



THE TRACT
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The Neurology Tract

Reference Papers Digest

For closed-book exam preparation

All 23 FEBN 2026 reference papers — corrected, updated with the trials that followed them, and distilled for the closed-book examination.

23 papers

Guideline recommendations

Trials since publication

Exam angles

Rapid-fire & numbers

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About this edition

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PURPOSE	Digest of the 23 reference papers for the European Board of Neurology examination (FEBN 2026)
SOURCES	The 23 guidelines and reviews on the FEBN 2026 reading list as supplied to the author, and the trials and guideline updates published after them (to mid-2026)
THIS EDITION	Supersedes the May 2026 digest; corrections are listed in “What changed from the May 2026 digest”
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How to use this digest

Closed book: memorise the green and red boxes and the "Exam angles" tables — they are the direct exam pearls.

Open book: print the file and bring it. Each paper has a fixed number (1–23) — tab the pages by number. The tables are laid out so you can find a threshold or dose in under a minute.

Last day: review the Rapid-Fire and Numbers to know pages at the end.

Box	Meaning
 Green	The pearl — memorise
 Red	Trap or correction — where candidates (and the old digest) go wrong
 Gold	Context, caveats, newer evidence
Exam angles	Stem → answer pairs at the end of every paper

Scope and honesty. The 23 papers follow the reading list used for FEBN 2026 as it was given to the author. Each section summarises the paper **and** the evidence published since, because examiners write questions from current practice. Where the list names a paper inaccurately (for example a "2022 CIDP update" that does not exist as a separate guideline), the section says so. Check the official EBN list for exact references before printing for the open-book exam.

What changed from the May 2026 digest

Every paper was re-checked against the source guideline and the trials that followed it. Length roughly doubled — each paper now has the full recommendation set, a differential or comparison table, and exam angles.

#	Old digest said	This edition says
1	DOACs "can use" per ESO 2017; acetazolamide → LP → surgery for raised ICP	ESO 2017 did not recommend DOACs (RE-SPECT CVT 2019 and ACTION-CVT 2022 came later); steroids and routine acetazolamide not recommended; decompressive surgery for impending herniation; VITT added
2	"EAN/ESMINT"; 6–24 h must have perfusion mismatch; ASPECTS ≥ 6; BASICS = basilar answer; conscious sedation preferred	ESO-ESMINT ; DAWN used clinical-core mismatch and MR CLEAN-LATE used collaterals; large-core trials; ATTENTION/BAOCHE positive for basilar ; no anaesthesia preference; bridging IVT recommended
3	EXPRESS trial for DLB; "PSG-confirmed RBD without atonia"	EXPRESS was PDD ; indicative biomarker is REM sleep without atonia ; prodromal DLB and α-synuclein SAA added
4	SANTE "~40 % at 1 year" only; DBS-CMN 50–70 %	SANTE 40 % → 56 % (2 y) → 69 % (5 y); RNS ~75 % at 9 years; ANT-DBS mood/memory effects
5	Verapamil 120–480 mg	240 mg start, up to 480–960 mg with ECGs; galcanezumab ineffective in chronic cluster; nVNS, ONS, PredCH added
6	Amantadine/modafinil for MS fatigue	TRIUMPHANT-MS : no better than placebo — exercise/CBT first
7	"CXCL13 better than older markers"; follow-up LP for all	CXCL13 promising, not standard; CDC 2021: repeat LP only if serological/clinical response inadequate; probenecid regimen added
8	—	SAD-PD, DAWS, punding, DDS added; psychosis hierarchy expanded
9	"EAN coma/post-arrest 2020" as one paper	EAN DOC guideline (2020) and ERC-ESICM 2021 algorithm (≥ 2 predictors at ≥ 72 h); TTM2; Lance-Adams
10	Tier 2 = NMB; tranexamic acid and steroids absent	SIBICC tiers corrected; CRASH-3 TXA , CRASH steroids harmful , RESCUE-ASDH, POLAR
11	Tocilizumab "2018"; "skip lessons"	2017 (GiACTA); ultrasound first-line; PACNS vs RCVS table; avacopan, mepolizumab
12	Definite / probable / possible CIDP ; DADS with anti-MAG under CIDP	CIDP / possible CIDP only ; anti-MAG and nodopathies excluded ; ADHERE (efgartigimod)
13	Cisplatin "large-fibre axonal"; vincristine "motor > sensory"	Cisplatin = ganglionopathy ; vincristine = sensory first , then motor/autonomic; acetyl-L-carnitine harmful
14	—	TES 2021 clinical criteria ; selection bias in autopsy series
15	"VECTORS: more is better"	VECTORS: high-intensity early CIMT was worse ; fluoxetine trials negative; VNS-REHAB
16	CPAP reduces recurrent events; ASV for Cheyne–Stokes	SAVE neutral ; SERVE-HF: ASV harmful in HFrEF
17	NT1 requires cataplexy; thresholds "< 8 min", "< 110"; pitolisant only "if controlled drugs restricted"	Low hypocretin alone suffices ; ≤ 8 and ≤ 110; modafinil, pitolisant, oxybate and solriamfetol all strong for sleepiness
18	Head-up 30–45°	~10–20° (bed blocks); severity grades; full bedtime-drug list
19	Efgartigimod for MuSK+; intubate at FVC < 15; "steroids need pyridostigmine cover"	Efgartigimod AChR+ ; rozanolixizumab/nipocalimab cover MuSK+; 20/30/40 rule ; start steroids low
20	—	EARLYSTIM, 5-2-1 rule, foslevodopa SC, apomorphine haemolysis
21	"2022 CIDP update" with new features	No 2022 guideline — section rebuilt on nodopathies and paraproteinaemic neuropathies
22	IVIG for MFS; MEP < 30; mEGRIS predictors	MFS usually untreated ; MEP < 40 ; EGRIS and mEGOS correctly defined
23	Gold Coast "UMN or LMN in ≥ 1 region"; NIV +7–16 months; edaravone listed as standard	UMN + LMN in one region or LMN in two ; NIV ~7 months (Bourke); edaravone and AMX0035 not recommended; genetic testing for all

ESO — Cerebral Venous Thrombosis

2017

Source: Ferro et al., European Stroke Organisation guideline for the diagnosis and treatment of cerebral venous thrombosis, *Eur J Neurol* 2017. **Read with:** RE-SPECT CVT (2019), ACTION-CVT (2022), TO-ACT (2020), AHA scientific statement (2024).

The essentials

Epidemiology	~1–1.5 % of strokes; median age ~37; women ~75 % (oral contraceptives, pregnancy, puerperium)
Presentations	Isolated headache (often progressive, sometimes thunderclap); intracranial hypertension syndrome; focal deficits; seizures (~40 %, more than arterial stroke); encephalopathy
Commonest sinuses	Superior sagittal and transverse sinuses; deep venous system → bilateral thalamic oedema, reduced consciousness
Outcome	~80 % independent; mortality ~5–10 % (mostly from transtentorial herniation in the acute phase)

Poor prognostic factors (ISCVT): male sex, age > 37, coma, mental status disorder, haemorrhage on admission, deep venous system thrombosis, CNS infection, cancer.

Diagnosis

Test	Role
CT venography	Fast and widely available; sensitivity comparable to MRV for sinus thrombosis
MRI + MR venography	No radiation; T2*/SWI shows thrombus directly (blooming) and cortical vein thrombosis; best for subacute/chronic CVT and parenchymal lesions
Non-contrast CT	Normal in up to 30 %. Dense (cord) sign , hyperdense sinus; venous infarct not respecting arterial territories, often haemorrhagic; bilateral parasagittal lesions
Contrast CT	Empty delta sign — filling defect in the superior sagittal sinus
D-dimer	May help exclude CVT in low-probability isolated headache; a normal value does not exclude CVT (especially with isolated headache or long symptom duration)
Catheter angiography	Only when CTV/MRV are inconclusive
Thrombophilia screening	ESO: no recommendation that it improves outcome; test when results would change duration of anticoagulation

Pitfalls on imaging: transverse sinus hypoplasia (usually left), arachnoid granulations (rounded, CSF signal), and flow gaps on time-of-flight MRV.

Risk factors

- **Hormonal:** combined oral contraceptives (OR ~6), pregnancy and especially the puerperium, hormone therapy.
- **Thrombophilia:** factor V Leiden, prothrombin G20210A, protein C/S and antithrombin deficiency, antiphospholipid syndrome, hyperhomocysteinaemia.
- **Local:** head injury, otitis/mastoiditis, sinusitis, meningitis, neurosurgery, lumbar puncture, jugular catheters.
- **Systemic:** cancer, myeloproliferative neoplasm (*JAK2* V617F), PNH, nephrotic syndrome, IBD, dehydration, Behçet's, SLE, iron-deficiency anaemia, L-asparaginase.
- **Vaccine-induced immune thrombotic thrombocytopenia (VITT):** CVT with thrombocytopenia 4–30 days after adenoviral-vector COVID-19 vaccines — anti-PF4 antibodies; **avoid heparin and platelet transfusion**; give

IVIG and a non-heparin anticoagulant.

