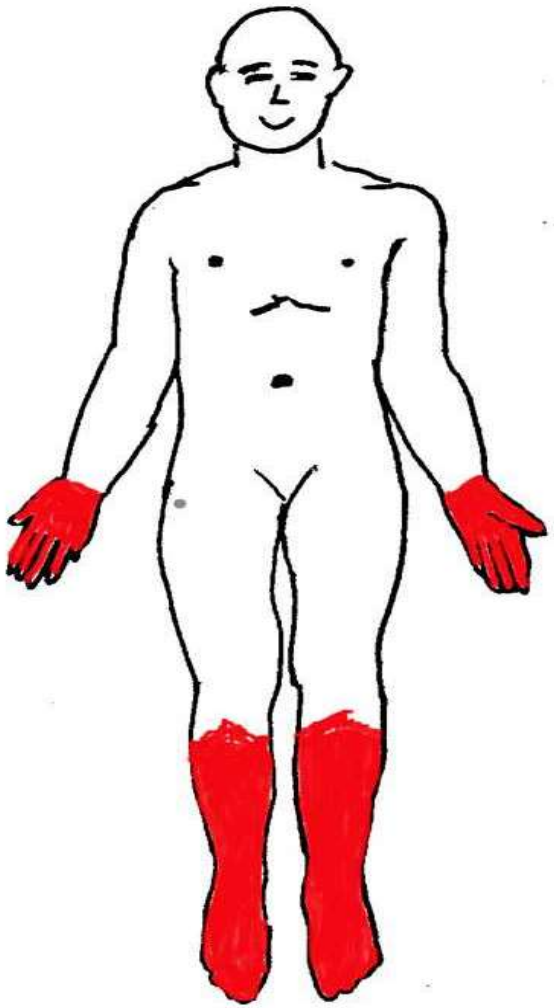
Clinical manifestation

- Acute onset, rapidly progressive in 2-4 wks.
- Distal, relatively symmetrical paresthesia follow by progressive limb weakness
- Widespread areflexia or hyporeflexia
- CN deficits
  - facial diplegia – 70%
  - dysphagia – 40%
  - extraocular motor dysfunction – 5%

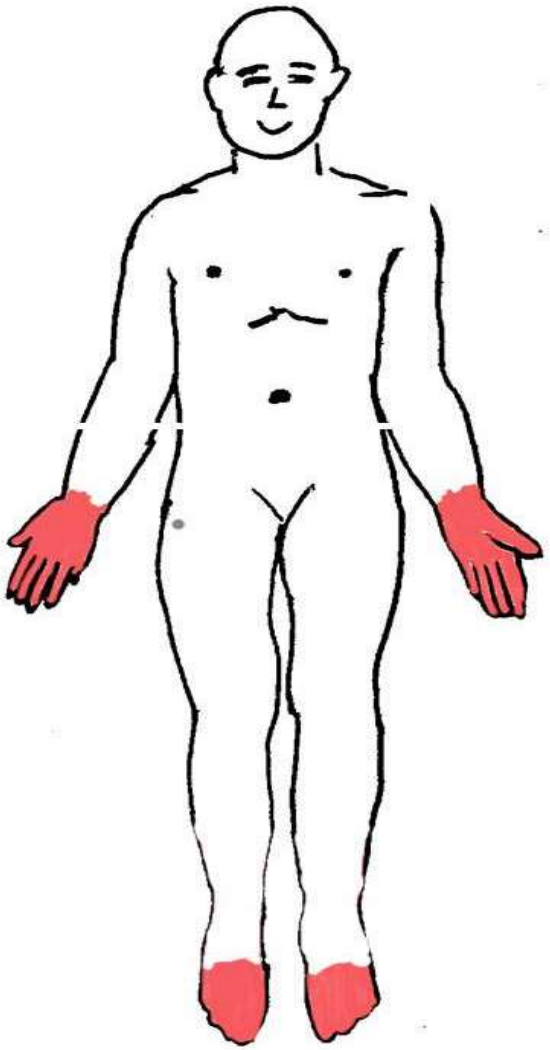
Clinical manifestation

- Sensory symptoms
  - numbness
  - ataxia
  - paraesthesia
  - pain 54–89%
- Autonomic dysfunction – 50%
- Respiratory failure - 25%

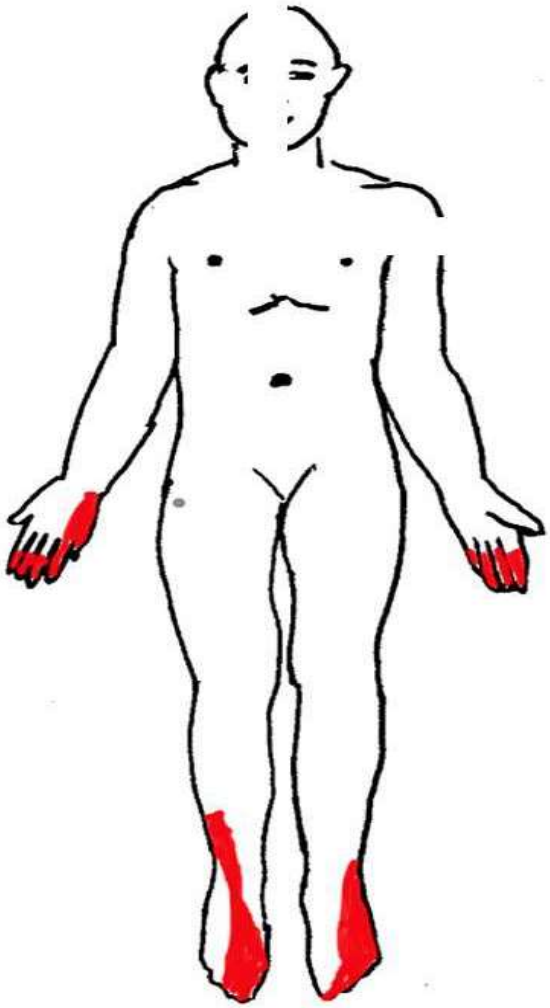
Nat. Rev. Neurol. 10, 469–482 (2014)



Axonopathy



Demyelination

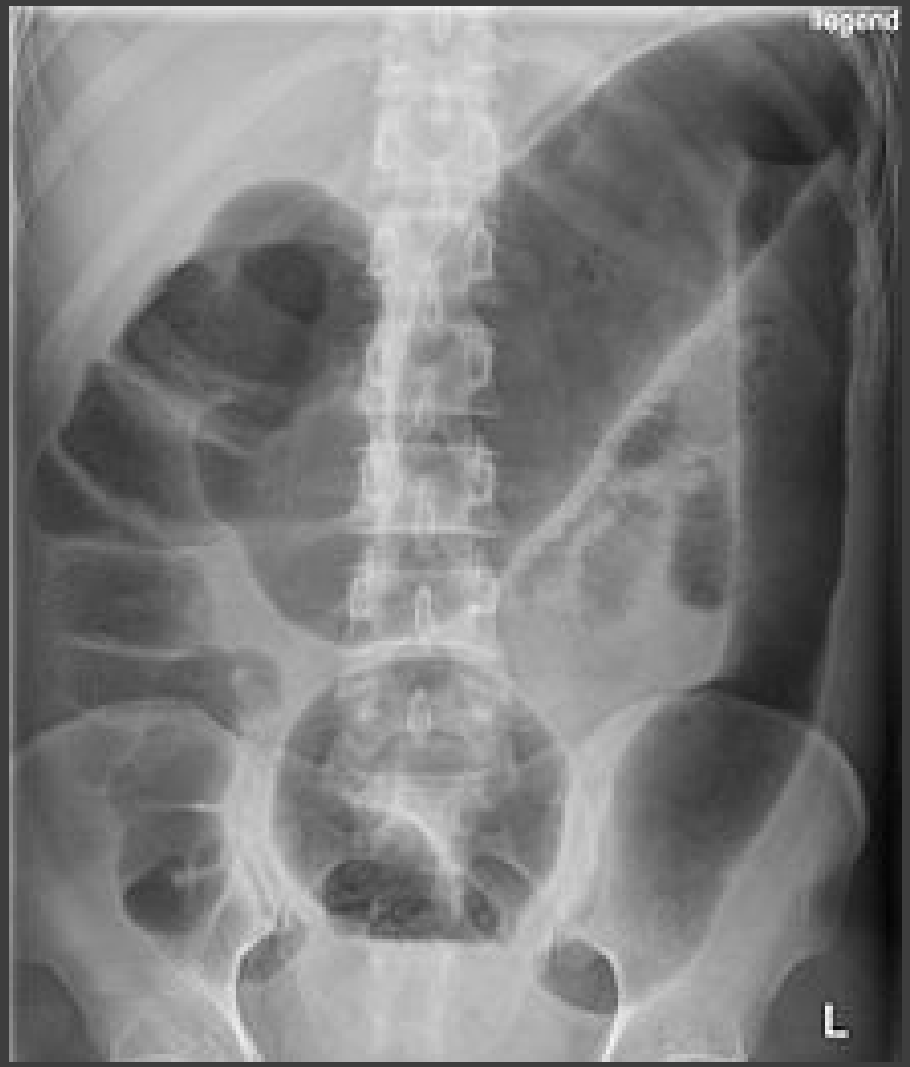


Multiple mononeuropathy

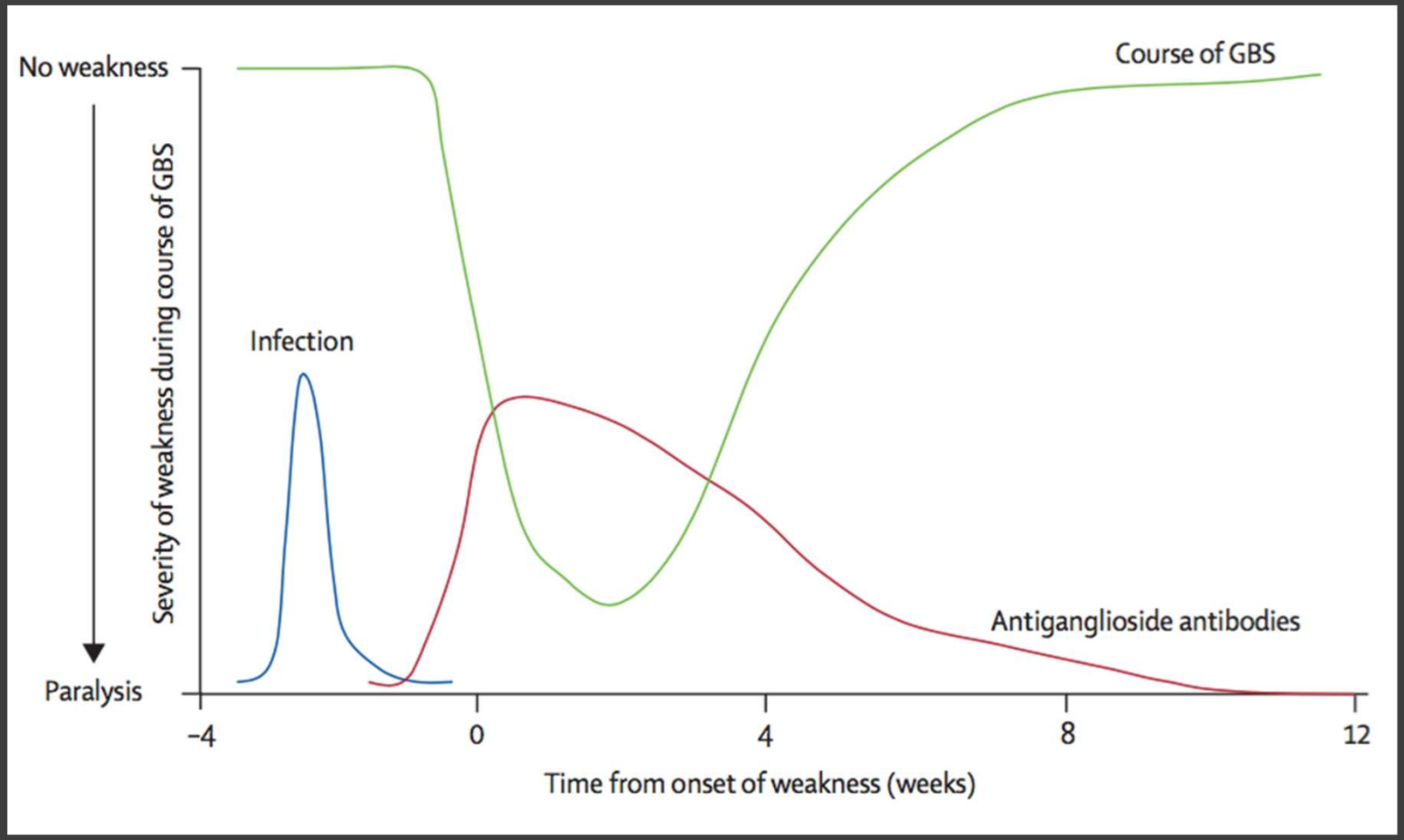
Autonomic dysfunction

- Sympathetic hyperactivity
  - arrhythmia, tachycardia
  - hypertension
  - decreased Intestinal Activity
- Parasympathetic hyperactivity
  - severe bradycardia, asystole
  - hypotension

Decreased Intestian Activity



Clinical course - GBS



Epidemiology

- Incidence - 0.6-2.4 cases per 100,000 per year
  - Europe – 60-80% AIDP
  - Asia – 30-60 % AMAN
- M:F - 3:2
- Antecedent infection
  - 2/3 URI or diarrhea
  - 2-4 wks. prior onset

Antecedent infection

- Bacterial infection
  - *C. jejuni* - 33%
  - Haemophilus influenzae
  - *Mycoplasma pneumonia*
  - Lyme disease
- Viral infection – EBV, Influenza virus, CMV, HEV
- HIV - seroconversion or early disease

Neurology 1998;51:1110–1115
Neurology 1996;47: 668–673

Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study

Van-Mai Cao-Lormeau, Alexandre Blake*, Sandrine Mons, Stéphane Lastère, Claudine Roche, Jessica Vanhomwegen, Timothée Dub, Laure Baudouin, Anita Teissier, Philippe Larre, Anne-Laure Vial, Christophe Decam, Valérie Choumet, Susan K Halstead, Hugh J Willison, Lucile Musset, Jean-Claude Manuguerra, Philippe Despres, Emmanuel Fournier, Henri-Pierre Mallet, Didier Musso, Arnaud Fontanet*, Jean Neil*, Frédéric Ghawché**

	viral RNA	IgM	IgG	Zika IgM/IgG					Neutralising antibodies	IgM Zika/IgM dengue			
				+/+	+/-	-/+	-/-	Zika virus positive		+/+	+/-	-/+	-/-
Guillain-Barré syndrome (N=42*)	0 (0)	39 (93%)	29 (69%)	27	12	2	1	41 (98%)	42 (100%)	8 (19%)	31 (74%)	0	3 (7%)
Control group 1 (N=98)	ND	17 (17%)	25 (26%)	7	10	18	63	35 (36%)	54 (56%)	6 (6%)	11 (11%)	8 (8%)	73 (75%)
Control group 2 (N=70)	70 (100%)	ND	5 (7%)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

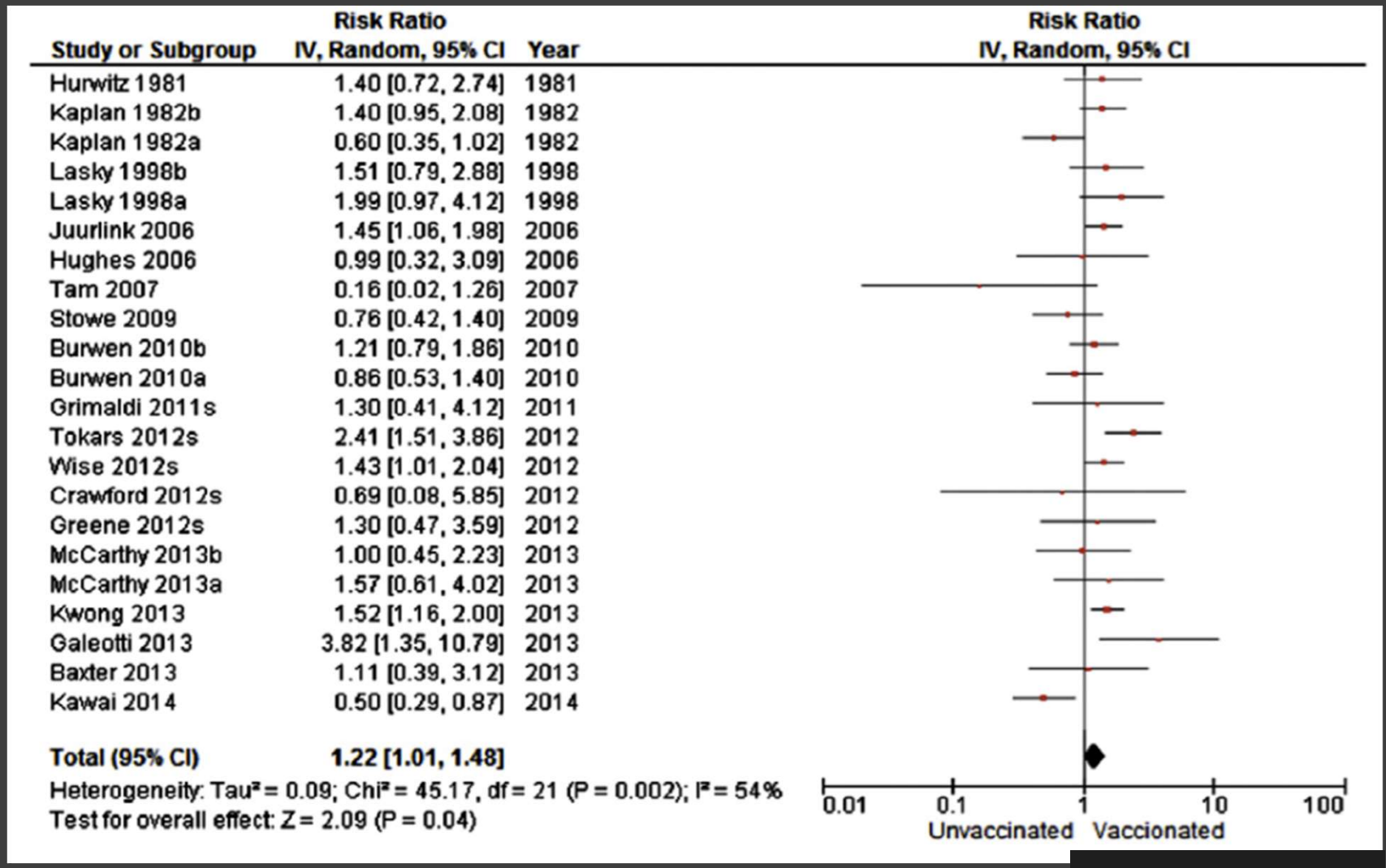
Data are n (%) or n. *RT-PCR was only done for 41 patients with Guillain-Barré syndrome; tested samples for patients with Guillain-Barré syndrome are late samples (around 3 months after admission), except for the RT-PCR (admission sample). ND=not done. IFA=immunofluorescent assay. MIA=microsphere immunoassay.

