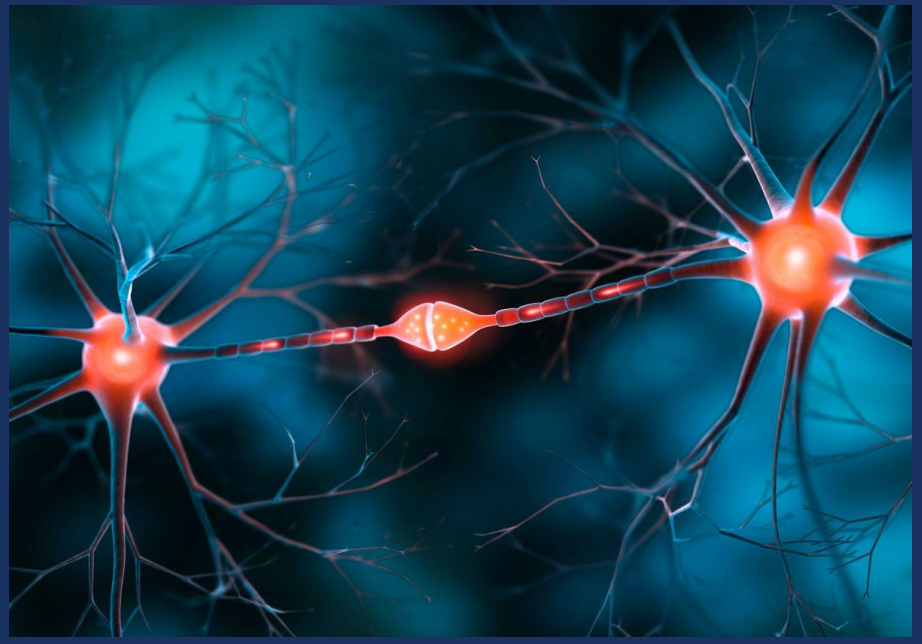
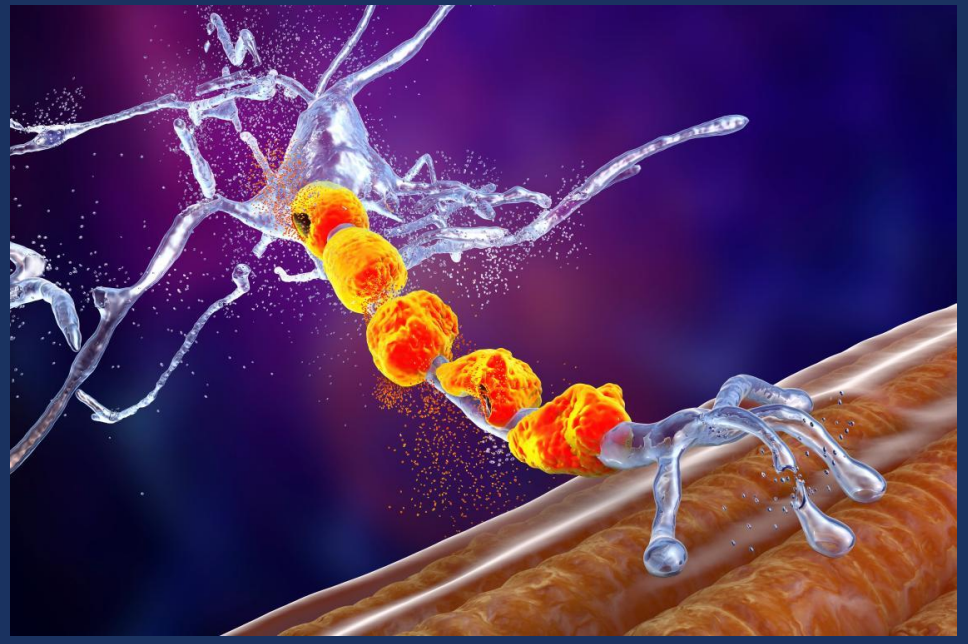
BASIC PATHOMECHANISM OF UPPER AND LOWER MOTOR NEURON SYNDROME

MUDR. MAREK BRENIŠIN, PHD.

INSTITUTE OF PATHOPHYSIOLOGY, P. J. SAFARIK UNIVERSITY, MEDICAL FACULTY, 2025/2026





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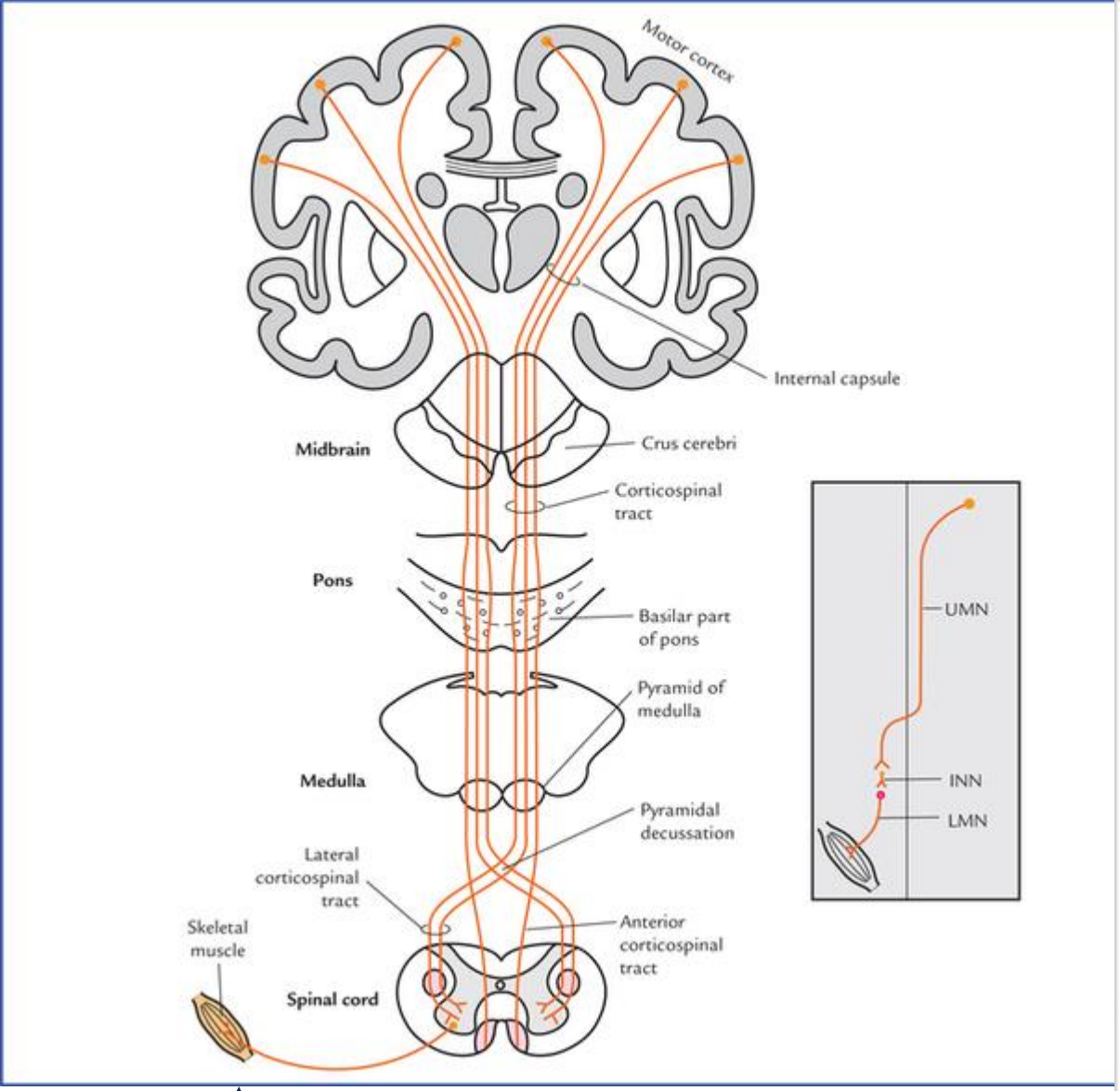
MOTOR FUNCTION PHYSIOLOGY BASICS

23. 3. 2026

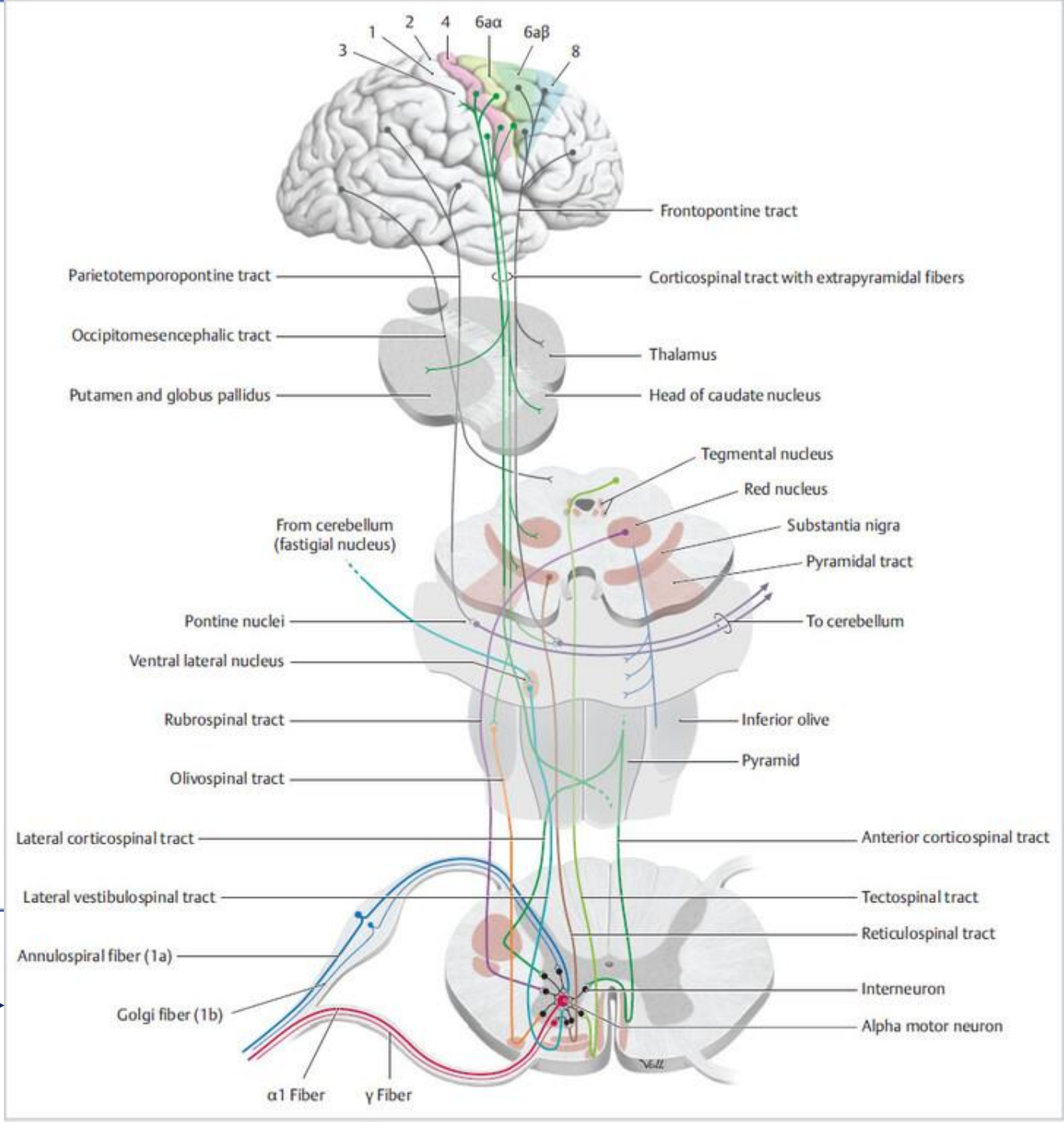
MOTOR SYSTEM PHYSIOLOGY

- Tracts classification
  - Pyramidal – two neurons, „voluntary control“
    - *Tr. corticospinalis* – truncal muscles (*tr. corticospinalis anterior*) and limbs (*tr. corticospinalis lateralis*)
    - *Tr. corticobulbaris* – cranial nerves
  - Extrapyramidal – „neuronal network“, involuntary movements, postural
    - *Tr. rubrospinalis* – flexors muscle tone regulation
    - *Tr. vestibulospinalis* – balance and postural action
    - *Tr. reticulospinalis* – autonomic functions, postural action, walking
    - *Tr. tectospinalis* – head and neck movements (various stimuli)
    - *Tr. olivospinalis* – motoric function (*medulla oblongata* and anterior spinal horns connection)



Pyramidal tract

Extrapyramidal system



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https://i0.wp.com/pocketdentistry.com/wp-content/uploads/2022/12/cs_18561635.jpg?w=960

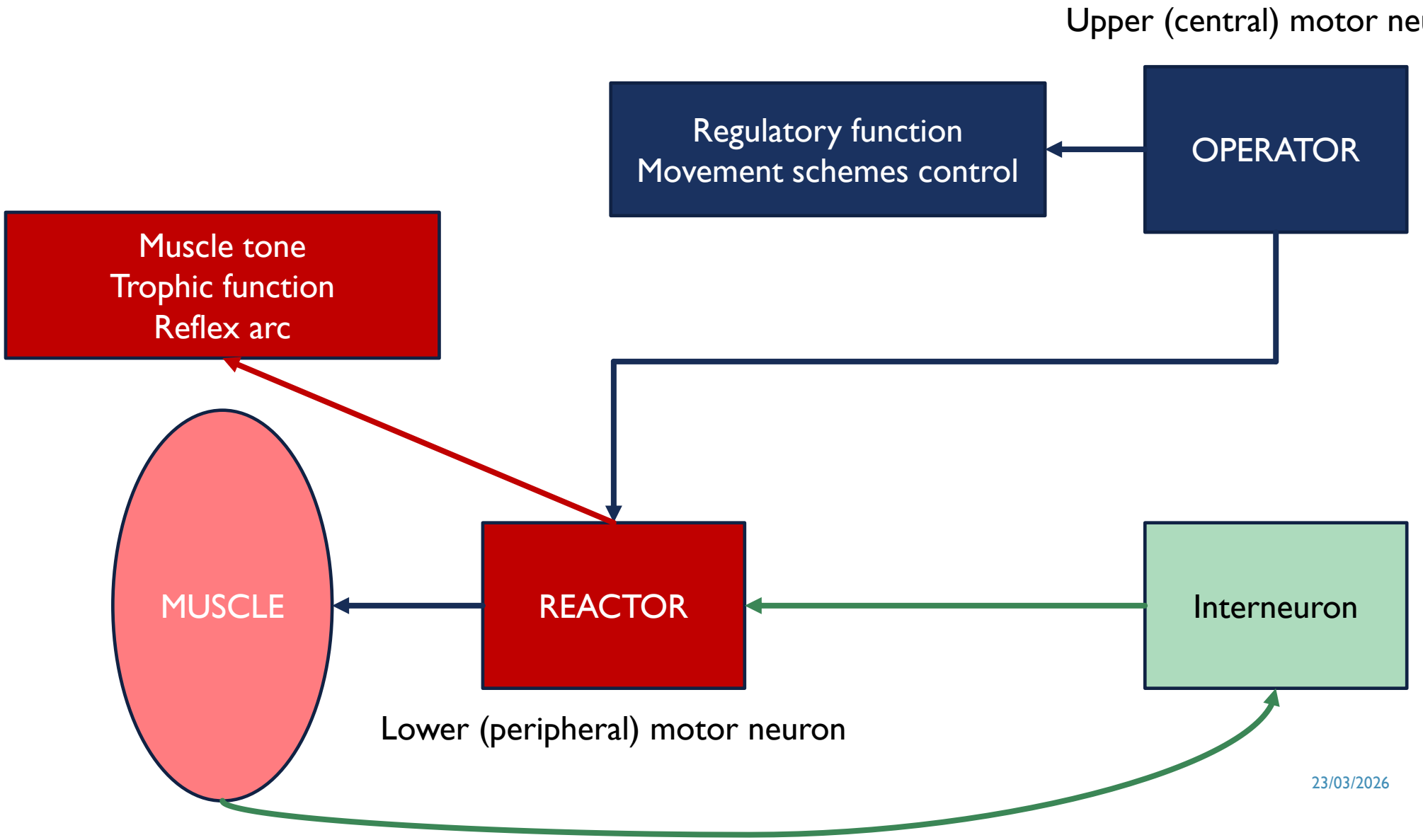
PYRAMIDAL TRACT – UPPER AND LOWER MOTOR NEURON

- Upper motor neuron
  - Location – area 4 (*gyrus precentralis*) -> primary motor cortex
    - 5 neuron layers – layers 2, 3, and 5 are excitatory
    - Impulses percepted from premotor cortex (area 6, learned movements) and supplementar motor cortex (medial area 6, planning, coordination and posturality)
  - Transmitter – glutamate
  - Tracts
    - 90 % crossing over – *decussatio pyramidum* -> *tr. corticospinalis lateralis* -> direct motor function, CONTRALATERAL
    - 10 % not crossing over -> *tr. corticospinalis anterior* -> axial and limbs movement control, CONTRALATERAL (crossing over at spinal level)