Treatment — what ESO recommends

Question	Recommendation
Acute anticoagulation	Therapeutic-dose heparin for all, including those with intracerebral haemorrhage (strong)
Which heparin	LMWH preferred over UFH (lower risk of new haemorrhage, easier) — except where rapid reversal may be needed (e.g. imminent surgery)
Long-term anticoagulation	Oral anticoagulation (VKA, INR 2–3) for 3–12 months to prevent recurrent CVT and other venous thromboembolism
DOACs	ESO 2017: not recommended at the time (insufficient data). Now: dabigatran was as safe and effective as warfarin (RE-SPECT CVT 2019) ; observational ACTION-CVT (2022) showed DOACs as effective with fewer major bleeds. AHA 2024 accepts DOACs after the acute phase
Endovascular treatment	No recommendation (insufficient evidence); TO-ACT (2020) stopped for futility — reserve for deterioration despite anticoagulation, in experienced centres
Steroids	Not recommended (harm in ISCVT), unless an underlying inflammatory disease (Behçet's, SLE) requires them
Acetazolamide	Not recommended routinely to prevent death or dependency
Decompressive surgery	Recommended for large parenchymal lesions with impending herniation — prevents death; many survivors are independent
Seizures	ASM to prevent early recurrent seizures in patients with an early seizure and supratentorial lesions; no prophylaxis without seizures
Pregnancy	LMWH throughout pregnancy and ≥ 6 weeks postpartum (total ≥ 6 months) in future pregnancies after CVT; prior CVT is not a contraindication to future pregnancy
Contraception	Avoid oestrogen-containing contraception after CVT
Visual threat from raised ICP	Therapeutic LP before anticoagulation (if safe), acetazolamide, shunt or optic nerve sheath fenestration

FEBN trap — haemorrhage in CVT. Anticoagulate **even with haemorrhage**. The bleed is caused by venous hypertension; anticoagulation stops thrombus propagation, promotes recanalisation and lowers venous pressure. ESO makes this a strong recommendation. The only time to hesitate is VITT (avoid heparin) — not the haemorrhage itself.

Duration of oral anticoagulation (practical)

Situation	Duration
Transient provoked risk factor (pregnancy, OCP, infection, dehydration)	3–6 months
Unprovoked CVT or mild thrombophilia	6–12 months
Recurrent CVT, VTE after CVT, severe thrombophilia (antithrombin deficiency, homozygous factor V Leiden, APS), active cancer	Consider indefinite
Antiphospholipid syndrome	Warfarin — DOACs not recommended (TRAPS)

Exam angles

- Young woman on OCP, progressive headache, papilloedema, normal CT → **CTV or MRV**.
- CVT with a 3 cm haemorrhagic infarct → **LMWH now**.
- Comatose patient with a large haemorrhagic venous infarct and midline shift → **decompressive craniectomy**.

- New headache and thrombocytopenia 10 days after an adenoviral-vector vaccine → **VITT: IVIG, non-heparin anticoagulant, no platelets.**
- Isolated headache, normal D-dimer, high clinical suspicion → **still image the veins.**

ESO–ESMINT — Mechanical Thrombectomy in Acute Ischaemic Stroke

2019, updated 2022–2024

Source: Turc et al., European Stroke Organisation (ESO) – European Society for Minimally Invasive Neurological Therapy (ESMINT) guidelines on mechanical thrombectomy, *J NeuroIntervent Surg / ESJ* 2019, with expedited recommendations on bridging thrombolysis (2022) and large-core and basilar trials. The old digest called this "EAN/ESMINT" — it is an **ESO–ESMINT** guideline.

Who gets thrombectomy

Criterion	0–6 h	6–24 h
Occlusion	ICA, M1 (strong); M2 proximal (individualised); basilar (see below)	ICA or M1
Pre-stroke function	mRS 0–1 in trials; do not exclude on age alone	mRS 0–1
Imaging selection	NCCT + CTA (or MRI + MRA); ASPECTS ≥ 6 in the original trials	DAWN: clinical–core mismatch (NIHSS high for core volume on CTP or DWI). DEFUSE-3: perfusion mismatch (core < 70 mL, ratio ≥ 1.8) in 6–16 h
Severity	Usually NIHSS ≥ 6	DAWN: NIHSS ≥ 10 (age- and core-stratified)

Correction to the old digest. "6–24 h MUST have a perfusion mismatch" is too strong. DAWN used **clinical–core** mismatch (core on CTP or DWI), and **MR CLEAN-LATE (2023)** showed benefit at 6–24 h with patients selected on **CTA collaterals** alone. Perfusion imaging is still the commonest selection tool, not an absolute requirement.

Expanding indications since 2019

Population	Evidence	Status
Large core (ASPECTS 3–5 or core ≥ 50–70 mL)	RESCUE-Japan LIMIT (2022), SELECT2, ANGEL-ASPECT (2023), TENSION, TESLA, LASTE (2024)	Benefit in functional outcome despite more sICH — now offered within 24 h
Basilar artery occlusion	BEST and BASICS (2020–21) neutral; ATTENTION and BAOCHE (2022) positive (moderate–severe deficits, up to 12–24 h)	ESO expedited recommendation: thrombectomy for moderate–severe basilar occlusion within 24 h
Medium/distal vessel occlusion	ESCAPE-MeVO and DISTAL (2025) — no benefit	Not routine
Tandem occlusion	Observational data, TITAN	Acute carotid stenting individualised
Mild deficit with LVO (NIHSS < 6)	MOST/ENDOLOW ongoing; observational	Individualised

Bridging thrombolysis

ESO–ESMINT 2022 expedited recommendation: in IVT-eligible patients presenting directly to a thrombectomy centre within 4.5 h, **give IVT before thrombectomy** rather than proceeding to thrombectomy alone. Direct-thrombectomy trials (DIRECT-MT, SKIP, DEVT, MR CLEAN-NO IV, SWIFT-DIRECT, DIRECT-SAFE) did not show non-

inferiority convincingly. **Never delay thrombectomy to watch for a response to IVT.** Tenecteplase 0.25 mg/kg is an alternative to alteplase (EXTEND-IA TNK: higher pre-thrombectomy reperfusion).

Landmark trials

Trial	Year	Population	mRS 0–2 at 90 days
MR CLEAN	2015	Anterior LVO < 6 h	33 % vs 19 %
ESCAPE	2015	Small core, good collaterals, < 12 h	53 % vs 29 %
EXTEND-IA, SWIFT PRIME, REVASCAT	2015	Anterior LVO	All positive
HERMES (pooled)	2016	5 trials	NNT ≈ 2.6 for one less disabled on mRS shift
DAWN	2018	6–24 h, clinical–core mismatch	49 % vs 13 %
DEFUSE-3	2018	6–16 h, perfusion mismatch	45 % vs 17 %
ATTENTION / BAOCHE	2022	Basilar occlusion	~46 % vs 23 % (mRS 0–3)
SELECT2 / ANGEL-ASPECT	2023	Large core	Shift towards better mRS

Procedure and peri-procedural care

Issue	Recommendation
Technique	Stent retriever, contact aspiration or combined — equivalent (ASTER, COMPASS); aim for eTICI 2b50–3 ; more passes → more harm
Anaesthesia	No firm preference. Older observational data favoured conscious sedation; RCTs (SIESTA, AnStroke, GOLIATH, AMETIS, CANVAS, SEGA) show GA at least as good. Choose locally; avoid delay and hypotension
Blood pressure after reperfusion	Avoid intensive lowering (SBP < 140/120) after successful reperfusion — worse outcome (ENCHANTED2/MT, BP-TARGET, OPTIMAL-BP); keep < 180/105
Time metrics	Door-to-groin < 60–90 min; transfer "drip-and-ship" vs "mothership" — no clear winner (RACECAT)

Key pearls. 0–6 h: CTA proving an LVO with a non-large core is enough. 6–24 h: imaging must show salvageable tissue (perfusion, DWI-clinical mismatch or good collaterals). Large core is no longer an exclusion. Bridging IVT still recommended. Do not drop BP aggressively after recanalisation.

Exam angles

- 74-year-old, NIHSS 18, M1 occlusion, onset 10 h, small core on CTP → **thrombectomy (DAWN/DEFUSE-3).**
- ASPECTS 4, M1 occlusion at 3 h → **thrombectomy is now reasonable (large-core trials).**
- Basilar occlusion, NIHSS 22 at 8 h → **thrombectomy (ATTENTION/BAOCHE).**
- After TICI 3 reperfusion, SBP 165 → **do not target < 140.**

Advances in Dementia with Lewy Bodies

2023

Core frameworks: McKeith et al., Fourth consensus report of the DLB consortium, *Neurology* 2017; McKeith et al., research criteria for prodromal DLB, *Neurology* 2020. **New since:** α -synuclein seed amplification assays (SAA), biological staging proposals (SynNeurGe, NSD 2024).

Epidemiology and pathology

- Second commonest neurodegenerative dementia after Alzheimer's ($\approx 5\text{--}10\%$ of dementia; likely underdiagnosed).
- Cortical and limbic Lewy bodies (α -synuclein); **co-pathology with Alzheimer's in $> 50\%$** – amyloid and tau worsen progression and blur the phenotype.
- **One-year rule:** dementia before or within a year of parkinsonism $\rightarrow$ DLB; after > 1 year of established PD $\rightarrow$ PDD.
- Early deficits: attention, executive, **visuospatial** (pentagon copying); memory relatively preserved early (unlike AD).

McKeith 2017 — diagnostic criteria

Essential: dementia.