Risk of GBS - 0.24 per 1000 Zika virus infection

Lancet 2016

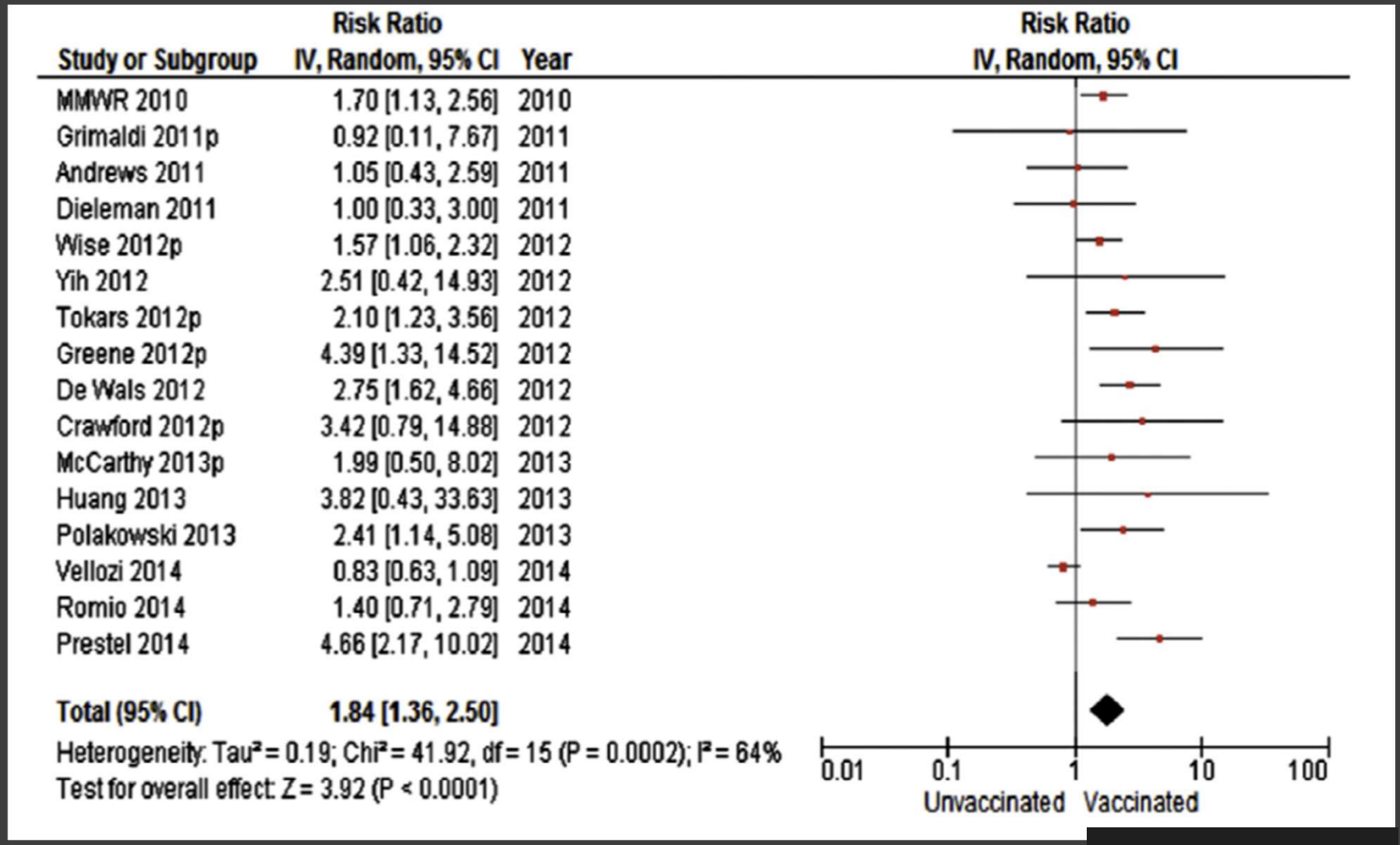
Influenza vaccine and GBS

Seasonal influenza vaccine and GBS



Vaccine 2015

Pandemic influenza vaccine and GBS



Vaccine 2015

Influenza Vaccine Effectiveness, 2016-17

US Flu VE Network
&
US Hospitalized Adult Influenza Vaccine Effectiveness Network (HAIVEN)

Jill Ferdinands, PhD
CDC Influenza Division

Meeting of the Advisory Committee on Immunization Practices (ACIP)

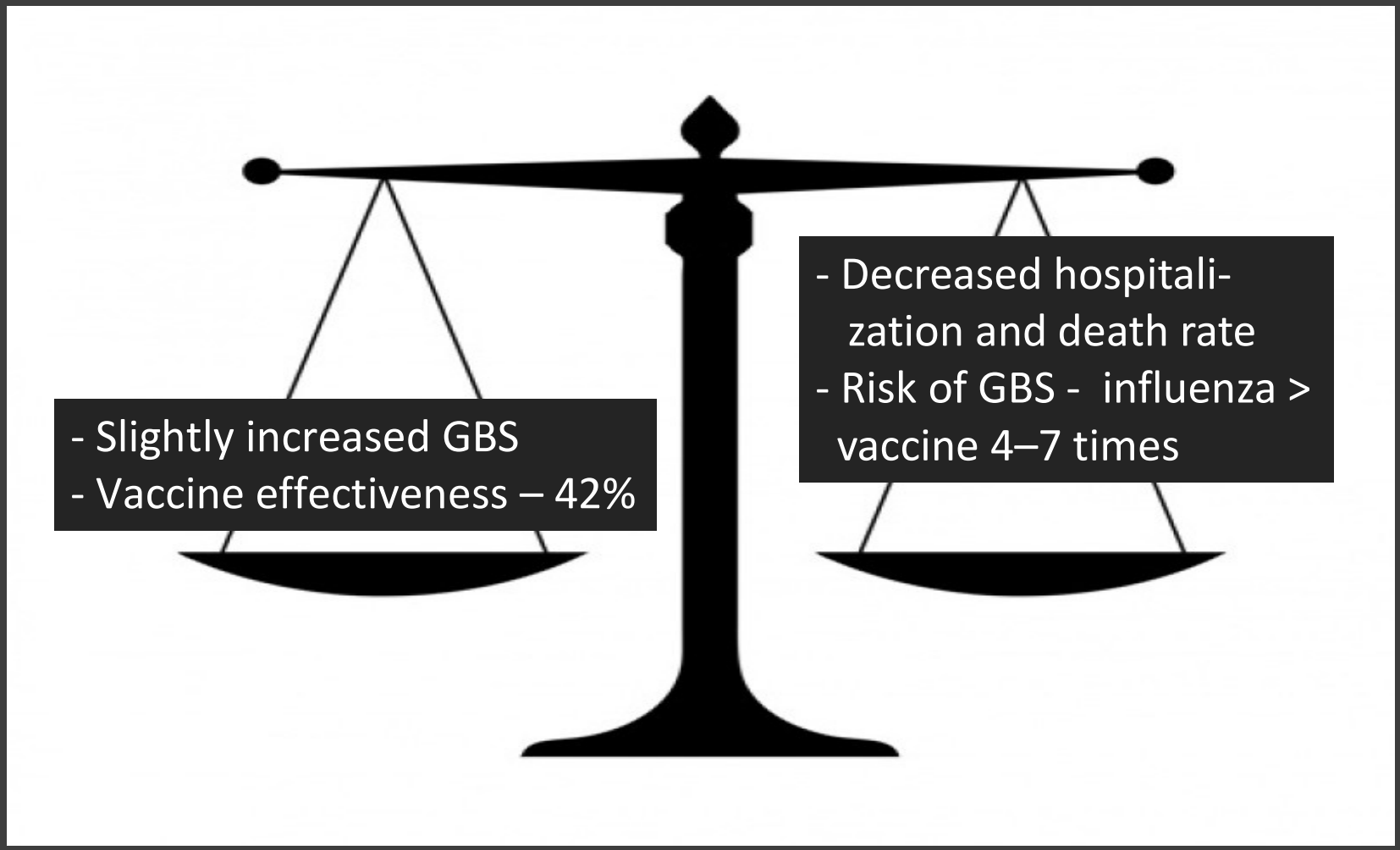
June 21, 2017

US Flu VE Network: Vaccine effectiveness against influenza A/B, 2016–17

	Influenza positive		Influenza negative		Vaccine Effectiveness			
					Unadjusted		Adjusted*	
Any influenza A or B virus	N vaccinated/Total	(%)	N vaccinated/Total	(%)	VE %	95% CI	VE %	95% CI
All ages	883/2052	(43)	2761/5153	(54)	35	(27 to 41)	**42**	**(35 to 48)**
Age group (yr)								
6 mo–8 yr	106/353	(30)	709/1318	(54)	63	(53 to 71)	**61**	**(49 to 70)**
9–17	123/402	(31)	245/606	(40)	35	(15 to 50)	**35**	**(13 to 61)**
18–49	203/529	(38)	716/1629	(44)	21	(3 to 35)	**19**	**(-1 to 34)**
50–64	203/442	(46)	537/909	(59)	41	(26 to 53)	**42**	**(26 to 55)**
≥65	248/326	(76)	554/691	(80)	21	(-8 to 43)	**25**	**(-5 to 46)**

* Multivariate logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, days from illness onset to enrollment, and calendar time of illness onset

Is it recommended to get a flu shot?

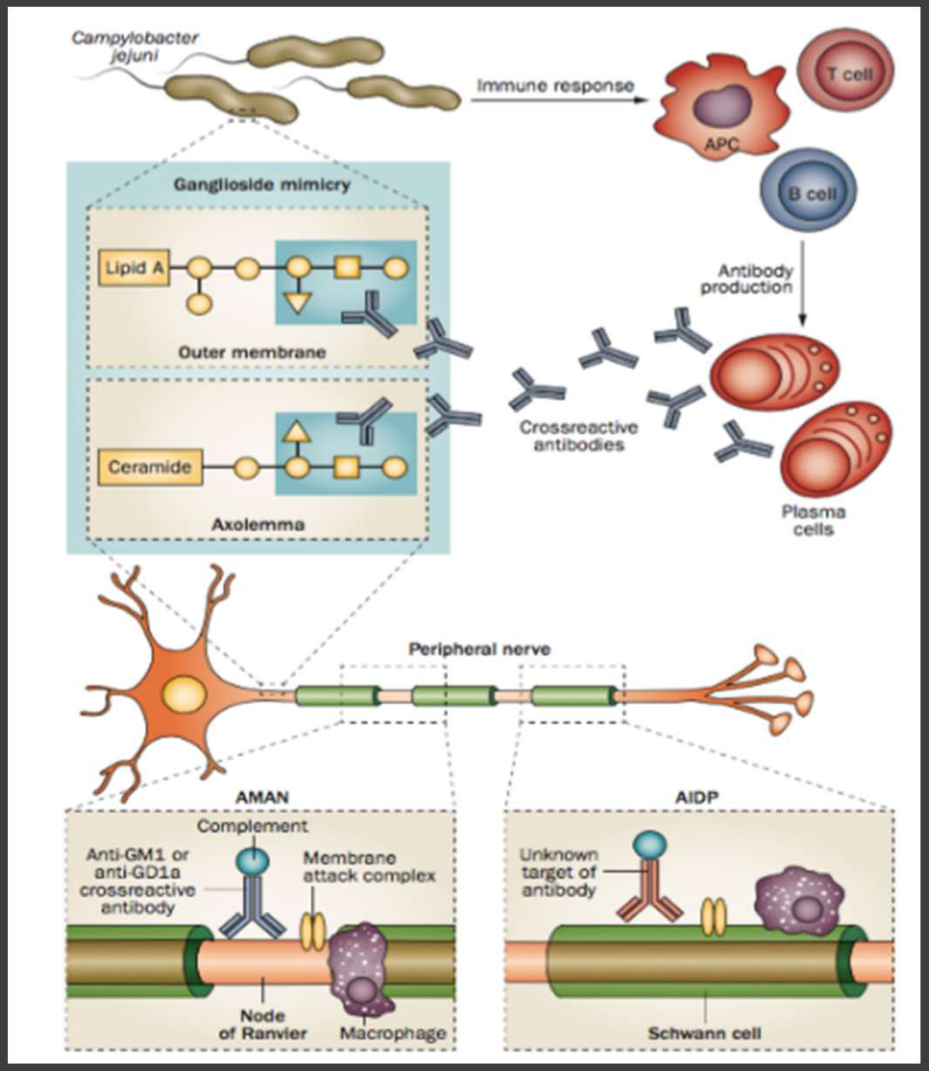


Vaccination in pts. with hx of GBS

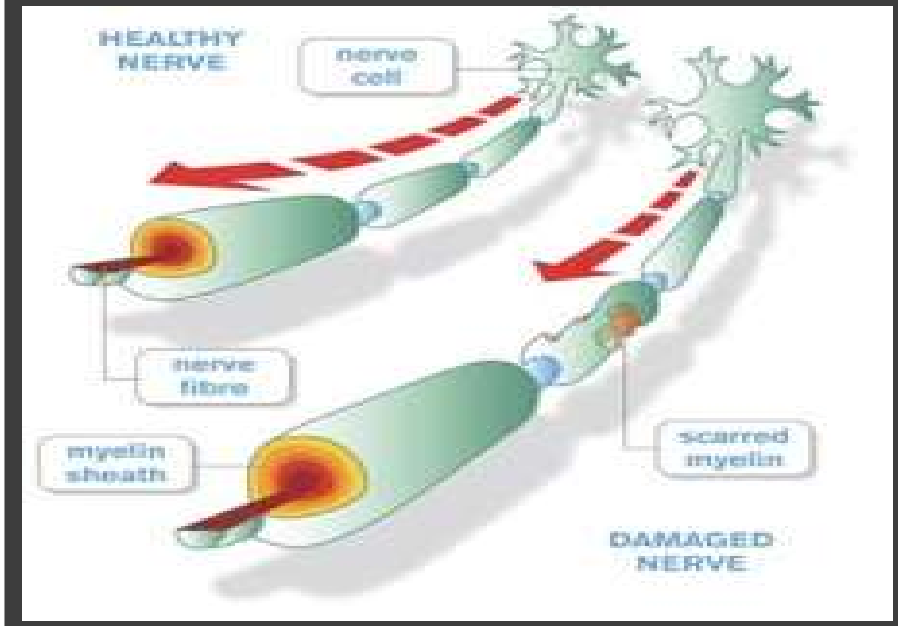
- Vaccination seems to be safe
  - onset of GBS > 6 wks. after vaccination
  - pts. who developed GBS > 3 mo. ago
  - 3.5% - repeat episode
  - 1.2% - serious GBS

Vaccine 30, 5801–5803 (2012).
J. Peripher. Nerv. Syst. 14, 310–315 (2009).