PYRAMIDAL TRACT – UPPER AND LOWER MOTOR NEURON

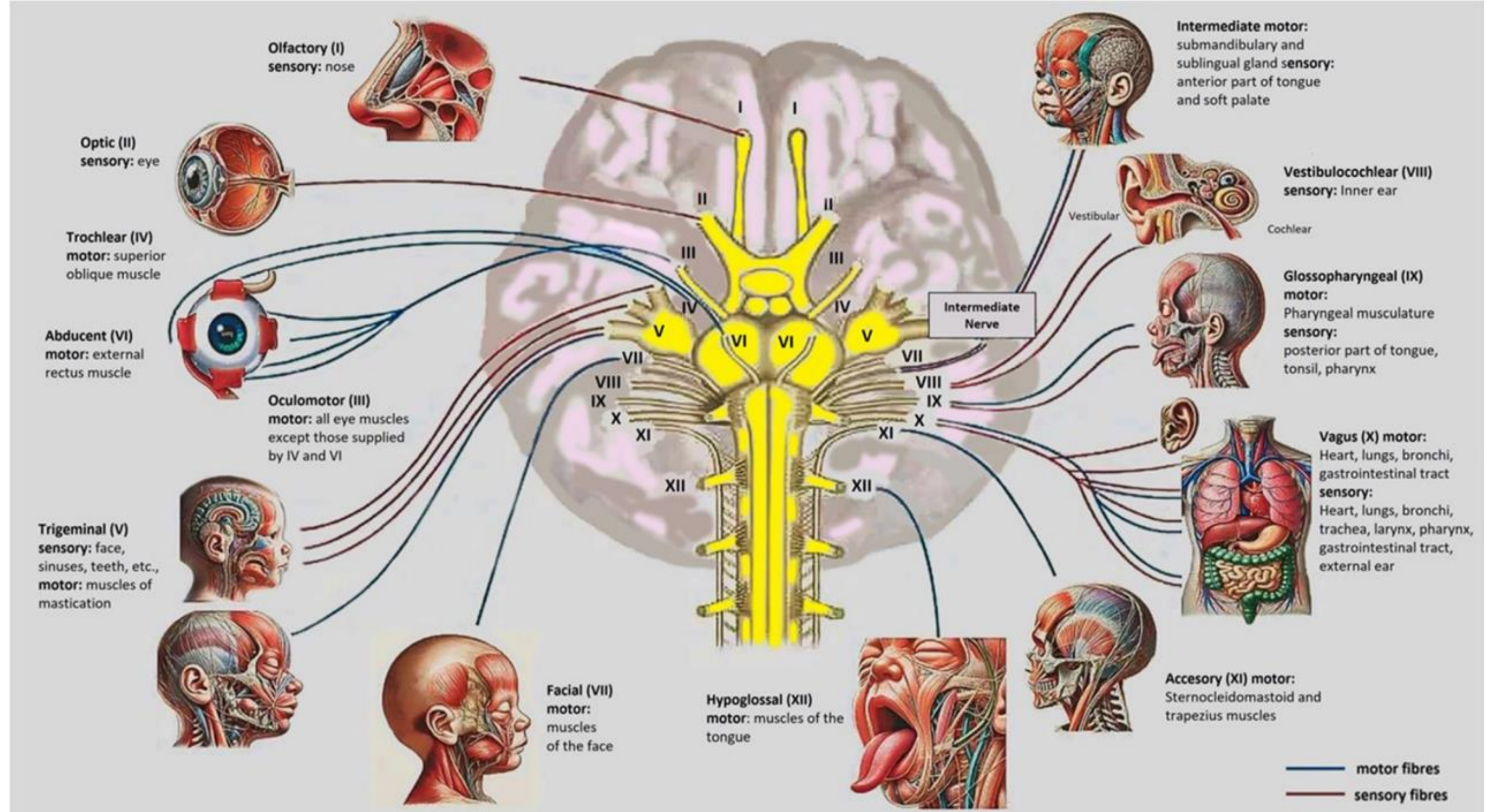
- Lower motor neuron
  - Location – anterior spinal horns
    - Ipsilateral muscular innervation
  - Transmitter – acetylcholine
    - Active on neuromuscular junction -> binding to Ach-R -> Na+ channels opened -> action potential -> Ca2+ release from endoplasmic reticulum -> muscular contraction -> Ach decomposed by acetylcholine esterase*

*synaptic space contains also an enzyme butyrilcholine esterase -> being non-specific, able to cleave other compounds, yet with only 25 % rate of acetylcholine esterase


Upper (central) motor neuron
Regulatory function
Movement schemes control
OPERATOR
Muscle tone
Trophic function
Reflex arc
MUSCLE
REACTOR
Interneuron
Lower (peripheral) motor neuron

MOTOR NEURON CATEGORIES

- Classification
  - Somatic (brainstem, anterior spinal horns)
    - Alpha – extrafusal fibres innervation (multiple fibres) -> synchronic contraction
    - Beta – extrafusal and intrafusal fibres - ???
    - Gamma – muscle spindles innervation -> sensitivity regulation (motoric „fine-tuning“)
  - Branchial (brainstem)
    - Cranial nerves innervation (motor function) -> n.V, VII, IX, X, XI
  - Visceral
    - Sympathetic -> Th1-L2
    - Parasympathetic – cranial nerves – III, VI, IX, X + S2-S4 segments



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Cranial nerves		Part		Distribution and function
No.	Name			
I	Olphactory	Specialised sensory		Olphactory nasal mucosa
II	Ophthalmic	Specialised sensory		Retina
III	Oculomotor	Motor		Intra and four extraocular muscles
IV	Trochlear	Motor		Extraocular muscle (superior oblique muscle)
V	Trigeminal	Mixed	Motor root	Mastication
			Sensory root	Facial sensory
VI	Abducens	Motor		Extraocular muscle
VII	Facial	Mixed	Motor root	Facial expression and movement
			Intermediary	Taste perception
VIII	Vestibulocochlear	Specialised sensory		Inner ear (hearing and balance)
IX	Glossopharyngeal	Mixed		Taste, gag reflex
X	Vagal	Mixed		Gag reflex, parasympathetic
XI	Accessory	Motor		Shoulders shrugging, neck movement
XII	Hypoglossal	Motor		Tongue, speech

„Oh-Oh-Oh-To-Touch-And-Feel-Very-Good-Velvet-Ah-Heaven“

UPPER MOTOR NEURON LESIONS

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UPPER MOTOR NEURON LESION CAUSES

- Stroke -> up to 80 % patients show upper motor neuron syndrome signs (UMS)
- Trauma, and injuries -> up to 33 % patients with UMS signs
  - Spinal shock including
- Demyelination disorders
  - Multiple sclerosis
- Neurodegenerative disorders
  - Amyotrophic lateral sclerosis
  - Primary lateral sclerosis
  - Atypical parkinsonism
- Nutrition – vitamin B12 deficiency
- Tumours

UPPER MOTOR NEURON SYNDROME (UMS)

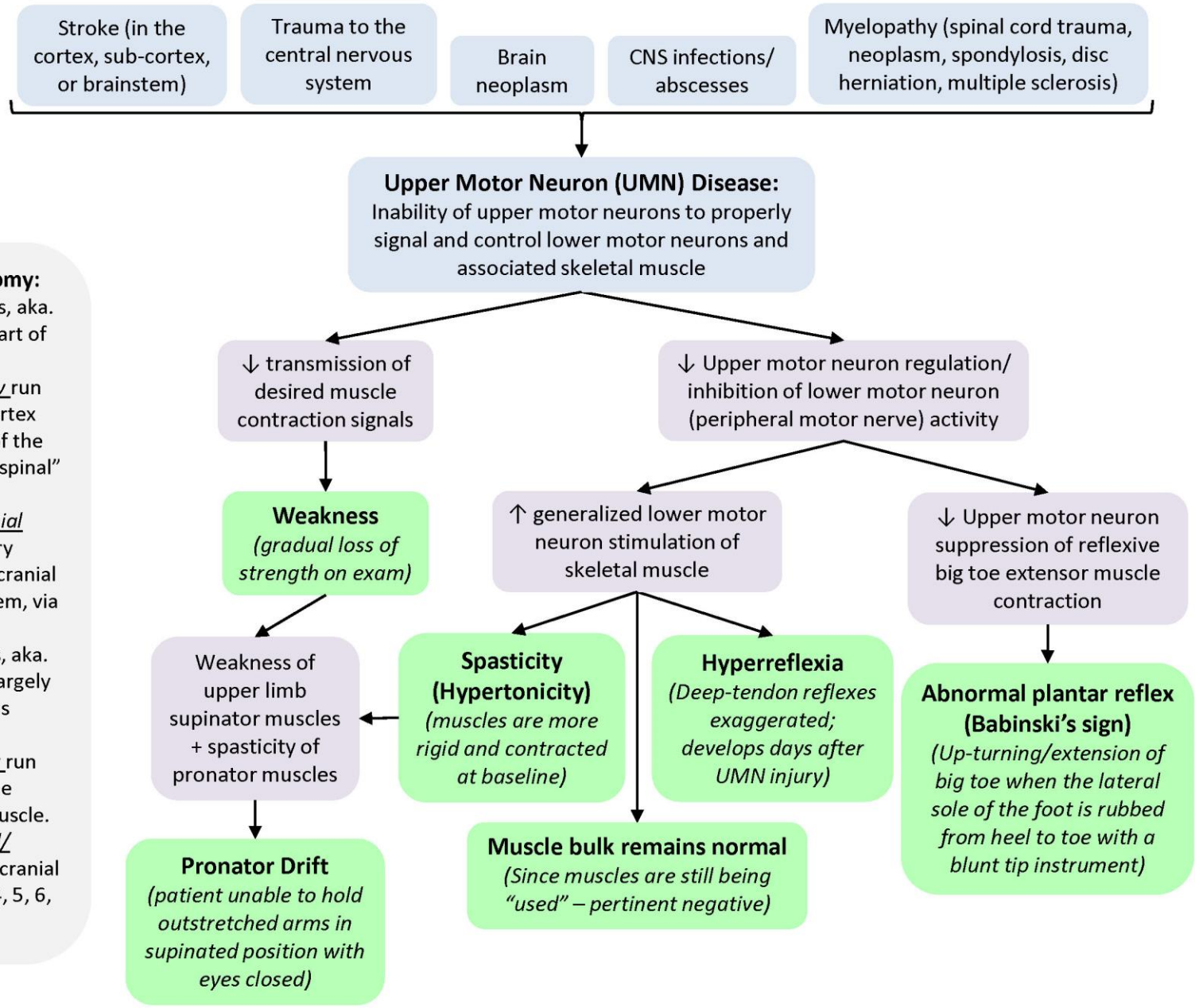
- Definition -> set of signs and symptoms caused by upper motor neuron lesion and function absence
  - „Reactor“ is not supervised -> uncontrolled force, deliberation phenomenon
- Typical signs
  - Muscle weakness -> pyramidal paresis
  - Spasticity -> „clasp knife“ phenomenon -> movement faces resistance which ceases abruptly then
  - Clonus -> rhythmical involuntary contractions (5 – 7 Hz)
  - Hyperreflexia of deep tendon reflexes -> reflex arc without supervision
  - Hyporeflexia of superficial reflexes (e.g. cremaster reflex) -> a complicated polyneural path required for a proper function
  - Synkinesis -> arm elevation causes leg movement
  - Co-contractions -> physiological function to stabilise joint; in UMS decrease movement abilities
  - Deliberation phenomenon -> Babinski, Hoffmann, Brissaud sign

Upper Motor Neuron (UMN) Disease: *Pathogenesis and Clinical Findings*

Author:
Yan Yu
Reviewers:
Owen Stechishin
Dustin Anderson
Scott Jarvis*
**MD at time of publication*

Note on terminology & anatomy:

- **Upper motor neurons** (UMNs, aka. "1st-order motor neurons", part of the central nervous system)
  - *UMNs innervating the body* run from the primary motor cortex down to the ventral horn of the spinal cord via the "corticospinal" or "pyramidal" tract.
  - *UMNs innervating the cranial nerves* run from the primary motor cortex down to the cranial nerve nuclei in the brainstem, via the "corticobulbar" tract.
- **Lower motor neurons** (LMNs, aka. "2nd-order motor neurons", largely part of the peripheral nervous system)
  - *LMNs innervating the body* run from the ventral horn of the spinal cord to the target muscle.
  - *LMNs innervating the head/ shoulders* are found in the cranial nerves themselves (CN 3, 4, 5, 6, 7, 9, 10, 11, 12)



Legend: Pathophysiology | Mechanism | Sign/Symptom/Lab Finding | Complications

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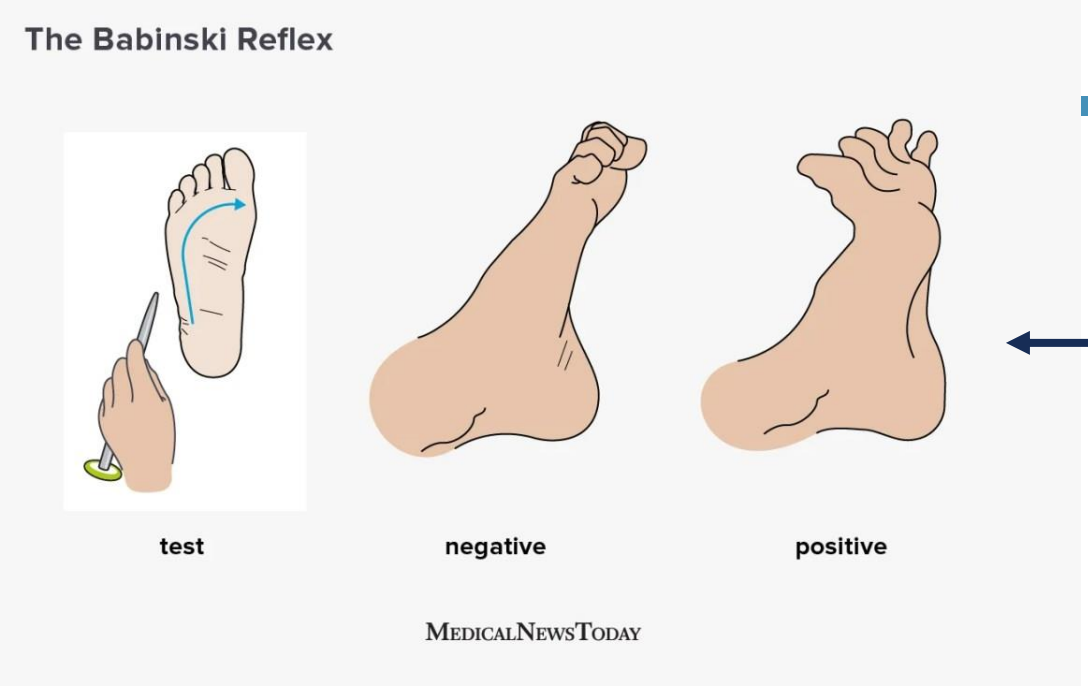
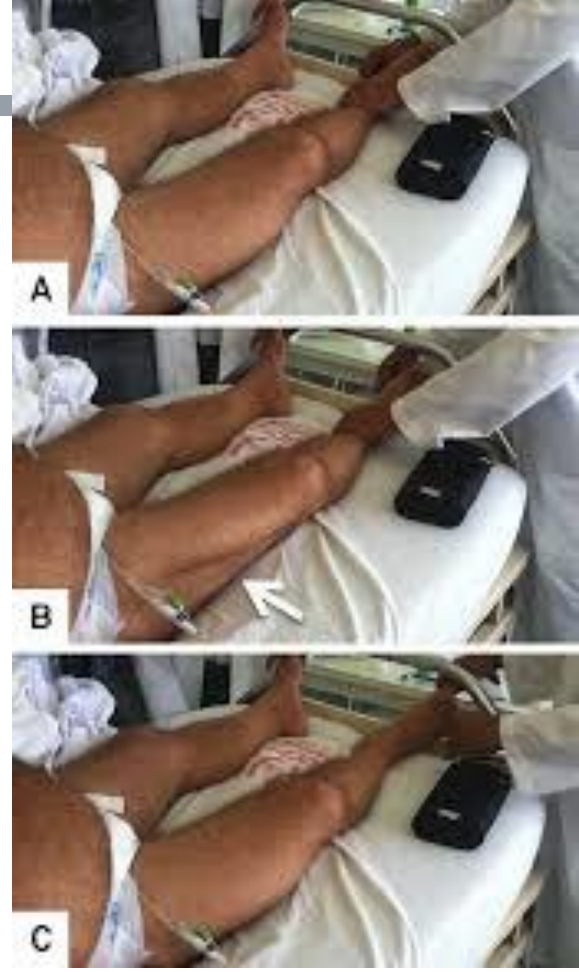
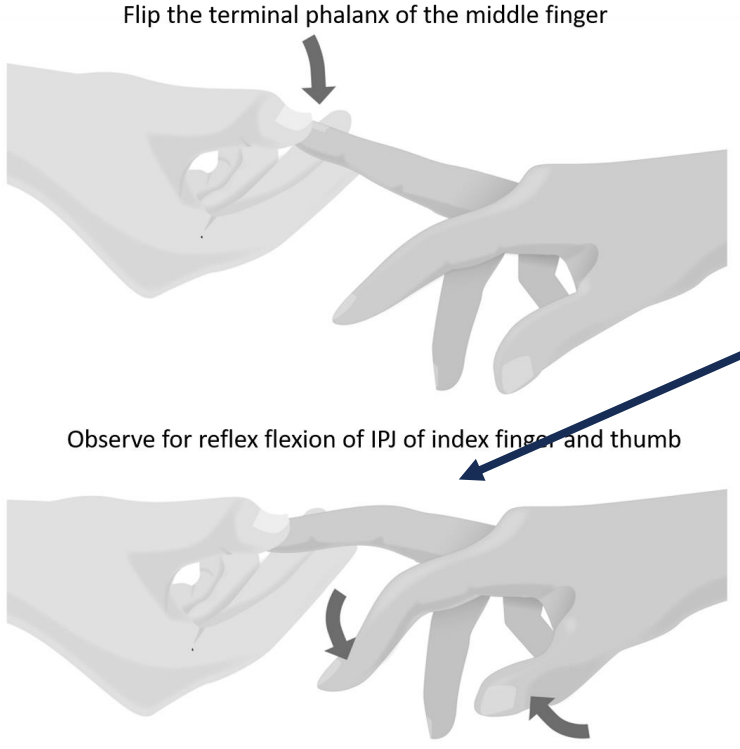


Babinski sign -> plantar irritiation by sharp object
Physiology – plantar flexion
Pathology – plantar extension and toes abduction





Hoffmann sign – middle finger held and nail twinkled
Physiology (neg) – no reaction
Pathology (posit.) – pointing finger and thumb flexion

Brissaud relfex – foot movement
Physiology (neg.) – no reaction
Pathology (posit.) – contraction of m. tensor fasciae latae (arrow)

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https://epomedicine.com/wp-content/uploads/2022/12/Hoffmann-reflex.png
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LOWER MOTOR NEURON SYNDROME

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LOWER MOTOR NEURON SYNDROME CAUSES

- Intervertebral discs herniation -> radiculopathies
- Peripheral nerves trauma
- Viral infections affecting anterior spinal horns -> poliovirus, enteroviral infections, herpes simplex (HSV 1 a 2), varicella-zoster, HIV, and HTLV, flaviviral infections (West Nile fever, Powassan, Japan encephalitis, tick borne encephalitis)
- Guillain-Barré syndrome
- Botulism
- Amyotrophic lateral sclerosis

LOWER MOTOR NEURON SYNDROME

- Definition – set of signs and symptoms caused by lower motor neuron function absence
  - „Reactor“ not working -> there is no „power“
- Typical signs and manifestations
  - Muscle paresis and palsy
  - Hypotonia and atonia -> absence of neural impulses
  - Loss of muscular electric activity control
    - Fasciculations -> muscle bundles
    - Fibrillations -> single muscular fibres/cells
  - Hypo- to areflexia -> efferent reflex arc part damaged
  - Muscular atrophy (progressing with time) -> absence of trophic signals from neuromuscular junction