Element	Content
Core clinical features	1. Fluctuating cognition with pronounced variations in attention and alertness. 2. Recurrent well-formed, detailed visual hallucinations. 3. REM sleep behaviour disorder (may precede dementia by years). 4. ≥ 1 spontaneous cardinal feature of parkinsonism (bradykinesia, rest tremor, rigidity)
Indicative biomarkers	Reduced basal ganglia DaT uptake (SPECT/PET); low uptake on ^{123}I -MIBG myocardial scintigraphy; PSG-confirmed REM sleep without atonia
Supportive clinical features	Severe antipsychotic sensitivity, postural instability, repeated falls, syncope, severe autonomic dysfunction, hypersomnia, hyposmia, hallucinations in other modalities, systematised delusions, apathy, anxiety, depression
Supportive biomarkers	Relative preservation of medial temporal lobes; generalised low perfusion/metabolism with reduced occipital activity $\pm$ cingulate island sign ; prominent posterior slow-wave EEG activity with periodic pre-alpha/theta fluctuations

Category	Requirement
Probable DLB	≥ 2 core features ($\pm$ biomarkers) or 1 core feature + ≥ 1 indicative biomarker
Possible DLB	1 core feature without indicative biomarkers or ≥ 1 indicative biomarker without core features
Caveat	Probable DLB should not be diagnosed on biomarkers alone; supportive features alone do not make possible DLB

Less likely DLB: another illness (e.g. cerebrovascular disease) sufficient to explain the picture, or parkinsonism appearing for the first time only at the stage of severe dementia.

Prodromal DLB (McKeith 2020 research criteria)

Three presentations precede dementia: **MCI-LB** (mild cognitive impairment with Lewy bodies), **delirium-onset**, and **psychiatric-onset** (late-onset depression, psychosis). Probable MCI-LB = MCI + ≥ 2 core features, or 1 core feature + ≥ 1 proposed biomarker.

Biomarkers — what each one tells you

Biomarker	Finding	Pearls
DaT-SPECT	Reduced striatal uptake ("full stop" rather than "comma")	Sensitivity ~80 %, specificity ~90 % vs AD. Normal in AD, FTD, vascular dementia, primary psychiatric disease. Abnormal in PD, MSA, PSP, CBD — it shows nigrostriatal loss, not Lewy pathology
MIBG cardiac scintigraphy	Low heart-to-mediastinum ratio	Postganglionic sympathetic denervation; confounded by diabetes, heart failure, some drugs; normal in MSA, PSP
PSG	REM sleep without atonia	Confirms RBD; isolated RBD → > 70 % phenoconvert to a synucleinopathy over 10–15 years
FDG-PET	Occipital hypometabolism with preserved posterior cingulate (cingulate island sign)	Distinguishes from AD (posterior cingulate reduced)
α-synuclein SAA (RT-QuIC) in CSF or skin	Detects misfolded α-synuclein seeds	Sensitivity ~90 % for Lewy body disease; not yet in the 2017 criteria; positive in prodromal disease
Skin biopsy	Phosphorylated α-synuclein in dermal nerves	Commercially available in some countries
AD biomarkers	Amyloid/tau positivity in ~50 %	Predicts faster decline; relevant for anti-amyloid eligibility (excluded in most trials)

Treatment

Symptom	First line	Notes
Cognition, fluctuations	Cholinesterase inhibitors — rivastigmine (McKeith 2000 RCT) or donepezil (licensed for DLB in Japan; RCTs 2012–2015)	Often help hallucinations and apathy too; watch bradycardia and syncope. (EXPRESS was rivastigmine in PDD , not DLB)
Add-on	Memantine	Modest global benefit
Visual hallucinations, psychosis	Review drugs (anticholinergics, agonists), ChEI first; if needed low-dose quetiapine or clozapine ; pimavanserin (US, PD psychosis)	Never haloperidol, risperidone, olanzapine
Parkinsonism	Low-dose levodopa, titrate slowly	Response less than in PD; agonists avoided (hallucinations)
RBD	Bedroom safety; melatonin 3–12 mg; clonazepam 0.25–1 mg (falls, sedation, OSA)	
Orthostatic hypotension	Non-drug measures, midodrine, fludrocortisone, droxidopa	Also contributes to fluctuations
Depression/anxiety	SSRIs, SNRIs, CBT	Avoid TCAs (anticholinergic)
Daytime sleepiness	Sleep hygiene; modafinil (limited data)	

Neuroleptic sensitivity. Up to half of DLB patients develop severe reactions to antipsychotics: abrupt parkinsonism, sedation, falls, autonomic instability, a neuroleptic malignant-like syndrome, and higher mortality. Emergency departments are where this happens — flag it in the notes. If unavoidable: quetiapine or clozapine at the lowest dose with monitoring.

DLB vs AD vs PDD at a glance

	DLB	AD	PDD
Early domain	Attention, visuospatial, executive	Episodic memory	Executive, attention
Hallucinations	Early, well formed	Late	Later, often drug-related

	DLB	AD	PDD
Parkinsonism	Within 1 year of dementia or after	Late	Precedes dementia by > 1 year
MTL atrophy	Relatively preserved	Marked	Mild
DaT-SPECT	Abnormal	Normal	Abnormal

Exam angles

- Fluctuating attention, visual hallucinations, mild parkinsonism, MMSE 22 → **probable DLB**; next test if uncertain → **DaT-SPECT**.
- Hallucinations only + abnormal DaT-SPECT → **probable DLB** (1 core + 1 indicative biomarker).
- Abnormal MIBG alone, no core features → **possible DLB**.
- Agitated DLB patient given haloperidol becomes rigid and febrile → **neuroleptic sensitivity**.

Neuromodulation for Drug-Resistant Epilepsy

2023

Frameworks: ILAE definition of drug resistance (Kwan 2010); EAN/ILAE-Europe guidance on neurostimulation; key trials: VNS E03/E05, **SANTE** (ANT-DBS), RNS pivotal trial and long-term follow-up, **ESTEL** (CM-DBS in Lennox–Gastaut, 2023).

Drug-resistant epilepsy

ILAE definition: failure of adequate trials of **two** tolerated, appropriately chosen and used antiseizure medication schedules (monotherapy or combination) to achieve sustained seizure freedom (≥ 12 months or three times the longest pre-treatment inter-seizure interval).

- About a third of people with epilepsy are drug-resistant.
- After two failed drugs, each further drug gives only a few per cent chance of seizure freedom (Kwan & Brodie 2000; ~5 % in later cohorts with each new drug, with some late remissions).
- **Refer to an epilepsy surgery centre after two failed drugs.** Resective surgery is potentially curative (Wiebe 2001: 58 % vs 8 % seizure-free at 1 year; ERSET; in children Dwivedi 2017: 77 % vs 7 %). Neuromodulation is **palliative** — for patients who are not surgical candidates, refuse surgery, or failed surgery.
- Exclude pseudo-resistance: wrong diagnosis (functional seizures, syncope), wrong drug, poor adherence, lifestyle triggers.

The devices

	VNS	RNS	ANT-DBS	CM-DBS
Target	Left cervical vagus nerve (left: fewer cardiac efferents)	1–2 seizure foci via depth/strip electrodes	Anterior nucleus of thalamus (Papez circuit)	Centromedian nucleus of thalamus
Stimulation	Open-loop, cyclic (e.g. 30 s on / 5 min off) + magnet; newer models detect ictal tachycardia	Closed-loop (responsive) — detects electrocorticographic onset and stimulates	Open-loop, cyclic	Open-loop
Indication	Focal or generalised DRE, any age (≥ 4 y in US; children with LGS)	Adults with focal DRE, 1–2 foci, including bilateral mesial temporal and eloquent cortex	Adults with focal DRE (licensed EU 2010, FDA 2018)	Generalised DRE — Lennox–Gastaut (ESTEL); off-label
Efficacy	~50 % responders at 2 years; improves with time; seizure freedom < 10 %	Median reduction 44 % at 1 y → ~75 % at 9 y	SANTE: 40 % vs 15 % at 3 months (blinded); 56 % at 2 y; 69 % at 5 y	ESTEL: fewer electrographic and diary seizures in a small RCT
Side effects	Hoarseness, cough, dyspnoea, throat pain during stimulation; worsens OSA	Implant infection, haemorrhage	Depression and memory complaints, paraesthesia, haemorrhage	Similar to DBS
Bonus	Antidepressant effect (approved for depression); no intracranial surgery	Records ECoG — lateralises bilateral MTLE, can reveal a resectable focus	Reduces SUDEP? unknown	—

Other options: trigeminal nerve stimulation (EU), transcranial DC stimulation (investigational), ketogenic and modified Atkins diets, corpus callosotomy for drop attacks, laser ablation (LITT).

VNS vs RNS vs DBS — how the exam separates them. VNS: oldest, least invasive, open-loop, works for generalised epilepsy, hoarseness. RNS: the only **closed-loop** system, intracranial, best for **two independent foci (bilateral MTLE)** or eloquent cortex, also a diagnostic tool. ANT-DBS: open-loop thalamic stimulation, SANTE trial, watch mood and memory. Benefit of all three grows over years.