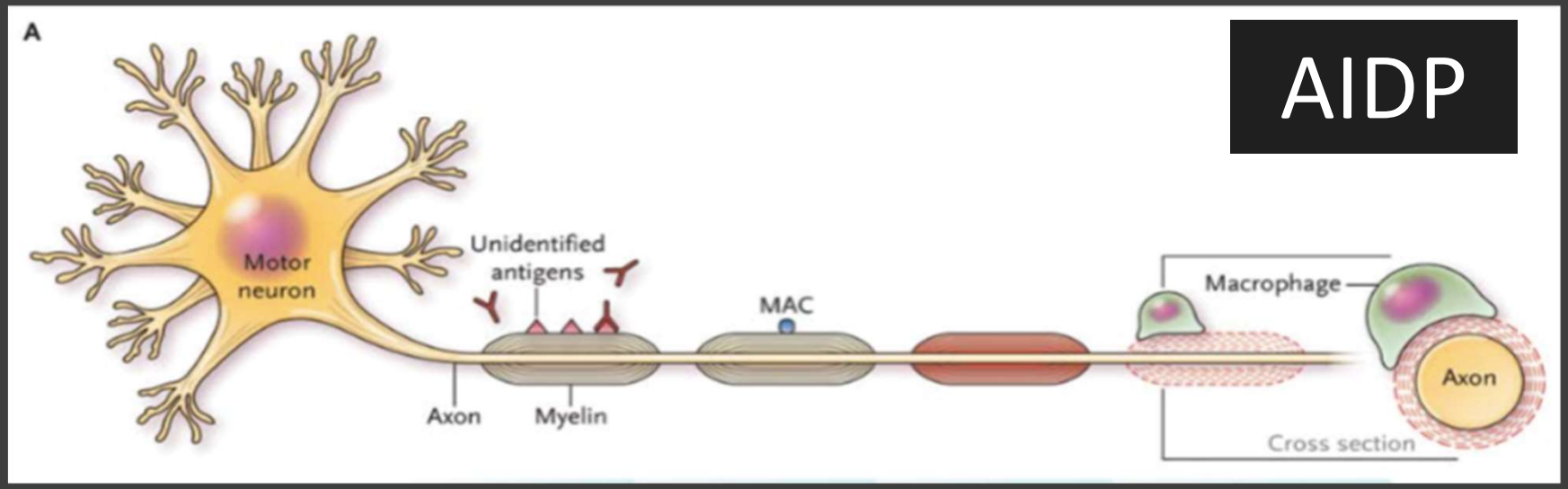
Pathogenesis

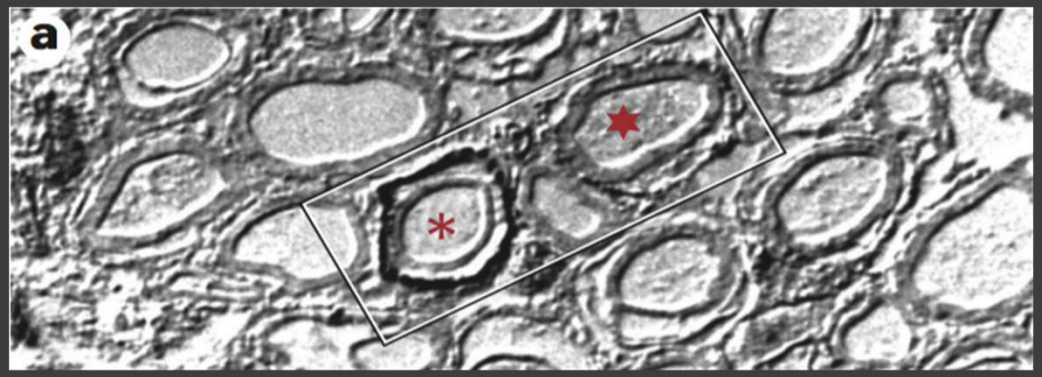


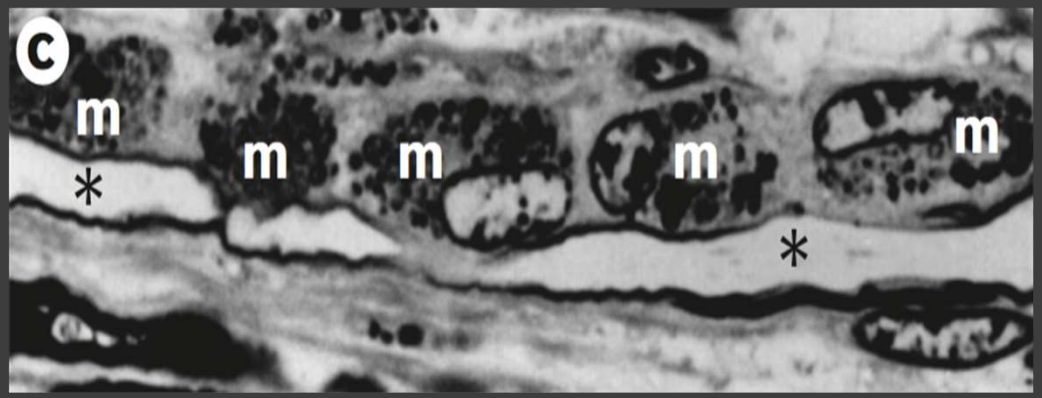
Teased fiber - Segmental demyelination

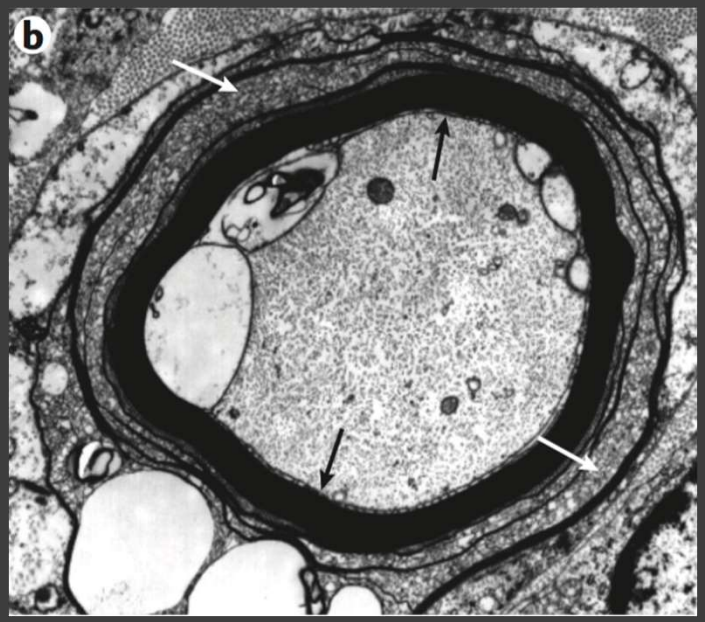


AIDP



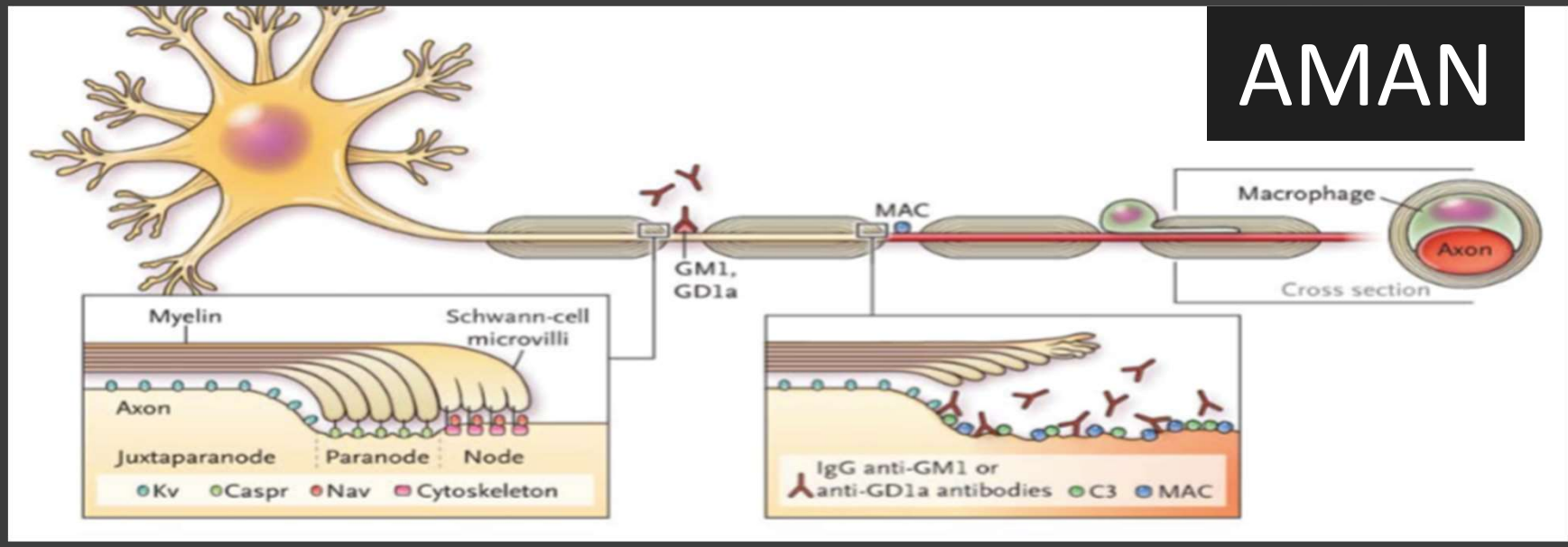


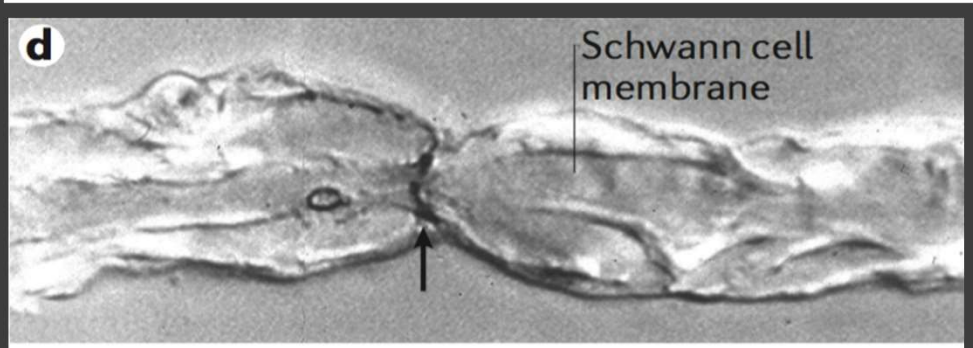


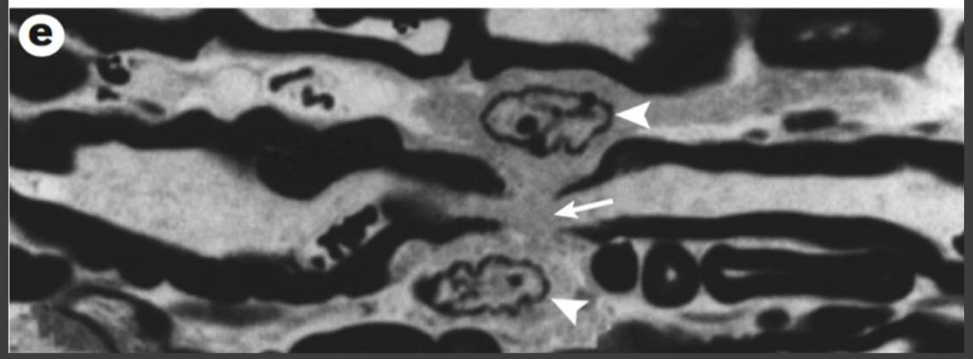


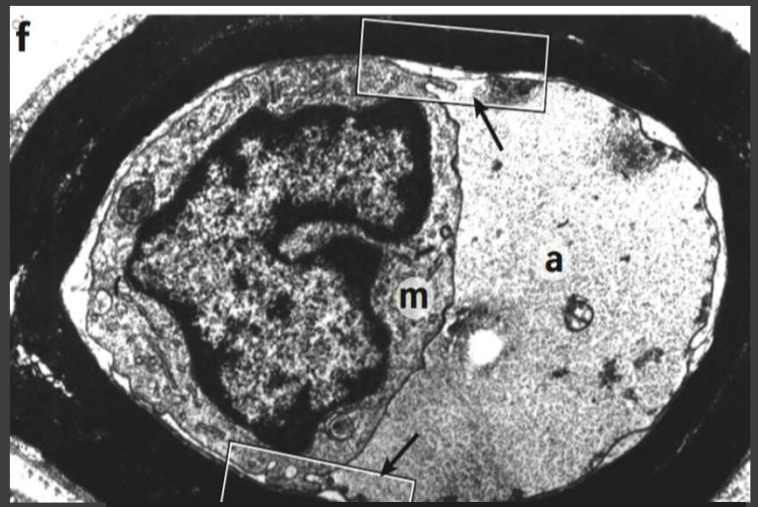
Ann. Neurol. 1996
N Engl J Med 2012

AMAN



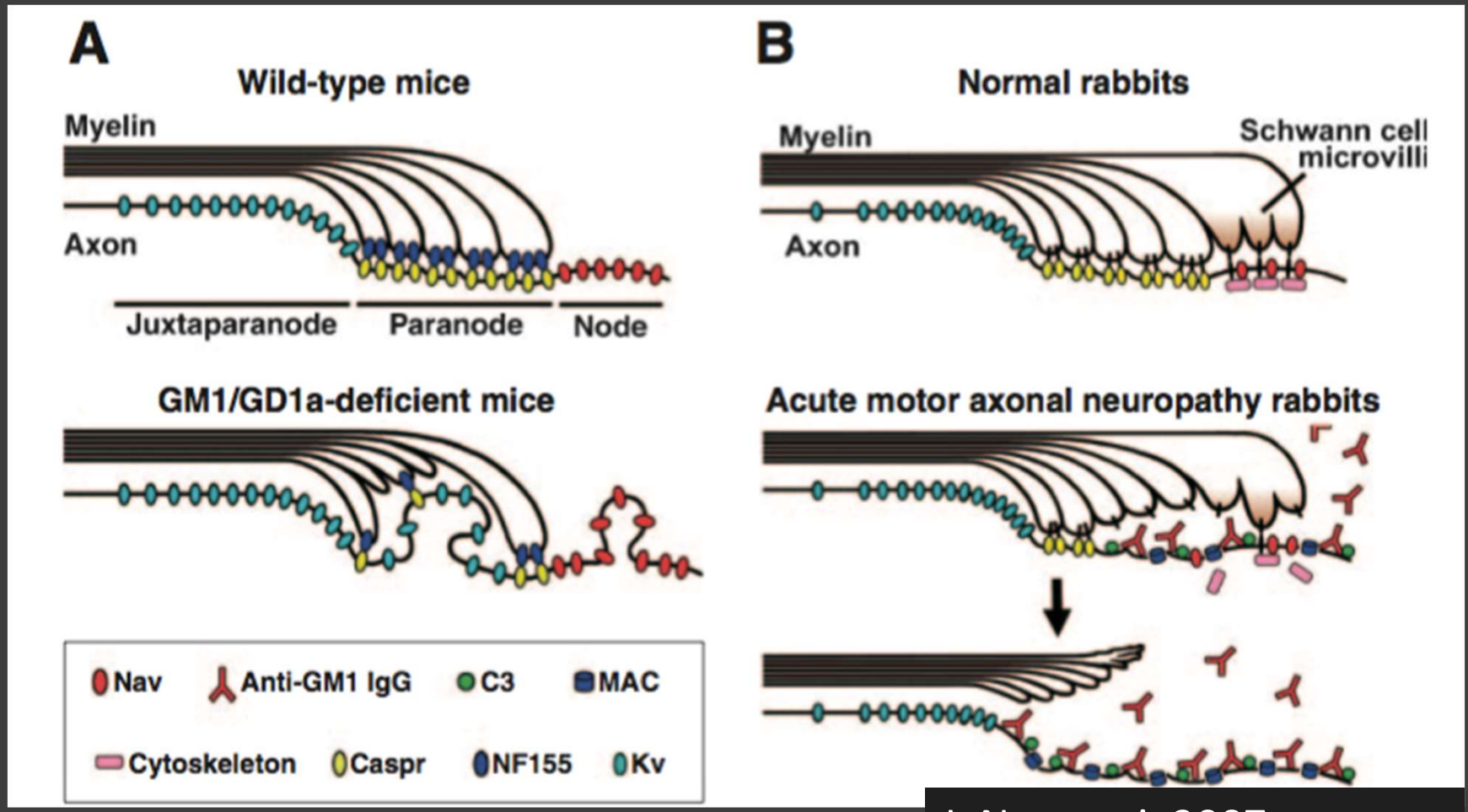






Annu. Rev. Neurosci. 1998
J. Neurocytol. 1996
N Engl J Med 2012

Role of gangliosides in nerve



J. Neurosci. 2007
Methods Mol. Biol. 2010
Proc. Jpn. Acad., Ser. 2012

Subtypes of GBS

Table 1 | GBS subtypes, clinical features and relevant antibodies[3,37,43]

GBS subtypes	Main clinical features	NCS findings	Antibodies*
Acute inflammatory demyelinating polyneuropathy (AIDP)	Sensorimotor GBS, often combined with cranial nerve deficits and frequent autonomic dysfunction	Demyelinating polyneuropathy	Various‡
Acute motor axonal neuropathy (AMAN)	Pure motor GBS; cranial nerves rarely affected	Axonal polyneuropathy, sensory action potential normal	GM1a, GM1b GD1a GalNAc-GD1a
Acute motor sensory axonal neuropathy (AMSAN)	Resembles severe AMAN, but sensory fibres are affected, leading to sensory deficits	Axonal polyneuropathy, sensory action potential reduced or absent	GM1, GD1a
Pharyngeal–cervical brachial variant	Prominent weakness of oropharyngeal, facial, neck and shoulder muscles	Normal in most patients, sometimes abnormalities in arms, mostly axonal pattern	GT1a>GQ1b >>GD1a
Miller Fisher syndrome	Ataxia, ophthalmoplegia, areflexia	Normal in most patients; discrete changes in sensory conduction or H-reflex may be present	GQ1b, GT1a

Nat. Rev. Neurol. 10, 469–482 (2014)

Table 1 | Clinical features of GBS, MFS and their subtypes

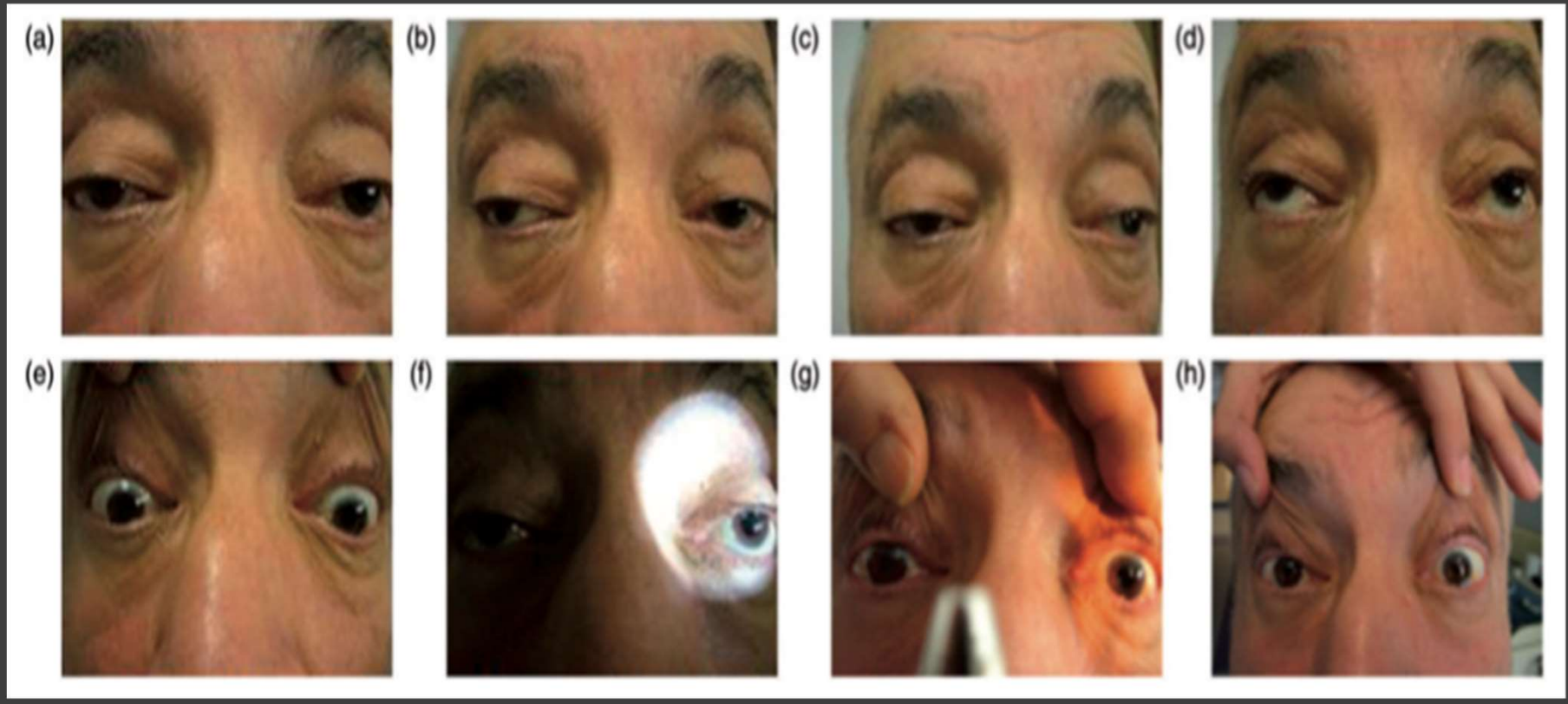
Category	Clinical features		
	Pattern of weakness	Ataxia	Hypersomnolence
GBS			
Classic GBS	Four limbs	No or minimal	No
Pharyngeal–cervical–brachial weakness*	Bulbar, cervical and upper limbs	No	No
Acute pharyngeal weakness‡	Bulbar	No	No
Paraparetic GBS*	Lower limbs	No	No
Bifacial weakness with paraesthesias*	Facial	No	No
MFS			
Classic MFS	Ophthalmoplegia	Yes	No
Acute ophthalmoparesis§	Ophthalmoplegia	No	No
Acute ataxic neuropathy§	No weakness	Yes	No
Acute ptosis§	Ptosis	No	No
Acute mydriasis§	Paralytic mydriasis	No	No
BBE‖	Ophthalmoplegia	Yes	Yes
Acute ataxic hypersomnolence¶	No weakness	Yes	Yes

Nat. Rev. Neurol. 10, 537–544 (2014)

CASE REPORT AND LITERATURE REVIEW

Pupillary Involvement in Miller Fisher Syndrome

Bahar Kaymakamzade[1], Ferda Selcuk[1], Aydan Koysuren[2], Ayse Ilksen Colpak[2], Senem Ertugrul Mut[1], and Tulay Kansu[2]