Lower Motor Neuron (LMN) Disease: *Pathogenesis and Clinical Findings*

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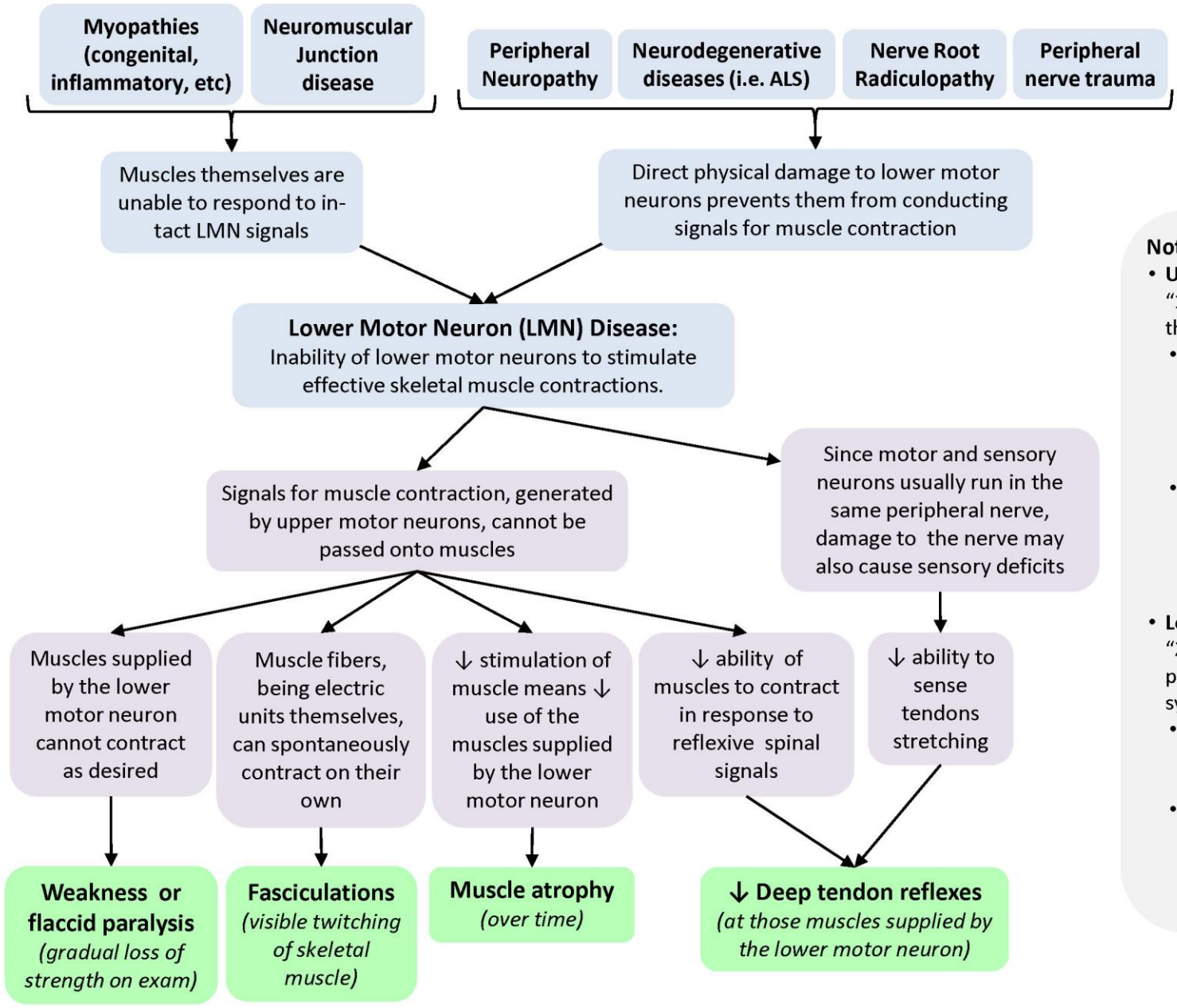

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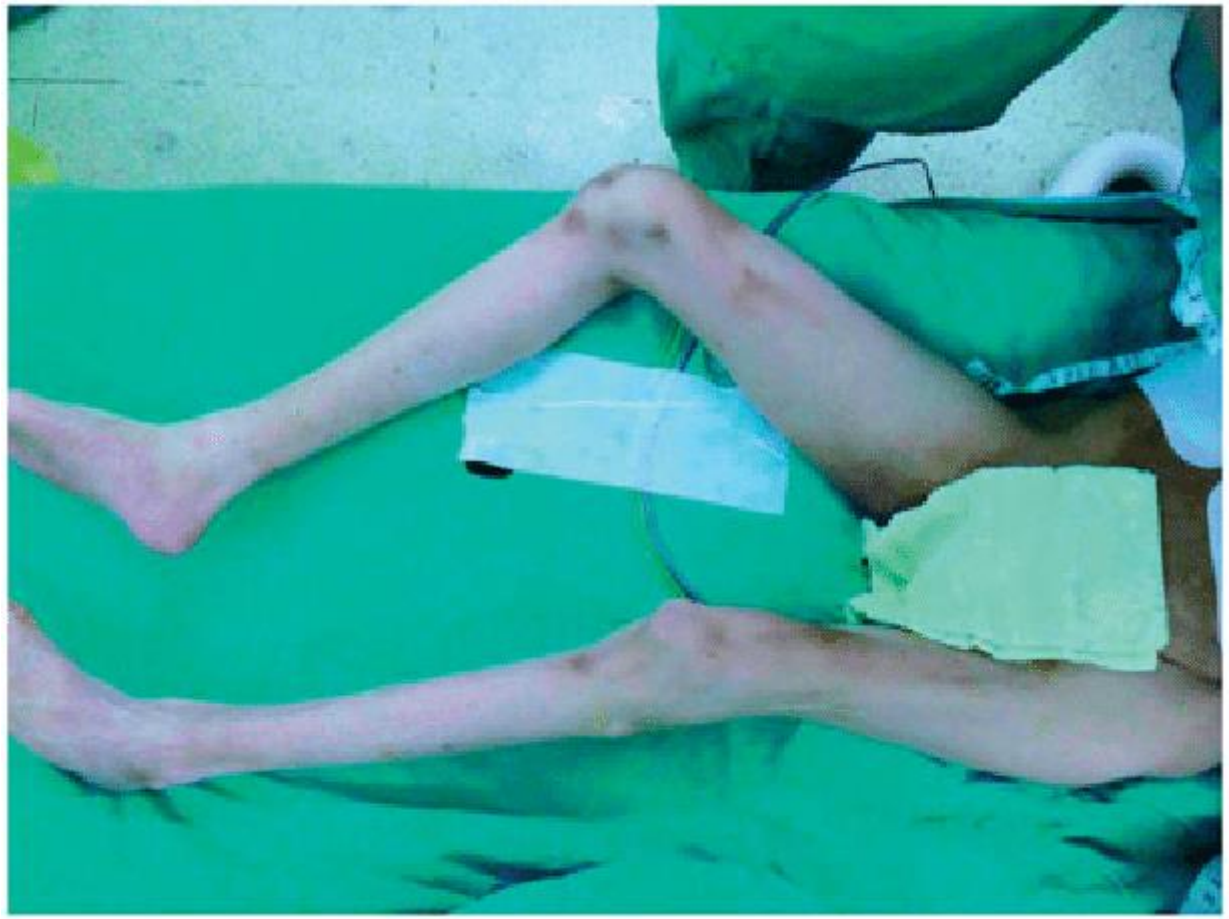

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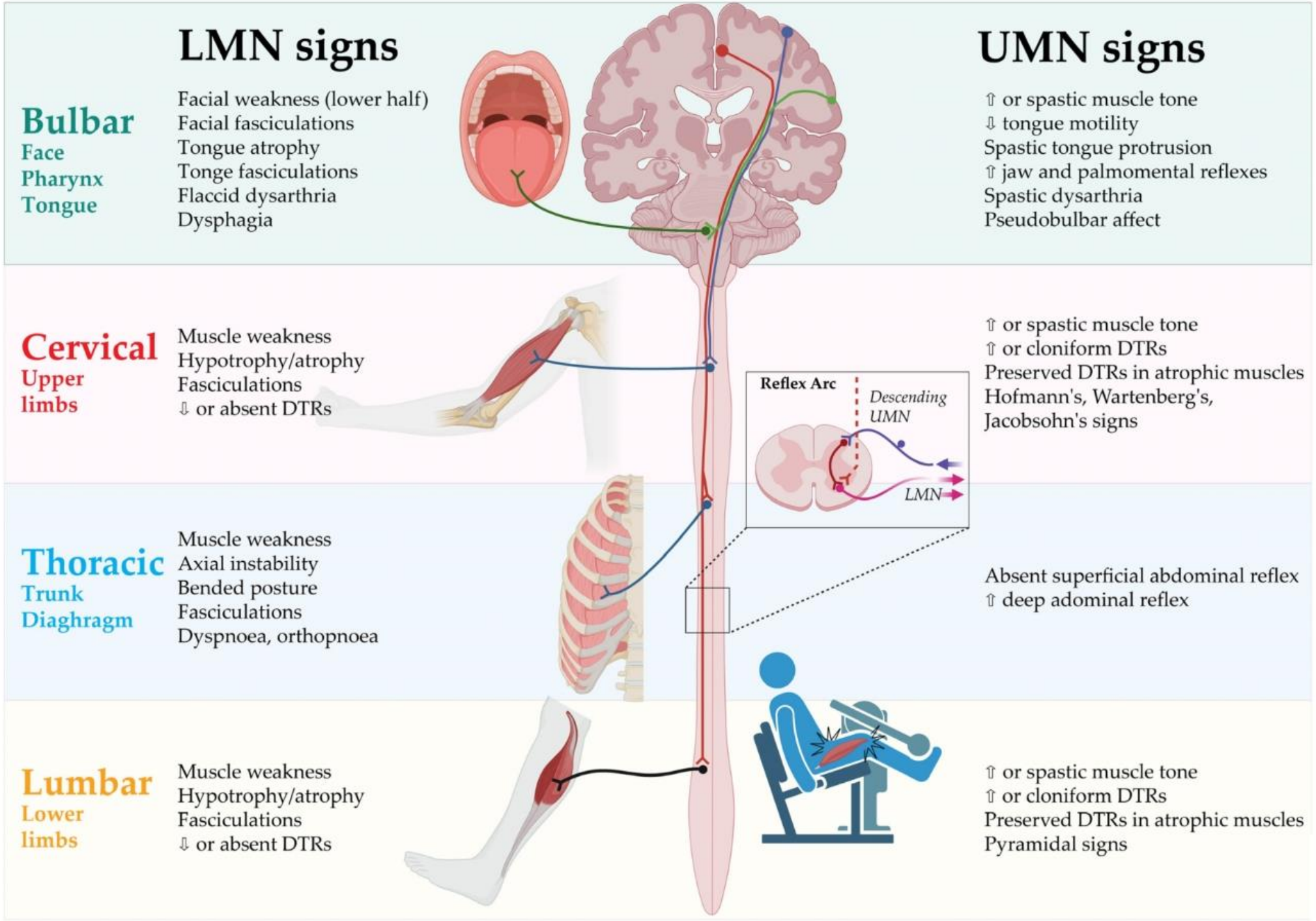

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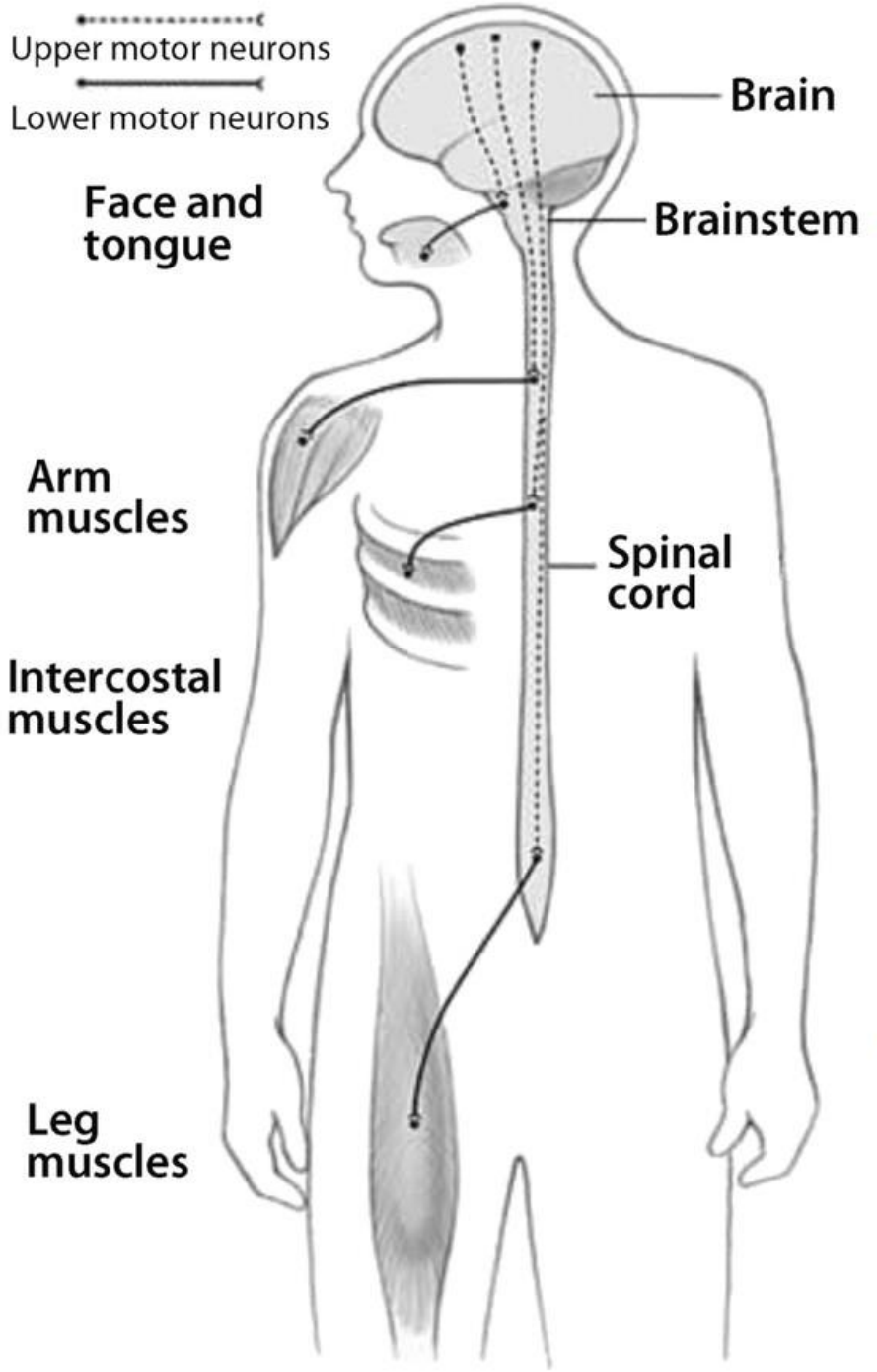

- **Upper motor neuron signs**
  - Very little wasting
  - Increased tone (spasticity)
  - Brisk reflexes (hyperreflexia)
  - Primitive reflexes (Babinski sign)
- **Lower motor neuron signs**
  - Wasting (atrophy)
  - Low or normal tone (flaccidity)
  - Reduced or absent reflexes (hyporeflexia or areflexia)
  - Fasciculations (low threshold for irritation of the motor neuron)

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CRANIAL NERVES MOTOR DISORDERS

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PSEUDOBULBAR PALSY

- Majority of cranial nerves shows bilateral innervation -> bilateral lesions necessary to affect neural functions
  - Exception -> facial nerve (n.VII) and hypoglossal nerve (XII)
- Definition -> bilateral cranial nerves lesion -> set of signs and symptoms
- Causes
  - Trauma, neoplasia, metabolic disorders
  - Vascular lesions -> repeated infarctions, „post-stroke“ state
  - Neurologic disorders -> amyotrophic lateral sclerosis, Parkinson disease, progressive supranuclear palsy; multiple sclerosis
  - Rare -> central pontine myelinolysis, bilateral thalamic infection, methotrexate, progressive multifocal leucoplakia, cerebral malaria, bacterial endocarditis, syphilis, meningioma, neurocysticercosis, autoimmunity (incl. Hashimoto‘s thyroiditis)

PSEUDOBULBAR PALSY PATHOMECHANISM

- Supranuclear lesion
- Disconnection with centres for laughter and crying -> „pseudobulbar“ crying
  - Physiology -> cerebellum communication with brain stem -> contextual emotions
  - Pseudobulbar crying may arise in subthalamic nucleus stimulation
- Cortico-ponto-cerebellar tracts lesions
  - Apathy
  - Emotional dysmetria

PSEUDOBULBARY PALSY COURSE

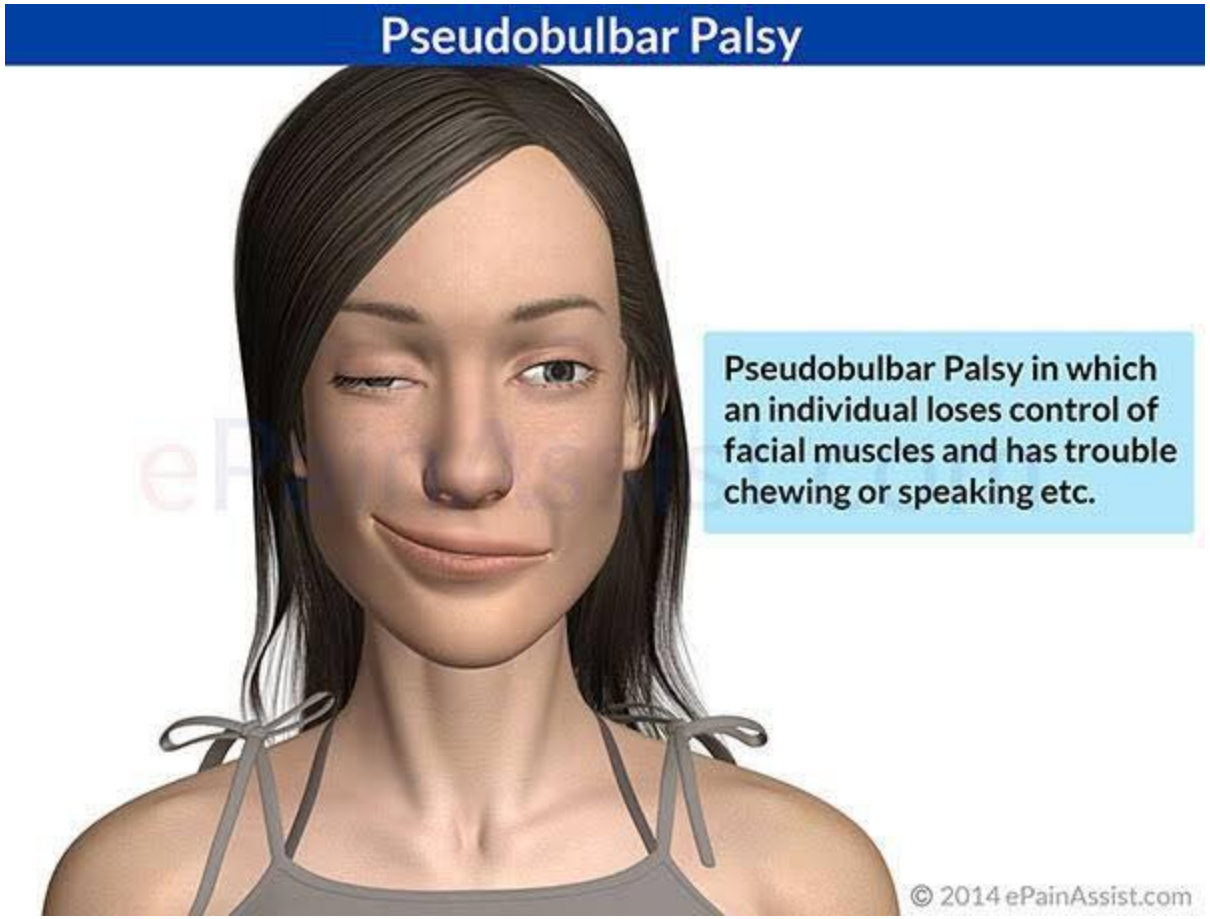
- Three main phases
  1. Shock -> swallowing and speech disorder (dysarthria)
  2. Motor function damage/loss -> lung functions reduction (FVC, FEV1, etc.)
  3. Function „release“ -> emotional incontinence