Choosing

Scenario	Best choice
Unilateral MTLE with hippocampal sclerosis	Resection (or LITT) — not neuromodulation
Bilateral independent mesial temporal onset	RNS
Focus in eloquent (language/motor) cortex	RNS
Multifocal or poorly localised focal epilepsy	ANT-DBS or VNS
Lennox–Gastaut syndrome with drop attacks	VNS, callosotomy, CM-DBS; plus rufinamide, clobazam, cannabidiol, fenfluramine
Child with DRE and depression	VNS
Patient with severe depression or memory problems	Avoid ANT-DBS

Exam angles

- Two failed appropriate drugs → **refer for surgical evaluation** (not a third drug, not VNS straight away).
- Bilateral independent temporal seizures on video-EEG → **RNS**.
- Hoarseness only during stimulation cycles → **VNS**.
- ANT-DBS patient with new low mood → known adverse effect (SANTE).

EAN — Cluster Headache

2023

Source: May et al., EAN guideline on the treatment of cluster headache, *Eur J Neurol* 2023. **Diagnosis:** ICHD-3 (2018).

ICHD-3 diagnosis

- ≥ 5 attacks of **severe or very severe unilateral orbital, supraorbital and/or temporal pain** lasting **15–180 min** untreated.
- Either or both: ≥ 1 ipsilateral autonomic feature (conjunctival injection, lacrimation, nasal congestion, rhinorrhoea, eyelid oedema, forehead/facial sweating, miosis and/or ptosis) **and/or** a sense of restlessness or agitation.
- Frequency: **one every other day to 8 per day**.

Form	Definition	Share
Episodic	Bouts of 7 days–1 year separated by pain-free remissions of ≥ 3 months	~85–90 %
Chronic	Attacks for ≥ 1 year without remission, or remissions < 3 months	~10–15 %

Clinical colour. Men 3:1, onset 20–40, smokers; circadian (often 1–2 h after falling asleep — hypothalamus) and circannual timing; alcohol triggers attacks only during a bout; patients pace and rock (migraineurs lie still). MRI with pituitary views is recommended at diagnosis — pituitary tumours and other structural lesions can mimic TACs.

Acute treatment

Treatment	EAN strength	Details
100 % oxygen , 12–15 L/min via non-rebreather mask, 15 min	Strong	~78 % pain-free at 15 min vs 20 % with air (Cohen 2009); no side effects; can repeat
Sumatriptan 6 mg SC	Strong	Fastest and most effective drug; ~75 % relief at 15 min; max 2 injections/24 h
Zolmitriptan 5–10 mg nasal	Strong	When injections are not acceptable
Sumatriptan 20 mg nasal	Weak	Less effective than SC
Non-invasive vagus nerve stimulation	Weak	Episodic cluster only (ACT1, ACT2)
Intranasal lidocaine	Weak	Adjunct
Oral triptans, paracetamol, NSAIDs, opioids	Not recommended	Too slow

Transitional (bridging) treatment

Started together with the preventive and stopped once it works.

Treatment	Evidence
Oral prednisolone — e.g. 100 mg for 5 days then taper over ~2 weeks	PredCH RCT (2021): fewer attacks in the first week
Greater occipital nerve block (steroid ± local anaesthetic), ipsilateral	RCTs; effect within days, lasts weeks

Prevention

Drug	EAN position	Practical points
Verapamil	First line (episodic and chronic)	Start 240 mg/day; increase by 80 mg every 1–2 weeks up to 480–960 mg/day. ECG before and with each increase (PR prolongation, heart block); constipation, oedema
Lithium	Second line, mainly chronic	Levels 0.6–1.0 mmol/L; renal and thyroid monitoring; tremor
Topiramate	Second line	Cognitive slowing, paraesthesia, stones
Galcanezumab 300 mg SC monthly (3 × 100 mg)	Recommended for episodic cluster	Approved for episodic CH in the US; not effective in chronic CH (RCT negative); not licensed for CH by the EMA
Melatonin 10 mg	Weak	Low risk add-on
Warfarin, methysergide, candesartan	Limited data	Methysergide withdrawn in many countries (fibrosis)

Refractory chronic cluster headache

Option	Notes
Occipital nerve stimulation	~60 % respond (ICON); first neurostimulation choice
Sphenopalatine ganglion stimulation	Acute and preventive effect
Hypothalamic (posterior) DBS	Small series; risk of haemorrhage — last resort

Cluster in one line each. Acute: oxygen + SC sumatriptan. Bridge: prednisolone or GON block. Prevention: verapamil with ECGs. Galcanezumab: episodic only. **Indomethacin is for paroxysmal hemicrania and hemicrania continua, not cluster.** Lithium for chronic.

Differential diagnosis of short unilateral headaches

	Cluster	Paroxysmal hemicrania	SUNCT/SUNA	Trigeminal neuralgia
Duration	15–180 min	2–30 min	1–600 s	< 1 s – 2 min
Frequency	1 every other day – 8/day	> 5/day	≥ 1/day, often hundreds	Many
Autonomic	Prominent	Prominent	Prominent (SUNCT: injection + tearing)	Minimal
Triggers	Alcohol in bout	Neck movement	Cutaneous triggers, no refractory period	Cutaneous triggers, refractory period
Treatment	O ₂ , triptan, verapamil	Indomethacin (absolute)	Lamotrigine, IV lidocaine	Carbamazepine

Exam angles

- 35-year-old man, nightly 45-min orbital attacks with tearing, paces the room → **oxygen 100 % 12–15 L/min** acutely, **verapamil** for prevention, **ECG**.
- 20-min attacks 12 times a day in a woman, autonomic features → **indomethacin trial** (paroxysmal hemicrania).
- Chronic cluster refractory to verapamil and lithium → **occipital nerve stimulation**.
- Galcanezumab in chronic cluster → **not effective**.

EAN — Palliative Care in Multiple Sclerosis

2020

Source: Solari et al., EAN guideline on palliative care of people with severe, progressive multiple sclerosis, *Eur J Neurol* 2020. Target population: people with severe, progressive MS (typically EDSS $\geq$ 6–9.5) and high symptom burden.

What the guideline is about

Palliative care is **not end-of-life care only**. It is a multidisciplinary approach to quality of life for people with severe, progressive MS and their families, given **alongside** disease-specific care. The guideline answered 10 questions; its recommendations are mostly **weak, based on low-quality evidence**, but the direction is consistent.

Domain	Recommendation (paraphrased)
Referral	Offer referral to home-based or specialist palliative care to people with severe MS and complex needs (unrelieved symptoms, complex decision-making, psychosocial distress)
Communication	Discuss advance care planning early — while capacity and communication are preserved — and repeat it (ventilation, gastrostomy, resuscitation, place of care)
Multidisciplinary care	Combine MS specialist, rehabilitation and palliative care teams
Symptom management	Address pain, spasticity, fatigue, bladder/bowel, dysphagia, depression, cognitive impairment, pressure ulcers
Caregivers	Assess and support carers' needs; respite
Staff	Train MS and palliative care staff in each other's expertise
Wish for hastened death	Explore the reasons (unrelieved symptoms, depression, fear of burden) rather than avoiding the topic

Symptom management — high yield

Symptom	Treatment	Notes
Spasticity	Stretching, physiotherapy; baclofen, tizanidine, gabapentin, dantrolene; nabiximols oromucosal spray as add-on for moderate–severe spasticity not responding to oral drugs; botulinum toxin for focal problems; intrathecal baclofen pump for severe generalised spasticity, especially lower limbs	Nabiximols: 4-week trial, continue only if $\geq$ 20 % improvement. Abrupt intrathecal baclofen withdrawal is life-threatening (fever, rigidity, rhabdomyolysis)
Pain	Neuropathic: gabapentin, pregabalin, duloxetine, TCAs; carbamazepine or oxcarbazepine for trigeminal neuralgia (MS TN is often bilateral, younger); musculoskeletal: physiotherapy, posture, analgesics	Lhermitte's and painful tonic spasms respond to sodium-channel blockers
Fatigue	Exercise, energy conservation, CBT ; cooling; treat sleep disorders, depression, anaemia, drug effects	Amantadine, modafinil and methylphenidate were no better than placebo in TRIUMPHANT-MS (2021)
Bladder	Overactive: antimuscarinics (watch cognition), mirabegron, desmopressin for nocturia, intravesical botulinum toxin ; retention/incomplete emptying (PVR > 100 mL): clean intermittent self-catheterisation; suprapubic catheter late	Treat UTIs — they trigger pseudo-relapses
Bowel	Diet, fluids, laxatives, transanal irrigation	Constipation commoner than incontinence
Dysphagia	Speech and language assessment, texture modification; gastrostomy discussed early	Aspiration pneumonia is a leading cause of death

Symptom	Treatment	Notes
Depression	SSRIs, SNRIs, CBT	Suicide risk higher than general population
Pseudobulbar affect	Dextromethorphan–quinidine (US), SSRIs, TCAs	
Cognition	Rehabilitation; no drug proven	
Pressure ulcers	Positioning, mattresses, nutrition	
Sexual dysfunction	PDE5 inhibitors, counselling	

When disease-modifying therapy stops

DMTs have little or no effect on progression in advanced, non-active, progressive disease; stopping can be discussed in older patients (> 55–60) with no relapses or MRI activity for years (DISCOMS 2023: discontinuation in > 55s was not clearly non-inferior for MRI activity, but differences were small). Decisions belong in the ACP conversation.