Neuro-Ophthalmology, 2013

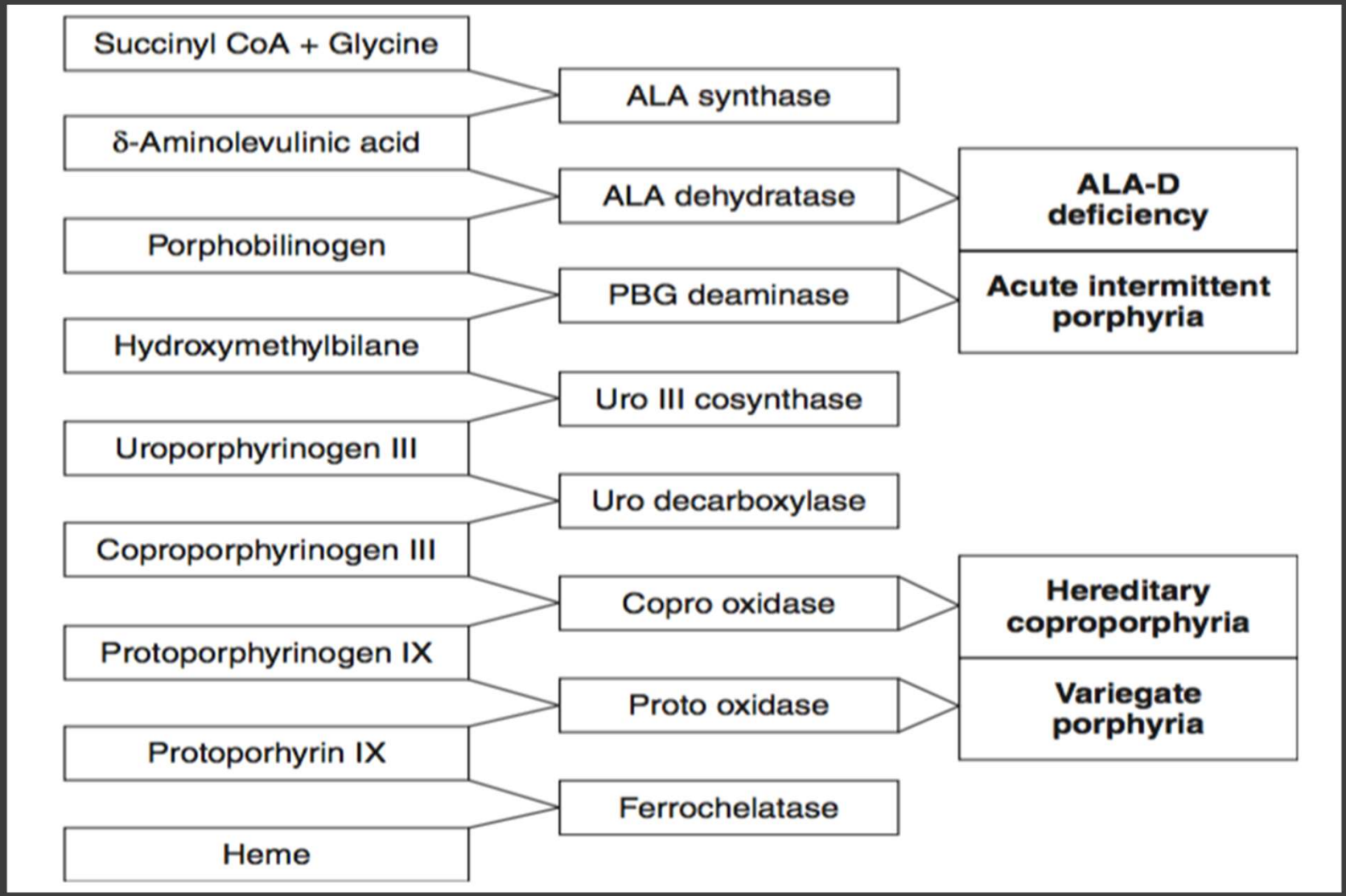
Atypical GBS

- Normal DTR - 2 – 9%, AMAN subtype
- Pure pandysautonomia
- Definite asymmetrical weakness – uncommon

Differential diagnosis

- Acute myelopathy
  - myelitis, ischemia
  - cord compression
- NMJ disease
  - Myasthenia gravis
  - Botulism
- Myopathy
  - DM, PM, NAM
  - rhabdomyolysis
  - toxic myopathy
  - critical illness myopathy
- Polyneuropathy
  - Diphtheria, CMV
  - acute intermittent porphyria
  - acute onset CIDP
  - vasculitic neuropathy
  - critical illness neuropathy
  - n-Hexane, arsenic, lead, thallium
  - toxic neuropathy
- Periordic paralysis
- Hypermanesemia

Porphyria


Succinyl CoA + Glycine
ALA synthase
δ-Aminolevulinic acid
ALA dehydratase
ALA-D deficiency
Porphobilinogen
PBG deaminase
Acute intermittent porphyria
Hydroxymethylbilane
Uro III cosynthase
Uroporphyrinogen III
Uro decarboxylase
Coproporphyrinogen III
Copro oxidase
Hereditary coproporphyria
Protoporphyrinogen IX
Proto oxidase
Variegate porphyria
Protoporhyrin IX
Ferrochelatase
Heme

Porphyric neuropathy

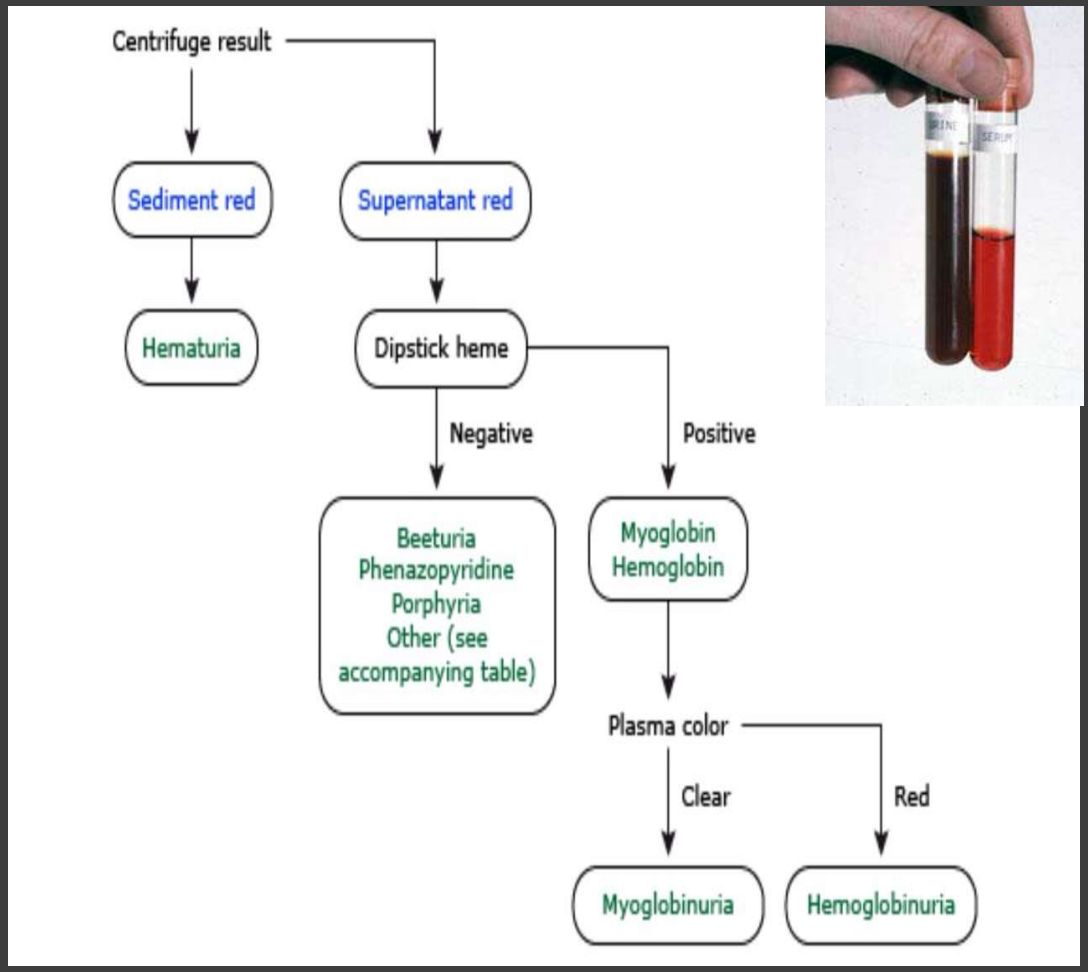
- CNS
  - psychiatric, anxiety, restlessness, insomnia, confusion
  - seizures
- Neuropathy
  - rapid progressive, motor predominant axonal neuropathy
  - areflexia, ascending weakness
  - respiratory, cranial nerve involvement can occur
- Autonomic features
  - tachycardia
  - constipation, gastroparesis, pseudo-obstruction, diarrhea, vomiting,

Investigation - Porphyria

Table 1. Characteristic patterns of abnormal levels of heme precursors in the urine and feces during an attack of hepatic porphyria.[2]

Type	Enzyme deficiency	Urine*	Feces†
ALA dehydratase deficiency	ALA dehydratase	↑ ALA, Copro	Normal
Acute intermittent	Hydroxymethylbilane (also called PBG deaminase)	↑ ALA, PBG, Uro	Normal
Hereditary coproporphyria	Copro oxidase	↑ ALA, PBG, Uro, Copro	↑ Copro > Proto
Variegate porphyria	Proto oxidase	↑ ALA, PBG, Uro, Copro	↑ Proto > Copro

Dark, brown urine



Prognosis - Porphyric neuropathy

- Abdominal pain, autonomic, CNS - rapidly resolved
- neuropathy – slowly resolved, months
  - depends on severity of axonal degeneration.
  - incomplete motor function

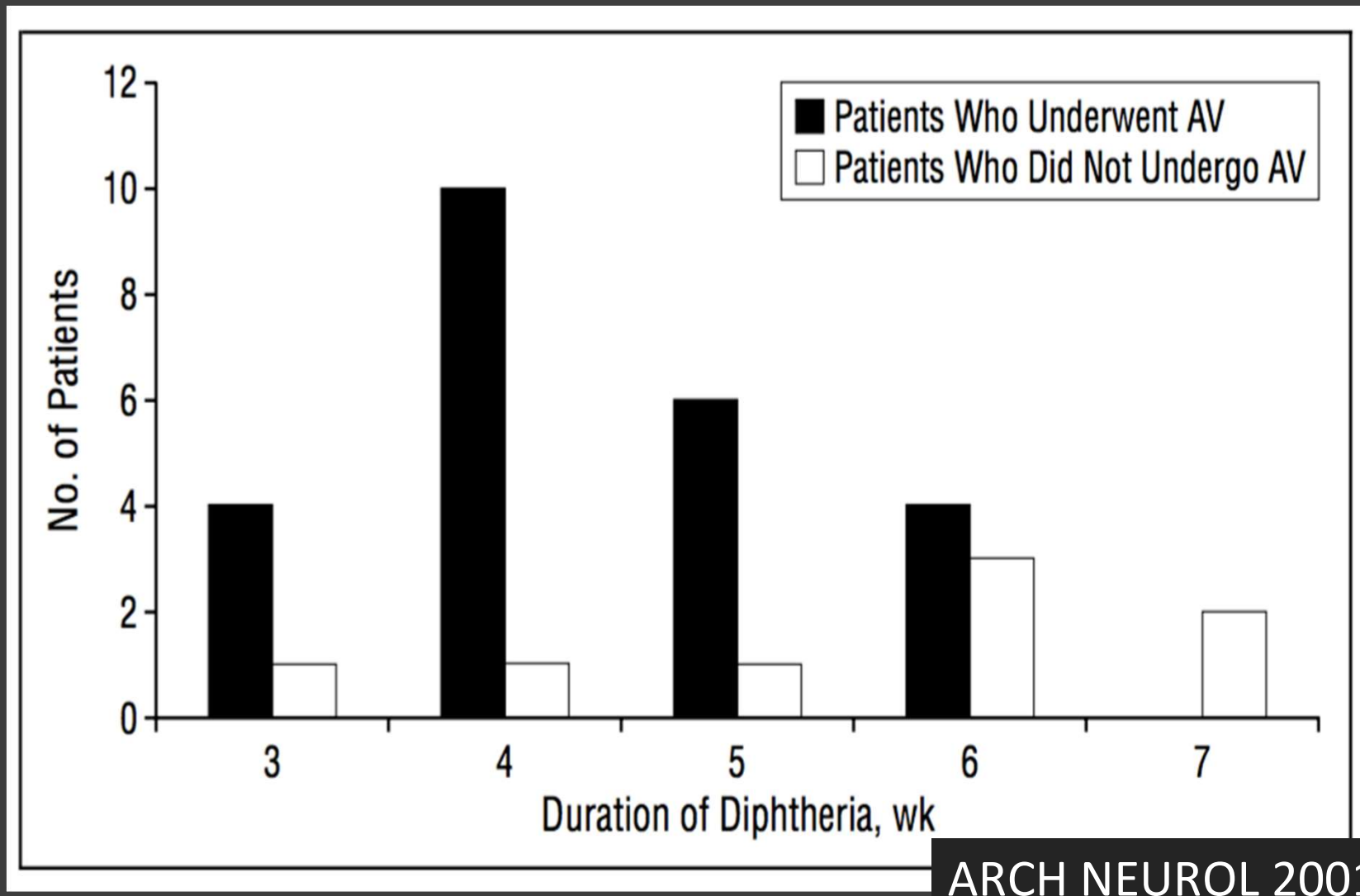
Table 2. Examples of medications and substances reported to be potentially safe, potentially unsafe, and unsafe for use in patients with hepatic porphyria.[1,2,4,25,97]

Potentially safe*	Potentially unsafe	Unsafe
Acetaminophen	Agents inducing cytochrome P450	Alcohol
Acyclovir	Alkylating agents	Barbiturates
Amantadine	Clonidine	Calcium channel blockers
Aspirin	Chloroquine	Carbamazepine
Atropine	Estrogens	Chloramphenicol
Beta blockers	Erythromycin	Chlorpropamide
Bromides	Hydralazine	Clonazepam
Cimetidine	Ketamine	Danazol
Chloral hydrate	Lidocaine	Ketamine
Chlorpromazine	Lidocaine	Dapsone
Colchicine	Methyldopa	Ergots
Dopamine	Nalidixic acid	Felbamate
Fentanyl	Nortryptyline	Griseofulvin
Gabapentin	Pentazocine	Halothane
Glucocorticoids	Phenoxybenzamine	Meprobamate
Haloperidol	Rifampin	Phenytoin
Insulin	Spirolactone	Primidone
Narcotic analgesics	Theophylline	Progestins
Neostigmine		Succinamides
Procaine		Sulfonamides
Penicillin		Theophylline
Phenothiazines		Tolazamide
Propofo		Tolbutamide
IPropranolol		Tranquilizers
Reserpine		Trimethadone
Serotonin reuptake inhibitors		Valproic acid
Streptomycin		
Tetracycline		
Vitamins		

Diphtheritic Polyneuropathy

- *Corynebacterium diph-theriae*
- Exudative pharyngitis
- Cervical lymphadenopathy
- Cardiomyopathy
- Demyelinating polyneuropathy 20-70%

Onset of Diphtheritic Polyneuropathy



ARCH NEUROL 2001

Diphtheritic Polyneuropathy

Table 1. Cranial Nerve Disturbances in 32 Patients With Diphtheritic Polyneuropathy

Cranial Nerves	Duration of Involvement, wk	Frequency*
IX and X	7-8	32 (100)
VII	7-8	28 (88)
III, IV, and VI	5-7	27 (84)
XI	7-9	27 (84)
XII	7-8	23 (72)
V	6-7	17 (53)

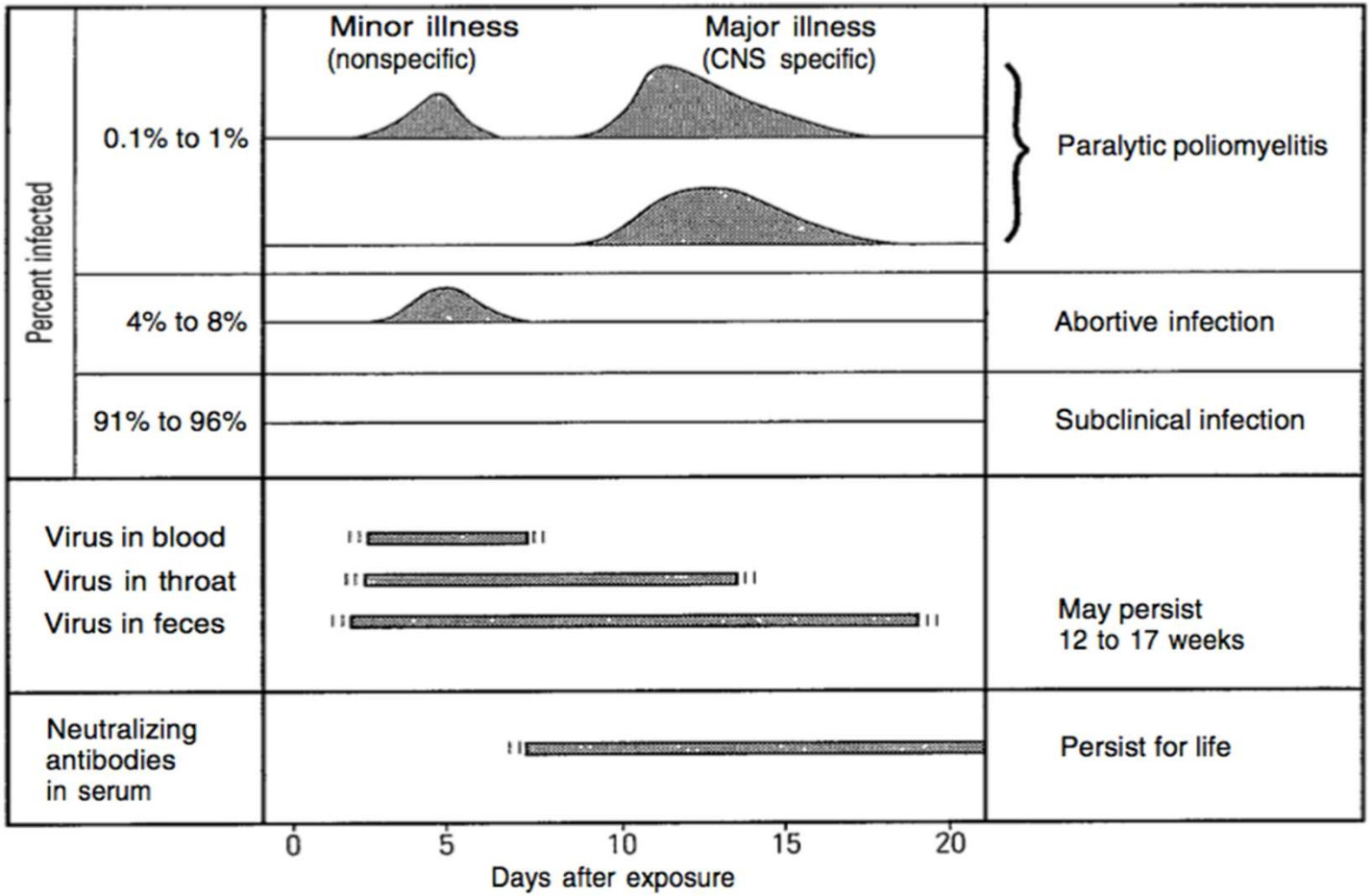
ARCH NEUROL 2001

CMV polyradiculopathy

- Host
  - HIV pts., late stage
  - immuno-compromised pts.
- Evidence of CMV infection
  - retinitis, enteritis
- Rapidly progressive lower ext. weakness and pain
- CSF pleocytosis, high protein, low glucose
- NCS - axonal polyradiculopathy

Poliomyelitis

Figure 1. Time course of events in infection with poliovirus.