PSEUDOBULBAR PALSY MANIFESTATIONS

- Dysarthria/anarthria
  - Slow and incomprehensible speech (mainly disease onset)
  - Palilalia frequent (words and syllables repetition)
- Dysphagia
- Sialorrhea, drooling
- Dysphonia, nasal voice („Donald duck/Duffy duck“)
  - Voice rhythm and colour disorders, incomprehensible speech
- Glossoplegia -> spastic tongue, function disorders
- Mastication disorders and facial muscles palsy

PSEUDOBULBAR PALSY MANIFESTATIONS

- Emotional instability
  - Laughter, crying bursts with poor facial mimics
  - Pathological laughter -> may indicate posterior fossa tumour
- Trism (masticatory muscles spasm)
  - Inability to open mouth more than 35-40 mm
  - Internal capsule damage signalling
- Jaw jerks and facial hyperreflexia
- Mouth angle and uvula deviated away from the lesion side
- Primitive reflexes reappear -> sucking, rooting, etc.
- Cognitive functions and epileptic seizures (up to 85 % paediatric patients)



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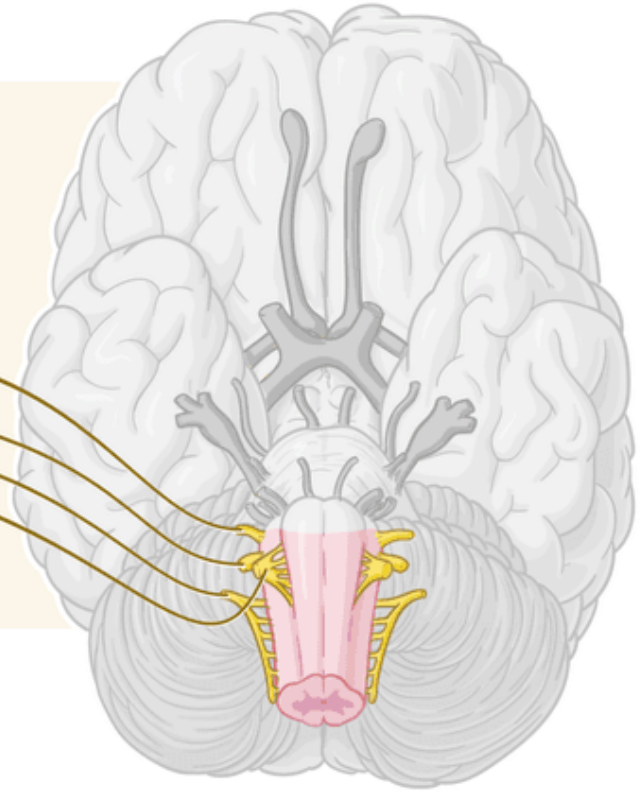
Parameter	Pseudobulbar palsy	Bulbar palsy	Depressive disorder
Duration	Seconds to minutes	Minutes to years	Weeks to months
Lesion localisation	Supranuclear	Lower motor neuron	N/A
Tongue	Spastic	Flaccid, fasciculations	No change
Jaw jerks	Yes	No	No
Speech	Spastic dysarthria, „Donald/Duffy duck“	Nasal	No change
Limbs	UMN signs	LMN signs	No change
Emotions	Labile	Stable	Vary
Decision ability and cognition	No changes	No changes	Alteration possible
Causes	Bilateral stroke, multiple sclerosis, neuron damage	Neuron damage, Guillain-Barré sy., poliomyelitis, brain stem infarction	Vary

BULBAR PALSY

- Definition – signs and symptoms set due to „lower cranial nerves“ damage – n. IX, n. X, n. XI, and n. XII.
  - Pathomechanism -> lower motor neuron damage (oblongate medulla nuclei)
- Classification
  - Progressive (frequent)
    - Causes – neurodegenerative disorders (e.g. amyotrophic lateral sclerosis), autoimmunity (e.g. Guillain-Barré sy.) or genetics (e.g. Kennedy disease)
  - Non-progressive (rare)
    - Causes – trauma, stroke, congenital disorders

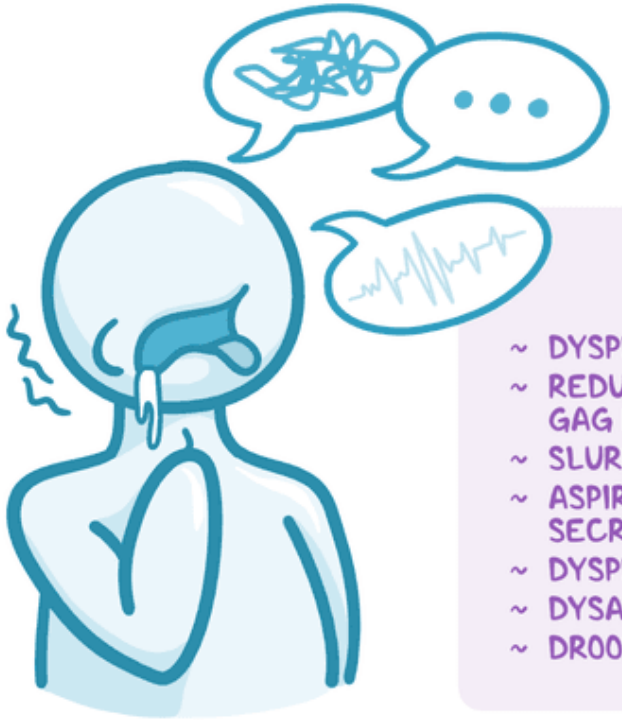
BACKGROUND

* **BULBAR PALSY** - SYMPTOMS LINKED to IMPAIRED FUNCTION of LOWER CRANIAL NERVES
  - CN IX - GLOSSOPHARYNGEAL
  - CN X - VAGUS
  - CN XI - ACCESSORY
  - CN XII - HYPOGLOSSAL
* CLASSIFIED as PROGRESSIVE or NON-PROGRESSIVE



CAUSES

* **BRAINSTEM STROKES & TUMORS**
* DEGENERATIVE DISEASES
  - AMYOTROPHIC LATERAL SCLEROSIS (ALS)
* AUTOIMMUNE DISEASES
  - GUILLAIN–BARRÉ SYNDROME
* GENETIC DISEASES
  - KENNEDY DISEASE
  - BROWN–VIALETTO–VAN LAERE (BVVL) SYNDROME
  - FAZIO–LONDE SYNDROME



SYMPTOMS

- DYSPHAGIA
- REDUCED/ABSENT GAG REFLEX
- SLURRED SPEECH
- ASPIRATION of SECRETIONS
- DYSPHONIA
- DYSARTHRIA
- DROOLING
- DIFFICULTY CHEWING
- NASAL REGURGITATION
- DIFFICULTY HANDLING SECRETIONS
- SPEECH LACKS MODULATION
- DIFFICULTY with CONSONANTS
- ATROPHIC TONGUE
- WEAK JAW/FACIAL MUSCLES
- NORMAL or ABSENT JAW JERK

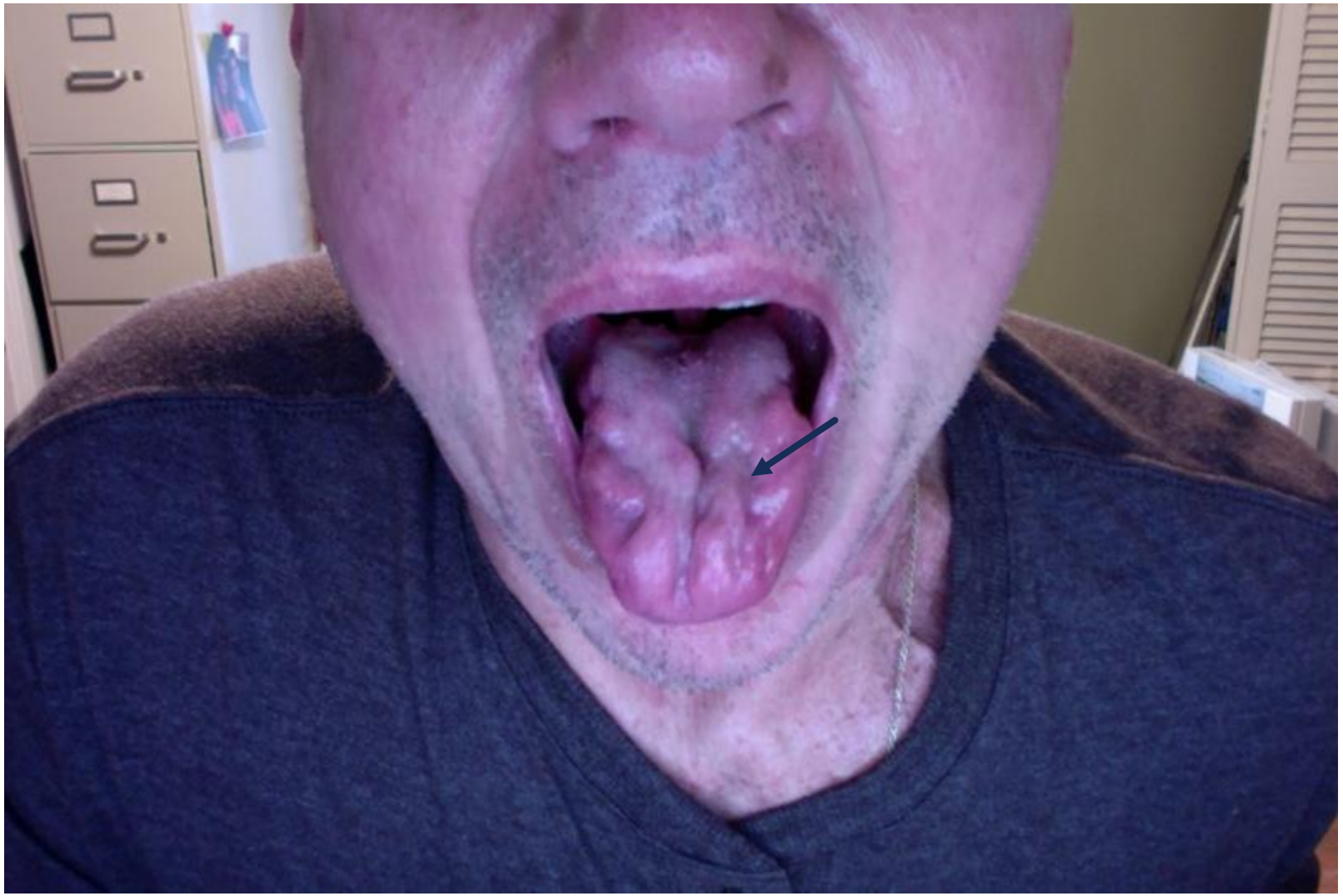
TREATMENT

* **NO KNOWN TREATMENT**
* SYMPTOM MANAGEMENT
  - MEDICATIONS (DROOLING)
  - FEEDING TUBE (DIFFICULTY SWALLOWING)
  - SPEECH & LANGUAGE THERAPY
* CONDITION-SPECIFIC TREATMENTS

BULBAR PALSY PATHOMECHANISM

- Main change -> single or multiple nerves damage -> symptoms may vary

- Glossopharyngeal nerve damage -> dysphagia, gag reflex lost
- Other nerves
  - Mastication diosrders
  - Nasal regurgitation
  - Mumbling, confluent (swallowed) speech, dysarthria
  - Secretions aspiration, drooling
  - Tongue atrophy -> fasciculations
- Emotions unchanged!



Bulbar paralysis onset (tongue fasciculations; arrow) in ALS patient

https://www.alsforums.com/community/attachments/tongue2-jpg.9930/

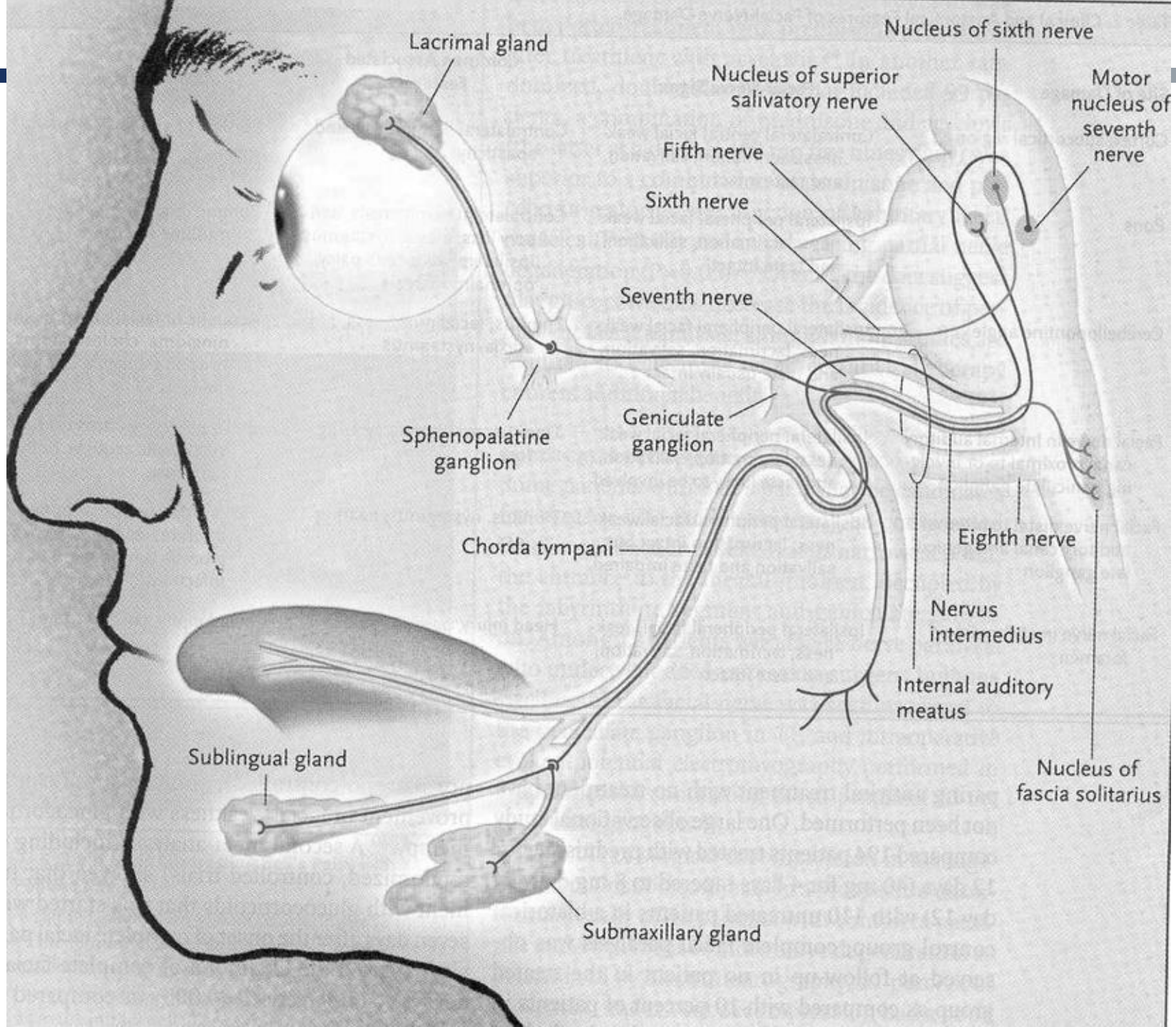
BULBAR PALSY PROGNOSIS AND TREATMENT

- Treatment
  - No curative therapy
  - DMD (disease modifying drugs) -> ALS (riluzol + edaravon), Guilain-Barré (corticosteroids)
  - Symptomatic
    - Dysphagia –> diet, liquid foods, nutrition drinks, nasogastric tube feeding
    - Respiratory disorders/failure -> tracheostomy, intubation
    - Dysarthria -> therapy
    - Drooling -> anticholinergics (glycopyrrolate, scopolamine patches)
    - Spasticity (advanced stages) -> myorelaxation drugs, physiotherapy
- Prognosis -> progressive fatal usually (1-3 years approx. survival), else depending on triggering cause treatment success

FACIAL NERVE LESIONS

- Anatomy -> facial nerve tract is long and often convoluted -> risk locations for neural functions
  - Facial muscles innervation -> forehead with bilateral innervation, rest unilateral

- Classification
  - Upper motor neuron –> contralateral lesion, mouth angle only
  - Lower motor neuron –> ipsilateral, half of face affected
- Epidemiology
  - 15 – 40/100000/yearly (2022 – 2024, worldwide)



https://www.researchgate.net/publication/233993535/figure/fig1/AS:393548118675462@1470840592256/Functional-anatomy-of-the-facial-nerve-Facial-nucleus-is-in-the-caudal-pons-The-facial.png