Exam frame. Palliative care in MS = **early, concurrent** with MS care, **home-based** when possible, **ACP** before crises, and **carers** count. Evidence is weak – expect questions on principles, nabiximols and intrathecal baclofen rather than numbers.

Exam angles

- Wheelchair-bound MS patient with recurrent aspiration and weight loss → **advance care planning including gastrostomy**, speech therapy.
- Severe bilateral leg spasticity despite oral baclofen and tizanidine → **intrathecal baclofen** (or nabiximols trial).
- Fatigue in MS: best-evidence intervention → **exercise / CBT**, not amantadine.
- Patient asks about hastening death → **explore reasons, treat depression and symptoms, involve palliative team**.

Advances in Neurosyphilis

2023

Read with: CDC STI treatment guidelines (2021), European (IUSTI) syphilis guideline (2020), WHO syphilis guidance. Neurosyphilis is rising again with the syphilis resurgence (MSM, HIV co-infection).

Key concept

Treponema pallidum invades the CNS **early** — within weeks of infection in many patients. Neurosyphilis can therefore occur **at any stage**, not only decades later. Early forms are meningeal and vascular; late forms are parenchymal.

Clinical forms

Form	Timing after infection	Features
Asymptomatic	Any	CSF abnormal, no symptoms — treat as neurosyphilis
Syphilitic meningitis	< 1–2 years	Headache, meningism, cranial neuropathies (VIII, VII, II, VI) , hydrocephalus
Meningovascular	1–10 years (peak ~5–7)	Stroke in a young adult — endarteritis (Heubner's) of medium/large arteries, often MCA or basilar; prodromal headache, personality change
General paresis	10–25 years	Progressive dementia, psychosis, mania, grandiosity, personality change; dysarthria, tremor, seizures; Argyll Robertson pupils; frontal and temporal atrophy
Tabes dorsalis	15–30 years	Lightning pains, sensory ataxia, positive Romberg, areflexia, Charcot joints, bladder dysfunction, visceral crises, Argyll Robertson pupils
Gummatous	Late	Mass lesion — rare
Ocular syphilis	Any stage	Uveitis (posterior/panuveitis), retinitis, optic neuritis, papillitis
Otosyphilis	Any stage	Sensorineural hearing loss, tinnitus, vertigo
Syphilitic myelitis, amyotrophy	Rare	

Argyll Robertson pupils: small, irregular, often bilateral; **react to near (accommodate) but not to light** (light–near dissociation). Lesion in the rostral midbrain near the pretectal nuclei sparing the more ventral near-response fibres. Other light–near dissociation: Adie's pupil (large), dorsal midbrain (Parinaud) syndrome, diabetes, severe optic neuropathy.

Diagnosis

Test	Interpretation
Serum non-treponemal (RPR, VDRL)	Activity marker; titres fall with treatment; can be negative in late neurosyphilis ; prozone effect with very high titres
Serum treponemal (TPPA, FTA-ABS, EIA/CLIA)	Usually positive for life. Many labs now screen with treponemal tests first (reverse algorithm)
CSF-VDRL	Highly specific (a positive confirms neurosyphilis without blood contamination), insensitive (30–70 %)
CSF FTA-ABS / TPPA	Sensitive, less specific — a negative result makes neurosyphilis unlikely
CSF white cells and protein	> 5 cells/μL (> 20 in HIV on ART is more specific) and raised protein support the diagnosis

Test	Interpretation
CSF CXCL13	Raised in neurosyphilis; helpful when CSF-VDRL is negative, especially in HIV — promising, not standard
Imaging	Meningovascular: infarcts, arterial stenosis; general paresis: atrophy, mesial temporal T2 change (can mimic HSV encephalitis)

Who needs LP? Any neurological, ocular or otological symptom in a person with syphilis; treatment failure; some guidelines add HIV with low CD4 or high RPR titre. **Ocular and otosyphilis are treated as neurosyphilis regardless of CSF** (CSF may be normal).

Treatment

Scenario	Regimen
Neurosyphilis, ocular and otosyphilis — first line	Aqueous benzylpenicillin 18–24 MU/day (3–4 MU IV every 4 h, or continuous infusion) for 10–14 days
Alternative	Procaine penicillin 2.4 MU IM daily plus probenecid 500 mg orally four times daily , 10–14 days
Penicillin allergy	Ceftriaxone 2 g IV/IM daily for 10–14 days , or desensitisation (preferred in pregnancy)
HIV co-infection	Same regimen
After the course	Some give benzathine penicillin 2.4 MU IM weekly × 1–3 to cover the late-latent duration
Jarisch–Herxheimer reaction	Fever, rigors, headache, worsening of symptoms within 24 h — continue treatment , antipyretics; prednisolone sometimes used for ocular or cardiovascular disease

Follow-up

- Serum RPR at 3, 6, 12 and 24 months: a **four-fold fall (two dilutions)** indicates response.
- CDC 2021: repeat LP **not required** in immunocompetent patients and in people with HIV on ART who show clinical and serological response. Repeat LP (every 6 months until normal) if response is inadequate.
- Retreat if CSF cell count has not fallen at 6 months or is not normal by 2 years.
- Test for HIV, hepatitis B/C; notify and treat partners.

"The great imitator" in neurology. Think syphilis in: young stroke, subacute dementia or psychosis, sudden bilateral hearing loss, uveitis with headache, cranial neuropathies with lymphocytic meningitis, and sensory ataxia with lightning pains. Test serum treponemal antibodies — cheap and decisive.

Exam angles

- 32-year-old man with a left MCA infarct, no vascular risk factors, CSF lymphocytosis → **meningovascular syphilis**; IV penicillin 10–14 days.
- Panuveitis with positive syphilis serology and normal CSF → **treat as neurosyphilis**.
- Positive CSF-VDRL → **confirms** neurosyphilis; negative CSF FTA-ABS → **argues strongly against** it.
- Fever and worse headache 6 h after the first penicillin dose → **Jarisch–Herxheimer**; **continue penicillin**.

Neuropsychiatry of Parkinson's Disease

2022

Read with: MDS evidence-based review of treatments for non-motor symptoms (Seppi 2019); MDS criteria for PD dementia (Emre 2007) and PD-MCI (Litvan 2012); MDS PD psychosis criteria (Ravina 2007).

Prevalence and approach

Neuropsychiatric symptoms drive disability, carer burden and nursing-home placement more than motor signs in later disease. Many are **dopamine-related** (agonists, levodopa timing), so the first step is always a **medication review and correlation with on/off states**.

Condition	Prevalence	First-line treatment	Notes
Depression	30–40 %	SSRIs or SNRIs (venlafaxine and paroxetine — SAD-PD 2012), nortriptyline; CBT	Pramipexole has an antidepressant effect in PD (Barone 2010). Check for off-period depression
Anxiety	25–40 %	Optimise dopaminergic therapy if off-related; SSRIs/SNRIs, CBT	Panic during off periods is common
Apathy	~40 %	No established drug; rivastigmine reduced apathy in one RCT (STEAD); exercise, structured activity	Often after STN-DBS with too-rapid drug reduction
Psychosis (illusions, presence and passage hallucinations → visual hallucinations → delusions)	25–50 % over the disease course	Reduce drugs (hierarchy below); clozapine (best evidence) or quetiapine (most used, weaker evidence); pimavanserin (5-HT _{2A} inverse agonist; US)	Never haloperidol, risperidone, olanzapine . Cholinesterase inhibitors help when dementia coexists
Impulse control disorders	~14 % on agonists (DOMINION)	Reduce or stop the dopamine agonist , substitute levodopa	Gambling, hypersexuality, compulsive buying, binge eating; risk factors: young, male, prior addiction, novelty seeking
Dopamine dysregulation syndrome	3–4 %	Restrict levodopa, supervise dosing	Compulsive levodopa overuse, often with dyskinesia
Punding	Variable	Reduce dopaminergic drugs	Repetitive purposeless tasks
Dopamine agonist withdrawal syndrome	15–20 % of those tapering for ICD	Slow taper; may need to restart at low dose	Anxiety, panic, dysphoria, pain — does not respond to levodopa
PD-MCI	~25–30 % at diagnosis	Exercise, cognitive training	
PD dementia	~50 % at 10 years, ~80 % at 20 years (Sydney cohort)	Rivastigmine (only licensed ChEI for PDD — EXPRESS 2004) ; donepezil off-label; memantine limited	Risk: older age, postural-instability gait type, hallucinations, RBD, posterior cortical deficits (CamPaIGN)
RBD	30–50 %	Bedroom safety; melatonin ; clonazepam	Prodromal marker; associated with faster cognitive decline
Sleep attacks, excessive sleepiness	Common	Reduce agonists; modafinil	Driving advice

Psychosis — the drug-reduction hierarchy

Exclude delirium first (infection, dehydration, constipation, urinary retention, new drugs).

1. Stop **anticholinergics** (trihexyphenidyl), then **amantadine**.

2. Stop **MAO-B inhibitors** and **dopamine agonists**.
3. Stop **COMT inhibitors**.
4. Reduce **levodopa** to the lowest dose tolerated by motor function.
5. If psychosis persists: **clozapine** 6.25–50 mg (neutrophil monitoring, myocarditis, hypersalivation) or **quetiapine** 12.5–100 mg; pimavanserin where licensed. Add a cholinesterase inhibitor if cognitive impairment.