CNS involvement - Poliomyelitis

- Nonparalytic aseptic meningitis
- Flaccid paralysis
  - spinal polio- myelitis - 79%
    - Asymmetric, limbs and trunk weakness
    - proximal > distal m.
    - lumbrosacral region – most common
  - bulbar poliomyelitis – 2%
    - CN VII, IX, X
    - respiratory m.involvement
  - bulbospinal poliomyelitis – 19%

Prognosis - Poliomyelitis

- Recovery may be complete in some pts.
- Motor weakness persists beyond 12 mo.
  - lifelong disability
- Death – 2-30%, bulbar poliomyelitis
- PPS - 22% to 85%
  - progressive motor weakness
  - begin 8 -71 yrs. (average 35 yrs.)

n-Hexane

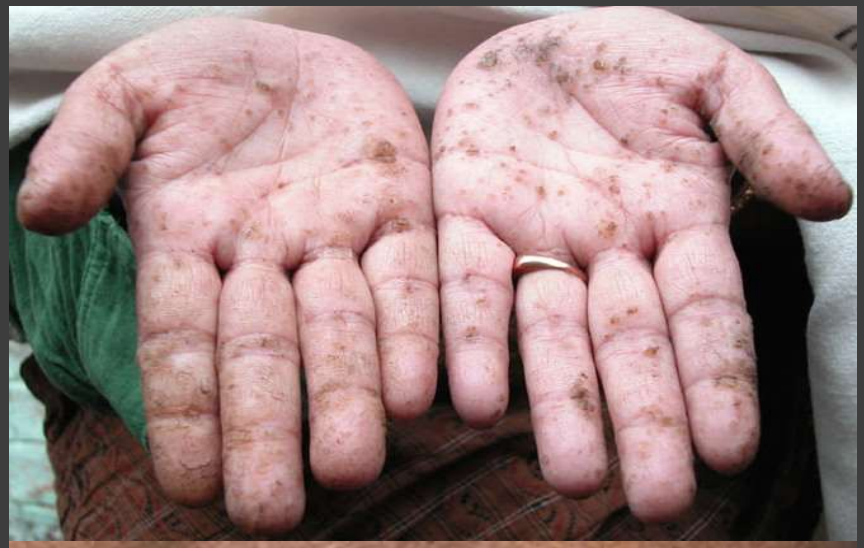
Hexacarbon neurotoxicity

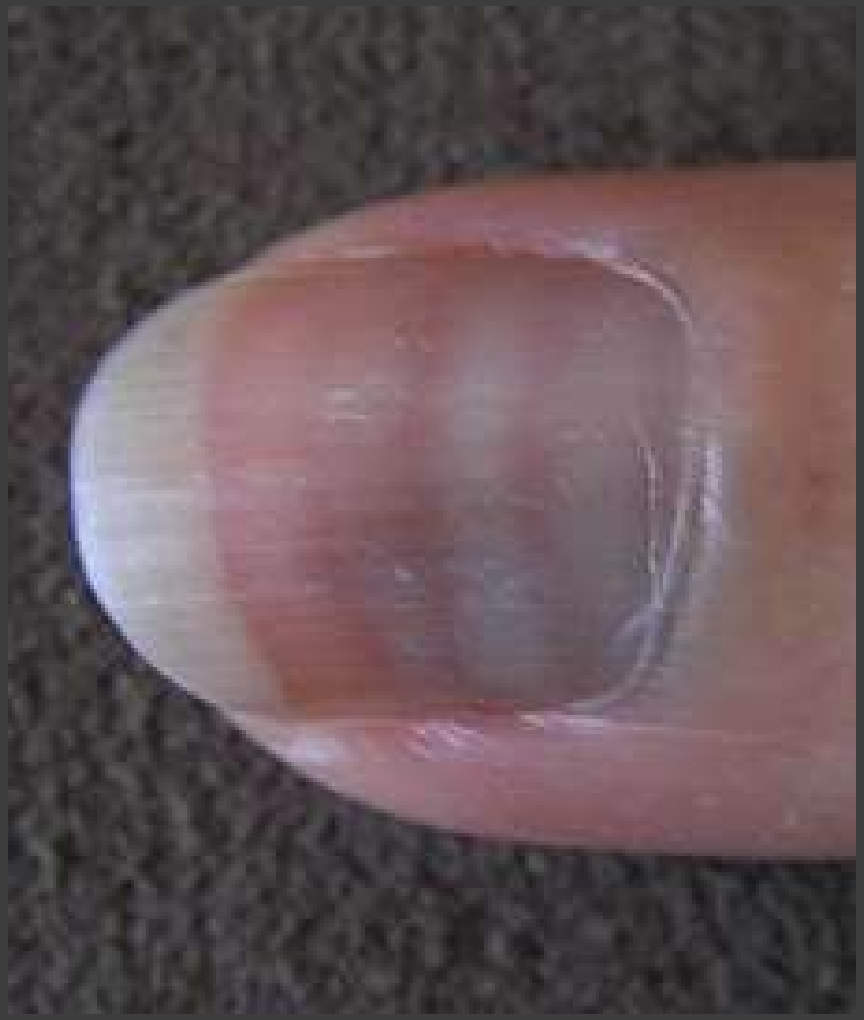
- Symmetrical, sensory predominant demyelinating polyneuropathy
  - sensory loss – all modality
  - distal weakness (proximal in severe case)
  - autonomic - rare
- Hyporeflexia or areflexia
- Insidious onset - subacute course can developed in excessive abuse
- Progression after stop exposure – 1 - 4 mo.
- Complete recovery in mild cases

Arsenic poisoning

- Acute GI symptoms
  - abdominal pain, nausea, vomiting, diarrhea
  - min. to hours after ingestion
- Polyneuropathy
  - painful neuropathy with progressive distal muscle weakness
  - onset - Day 10 - 3 wks.
  - may progress up to 5 wks.
- Acute and severe poisoning
  - drowsiness, confusion, stupor, psychosis, delirium
  - Hypotension, cardiomyopathy, cardiac arthymia, respiratory m. Involvement
  - death within 24 hrs.

Arsenic poisoning

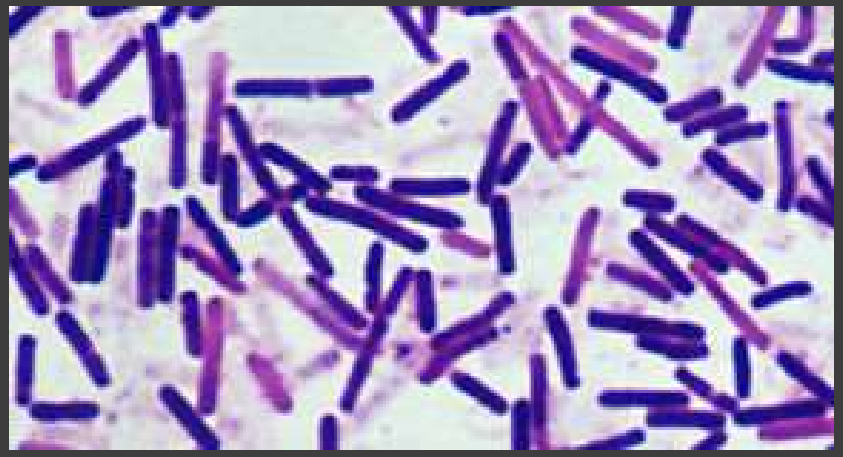




Organophosphate and Carbamate

- Inhibitacetyl cholinesterase
- salivation, lacrimation, diarrhea, nausia
- Weakness
- Bronchospasm, pulmonary edema, cyanosis
- Bradycardia, chest pain
- Tremor
- Convulsions, coma

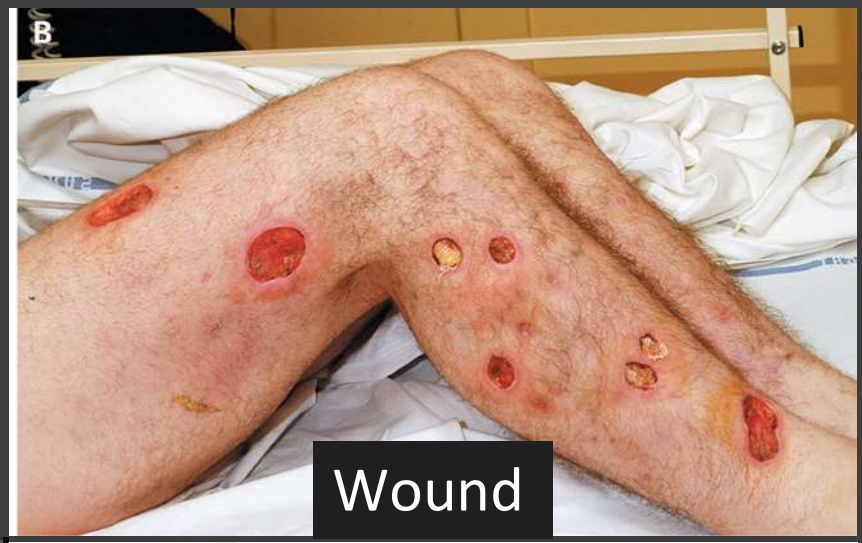
Botulism



- *Clostridium botulinum*
  - Anaerobic, gram positive, spore-forming, rod-shaped bacterium
- Botulinum toxin
  - colorless, odorless, tasteless
  - inactive by heat (□85°C for 5 min.
- Spores resistant to heat
  - survive in home-canning at temp < 120°C

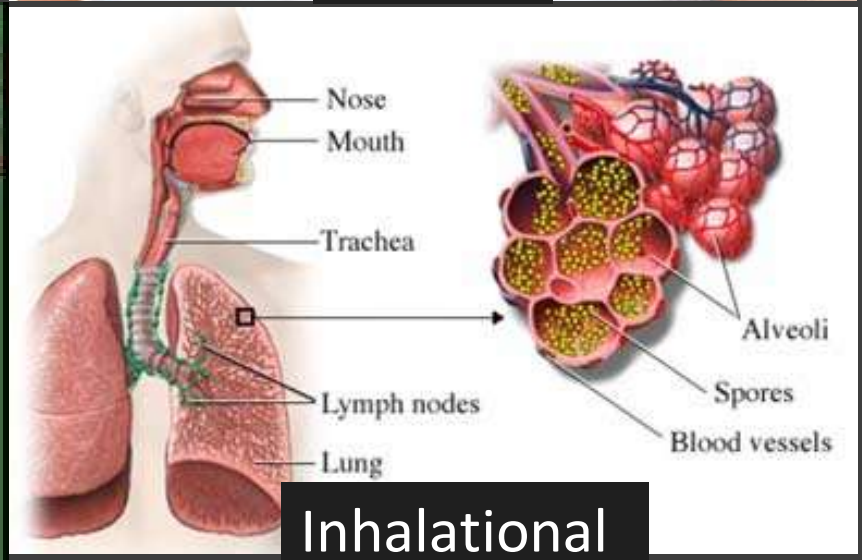
Human botulism


Foodborne



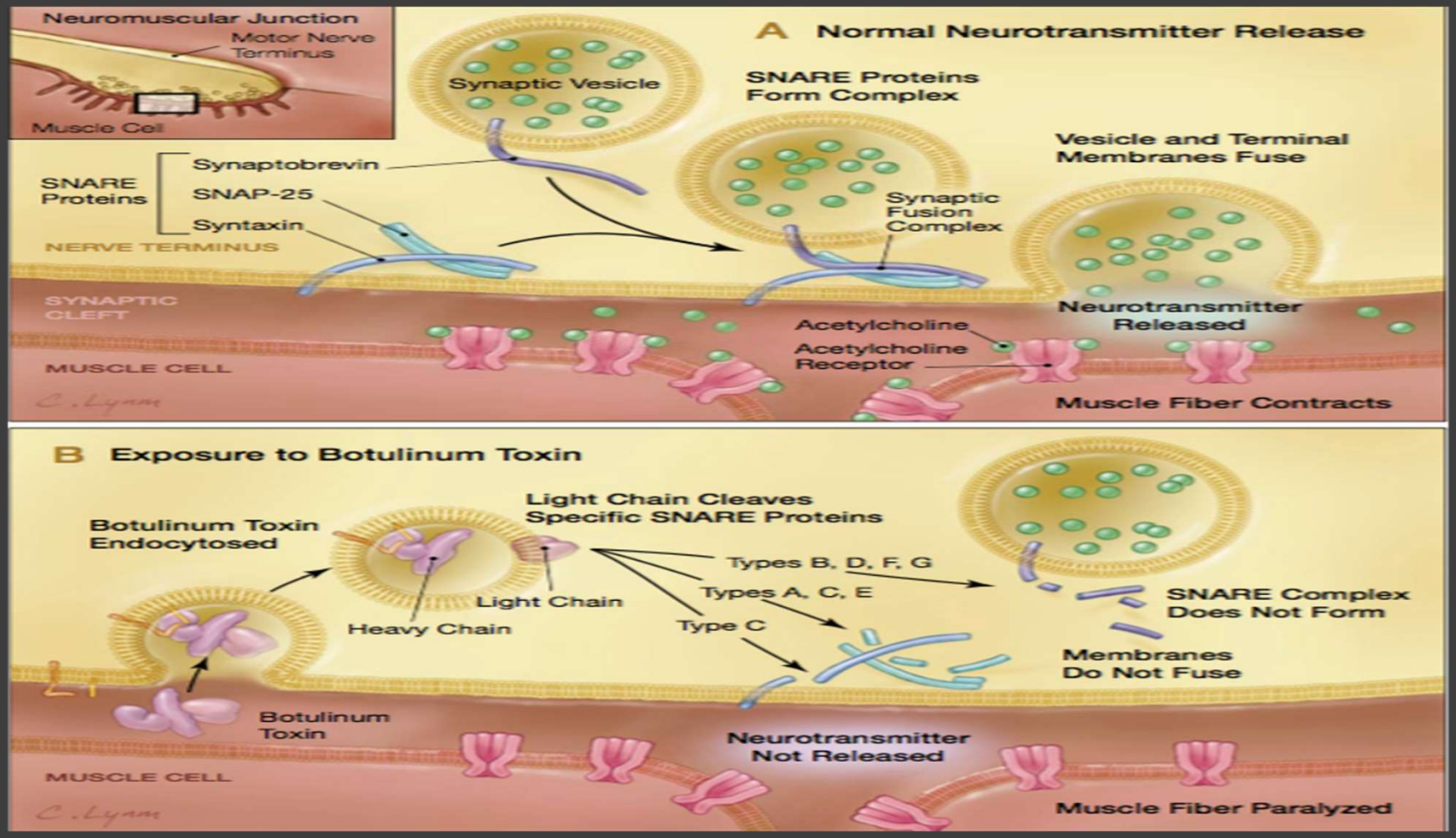
Wound


Intestinal



Inhalational

Pathogenesis - Botulism



Clinical manifestation - Botulism

- Acute, afebrile, symmetric, descending flaccid paralysis
  - ptosis, diplopia, blurred vision
  - enlarged or sluggishly reactive pupils
  - dysarthria, dysphonia, dysphagia
  - dry mouth and injected pharynx
- No sensory changes
  - except circum-oral, peripheral paresthesia from hyperventilation

Diagnostic Tests - Botulism

- Botulinum toxin
  - Mouse bioassay
  - Immunoassay for toxin
  - Polymerase chain reaction (PCR) for toxin
  - Specimen – serum, stool, gastric content, enema, suspect food
- C/S for *Clostridium botulinum*
  - Stool, gastric content