FACIAL NERVE LESIONS TYPES

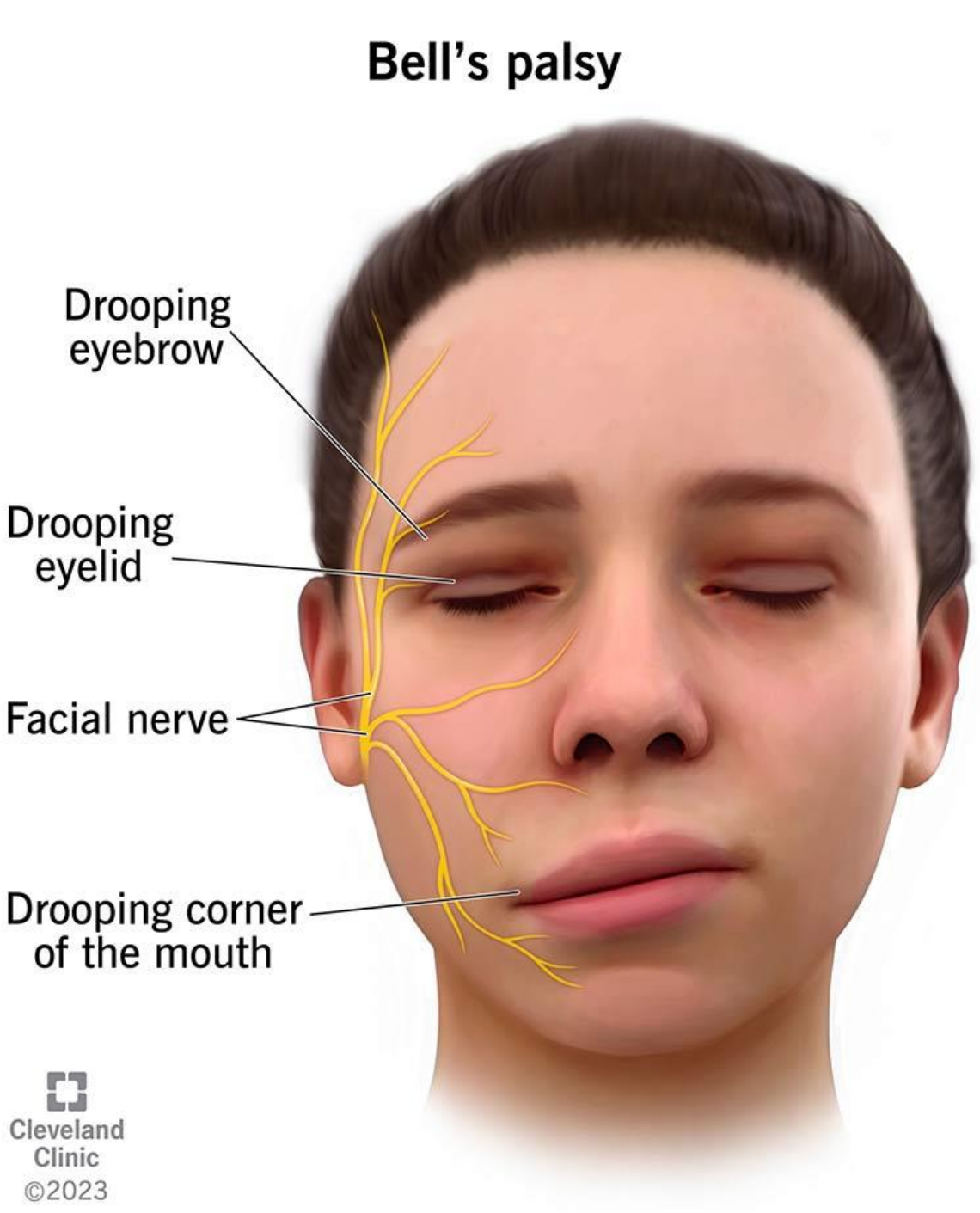
1. Idiopathic/Bell‘s palsy (70 %)
2. Trauma (10 – 23 %)
3. Infections (4,5 – 7 %)
4. Neoplasia (2,2 – 5 %)
5. Facial nerve palsy in children
6. Bilateral facial nerve palsy (0,3 – 2 %)

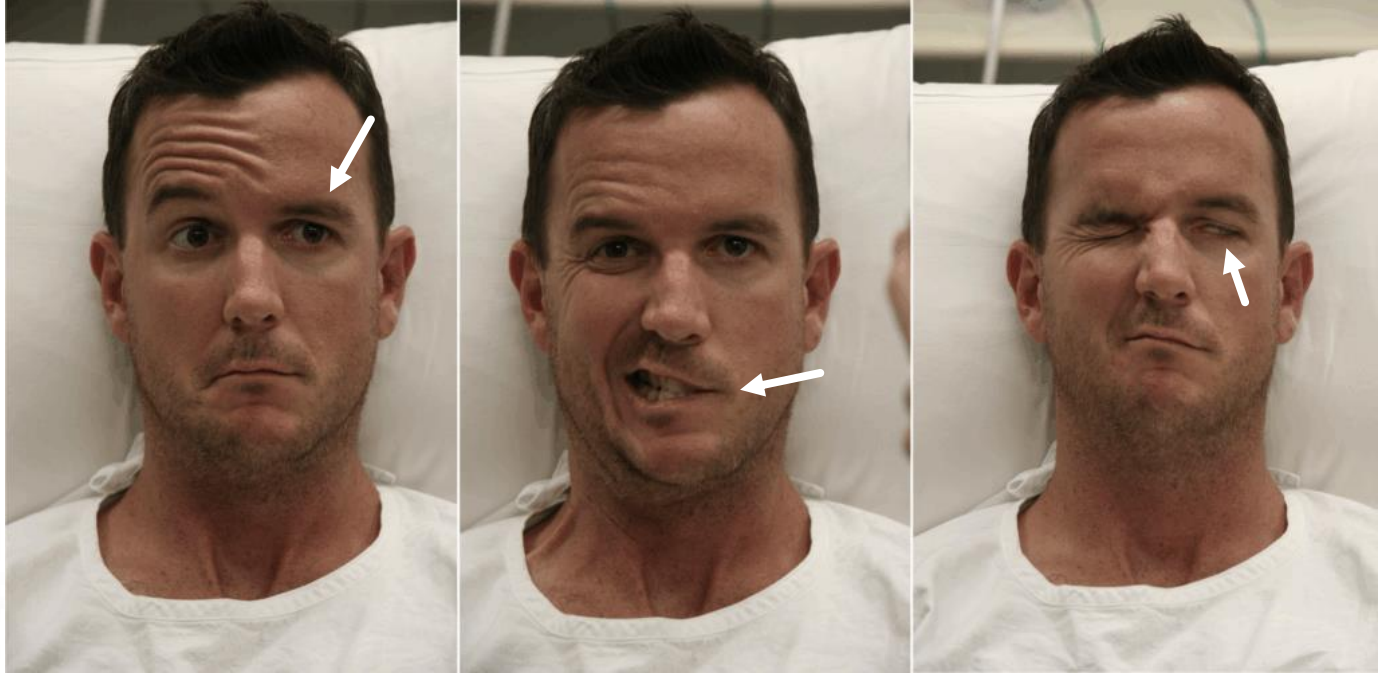
IDIOPATHIC/BELL‘S PALSY

- Definition -> unilateral facial nerve function loss (lower motor neuron loss)
- Aetiology -> unknown
  - Viral infection in recent medical history often recorded
- Gender -> no differences
- Epidemiology -> 10–40/100000/year (2022 – 2024, worldwide)
- Risk factors
  - Diabetes mellitus
  - Upper respiratory tract infection
  - Pregnancy
- Prognosis -> 85 % improved in 3 weeks, 15 % up to 3-6 months

IDIOPATHIC/BELL‘S PALSY

- Hypothesised pathomechanism
  - Viral infection -> stylomastoid foramen swelling -> facial nerve oppression
    - Some samples showed herpes simplex virus positivity (HSV-1), possible varicella-zoster infection influence (VZV)
    - HSV-1 causes demyelination sometimes -> immune response mistaken -> not directly connected with Bell‘s palsy
  - Inflammation decreases palsy course
- Per exclusion diagnosis -> known cause excludes Bell‘s palsy
- Treatment
  - Corticosteroids -> improve disease course
  - Antiviral drugs -> benefits controversial
  - Eye protection + physiotherapy
  - Surgery -> only in conventional therapy failure (Cochrane review)





Bell's palsy (left side) – patient does not rise eyebrows, has dropped mouth angle and does not close his eye properly (arrows)

https://my.clevelandclinic.org/-/scassets/images/org/health/articles/5457-bells-palsy
https://litfl.com/wp-content/uploads/2025/03/Left-Bells-Palsy-2048x1004.png

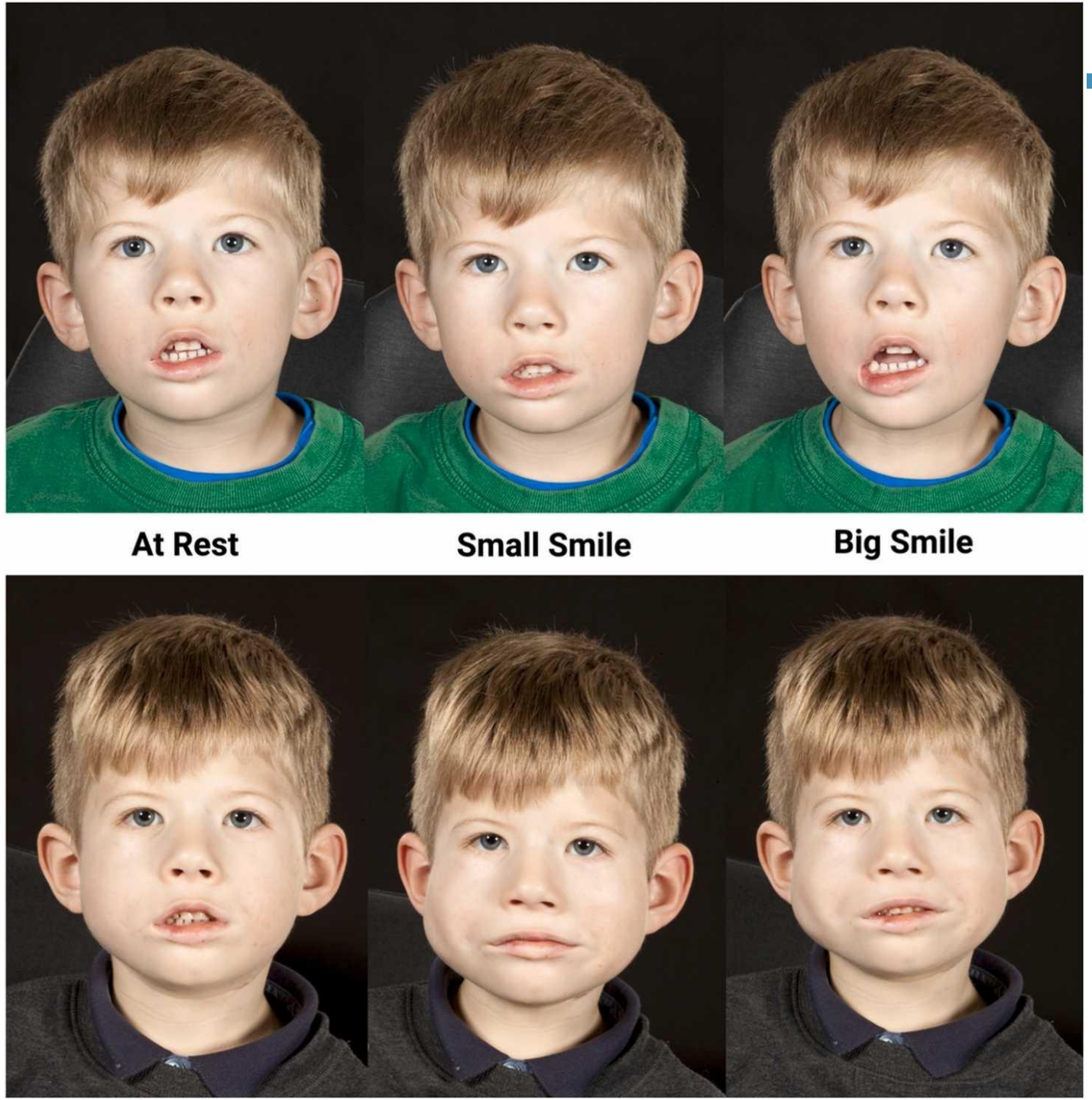
TRAUMA AND INFECTIONS

- Trauma -> rare (+haemotympanum, injury signs, nystagmus)

- Infections
  - Ramsay-Hunt syndrome (VZV)
    - Viral dormancy in geniculate ganglion -> ganglionitis
    - Glossopharyngeal signs -> vesicles in external ear and soft palate
    - 40 % patients show vertigo signs -> vestibulocochlear nerve affected
    - Prognosis – poor (21 % recovery in 12 months)
  - Bacterial -> acute otitis media, Lyme borreliosis

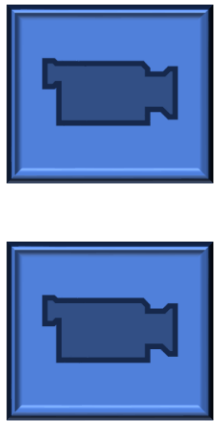
NEOPLASIA AND FACIAL NERVE PALSY IN CHILDREN

- Neoplasia -> parotic gland, neuroma, meningioma, arachnoid cysts
  - Tumour removal leads to improvement of clinical condition
- Facial nerve palsy in children
  - Causes
    - Delivery trauma -> macrosomia, forceps, premature delivery, Caesarean section
    - Craniofacial syndromes and anomalies -> Moebius syndrome, Goldenhare syndrome, Arnold Chiari malformations
    - Genetics – hereditary myopathies (myasthenia and myotonic dystrophies) -> 3q21-22 a 10q21.3-22.1
  - Surgical decompression not recommended -> benefit not outweighing the risks
    - Neural grafts and muscular transfers may lead to improvement



Moebius syndrome

- Spontaneous mutations in genes like PLXND1, REV3L
- Abducens nerve malvolution – inability to perform eyes side-to-side movement
- Facial nerve malvolution – smile inability and facial palsy



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„Love is always coming frim the heart.“
- Alex Barker and Erin Smith, both having Moebius syndrome

https://images.seattletimes.com/wp-content/uploads/2017/12/b6b427ee35df4dce883efcbd584e0d30.jpg?d=640x440

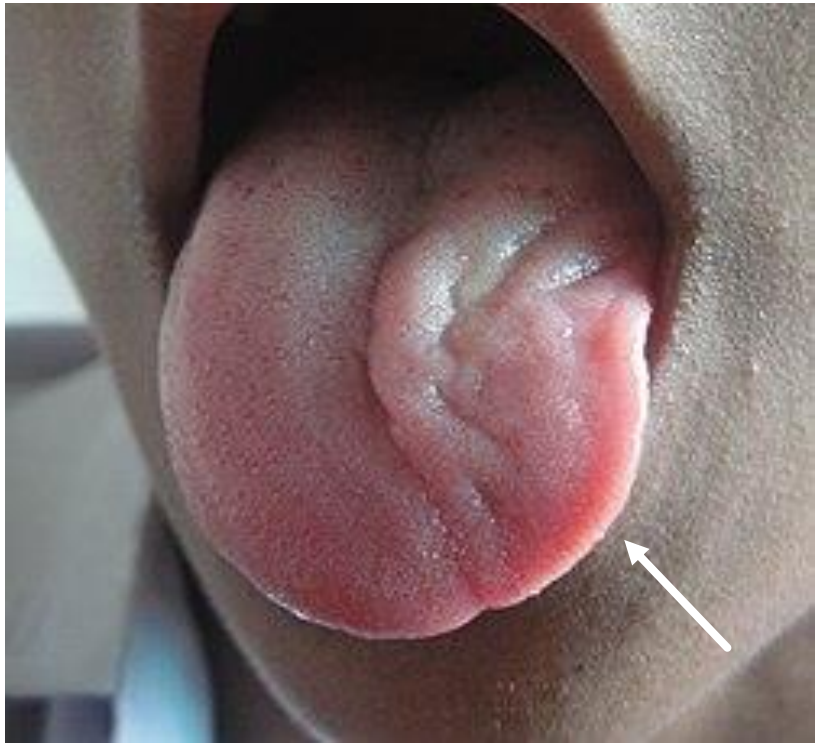
BILATERAL FACIAL NERVE PALSY

- Rare (0,3–2 %), yet significant -> signalling systemic disease

- Systemic diseases
  - Lyme borreliosis (35 % bilateral palsy cases)
  - Guillain-Barré sy.
  - Sarcoidosis
  - Diabetes mellitus
- Neurodegenerative disorders
  - Parkinson‘s disease
  - Multiple sclerosis
  - Pseudo/bulbar palsy

HYPOGLOSSAL NERVE PALSY

- Isolated lesions rare, often being part of syndromes
  - Cause – trauma, gunshots
  - Often part of multiple damage to trigeminal and facial nerve due to vertebrobasilar insufficiency
- Manifestation
  - Tongue -> atrophy, deviated to lesion side
  - Speech -> difficulties, slurred, feeling of numb tongue
  - Mastication difficulties
- Some cases might be relieved with anastomosis to facial nerve -> function restoration



Hypoglossal nerve lesion (left side)