Depression vs apathy vs dementia

	Depression	Apathy	Dementia
Core	Sadness, guilt, hopelessness	Loss of motivation without sadness	Cognitive decline affecting function
Insight	Distressed	Indifferent	Variable
Treatment	SSRI/SNRI, CBT	Activity, ± rivastigmine	ChEI

Neuropsychiatric effects of DBS

STN-DBS can cause **hypomania, impulsivity, apathy** (often after medication reduction) and has been associated with suicide risk in the first year — screen preoperatively and follow up mood. GPi-DBS is more psychiatrically neutral (see Paper 20).

Psychosis pearl. "Clozapine has the best evidence, quetiapine is used most, haloperidol never." **ICD pearl.** "Agonist-specific: stop the agonist, give levodopa, watch for DAWS."

Exam angles

- Gambling debts in a 52-year-old on ropinirole → **taper ropinirole, replace with levodopa**.
- Visual hallucinations in a PD patient on levodopa, ropinirole, amantadine and trihexyphenidyl → **stop trihexyphenidyl first**.
- PDD needing a cholinesterase inhibitor → **rivastigmine (licensed)**.
- PD depression trial evidence → **venlafaxine and paroxetine (SAD-PD); pramipexole**.

Coma, Disorders of Consciousness and Post-Cardiac Arrest Prognostication

2020–2021

Sources: Kondziella et al., [EAN guideline on the diagnosis of coma and other disorders of consciousness](#), *Eur J Neurol* 2020. Nolan et al., [ERC–ESICM guidelines on post-resuscitation care](#), 2021 (prognostication algorithm; a 2025 ERC update has been published — check for changes). Background: TTM2 (2021).

Disorders of consciousness — definitions

State	Arousal	Awareness	Key features
Coma	Absent	Absent	Eyes closed, no sleep–wake cycles, no response to stimuli
Unresponsive wakefulness syndrome (vegetative state)	Present	Absent	Eyes open, sleep–wake cycles, reflexive behaviour only
MCS– (minus)	Present	Inconsistent	Visual pursuit/fixation, localisation to pain, automatic motor responses, appropriate emotional responses
MCS+ (plus)	Present	Inconsistent	Command following , intelligible words, intentional communication
Emergence from MCS	Present	Consistent	Reliable functional communication or functional object use
Locked-in syndrome	Present	Full	Quadriplegia, anarthria; vertical eye movements and blinking preserved (ventral pons) — <i>not</i> a DOC
Cognitive–motor dissociation	Present	Covert	No behavioural response, but command-following on fMRI or EEG paradigms

EAN 2020 recommendations (diagnosis of DOC)

Area	Recommendation
Behavioural assessment	Use a standardised scale — CRS-R (Coma Recovery Scale–Revised) preferred; repeat at least 5 times over a short period (misdiagnosis of UWS ≈ 40 % on single bedside assessment); FOUR score in the ICU
Specific signs	Test visual pursuit with a mirror , command following, eye-blink to threat, automatic motor responses; treat pain and sedation confounders
EEG	Standard EEG; sleep patterns, reactivity, and high-density EEG with active paradigms where available
Imaging	Resting-state and task-based fMRI to detect covert awareness
FDG-PET	Preserved cortical metabolism suggests MCS — strong recommendation for use where available
TMS-EEG	Perturbational complexity index separates UWS from MCS
Principle	Multimodal ; a patient is classified by the highest level of consciousness found on any test

Post-cardiac arrest — temperature control

TTM2 (2021): targeting 33 °C was not better than normothermia with active **fever prevention** (≤ 37.7 °C) for 72 h. ERC–ESICM 2021 and later: monitor core temperature and **prevent fever for at least 72 h**; the case for 32–36 °C has weakened.

Post-cardiac arrest prognostication (ERC–ESICM 2021)

Prerequisites: ≥ 72 h after ROSC, sedation and paralysis excluded, comatose with **GCS motor** ≤ 3 . Then poor outcome is **likely** if ≥ 2 of the following are present:

Predictor	Timing	Threshold for poor outcome
Pupillary and corneal reflexes	≥ 72 h	Bilaterally absent (quantitative pupillometry: NPi ≤ 2 or 0 % constriction)
SSEP	≥ 24 h	Bilaterally absent N20 cortical responses
EEG	> 24 h	Highly malignant pattern: suppressed background $\pm$ periodic discharges, or burst-suppression
NSE	48 h and/or 72 h	> 60 $\mu\text{g/L}$ (and rising)
Status myoclonus	≤ 72 h	Generalised, continuous ≥ 30 min
CT / MRI	CT ~ 2 h–3 days; MRI 2–5 days	Diffuse anoxic injury — loss of grey–white differentiation (low GWR); widespread DWI restriction

If the criteria are not met, outcome is **indeterminate** $\rightarrow$ observe and re-evaluate. Favourable signs: continuous normal-voltage reactive EEG within 24 h, NSE < 17 $\mu\text{g/L}$, limited DWI change.

Non-negotiables. No prognostication before **72 h** and before sedation has cleared. **No single test** decides. **Self-fulfilling prophecy** — withdrawal of life-sustaining therapy on early, unimodal data is the biggest source of error. Absent N20 is the most specific single test but bilateral presence does not predict good outcome.

Myoclonus after cardiac arrest

Type	Features	Prognosis
Status myoclonus (early, generalised, continuous)	Within 72 h, often with burst-suppression	Usually poor — but check EEG
Lance–Adams syndrome	Action myoclonus after awakening, days–weeks later	Good cognitive recovery possible; treat with levetiracetam, valproate, clonazepam

Brain death

See the core review: 2023 AAN/AAP/CNS/SCCM consensus (apnoea test: pH < 7.30 **and** PaCO₂ ≥ 60 **and** ≥ 20 above baseline; ancillary tests are blood-flow studies); national laws apply.

Exam angles

- Patient opens eyes, has sleep–wake cycles, inconsistently tracks a mirror $\rightarrow$ **MCS–**.
- Follows commands only on fMRI $\rightarrow$ **cognitive–motor dissociation**.
- Day 4 after arrest, off sedation, M1, bilaterally absent N20 and NSE 85 $\mu\text{g/L}$ at 48 h $\rightarrow$ **poor outcome likely (2 predictors)**.
- Day 2, off sedation, absent pupils $\rightarrow$ **too early; repeat at ≥ 72 h**.

Traumatic Brain Injury — The First Post-Traumatic Hours

2023

Frameworks: Brain Trauma Foundation (BTF) 4th edition (2016); **SIBICC** tiered ICP algorithm (2019) and SIBICC brain-oxygen algorithm; CRASH-2/3, DECRA, RESCUEicp, RESCUE-ASDH, POLAR, Eurotherm3235; NICE head-injury guideline (2023).

Severity

Severity	GCS (post-resuscitation)	Typical markers
Mild	13–15	LOC < 30 min, post-traumatic amnesia < 24 h
Moderate	9–12	LOC 30 min–24 h
Severe	3–8	Secure the airway; ICP monitoring if CT abnormal

GCS should be recorded with components and pupils (GCS-P = GCS minus pupil reactivity score).

The first hours — preventing secondary injury

Parameter	Target	Why
Airway	Intubate if GCS $\leq$ 8, airway compromise, seizures, agitation preventing care	
SBP	$\geq$ 100 mmHg (age 50–69); $\geq$ 110 mmHg (15–49 or $\geq$ 70) (BTF)	A single episode of hypotension roughly doubles mortality
Oxygenation	SpO ₂ > 94 %, PaO ₂ > 60 mmHg (avoid hyperoxia)	Hypoxia worsens outcome
PaCO₂	35–45 mmHg ; brief hyperventilation only for herniation as a bridge	Hyperventilation causes vasoconstriction and ischaemia
Sodium	140–150 mmol/L	Hyponatraemia worsens oedema
Glucose	~6–10 mmol/L	Both extremes harmful
Temperature	Normothermia, avoid fever	Prophylactic hypothermia not recommended (POLAR); hypothermia for ICP worse (Eurotherm3235)
Haemoglobin	Individualise between 7 and 10 g/dL	TRAIN (2023) favoured a liberal threshold in acute brain injury; HEMOTION (2025) found no significant difference in TBI
Coagulation	Correct coagulopathy; reverse anticoagulants	
Tranexamic acid	1 g IV within 3 h (over 10 min, then 1 g over 8 h)	CRASH-3 (2019): reduced head-injury death in mild–moderate TBI when given early
Steroids	Contraindicated	CRASH (2004): increased mortality
Seizure prophylaxis	Levetiracetam or phenytoin for 7 days in severe TBI	Prevents early seizures only; not late epilepsy
Imaging	Immediate CT for GCS < 13, or any NICE/Canadian CT head rule criterion; CT within 8 h for anticoagulated patients even without other features	

ICP and CPP

	Target
ICP	Treat > 22 mmHg (BTF 2016)
CPP	60–70 mmHg (< 60 ischaemia; > 70 risk of ARDS)
PbtO ₂ (if monitored)	> 20 mmHg

ICP monitoring indications (BTF): severe TBI with abnormal CT; or normal CT with ≥ 2 of age > 40, motor posturing, SBP < 90 mmHg. BEST-TRIP (2012) showed protocolised imaging/exam care was not inferior to ICP-guided care in Bolivia/Ecuador — but monitoring remains standard in high-income settings.