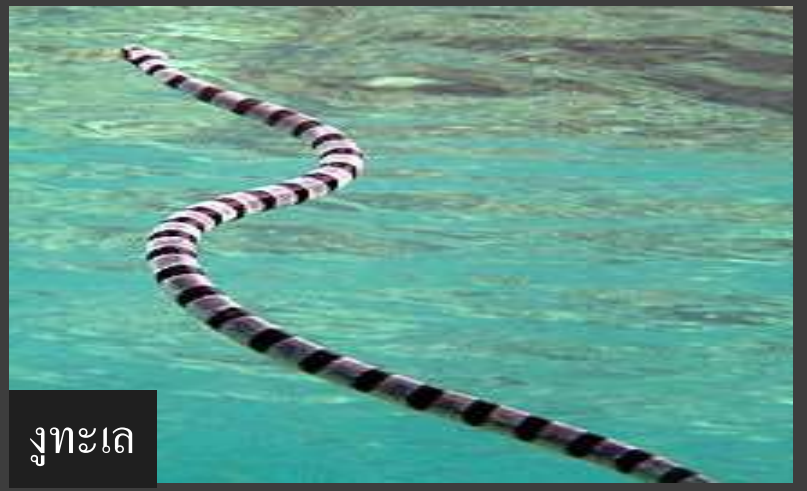
Tetrodotoxin and Saxitoxin

Snake venom

งูเห่า งูจงอาง

งูสามเหลี่ยม

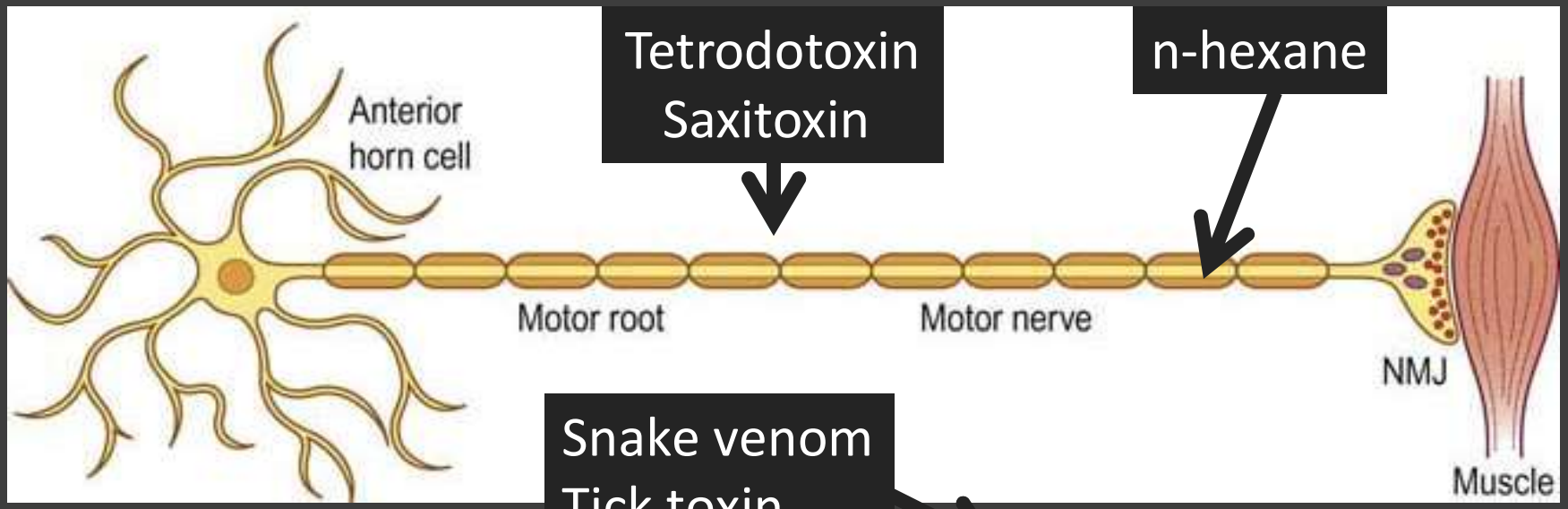
งูทับสมิงคลา



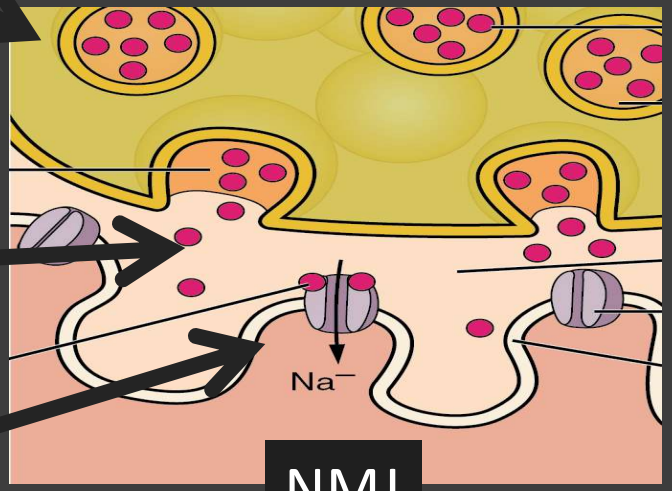
งูทะเล

Tick paralysis

Toxin



Snake venom
Tick toxin
Botulism

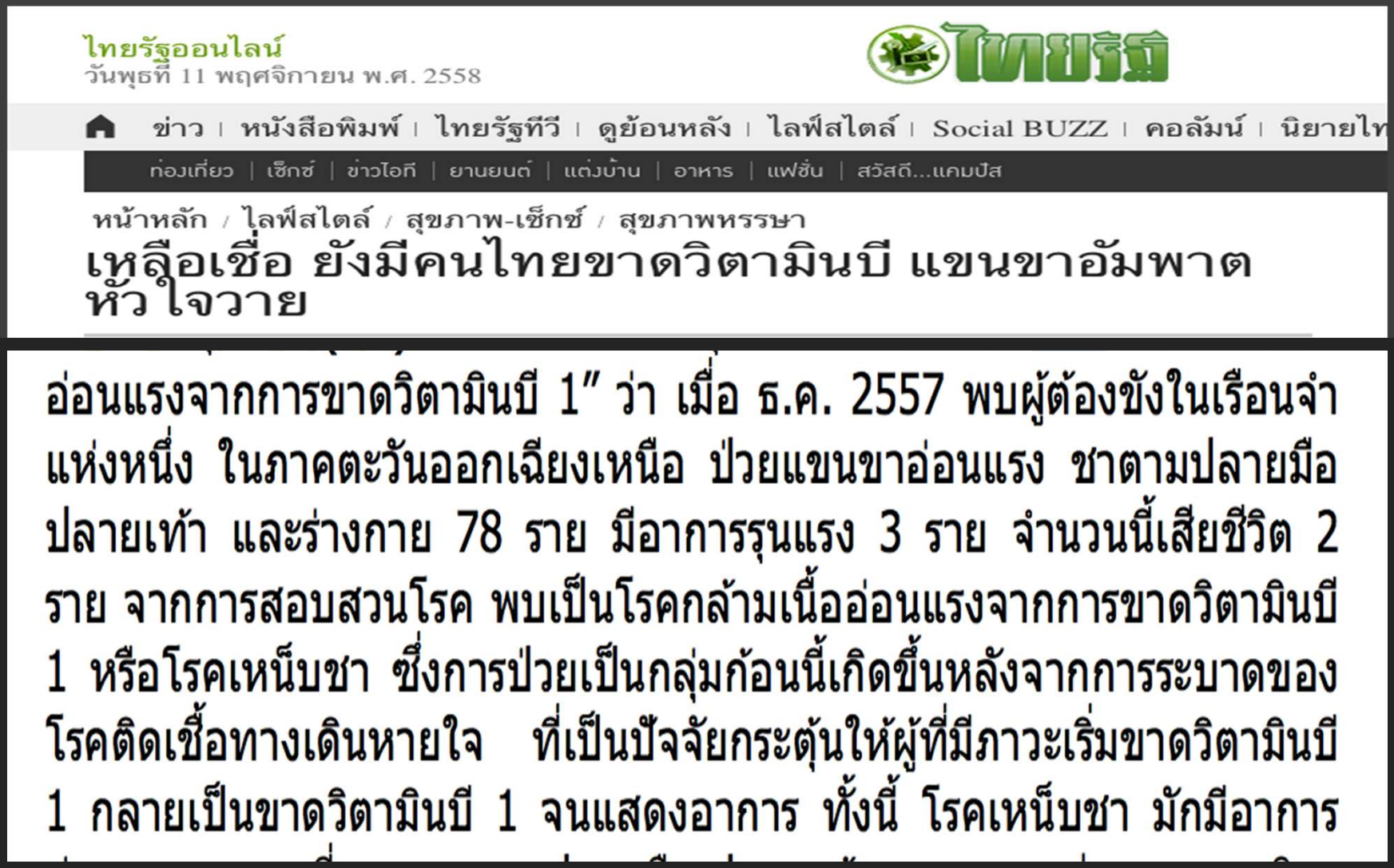


Organophosphate
Carbamate

Snake venom

NMJ

Thiamine deficiency



ไทยรัฐออนไลน์
วันพุธที่ 11 พฤศจิกายน พ.ศ. 2558

ไทยรัฐ

ข่าว | หนังสือพิมพ์ | ไทยรัฐทีวี | ดูย้อนหลัง | ไลฟ์สไตล์ | Social BUZZ | คอลัมน์ | นิยายไท

ท่องเที่ยว | เซ็กซ์ | ข่าวไอที | ยานยนต์ | แต่งบ้าน | อาหาร | แฟชั่น | สวัสดี...แคมปัส

หน้าหลัก / ไลฟ์สไตล์ / สุขภาพ-เซ็กซ์ / สุขภาพหรรษา

เหลือเชื่อ ยังมีคนไทยขาดวิตามินบี แขนขาอัมพาต หัวใจวาย

อ่อนแรงจากการขาดวิตามินบี 1" ว่า เมื่อ ธ.ค. 2557 พบผู้ต้องขังในเรือนจำแห่งหนึ่ง ในภาคตะวันออกเฉียงเหนือ ป่วยแขนขาอ่อนแรง ชาตามปลายมือปลายเท้า และร่างกาย 78 ราย มีอาการรุนแรง 3 ราย จำนวนนี้เสียชีวิต 2 ราย จากการสอบสวนโรค พบเป็นโรคกล้ามเนื้ออ่อนแรงจากการขาดวิตามินบี 1 หรือโรคเหน็บชา ซึ่งการป่วยเป็นกลุ่มก้อนนี้เกิดขึ้นหลังจากการระบาดของโรคติดเชื้อทางเดินหายใจ ที่เป็นปัจจัยกระตุ้นให้ผู้ที่มีภาวะเริ่มขาดวิตามินบี 1 กลายเป็นขาดวิตามินบี 1 จนแสดงอาการ ทั้งนี้ โรคเหน็บชา มักมีอาการ

Thiaminase

Thiamine antagonists

Investigation

Lumbar puncture

- Albuminocytological dissociation - 64%
  - elevated CSF protein
    - 50% within first 3 days
    - 90% at nadir
  - normal cell counts

- CSF cell counts >50 cells/µl
  - Leptomeningeal metatasis, lymphoma
  - CMV, early HIV infection, Poliomyelitis
  - Lyme, sarcoidosis

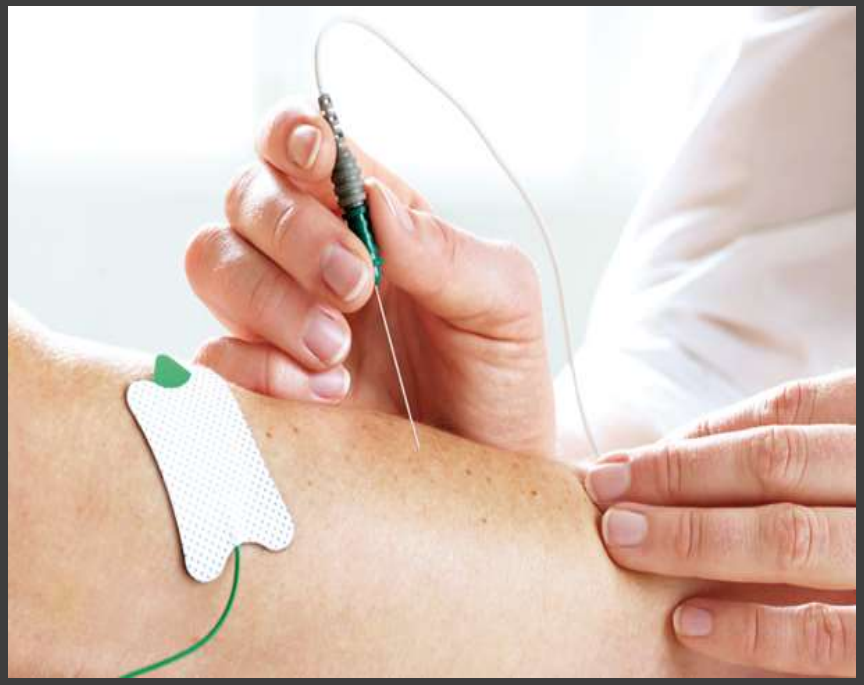
Brain 137, 33–43 (2014)

Antiganglioside antibodies

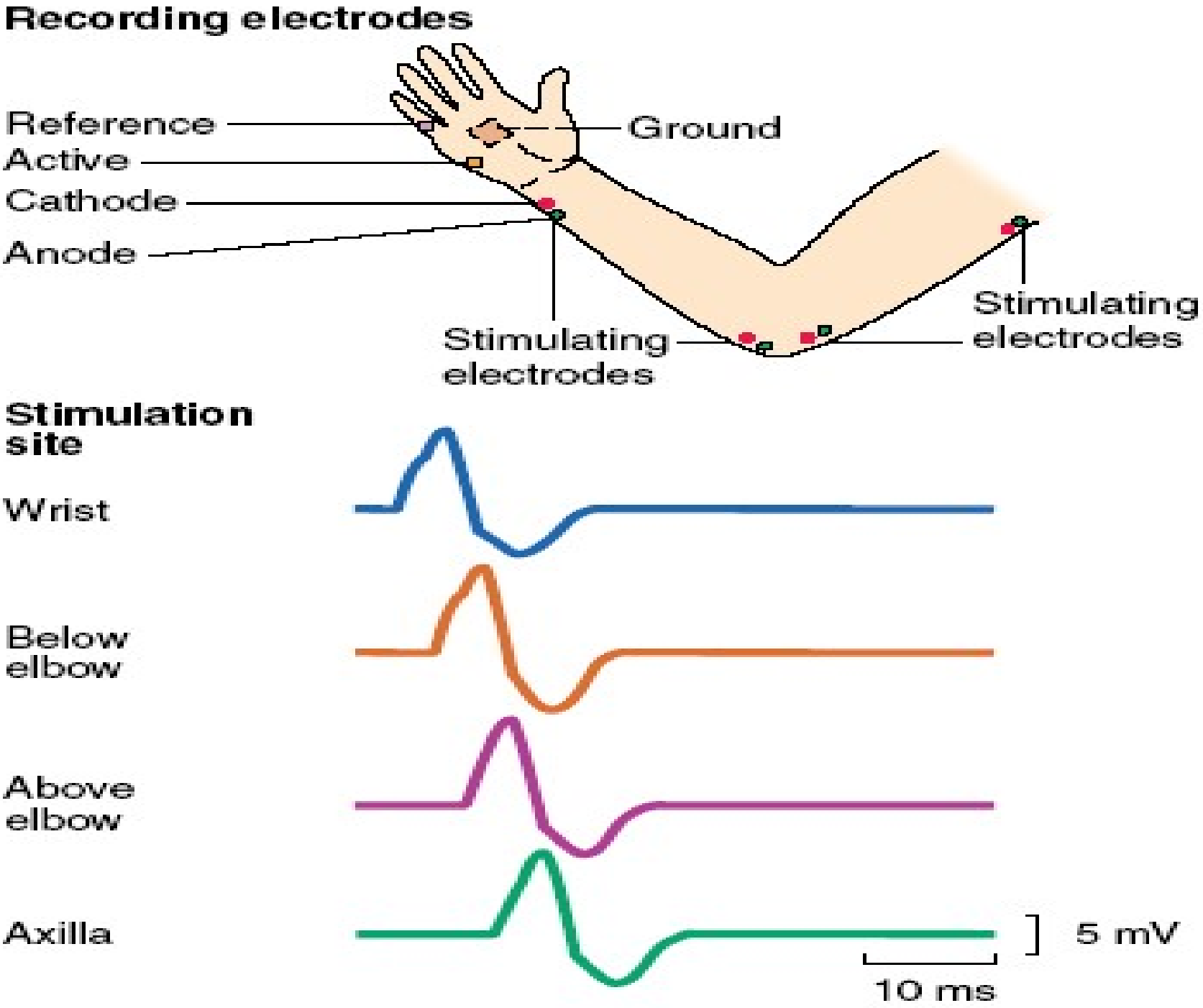
- No role in diagnosis except anti-GQ1b Ab
  - low negative predictive value
  - can occur in other diseases

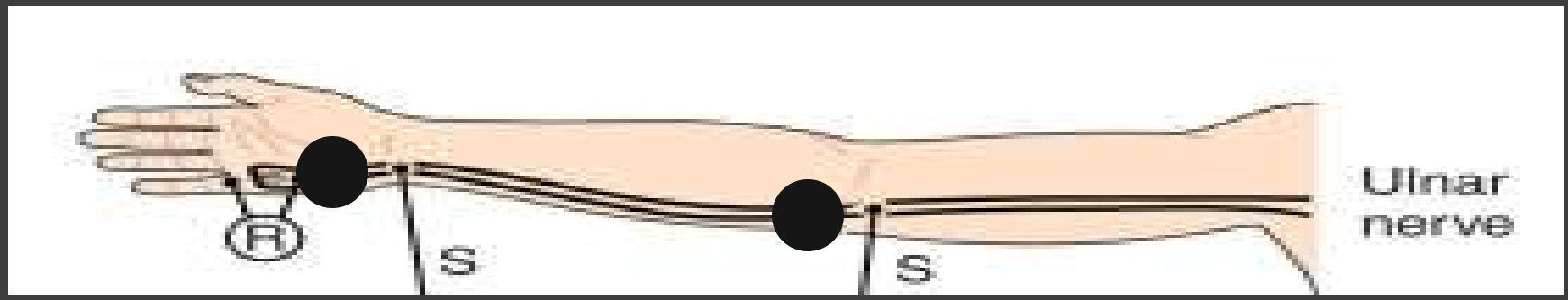
Electrodiagnosis study

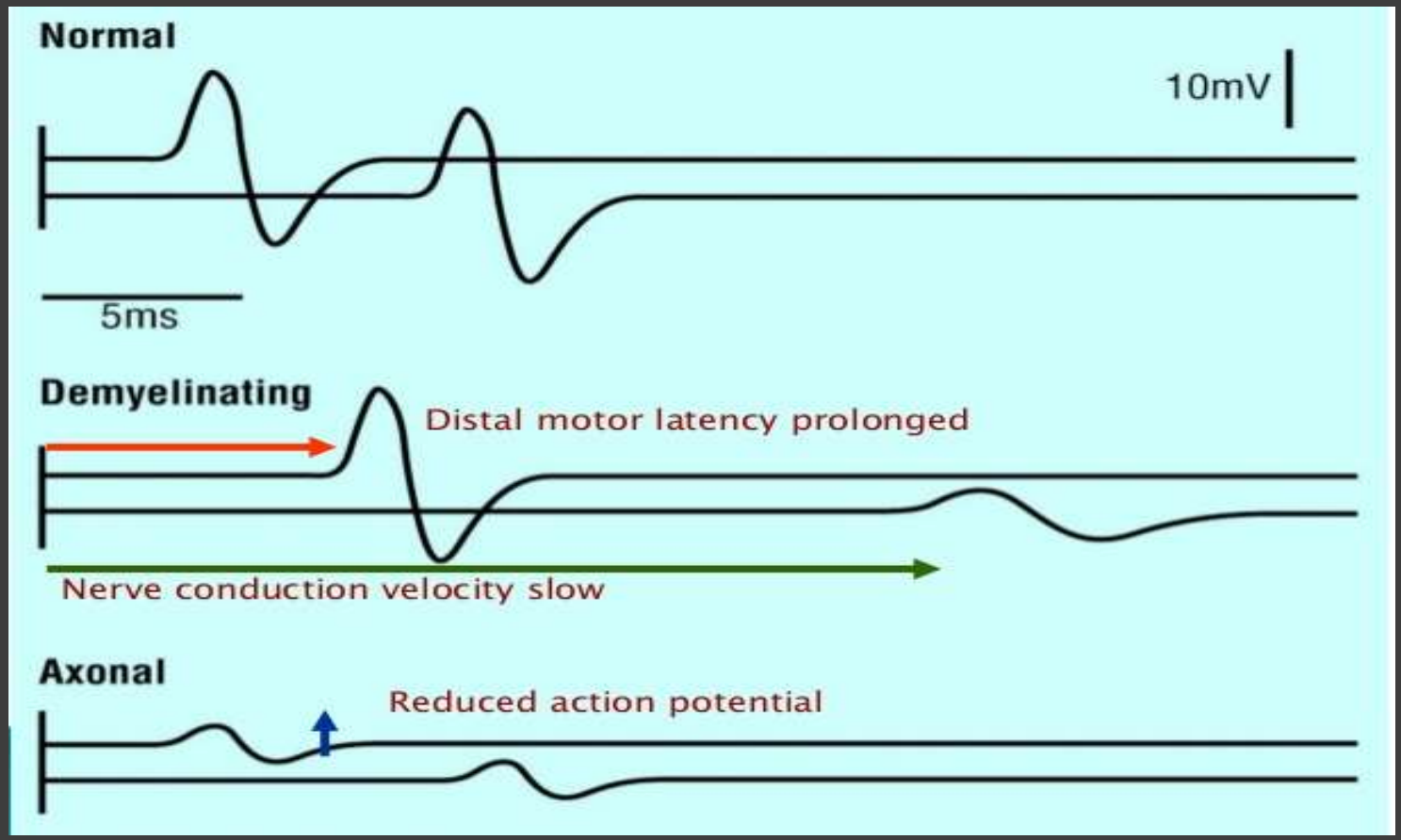
Nerve conduction study



Electromyography


Recording electrodes
Reference
Active
Cathode
Anode
Ground
Stimulating electrodes
Stimulating electrodes
Stimulation site
Wrist
Below elbow
Above elbow
Axilla
5 mV
10 ms


R
S
S
Ulnar
nerve


Normal
10mV
5ms
Demyelinating
Distal motor latency prolonged
Nerve conduction velocity slow
Axonal
Reduced action potential

Panel 2: Neurophysiological criteria for AIDP, AMSAN, and AMAN

AIDP

At least one of the following in each of at least two nerves, or at least two of the following in one nerve if all others inexcitable and dCMAP>10% LLN:

Motor conduction velocity <90% LLN (85% if dCMAP <50% LLN)

Distal motor latency >110% ULN (>120% if dCMAP <100% LLN)

pCMAP/dCMAP ratio <0·5 and dCMAP>20% LLN

F-response latency >120% ULN

AMSAN*

None of the features of AIDP except one demyelinating feature allowed in one nerve if dCMAP <10% LLN

Sensory action potential amplitudes <LLN

AMAN*

None of the features of AIDP except one demyelinating feature allowed in one nerve if dCMAP <10% LLN

Sensory action potential amplitudes normal

Inexcitable

dCMAP absent in all nerves or present in only one nerve with dCMAP <10% LLN

dCMAP=compound muscle action potential amplitude after distal stimulation; pCMAP=compound muscle action potential amplitude after proximal stimulation; LLN=lower limit of normal. ULN=upper limit of normal. *In the original definitions the difference between AMSAN and AMAN proposed here is implied but not stipulated.