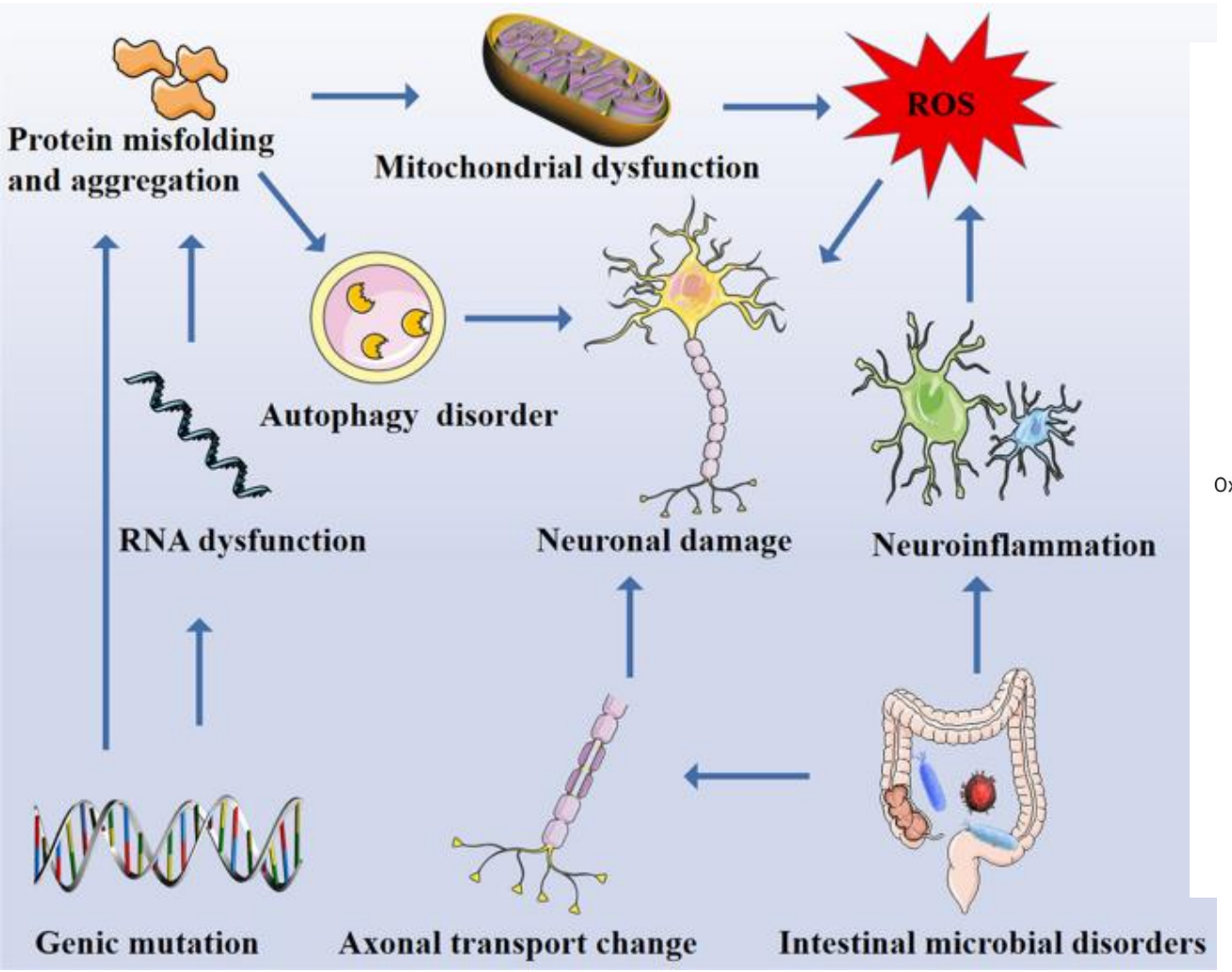
https://upload.wikimedia.org/wikipedia/commons/thumb/9/94/Unilateral_hypoglossal_nerve_injury.jpeg/250px-Unilateral_hypoglossal_nerve_injury.jpeg

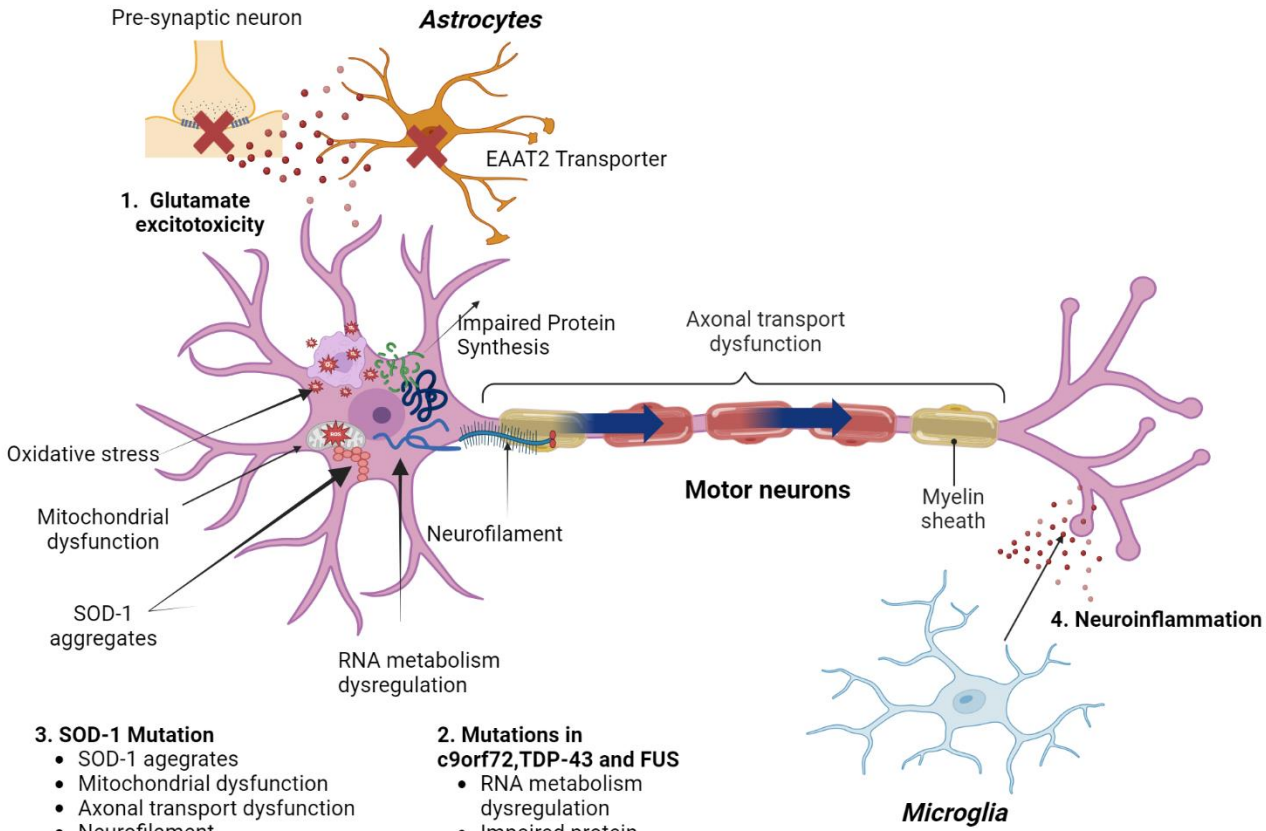
AMYOTROPHIC LATERAL SCLEROSIS

- Degenerative disease with progressive anterior spinal horns, lateral fascicles, cranial nerves motor neurons and cortical motor neurons destruction
- Causes
  - Familial – rare
    - 15-20 % associated with superoxide dismutase gene (ALS1) – adult form
    - Alsin (ALS2) gene mutations – juvenile form
    - Tau protein mutations – combined with dementia and Parkinson‘s disease
  - Lou-Gehring disease (sporadic)
    - Onset around 40-65 years, M:F - (2-3):1
    - Unknown case in most patients

AMYOTROPHIC LATERAL SCLEROSIS MANIFESTATION

1. Initial manifestation
   - 80 % - lower motor neuron syndrome -> loss of limb muscle strength, muscle atrophy, fasciculation
   - 20 % - bulbar manifestation -> may be combined with upper motor neuron syndrome
2. Remission and spreading to other regions
   - Onset signs may subside -> spreading to another region and cycle repetition
3. Upper motor neuron lesion
   - Spasticity, „clasp knife“ phenomenon, reflexes may vary
   - Emotions damage possible -> pseudobulbar palsy syndrome
   - Frontotemporal dementia (10–15 %) -> voluntary control loss, phrases and gestures repetition





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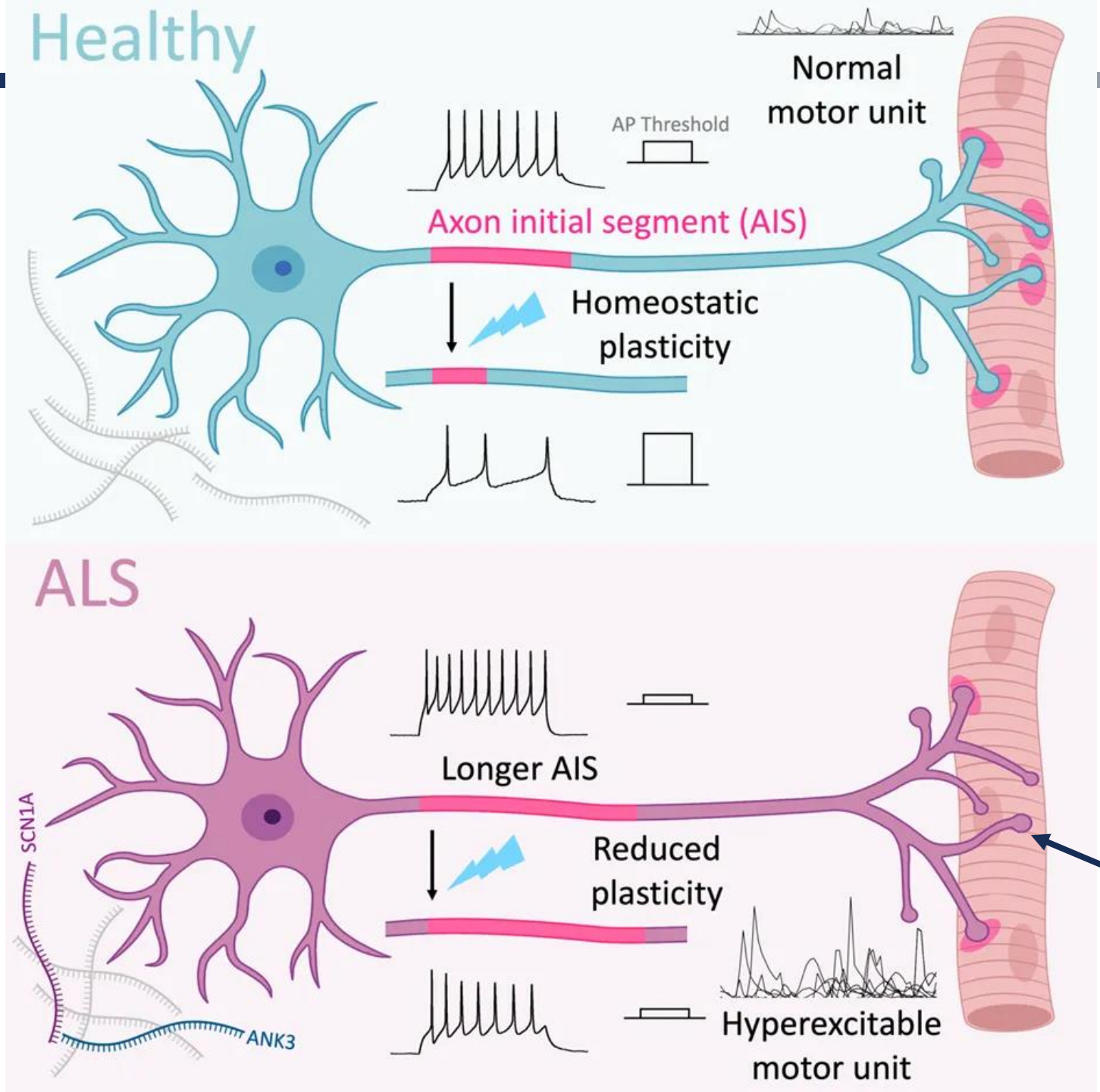


https://www.kcl.ac.uk/newimages/ioppn/neuroscience/misc/lieberam-burrone-2023-graph.x0f40790c.png?f=webp

Synapse failure

AMYOTROPHIC LATERAL SCLEROSIS SUBTYPES

Form	Upper motor neuron lesion	Lower motor neuron lesion	Prognosis
Classical (70 %)	Yes	Yes	Fatal in 3-5 years
Primary lateral sclerosis (5 %)	Yes	No	Good Respiration spared Less severity of body functions affected
Progressive muscular atrophy (5 %)	No	Yes	Fatal Progresses slower compared to the classical form

AMYOTROPHIC LATERAL SCLEROSIS SCALING SYSTEMS

King‘s ALS Scaling System

	Stage I	Stage II	Stage III	Stage IV
Stage description	Symptoms onset First region affected	2A – Diagnosis 2B – Second region	Third region	4A – nasogastric tube feeding necessary 4B – non-invasive ventilation necessary
Time median to stage progression	13,5 months	17,7 months	23,3 months	4A – 17,7 months 4B – 30,3 months

AMYOTROPHIC LATERAL SCLEROSIS SCALING SYSTEMS

Milano-Torino Functional Assessment

	Stage 0	Stage I	Stage II	Stage III	Stage IV	Stage V
Stage description	No functional domain loss	One domain loss	Two domains loss	Three domains loss	Four domains loss	Death
Death probability	7 %	26 %	33 %	33 %	86 %	N/A

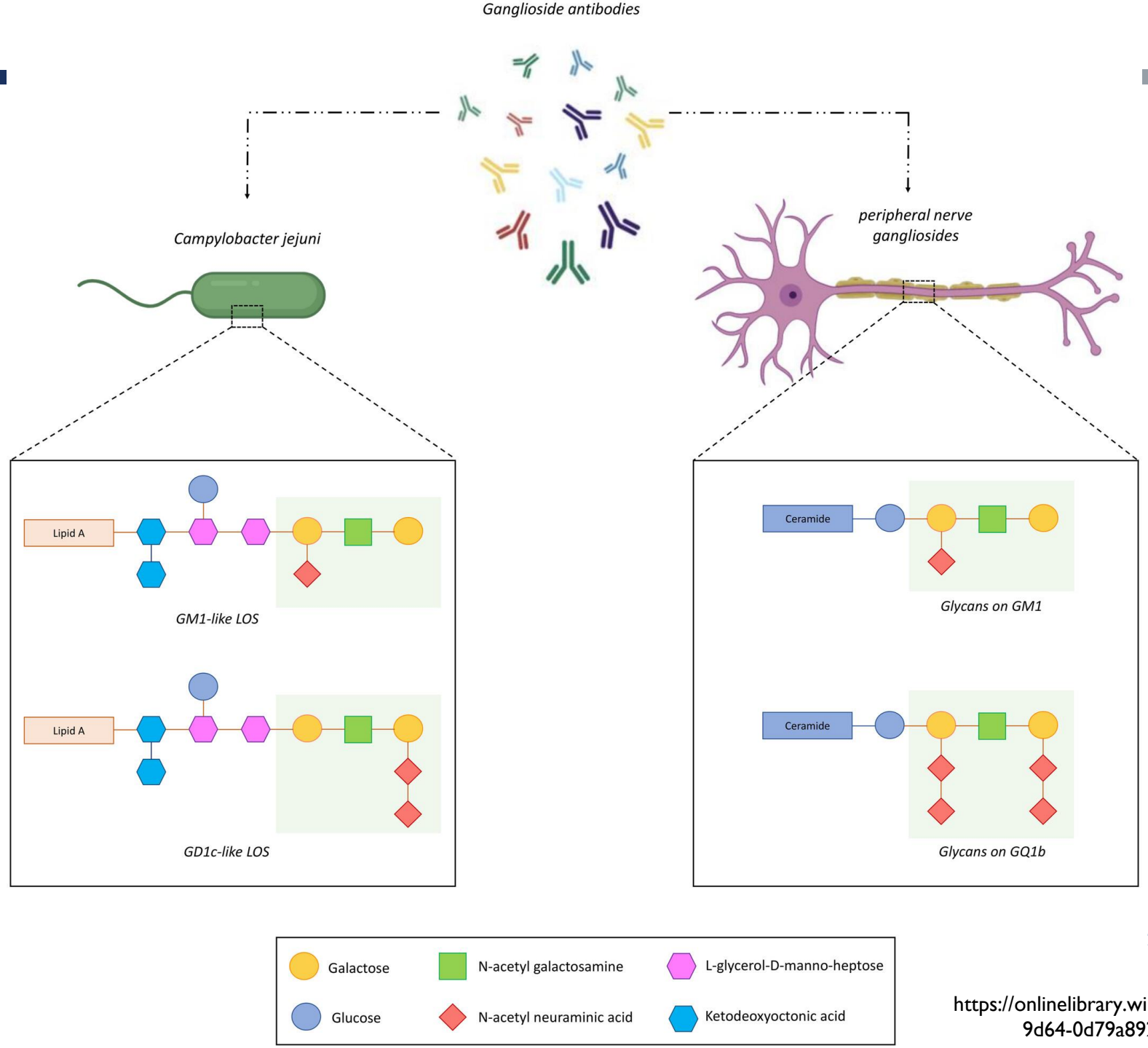
AMYOTROPHIC LATERAL SCLEROSIS MANIFESTATION

- Manifestation
  - Palsy, hypotonic, muscular atrophy
  - Fasciculation are typical for the disease
  - Hyperreflexia and spasticity follow later (with extrapyramidal signs)
  - Progresses to proximal muscles
  - Axonal degeneration, glial proliferation and sclerotisation
  - Bulbar palsy – neural lesions in n. VII, IX, X, XI, XII
  - Oculomotor nerves spared – n. III, IV, VI

http://www.thefamouspeople.com/profiles/images/stephen-hawking-4.jpg

GUILLAIN-BARRÉ SYNDROME

- Affects myelin sheaths of Schwann cells, primarily spares axons
- Epidemiology – 1,1 – 1,8/100000/yearly (2026)
- Main feature – combination of genetics and autoimmunity
  - Recent infections in medical history (approx. 14 days prior to the manifestation)
    - *Campylobacter jejuni*, viral hepatitis E, cytomegalovirus, *Mycoplasma pneumoniae*, EBV, HIV, varicella-zoster virus, *Haemophillus influenzae*
    - Arboviruses – Zika, dengue, chikungunya, Japan encephalitis
    - Possible yet unclear link with SARS-CoV-2 (Covid-19)
  - Vaccinations
    - Increased risk in adenoviral Covid-19 vaccines – Ad26.COV2.S (Janssen/Johnson & Johnson) a ChAdOx1 (not mRNA)
    - Influenzas (varies, modern vaccines with low risk), HBV, recombinant zoster vaccine, meningococcal -> benefits still outweigh risks