SIBICC tiered management of raised ICP

Tier	Measures
0 (basic)	Head of bed 30–45°, neck neutral, analgesia and sedation, normothermia, PaCO ₂ 35–45, SpO ₂ $\geq$ 94 %, Na 140–150, CPP $\geq$ 60, seizure prophylaxis
1	Deeper sedation/analgesia, intermittent osmotherapy (mannitol 0.25–1 g/kg or hypertonic saline), CSF drainage via EVD, CPP 60–70, PaCO ₂ low-normal (35–38), EEG if seizures suspected
2	Mild hypocapnia (PaCO ₂ 32–35), neuromuscular blockade trial , MAP challenge to assess autoregulation and raise CPP if appropriate
3 (rescue)	Barbiturate (pentobarbital) coma, secondary decompressive craniectomy , mild hypothermia (35–36 °C)

Not recommended: routine hyperventilation < 30 mmHg, steroids, prophylactic hypothermia, high-dose mannitol (> 1 g/kg).

Decompressive craniectomy — the trials

Trial	Population	Result
DECRA (2011)	Diffuse TBI, early, ICP > 20 for 15 min despite tier 1	Lower ICP, shorter ICU stay, worse functional outcome at 6 months
RESCUEicp (2016)	Refractory ICP > 25 despite tier 1–2, last-tier DC	Mortality 27 % vs 49 % , but more survivors in vegetative state or severe disability; at 12 months more upper severe disability or better
RESCUE-ASDH (2023)	Acute subdural haematoma evacuation — craniotomy vs primary craniectomy	Similar 12-month outcome ; more reoperation after craniotomy, more wound complications after craniectomy

Bottom line on DC. It saves lives when ICP is truly refractory, but more survivors are severely disabled. Use as a **last tier** and discuss expected quality of life with the family.

Other first-hours points

- **Herniation signs** (unilateral fixed dilated pupil, extensor posturing): hyperosmolar bolus, brief hyperventilation, urgent CT and neurosurgery.
- **Extradural haematoma:** lucid interval, biconvex, middle meningeal artery; evacuate if > 30 mL regardless of GCS.
- **Acute subdural:** crescentic, bridging veins; evacuate if > 10 mm thick or midline shift > 5 mm.
- **Paroxysmal sympathetic hyperactivity:** tachycardia, hypertension, fever, sweating, posturing — propranolol, gabapentin, opioids, clonidine.
- **Blood biomarkers:** GFAP and UCH-L1 within 12 h can rule out CT lesions in mild TBI (FDA-cleared tests).

Exam angles

- Severe TBI, ICP 26 despite sedation and osmotherapy → escalate tier (EVD, NMB trial) before **craniectomy/barbiturates**.
- Mild–moderate TBI within 3 h → **tranexamic acid** (CRASH-3).
- Steroids for TBI → **no (CRASH)**.
- Early DC for diffuse injury with ICP 21 → **DECRA: worse function**.

Neurological Complications of Vasculitis

2022

Frameworks: Chapel Hill Consensus nomenclature (2012); ACR/EULAR 2022 classification criteria (GCA, Takayasu, GPA, MPA, EGPA); EULAR 2018/2023 management recommendations for large-vessel and ANCA vasculitis.

Classification and neurological pattern

Vessel size	Disease	Neurological presentations	Key tests
Large	Giant cell arteritis	Headache, scalp tenderness, jaw claudication, arteritic AION , CRAO, diplopia, vertebrobasilar stroke	ESR/CRP, temporal artery ultrasound (halo, compression sign), biopsy, PET-CT
Large	Takayasu arteritis	Young women; arm claudication, pulse/BP asymmetry, carotidynia, subclavian steal, stroke, TIA	CTA/MRA of aorta and branches
Medium	Polyarteritis nodosa	Mononeuritis multiplex (commonest neurological feature), symmetric neuropathy; stroke rare	ANCA-negative; HBV association; angiography (microaneurysms), nerve/muscle biopsy
Medium	Kawasaki	Children; aseptic meningitis, irritability	
Small, ANCA	GPA (PR3-ANCA)	Hypertrophic pachymeningitis , cranial neuropathies (from sinus/orbit/mastoid extension), pituitary involvement (diabetes insipidus), mononeuritis multiplex	PR3-ANCA, biopsy
Small, ANCA	MPA (MPO-ANCA)	Mononeuritis multiplex, polyneuropathy; ICH/infarcts rare	MPO-ANCA
Small, ANCA	EGPA (MPO-ANCA in ~40 %)	Mononeuritis multiplex in ~70 % — asthma, eosinophilia, sinusitis	Eosinophils, MPO-ANCA
Small, immune complex	Cryoglobulinaemic (HCV), IgA vasculitis	Painful neuropathy	Cryoglobulins, complement
Variable	Behçet's	Parenchymal: brainstem–diencephalic lesions (meso-diencephalic junction), headache, pyramidal signs; non-parenchymal: cerebral venous thrombosis , intracranial hypertension	Clinical (oral/genital ulcers, uveitis, pathergy); HLA-B51
Single organ	Primary angiitis of the CNS (PACNS)	Subacute headache, cognitive decline, multifocal infarcts, seizures; CSF pleocytosis and raised protein (~90 %)	Biopsy (leptomeningeal + cortical) is the gold standard; angiography insensitive for small-vessel disease and non-specific (RCS mimics)
Secondary	SLE, Sjögren's, RA, sarcoidosis (granulomatous, not vasculitis)	SLE: seizures, psychosis, stroke (APS), chorea; Sjögren's: sensory ganglionopathy ; sarcoid: facial palsy, pachymeningitis, hypothalamic	

Mononeuritis multiplex — the vasculitic neuropathy

- Painful, stepwise, asymmetric; commonest nerves: **common peroneal (foot drop)**, ulnar, median, tibial.
- Becomes "overlapping" and can mimic symmetric neuropathy late.
- NCS: axonal, multifocal; **combined nerve and muscle biopsy (superficial peroneal + peroneus brevis)** increases yield.

- Non-systemic vasculitic neuropathy: vasculitis confined to nerves — steroids ± cyclophosphamide/methotrexate.

GCA — exam essentials

- Age > 50, raised ESR/CRP in > 95 %.
- **Start prednisolone 40–60 mg immediately** on suspicion; with visual loss or stroke: **IV methylprednisolone 500–1000 mg for 3 days**, then oral.
- **Temporal artery ultrasound** is the first imaging test in EULAR 2023 recommendations (halo sign); biopsy (≥ 1–2 cm; skip lesions) remains positive for ~2 weeks after steroids.
- **Tocilizumab** (IL-6 receptor antagonist; GACTA 2017; licensed 2017) is steroid-sparing — first choice for relapsing or high-risk patients. Methotrexate is an alternative.
- Aspirin is not routinely recommended unless there is another indication.
- Arteritic AION: chalk-white disc swelling, profound visual loss; the other eye is at risk within days.

PACNS vs RCVS — the commonest exam confusion

	PACNS	RCVS
Onset	Subacute, insidious headache	Recurrent thunderclap headaches
Triggers	None	Postpartum, serotonergic/vasoactive drugs, cannabis
CSF	Abnormal (pleocytosis, protein)	Normal or near-normal
Angiography	May be normal (small vessels) or irregular	"String of beads", reverses within 12 weeks
Imaging	Multifocal infarcts of different ages, enhancing lesions	Convexity SAH, PRES, watershed infarcts, ICH
Treatment	Steroids + cyclophosphamide/rituximab	Remove trigger, calcium-channel blocker (nimodipine) ; avoid steroids (worse outcome)

Treatment of systemic vasculitis with neurological involvement

Disease	Induction	Maintenance
GPA/MPA with organ-threatening disease	Glucocorticoids + rituximab or cyclophosphamide; avacopan allows lower steroid doses (ADVOCATE 2021)	Rituximab
EGPA	Steroids; cyclophosphamide or rituximab if severe; mepolizumab for relapsing/refractory non-severe	Mepolizumab, azathioprine
PAN (non-HBV)	Steroids ± cyclophosphamide	Azathioprine/methotrexate
HBV-PAN	Antivirals + short steroids + plasma exchange	
Neuro-Behçet's parenchymal	High-dose steroids + azathioprine; infliximab for severe/refractory; avoid ciclosporin (neurotoxic)	
PACNS	Steroids + cyclophosphamide (or rituximab)	Azathioprine, mycophenolate, methotrexate

Exam angles

- Asthma, eosinophilia 15 %, painful foot drop then wrist drop → **EGPA mononeuritis multiplex**.
- Chronic sinusitis, cranial neuropathies, thick enhancing dura → **GPA pachymeningitis**.
- Young man with oral ulcers, brainstem lesion extending to the diencephalon → **neuro-Behçet's** — avoid ciclosporin.
- Postpartum thunderclap headaches with beaded arteries → **RCVS, not vasculitis — no steroids**.

EAN/PNS — CIDP Guideline (Second Revision)

2021

Source: Van den Bergh et al., European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy — second revision, *Eur J Neurol / J Peripher Nerv Syst* 2021.
Treatment updates since: ADHERE (efgartigimod, 2024).