Lancet 2005

Diagnostic criteria

- Required features
  - progressive weakness in both arms and legs
  - areflexia or hyporeflexia
- Features supportive of diagnosis
  - progression of symptoms over days to 4 weeks
  - relative symmetry
  - mild sensory signs or symptoms
  - CN involvement, especially bilateral facial weakness
  - recovery beginning 2 to 4 weeks after progression ceases
  - autonomic dysfunction
  - absence of fever at onset

Ann Neurol 1990

Diagnostic criteria

- CSF - albuminocytologic dissociation
- NCS - demyelinating features
- Features that rule out the diagnosis
  - Hexacarbon abuse
  - abnormal porphyrin metabolism
  - recent diphtheria infection
  - Lead intoxication
  - excluded - poliomyelitis, botulism, hysterical paralysis, toxic neuropathy

Ann Neurol 1990

Red flags in diagnostic of GBS

- Clinical
  - fever at onset
  - bladder or bowel dysfunction at onset or persistent
  - sharp sensory level
  - persistent asymmetry of weakness
  - severe pulmonary dysfunction with limited limb weakness at onset
  - severe sensory signs with limited weakness at onset
- Lab
  - increased wbc in CSF (>50 /µl)
  - PMN in cerebrospinal fluid

Ann Neurol 1990

Treatment of GBS

GBS disability scale

0 - Healthy state

1 - Minor symptoms and capable of running

2 - Able to walk 10m or more without assistance but unable to run

3 - Able to walk 10m across an open space with help

4 - Bedridden or chair bound

5 - Requiring assisted ventilation for at least part of the day

6 - Dead

Indication of IVIg or Plasmapheresis

Consider specific treatment with IVIg or PE

Indications to start IVIg or PE:

- Severely affected patients (inability to walk unaided, GBS disability scale ≥3)[94,97]
- Start IVIg preferably within first 2 weeks from onset: 0·4 g/kg for 5 days (unknown whether 1·0 g/kg for 2 days is superior); or 5× PE with total exchange volume of five plasma volumes in 2 weeks

Unknown whether IVIg is effective:

- Mildly affected patients (GBS disability scale ≤2) or MFS patients

Indications for re-treatment with IVIg:

- Secondary deterioration after initial improvement or stabilisation (treatment-related fluctuation): treat with 0·4 g/kg for 5 days
- No proven effect of re-treatment with IVIg in patients who continue to worsen

IVIg vs.Plasmapheresis

IVIg

- Start improving < 1 wk
- Benefit – 3-6 wk.
- Complication
  - headache, nausea
  - chills, myalgia
  - chemical meningitis
  - acute renal failure
  - anaphylaxis
  - hyper-viscocity syndrome

Plasmaphoresis

- Start improving within days
- Benefit - 3-4 wk.
- Complication
  - infection
  - Thrombosis
  - Bleeding
  - Hypotension
  - cardiac arrhythmias
  - toxic reaction to the citrate used in procedure

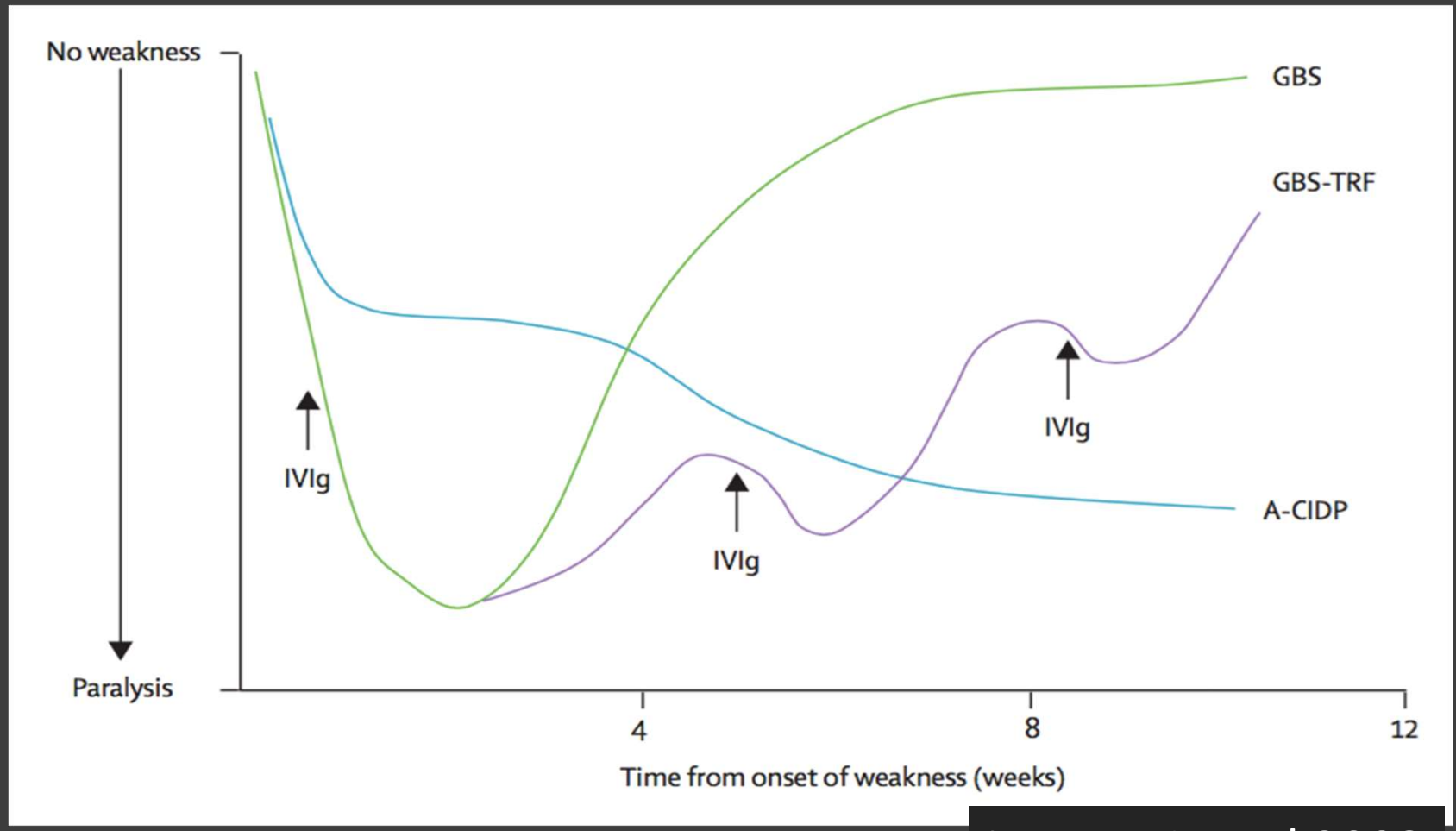
Cochrane Database Syst Rev. 2006 Apr 19;(2):CD001446.

Corticosteroids for Guillain-Barré syndrome.

Hughes RA[1], Swan AV, van Koningsveld R, van Doorn PA.

- Corticosteroid and non–corticosteroid
  - no difference in disability grade
  - less clinical improvement after 4 wks.
- IVMP alone - no benefit or harm
- IVMP + IVIg
  - may hasten recovery but does not significantly affect the long-term outcome

Repeated dose of IVIg



Lancet Neurol 2008

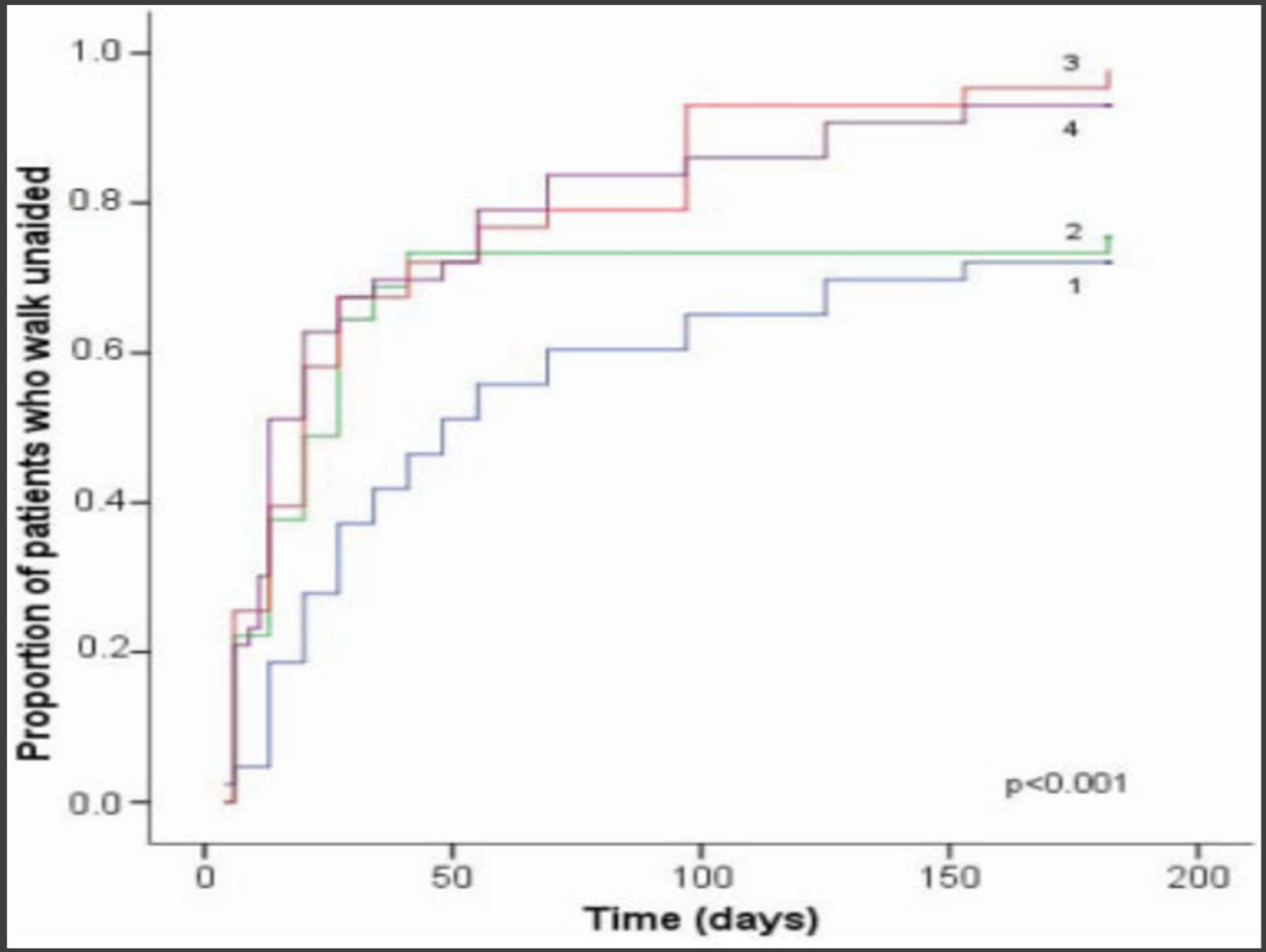
Table 2 | Differentiating characteristics of GBS, GBS-TRF, A-CIDP and CIDP[130]

Characteristic	GBS	GBS-TRF	A-CIDP	CIDP
Time to nadir	<2 weeks (maximum 4 weeks)	<2 weeks (maximum 4 weeks)	4–8 weeks, followed by progression with deteriorations	>8 weeks
Disease course	Monophasic	1–2 deteriorations within 8 weeks	>2 deteriorations or deterioration after 8 weeks	Progressive, stepwise or fluctuating
Severity	Highly variable between patients, ranging from mild symptoms to paralysis	Highly variable between patients, ranging from mild symptoms to paralysis	Mostly moderate	Mostly moderate, distal and proximal weakness
Ventilator dependence	20–30%	20–30%	Almost never	Almost never
Cranial nerve deficits	Often	Often	Sometimes	Sometimes
Response to IVIg	Good	Good, with fluctuations	Variable	Good
EMG/NCS*	Sometimes no classification possible at first EMG/NCS	Sometimes no classification possible at first EMG/NCS	Often demyelinating polyneuropathy at first EMG/NCS	Demyelination
Treatment	IVIg or plasma exchange	Repeat IVIg or plasma exchange	IVIg or plasma exchange, on confirmed diagnosis of CIDP consider also switch to prednisolone maintenance treatment	IVIg, prednisolone or plasma exchange

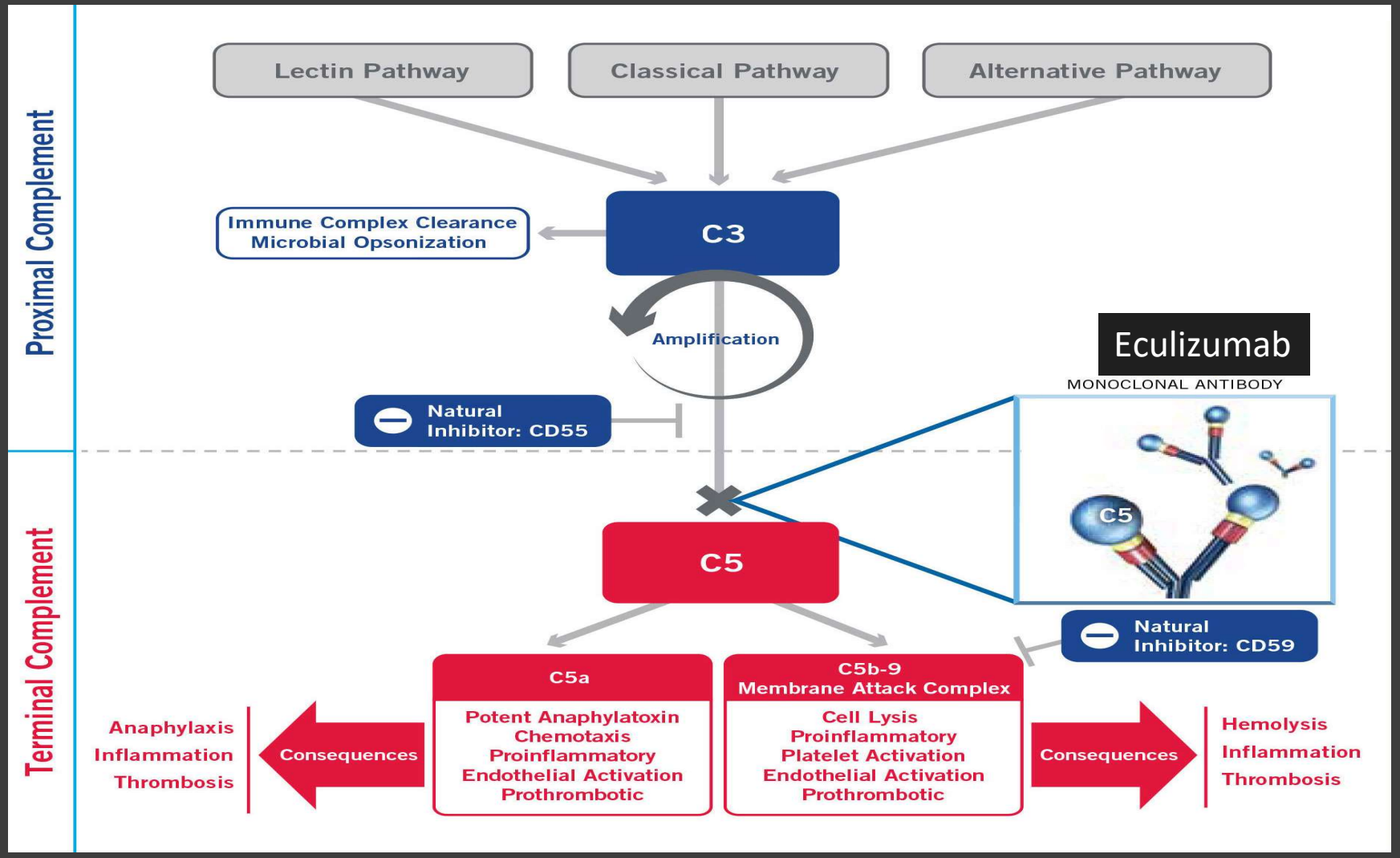
Pharmacokinetics of IVIG

Table. **Baseline Characteristics, Clinical Course, and Outcome in Quartiles of Patients Based on the Increase in ΔIgG Levels 2 Weeks After Treatment With a Standard High Dose of Intravenous Ig**

	Quartiles Based on ΔIgG at 2 wks				*p*
	1	2	3	4	
ΔIgG, g/L	<3.99	3.99–7.30	7.31–10.92	>10.92	
No.	43	45	43	43	
Serum IgG level, g/L					
Pretreatment	12.5 (3.8)	10.8 (2.4)	10.4 (2.6)	10.4 (3.0)	
2 wk after treatment	13.5 (4.2)	16.6 (2.7)	19.4 (2.8)	25.7 (4.8)	
Baseline characteristics					
Demographic features					
Age, y	52.1 (22.9)	49.2 (20.6)	51.8 (17.2)	45.4 (19.2)	0.20
Males	23 (54%)	29 (64%)	24 (56%)	23 (54%)	0.79
Bodyweight, kg	71.0 (19.7)	74.4 (15.1)	75.2 (13.9)	75.2 (16.1)	0.24
Preceding infections					
Diarrhea	9 (21%)	8 (18%)	11 (26%)	13 (31%)	0.19
Upper respiratory tract infection	17 (40%)	17 (38%)	13 (30%)	13 (31%)	0.31
Clinical severity at entry					
GBS disability score	4.0 (0.44)	3.8 (0.56)	3.7 (0.58)	3.7 (0.56)	0.007
≥4	39 (91%)	34 (76%)	29 (67%)	28 (65%)	0.004
MRC sum score	35.8 (11.3)	39.0 (13.0)	42.7 (10.1)	43.7 (9.8)	<0.001
≤40	25 (58%)	19 (42%)	14 (33%)	12 (28%)	0.003
Outcome characteristics					
Clinical severity at nadir					
GBS disability score	4.6 (0.7)	4.0 (0.7)	3.9 (0.7)	4.0 (0.5)	<0.001
>4	25 (58%)	10 (22%)	7 (16%)	5 (12%)	<0.001
MRC sum score	23.0 (16.0)	32.9 (17.3)	37.9 (14.4)	39.1 (15.3)	<0.001
≤40	36 (84%)	25 (56%)	20 (47%)	16 (37%)	<0.001
Mechanical ventilation					
Frequency[a]	22 (52%)	9 (23%)	5 (12%)	5 (13%)	<0.001
Outcome at 6 mo					
GBS disability score >2	12 (28%)[b]	11 (24%)[c]	1 (2%)[d]	3 (7%)[e]	0.001


Proportion of patients who walk unaided
1.0
0.8
0.6
0.4
0.2
0.0
0
50
100
150
200
Time (days)
3
4
2
1
p<0.001