23. 3. 2026

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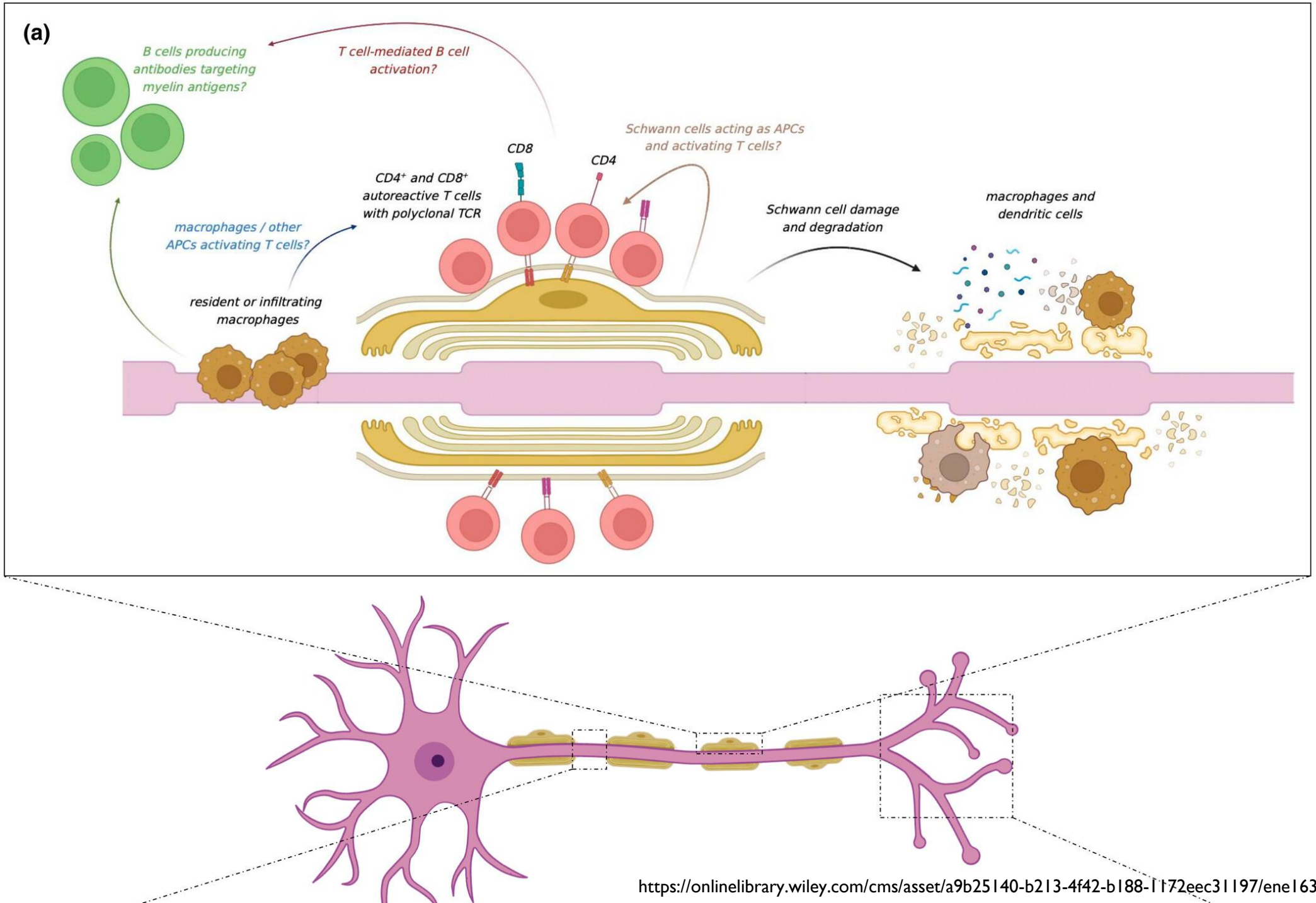
GUILLAIN-BARRÉ SYNDROME PATHOMECHANISM

- Molecular mimicry manifestation
  - *Campylobacter jejuni* -> gangliosides
  - *Mycoplasma pneumoniae* -> galactocerebrosides
  - Cytomegalovirus -> galactocerebrosides, sialosylneolactotetrasylceramide, moesine
- Mechanism
  - Ag pathogen detected -> APC -> T_{FH} -> (?) T_{reg} failure -> autoreactive clones – T_{H17}
  - B-Ly stimulation -> Plasma cells -> antibodies with complement damage -> blood-brain barrier breach (IL-17 a IL-22)
  - T_{H1} -> macrophages stimulation -> Schwann cells antigens detected
  - T_{H2} -> B-Ly -> plasma cells -> antibodies production (IgG1 a IgG3)
  - T_{reg} failure -> microglial activation -> „neuroinflammation“



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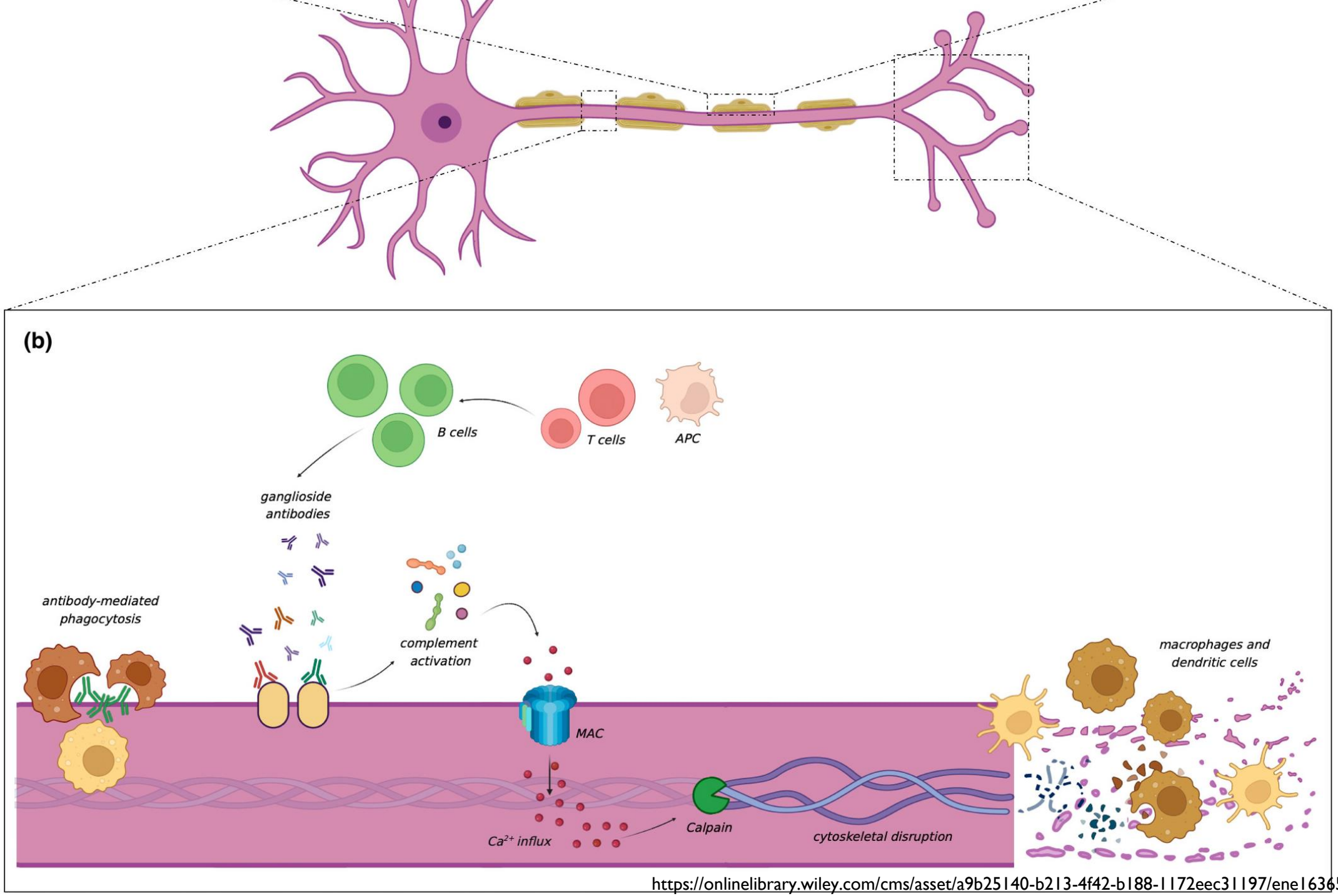

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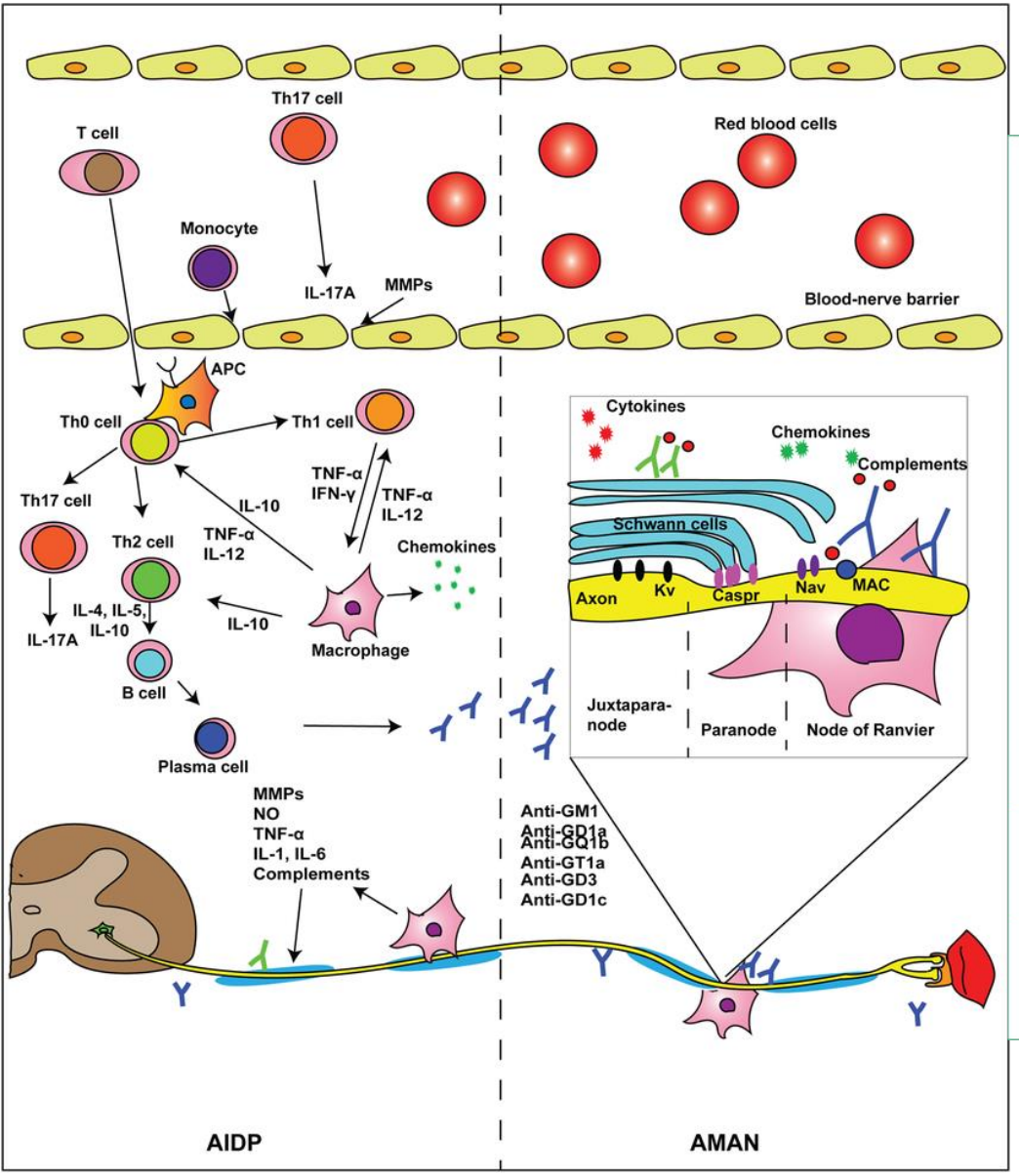
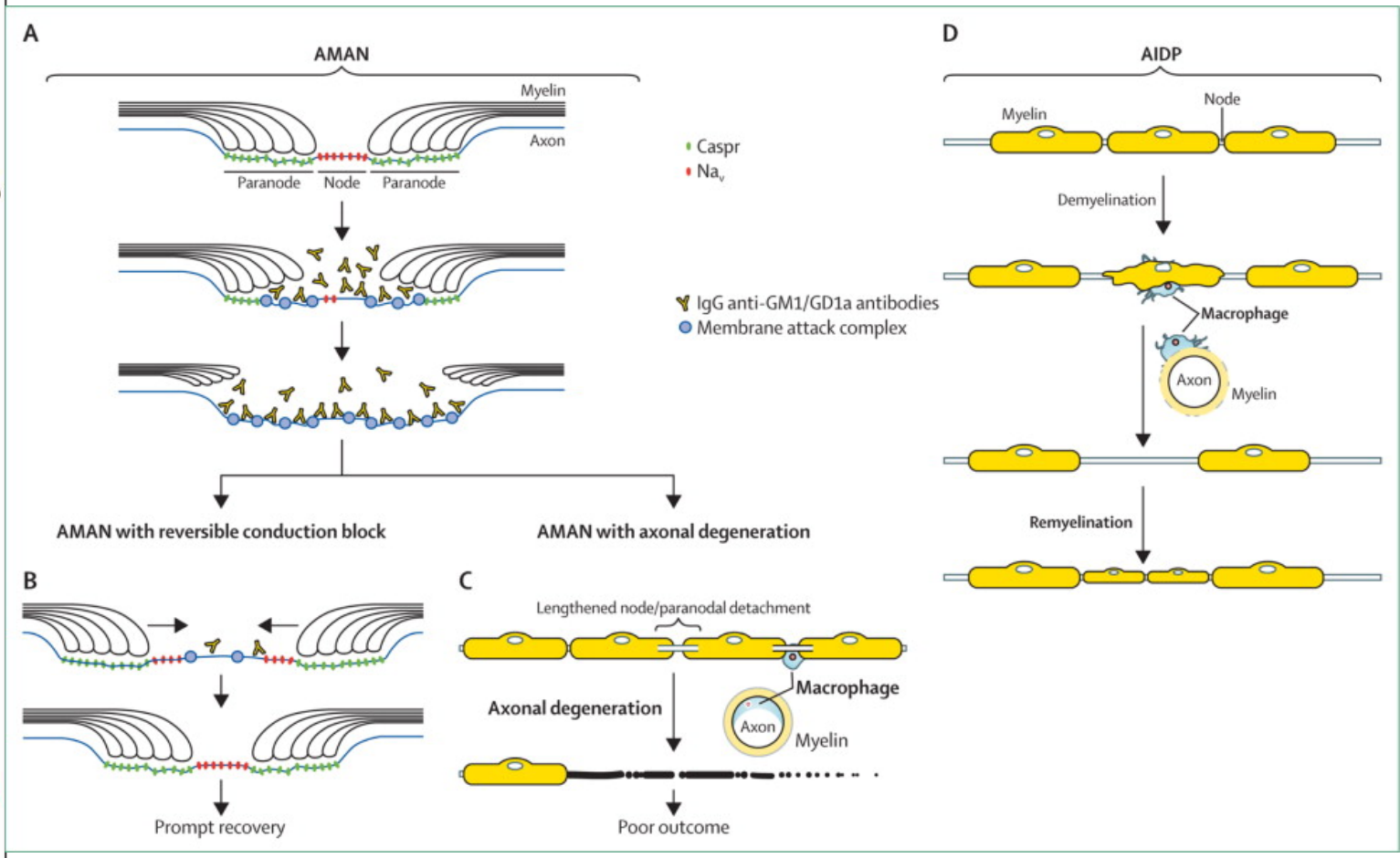
GUILLAIN-BARRÉ SYNDROME SUBTYPES – ELECTROPHYSIOLOGIC DIVISION

1. Acute motor axonal neuropathy (AMAN) (22 %)
2. Acute inflammatory demyelinating polyneuropathy (AIDP) (57 %)
3. Miller-Fisher syndrome group (MFS) (7 %)
4. Cranial nerves variant (CNV)
5. Bickerstaff brain stem encephalitis overlapping with GBS (BBE-GBS)
6. Acute motor-sensory axonal neuropathy
7. Sensory ataxia variant
8. Paraparetic variant
9. Acute sensory neuropathy
10. Acute small fibers neuropathy
11. Acute autonomic neuropathy/Acute pandysautonomy

AMAN VS. AIDP

- AMAN
  - Ganglioside antigens struck at nodal structures, ventral roots and nerve fibers (complement activation -> MAC formation)
  - Complement + MAC -> voltage-gated Na^+ canals loss with paranodal demyelination (reversible with quick treatment)
  - Progress -> Ca^{2+} accumulation + Na^+/K^+-ATPase suppression + MAC mediated axolemal perforation
- AIDP
  - MAC -> vesicular myelin degeneration
  - Macrophages engulf myelin debris
  - Schwann cells able to regenerate axons partially
  - Intense inflammation may lead to secondary axons loss





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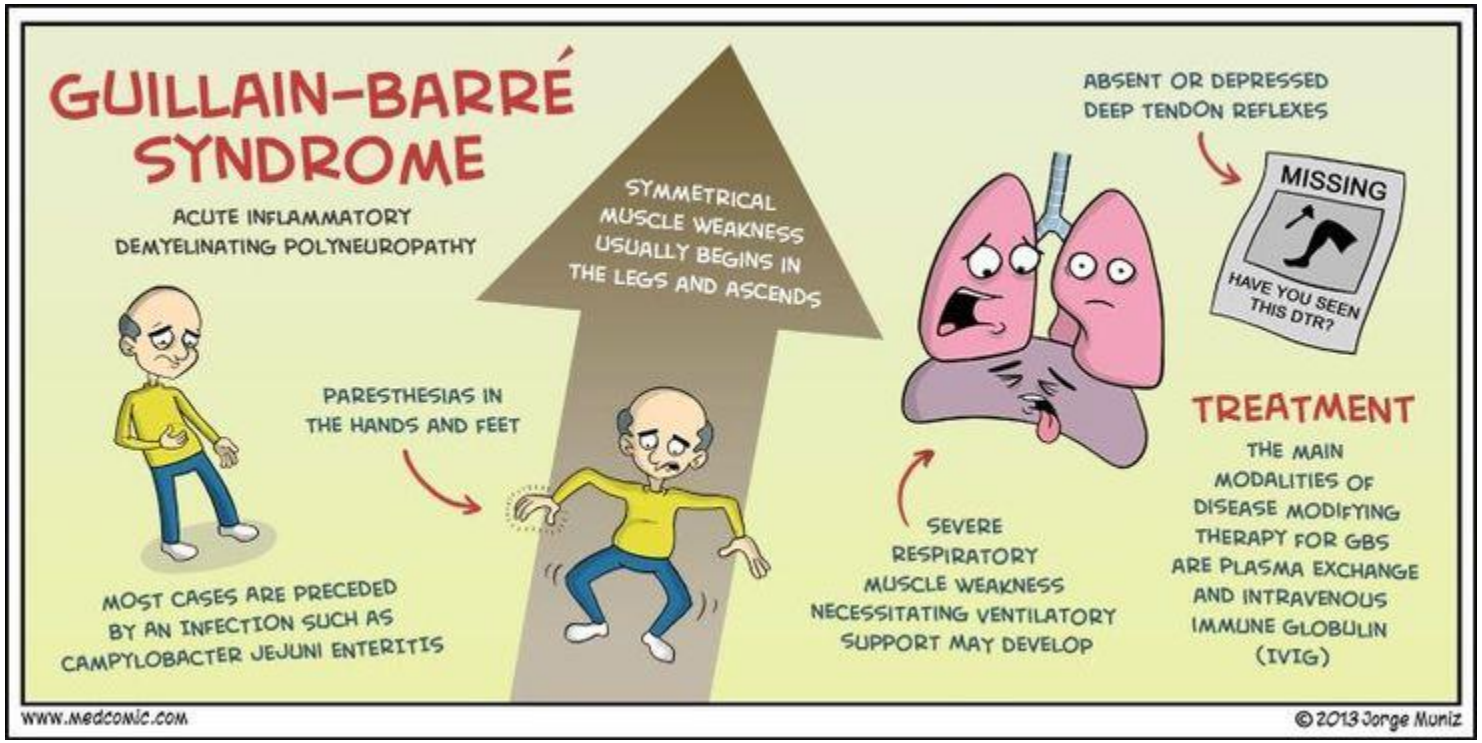
https://www.thelancet.com/cms/attachment/2009190191/2031662136/gr3.jpg