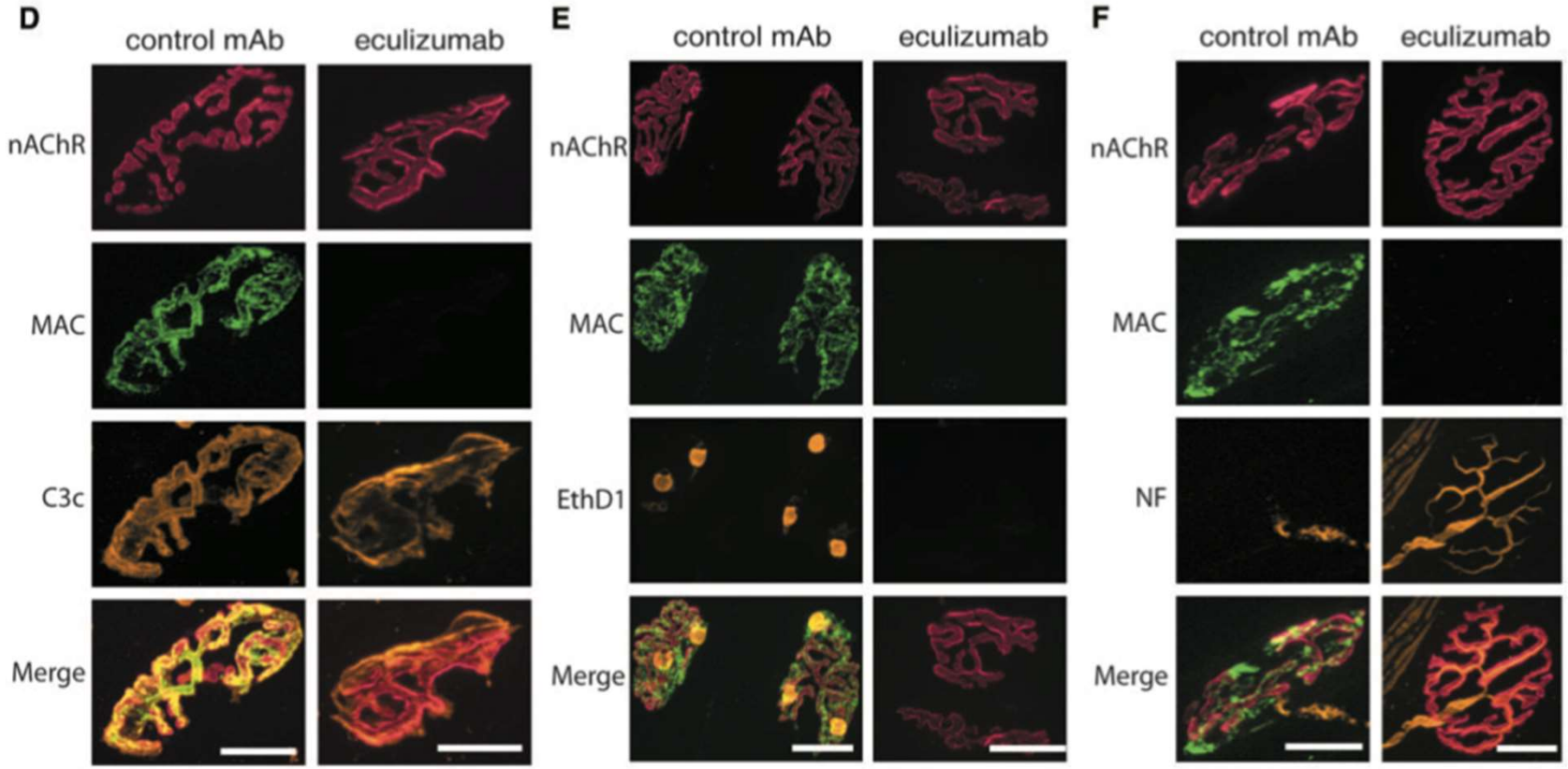
Eculizumab


Proximal Complement
Terminal Complement
Lectin Pathway
Classical Pathway
Alternative Pathway
Immune Complex Clearance
Microbial Opsonization
C3
Amplification
Natural
Inhibitor: CD55
Eculizumab
MONOCLONAL ANTIBODY
C5
C5
Natural
Inhibitor: CD59
C5a
Potent Anaphylatoxin
Chemotaxis
Proinflammatory
Endothelial Activation
Prothrombotic
C5b-9
Membrane Attack Complex
Cell Lysis
Proinflammatory
Platelet Activation
Endothelial Activation
Prothrombotic
Anaphylaxis
Inflammation
Thrombosis
Consequences
Consequences
Hemolysis
Inflammation
Thrombosis

doi:10.1093/brain/awm316 *Brain* (2008), **131**, 1197–1208

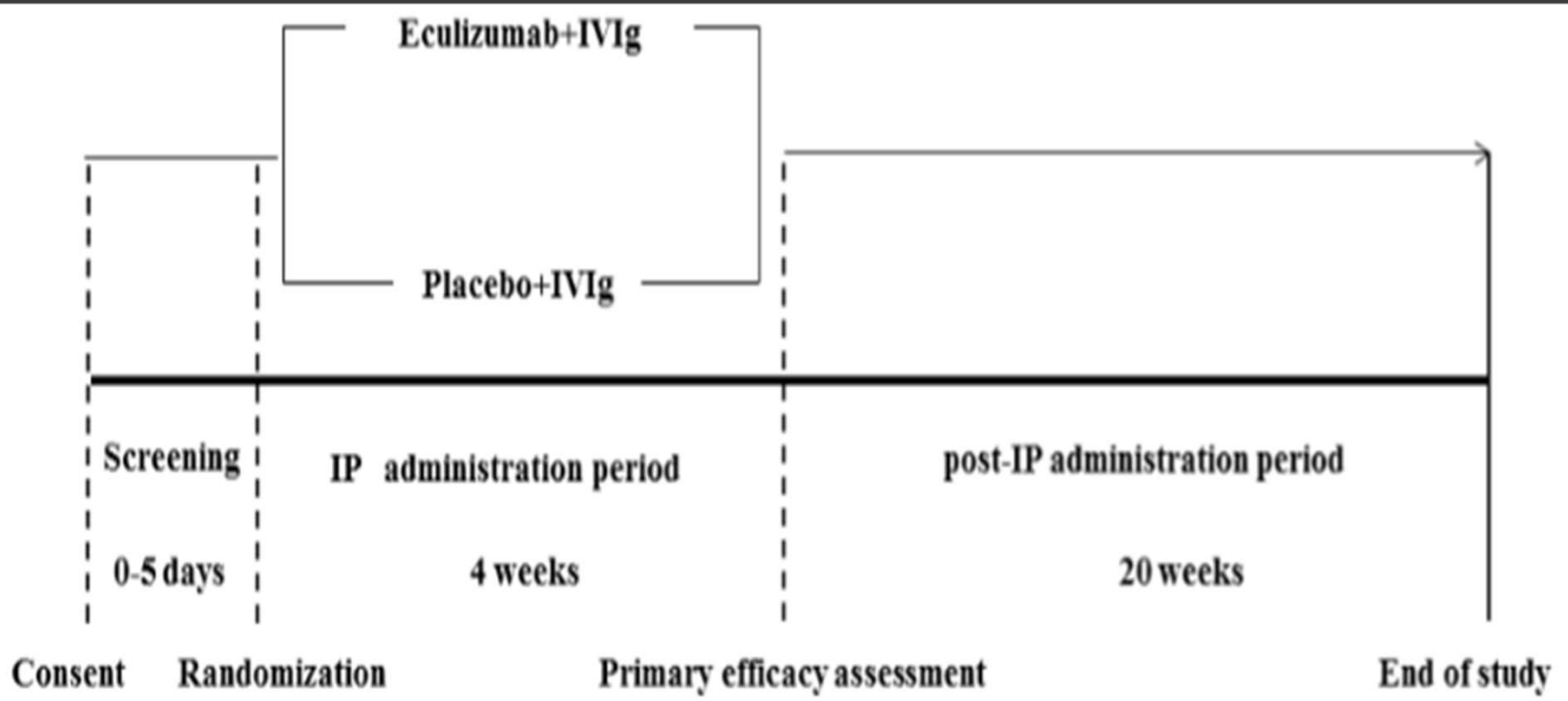
Eculizumab prevents anti-ganglioside antibody-mediated neuropathy in a murine model

Susan K. Halstead,[1,*] Femke M. P. Zitman,[2,3,*] Peter D. Humphreys,[1] Kay Greenshields,[1] Jan J. Verschuuren,[2] Bart C. Jacobs,[4] Russell P. Rother,[5] Jaap J. Plomp[2,3] and Hugh J. Willison[1]



A Prospective, Multicenter, Randomized Phase II Study to Evaluate the Efficacy and Safety of Eculizumab in Patients with Guillain-Barré Syndrome (GBS): Protocol of Japanese Eculizumab Trial for GBS (JET-GBS)

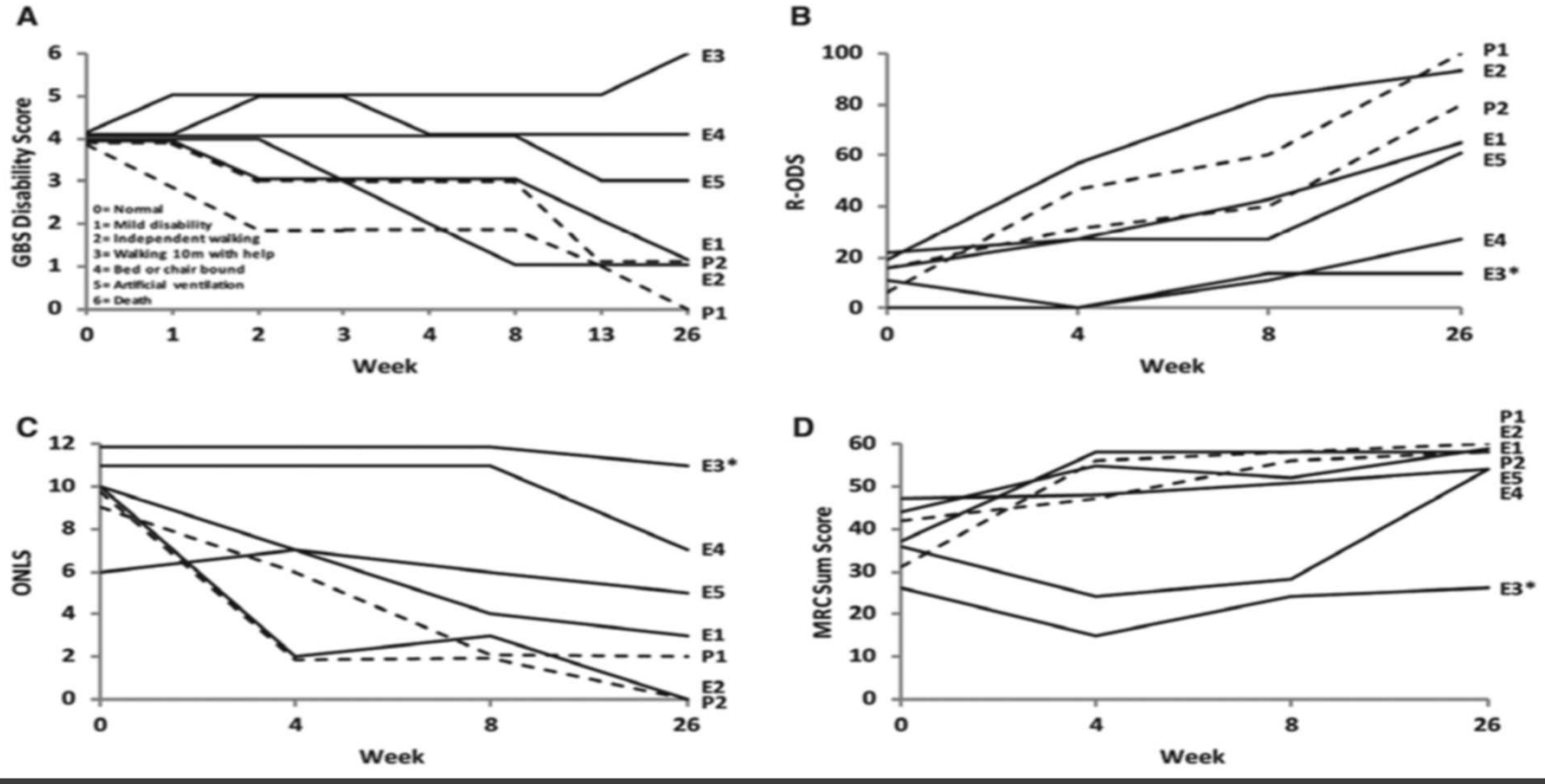
Nobuko Yamaguchi[1], BSc; Sonoko Misawa[2], PhD, MD; Yasunori Sato[3], PhD; Kengo Nagashima[3], PhD; Kanako Katayama[1], MSc; Yukari Sekiguchi[2], PhD, MD; Yuta Iwai[2], PhD, MD; Hiroshi Amino[2], MD; Tomoki Suichi[2], MD; Takanori Yokota[4], PhD, MD; Yoichiro Nishida[4], PhD, MD; Nobuo Kohara[5], PhD, MD; Koichi Hirata[6], PhD, MD; Kazutoshi Nishiyama[7], PhD, MD; Ichiro Yabe[8], PhD, MD; Ken-Ichi Kaida[9], PhD, MD; Norihiro Suzuki[10], PhD, MD; Hiroyuki Nodera[11], MD; Shoji Tsuji[12], PhD, MD; Haruki Koike[13], PhD, MD; Jun-Ichi Kira[14], PhD, MD; Hideki Hanaoka[1], PhD, MD; Susumu Kusunoki[15], PhD, MD; Satoshi Kuwabara[2], PhD, MD; JET-GBS Group[4,5,6,7,8,9,10,11,12,14,15]



RESEARCH REPORT

Inhibition of complement in Guillain-Barré syndrome: the ICA-GBS study

Amy I. Davidson[1,2], Susan K. Halstead[1], John A. Goodfellow[1,2], Govind Chavada[2], Arup Mallik[3], James Overell[2], Michael P. Lunn[4], Alex McConnachie[5], Pieter van Doorn[6], and Hugh J. Willison[1,2]



J Peripher Nerv Syst. 2017

Prognosis

- Most improvement occurs within the 1st yr. after onset
  - complete or almost complete recovery - 62%
  - unable to walk unaided - 9%
  - unable to run - 17%
  - bedbound or ventilator dependent - 4%
- Died - 8% (all > 60)

JNNP. 1998

The Erasmus GBS outcome score

	Categories	Score
Age at onset (years)	>60	1
	41–60	0·5
	≤40	0
Diarrhoea (≤4 weeks)	Absence	0
	Presence	1
GBS disability score (at 2 weeks after entry)	0 or 1	1
	2	2
	3	3
	4	4
	5	5
Erasmus GBS outcome score		1–7

Table 3: The Erasmus GBS outcome score

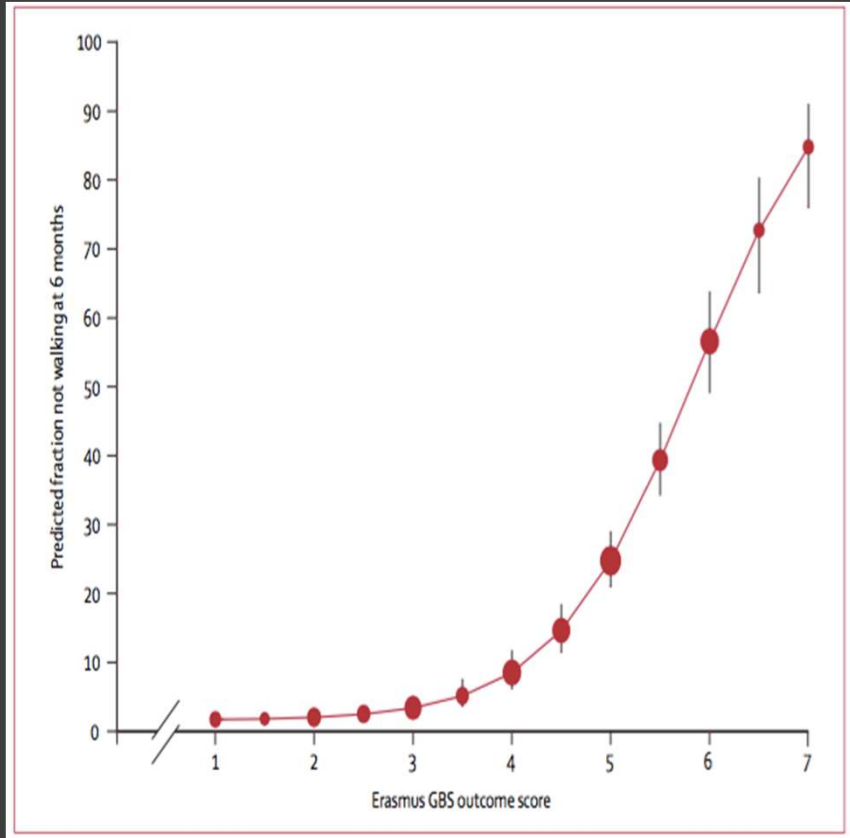
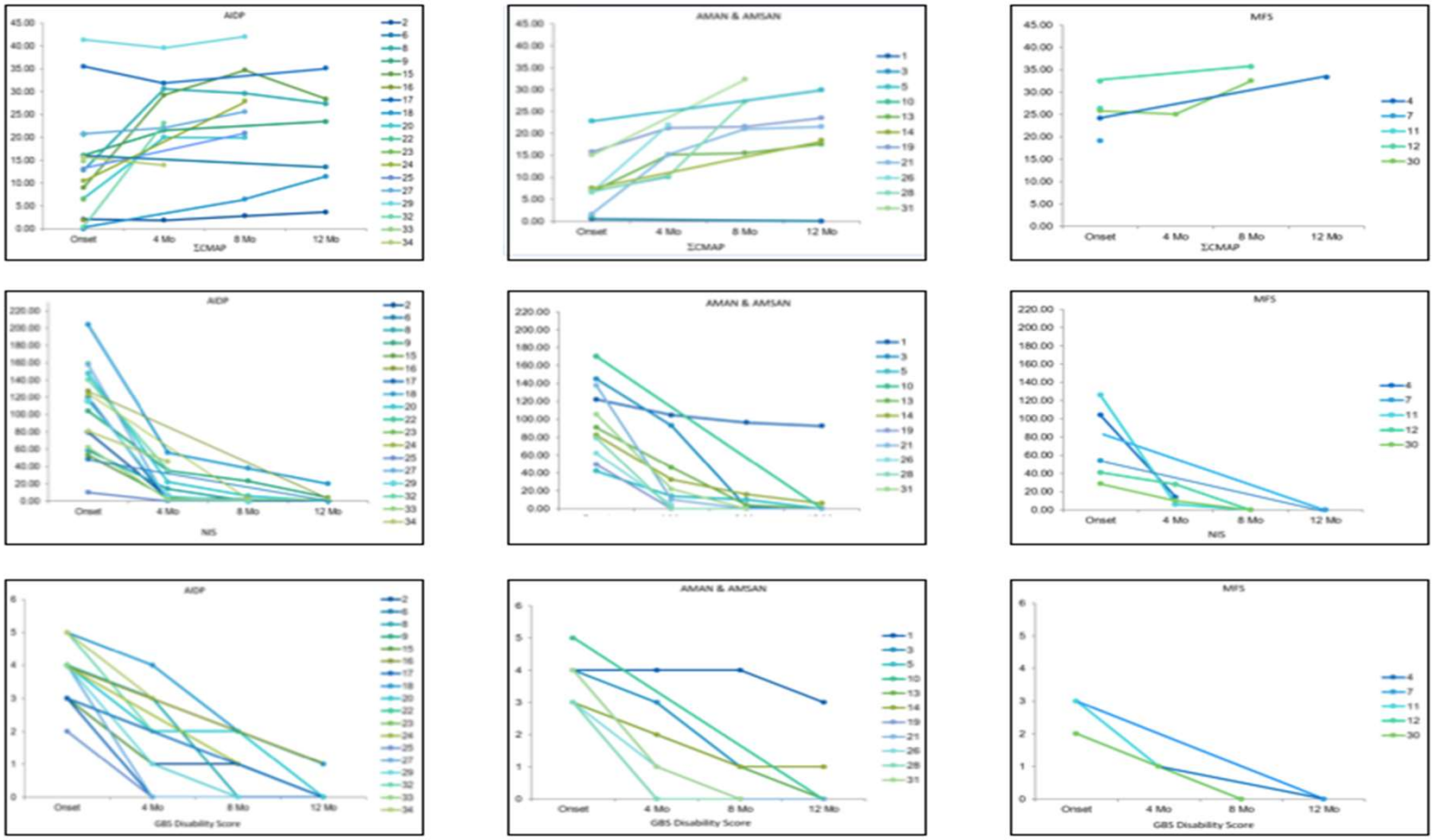


Figure: Predicted fraction of patients unable to walk independently at 6 months after randomisation on the basis of the Erasmus GBS outcome score (n=762)

Lancet Neurol 2007; 6: 589–94

Prognosis of Thai GBS patients



Unpublished data