HUGHES DYSFUNCTION SCALE IN GBS

Degree	Description
0	No signs, healthy
1	Mild signs, able to run
2	Walks over 10 meters without support, unable to run
3	Walks over 10 meters with support
4	Immobile/Bedridden patient
5	Ventilation support necessary for at least a part of day
6	Death

GUILLAIN-BARRÉ SYNDROME

- Manifestation
  - Muscle weakness and paresthesias
  - Symetric lesions, quick development (days)
  - Hyporeflexion may occur
  - Frequent facial nerve dysfunctions
  - Vegetative neural system affected -> dysrrhythmias, postural hypotension
  - Respiratory failure imminent -> phrenic and intercostal nerves affected
  - „Socks and gloves sensation“ type loss
  - Elevated proteins liquor concentrations, cells are in normal range
- Excellent prognosis – approx. 80 % cases recover



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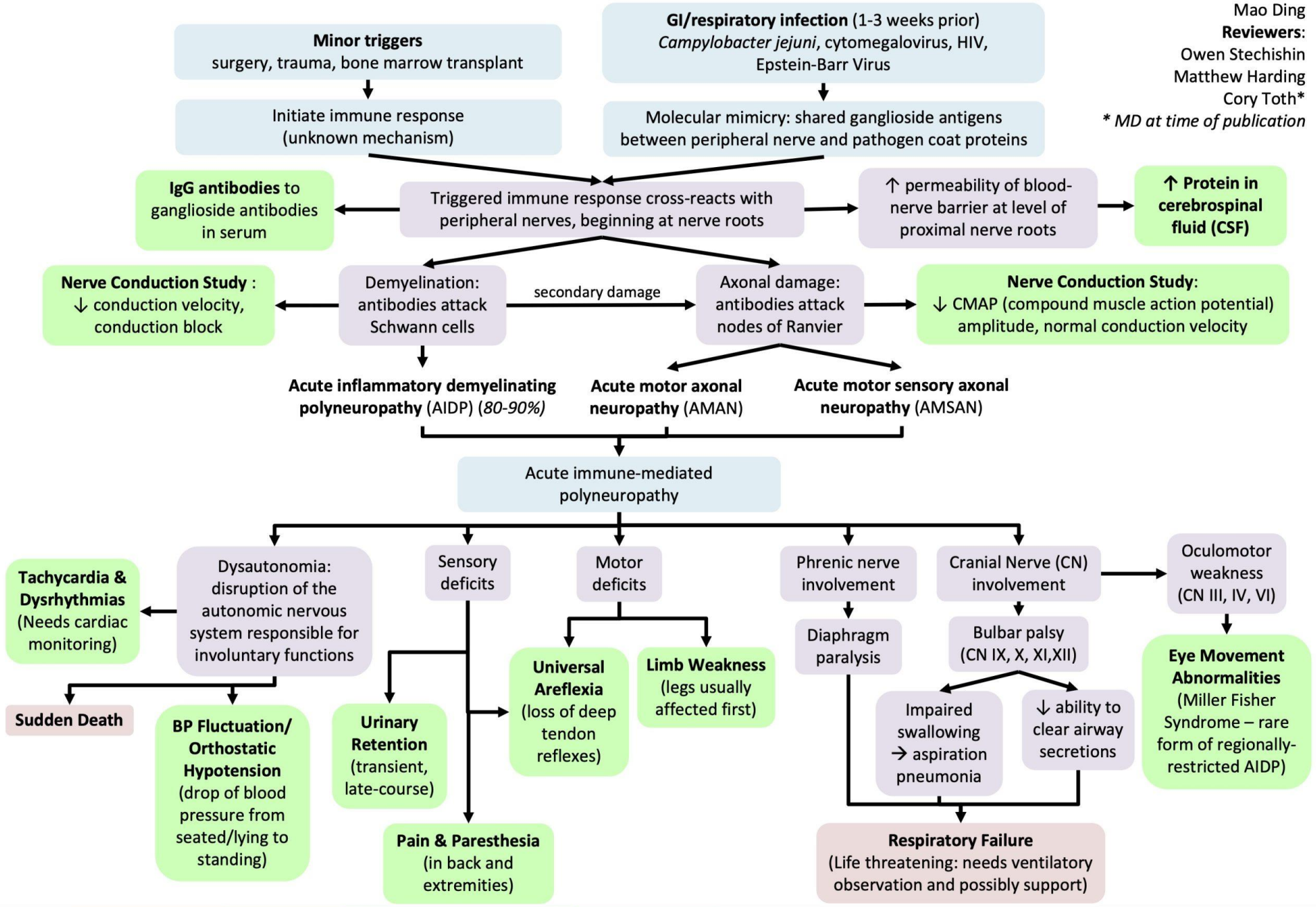
Guillain-Barré Syndrome: *Pathogenesis and clinical findings*

Author:
Nissi Wei
Mao Ding
Reviewers:
Owen Stechishin
Matthew Harding
Cory Toth*
** MD at time of publication*



Legend: Pathophysiology | Mechanism | Sign/Symptom/Lab Finding | Complications

Published **Nov 1, 2013,** updated **Oct 15, 2023** on www.thecalgaryguide.com

https://calgaryguide.ucalgary.ca/wp-content/uploads/2015/05/Guillain-Barre-Syndrome-2023-scaled.jpg

SPINAL CORD INJURY – GENERAL CHARACTERISTICS

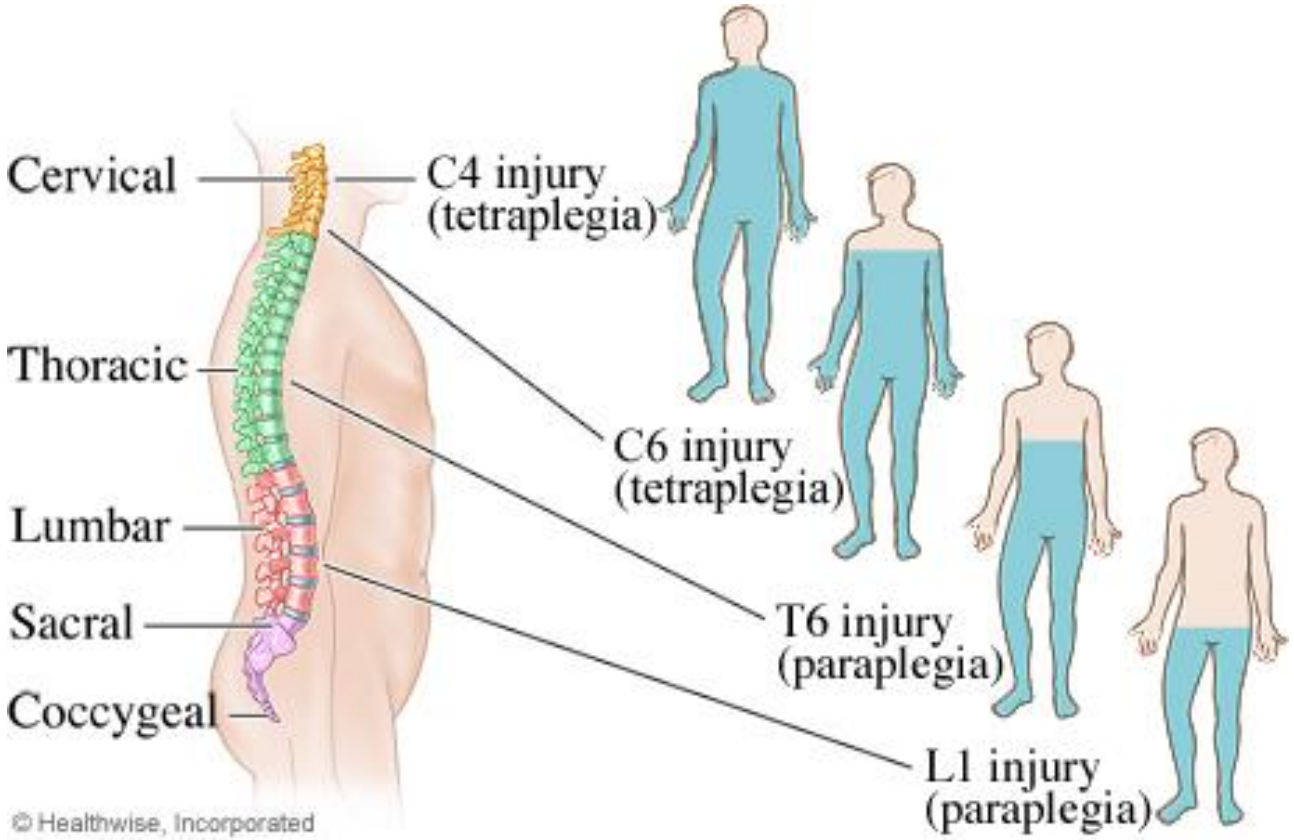
- Partial or total function loss
  - Motor control
  - Sensory perception
  - Autonomic neural system
- Usually ends as spastic palsy, hyperreflexia with loss of sensory and vegetative functions
- Primary causes
  - Spinal cord trauma and/or compression
  - Grey matter affected more
  - Irreversible changes after 1 and 3 hours (grey, and white matter respectively)
- Secondary
  - Ischemia/reperfusion, bleeding, excitation neurotransmitters toxicity (glutamate, cainate), elevated Na^{+} a Ca^{2+}concentration, immune system response

SPINAL CORD INJURY – CERVICAL SEGMENT

- Total loss of C1-4 innervation is a life-threatening event
  - Acute respiratory failure imminent (phrenic nerve rises from C4-7 segments)
- Lower parts
  - Diaphragm function spared
  - Lung vital capacity decreased (-> restrictive lung disorder)
  - Normal levels of blood carbon dioxide
- Tetraplegia or quadriplegia
  - Sensory functions loss correspond with motor dysfunction

SPINAL CORD INJURY – CERVICAL SEGMENT

- Vegetative neural system
  - Peripheral vasoconstriction dysfunction -> tends to be well compensated
  - Postural hypotension frequent
  - Decreased heart response to hypotension (slower tachycardia development)
  - Some reflexes may be supressed (full bladder causes peripheral vasoconstriction and arterial hypertension)
  - Voluntary defecation reflex control loss (caudal parasympathetic system dysfunction)
    - Inhibition (retention) or activation (incontinence)
  - Loss of voluntary miction reflex control (bladder distension, incontinence due to overflow)



https://myhealth.alberta.ca/Health/_layouts/15/healthwise/media/medical/hw/h9991288_003.jpg

SPINAL CORD INJURY – THORACIC, LUMBAL AND SACRAL SEGMENT

- Ventilation spared, sympathetic activity normal
- „Voluntary“ motor and sensory function lost only in the lower body half (paraplegia)
  - Storage and emptying function of bladder and rectum affected
  - Intestinal motility may be decreased
- Pregnancy possible
  - Th10-above lesions cause painless delivery
- Erection and ejaculation affected temporarily
  - Functions may restore after initial shock phase in case of sacral segment spared

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GENERAL CHARACTERISTICS OF SPINAL SHOCK

- Spinal shock
  - Flaccid palsy
  - Temporary spinal reflexes loss
  - Sensory functions disorders
  - Bladder, intestines and rectum dysfunction
  - Thermoregulation dysfunction with blood pressure regulation instability
- Neurogenic shock
  - Sudden sympathetic activity decrease with parasympathetic overactivation
  - Vasodilation, bradycardia, decreased cardiac output, hypotension
- Spinal shock may last days to weeks and is possible to recover spontaneously

CRANIAL SPINAL CORD INJURY SPINAL SHOCK

- Pulmonary ventilation disorders
- Cough reflex absence!
- Areflexia, flaccid palsy of trunk and limbs with sensory loss
- Unable to mount shivering response in body core temperature drop -> thermoregulation disorder
  - Hypo/hyperthermia may develop more quickly in milder environmental changes
- Vasodilation may impair venous return
  - Increased deep venous thrombosis risk
  - Stable blood pressure but rapid fluctuations may occur

CRANIAL SPINAL CORD INJURY SPINAL SHOCK

- Miction disorders
  - Bladder distension, incontinence due to „leaking“
  - Detrusor muscle may be impaired due to distension
- Defecation reflex loss
- Erection and ejaculation damaged
- Negative nitrogen balance
  - Proteins catabolism
  - K^+, Ca^{2+}, PO_4^{3-} loss by urine –> possible stones emerge

CAUDAL SPINAL CORD INJURY SPINAL SHOCK

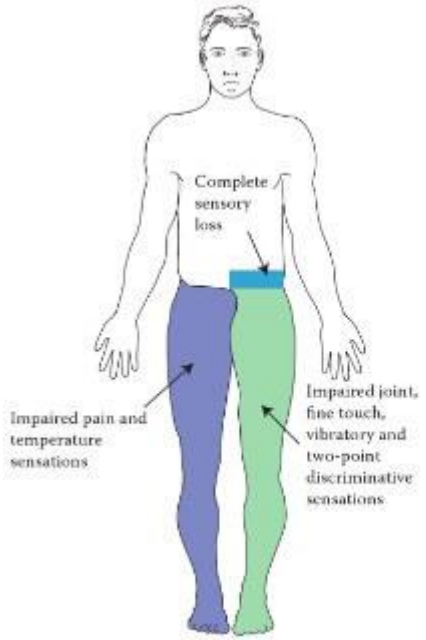
- Ventilation and thermoregulation spared
- Sacral segments and cauda equina damage
  - Flaccid palsy of affected area -> turning to a permanent one
  - Sensory function loss
  - Miction reflex impaired permanently

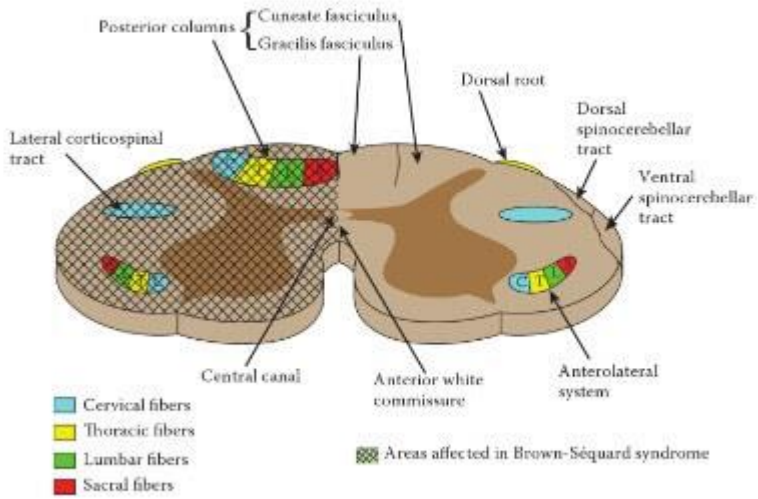
SPINAL SHOCK CESSATION

- Reflexes being restored in caudo-cranial way
  - Anal sphincter reflex restored among first ones
- Miction reflex restored in case of intact sacral segment and cauda equina
- Flaccid palsy turns to spastic with hyperreflexia
- Sensory loss still present

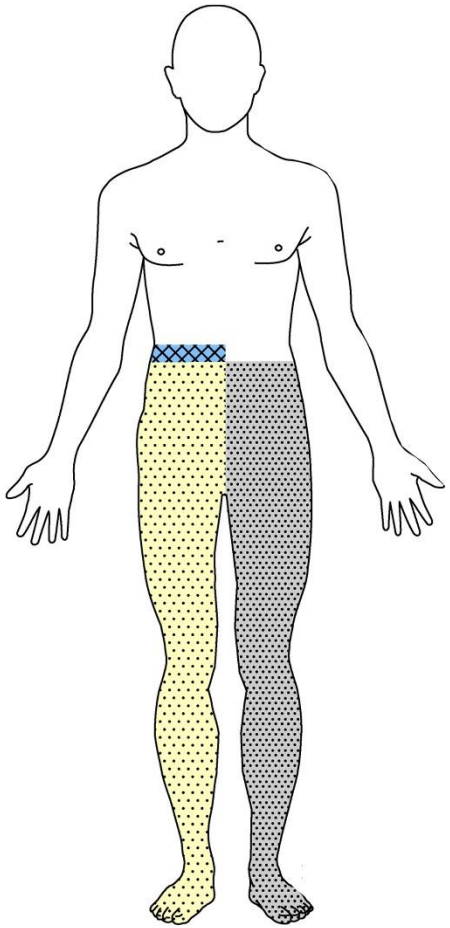
DISSOCIATION ANAESTHESIA

- Syringomyelic dissociation
  - Spinothalamic tract in ventrolateral fascicle damaged
  - CONTRALATERAL LOSS –> thermal, pressure, protopathic sensory and pain perception
  - Deep (staaesthesia, pallaesthezia, kinaesthesia, baraesthesia) and epicritic superficial sensory functions maintained
- *Tabes dorsalis*
  - Posterior fascicles damaged (fasciculus gracilis et cuneatus)
  - IPSILATERAL LOSS –> deep and epicritic sensory loss
  - Pain, thermal, pressure and protopathic sensory functions maintained
- Brown-Séquard spinal hemi-syndrome
  - Half of spinal cord disrupted
  - All sensory functions lost at the lesion level, flaccid palsy ipsilateral
  - Below lesion -> contralateral syringomyelic, ipsilateral tabic; spastic palsy ipsilateral (paraparesis)





http://epomedicine.com/wp-content/uploads/2016/07/Brown-sequard-syndrome.jpg



Ipsilateral loss of all sensory modalities at the level of the lesion

Ipsilateral flacid paralysis at the level of the lesion

Ipsilateral spastic paraparesis below the lesion

Ipsilateral loss of vibration and position sense below the lesion

Contralateral loss of pain and temperature below the lesion

http://www.thelancet.com/cms/attachment/2002726259/2009696161/gr2_lrg.jpg

marek.brenisin@upjs.sk