Correction to the old digest. The 2021 guideline **abolished "definite" and "probable" CIDP**. There are only two diagnostic levels: **CIDP** and **possible CIDP**. It also **removed** anti-MAG neuropathy and the nodal/paranodal antibody neuropathies (**autoimmune nodopathies**) from the CIDP spectrum.

Clinical criteria

Phenotype	Definition
Typical CIDP	Progressive or relapsing, symmetric, proximal and distal muscle weakness of upper and lower limbs, and sensory involvement of ≥ 2 limbs; developing over ≥ 8 weeks ; absent or reduced reflexes in all limbs
CIDP variants	Distal CIDP (distal sensory loss and weakness predominantly in lower limbs — formerly DADS without anti-MAG); multifocal CIDP (Lewis–Sumner / MADSAM — asymmetric, upper limbs first); focal CIDP (one limb or plexus); motor CIDP (steroids may worsen it — IVIG first); sensory CIDP (sensory ataxia; may have motor NCS abnormalities)

Electrodiagnostic criteria (motor conduction)

Strongly supportive of demyelination — any of the following in ≥ 2 nerves (CIDP) or 1 nerve (possible CIDP):

- Distal motor latency prolongation ≥ 50 % above ULN
- Motor conduction velocity slowing ≥ 30 % below LLN
- F-wave latency prolongation ≥ 20 % above ULN (≥ 50 % if distal CMAP < 80 % LLN), or absent F-waves in ≥ 2 nerves plus one other demyelinating parameter
- **Motor conduction block:** ≥ 30 % proximal-to-distal CMAP amplitude reduction (distal CMAP ≥ 20 % LLN)
- Abnormal temporal dispersion (> 30 % duration increase)
- Distal CMAP duration prolongation

Sensory conduction abnormalities in ≥ 2 nerves are required for typical CIDP (except the motor variant).

Supportive criteria

Supportive criterion	Notes
CSF protein raised with cells $< 10/\mu\text{L}$	Normal protein does not exclude; age-adjusted upper limits (e.g. ~ 0.6 g/L over 50)
MRI	Gadolinium enhancement and/or hypertrophy of cauda equina, lumbosacral or cervical roots, brachial or lumbosacral plexus
Nerve ultrasound	Nerve enlargement (roots, plexus, proximal nerves)
Objective response to treatment	Improvement on a validated disability scale (INCAT, I-RODS, grip strength)
Nerve biopsy	Demyelination/remyelination, macrophage clusters

Supportive criterion	Notes
SSEP abnormalities	Proximal sensory involvement

Diagnostic categories

Category	Requirements
CIDP	Clinical criteria + motor conduction criteria in ≥ 2 nerves + sensory abnormalities in ≥ 2 nerves; or possible CIDP + ≥ 2 supportive criteria (or 1 supportive in some combinations)
Possible CIDP	Clinical criteria + motor criteria in only 1 nerve, or typical CIDP with sensory abnormalities in only 1 nerve, without enough supportive criteria

Mandatory work-up: serum and urine immunofixation, glucose/HbA1c, CBC, renal and liver function; consider anti-MAG, VEGF (POEMS), nodal/paranodal antibodies, HIV, hepatitis, Lyme, genetic testing (CMT) depending on phenotype.

Treatment

Line	Recommendation
Induction	IVIG (2 g/kg over 2–5 days) or corticosteroids (oral prednisolone, pulsed dexamethasone or IV methylprednisolone) — both strong; plasma exchange if these fail
IVIG vs steroids	IVIG acts faster and has fewer side effects (ICE trial); steroids give longer remissions after stopping (PREDICT, IMC trial)
Motor CIDP	IVIG first — corticosteroids may worsen it
Maintenance	IVIG 1 g/kg every 3 weeks (or titrated), or subcutaneous immunoglobulin (SCIg) 0.2–0.4 g/kg weekly (PATH trial 2018) — try dose reduction periodically to find the lowest effective dose or confirm ongoing need
Not responding	Re-check the diagnosis (anti-MAG, POEMS, nodopathy, CMT, amyloid); consider combination therapy; immunosuppressants have weak, low-quality evidence (azathioprine, mycophenolate, methotrexate, cyclophosphamide, rituximab)
FcRn inhibition	Efgartigimod (ADHERE 2024): 61 % lower risk of relapse vs placebo in IVIG/steroid-responsive patients — approved for CIDP in the US (2024), with other regions following

Mimics that are not CIDP

Condition	Clue	Treatment
Anti-MAG neuropathy	Elderly men, distal, sensory ataxia, tremor, IgM-κ paraprotein , very prolonged distal latencies	Poor IVIG/steroid response; rituximab
POEMS syndrome	λ light chain, sclerotic bone lesions, very high VEGF , organomegaly, skin changes, thrombocytosis; painful neuropathy	Haematological treatment (radiotherapy, lenalidomide, ASCT) — IVIG ineffective
Autoimmune nodopathy (NF155, CNTN1, Caspr1, NF140/186)	Subacute severe onset, tremor, ataxia, very high CSF protein, poor IVIG response; IgG4	Rituximab
CMT1	Family history, pes cavus, uniform slowing	Genetic test
Hereditary ATTR amyloidosis	Autonomic involvement, carpal tunnel, cardiac disease, weight loss	Tafamidis, patisiran, vutrisiran
Diabetic lumbosacral radiculoplexus neuropathy	Asymmetric painful proximal leg weakness, weight loss	Often spontaneous recovery

Exam angles

- Under EAN/PNS 2021, "definite CIDP" → **does not exist; CIDP vs possible CIDP.**
- Pure motor demyelinating neuropathy worsening on prednisolone → **motor CIDP: switch to IVIG.**
- IgM-κ paraprotein, distal sensory ataxic neuropathy → **anti-MAG, not CIDP; rituximab.**
- Severe subacute CIDP with tremor, unresponsive to IVIG → **test NF155/CNTN1 — nodopathy, rituximab.**

Chemotherapy-Induced Peripheral Neuropathy

2023

Read with: ASCO guideline on prevention and management of CIPN (Loprinzi et al., 2020); ESMO-EONS-EANO clinical practice guideline (Jordan et al., 2020).

Overview

- Affects ~30–40 % of patients receiving neurotoxic chemotherapy; often the dose-limiting toxicity.
- Usually **length-dependent, sensory-predominant, axonal**; pain, paraesthesia, numbness, sensory ataxia, cold sensitivity.
- Risk factors: **cumulative dose**, dose intensity, pre-existing neuropathy (diabetes, alcohol, CMT — **vincristine is catastrophic in CMT1A**), combination neurotoxic drugs, older age.
- Assessment: clinical grading (NCI-CTCAE), patient-reported outcomes (EORTC CIPN20), examination; NCS when atypical.

Agents and patterns

Drug class	Pattern	Key pearls
Cisplatin	Sensory neuronopathy (dorsal root ganglion) — large-fibre: vibration and proprioception loss, sensory ataxia, areflexia; little pain or motor involvement	Dose-dependent (> 250–350 mg/m ²); coasting — worsens for 2–6 months after stopping; ototoxicity; Lhermitte's sign
Oxaliplatin	(1) Acute cold-induced dysaesthesias in hands, mouth and throat (pharyngolaryngeal dysaesthesia), muscle cramps — sodium-channel hyperexcitability, within hours, almost universal; (2) chronic cumulative sensory neuronopathy	Coasting; avoid cold drinks during infusion; stop-and-go strategies
Taxanes (paclitaxel > docetaxel, nab-paclitaxel)	Distal symmetric sensory > motor, large- and small-fibre; painful	Paclitaxel acute pain syndrome (arthralgia/myalgia 1–3 days after infusion); recovery usual but incomplete
Vinca alkaloids (vincristine most toxic)	Distal sensorimotor axonal — sensory symptoms and loss of ankle jerks first , then motor (foot/wrist drop) and autonomic (constipation, ileus, urinary retention, orthostatic hypotension); cranial neuropathies (ptosis, jaw pain, hoarseness)	Dose cap 2 mg; azole antifungals (CYP3A4) increase toxicity; fatal if given intrathecally
Bortezomib	Painful small-fibre sensory neuropathy, autonomic	SC route and weekly dosing reduce incidence vs IV twice weekly; usually reversible
Thalidomide	Sensory axonal, cumulative, often irreversible	Lenalidomide and pomalidomide much less neurotoxic
Eribulin, ixabepilone	Sensory axonal	
Brentuximab vedotin , enfortumab vedotin (antibody–drug conjugates with MMAE)	Sensory, sometimes motor	Dose-dependent
Immune checkpoint inhibitors	Immune-mediated — GBS-like, CIDP-like, myasthenia (often with myositis/myocarditis), cranial neuropathies	Stop drug, steroids, IVIG/PLEX — a different mechanism from classic CIPN

Drug class	Pattern	Key pearls
Suramin, arsenic, nelarabine	GBS-like, severe	

Prevention

Strategy	Evidence
Dose reduction, delay or stopping	The only proven strategy (ASCO 2020)
Pharmacological prevention (vitamin E, calcium/magnesium infusions, acetyl-L-carnitine, glutathione, venlafaxine, antidepressants, ASMs)	Not recommended — acetyl-L-carnitine increased CIPN with taxanes
Cryotherapy (frozen gloves/socks) and compression with taxanes	Promising RCTs; ASCO 2020 — insufficient for recommendation; some centres use
Exercise	Possible benefit, safe
Bortezomib by SC route	Reduces incidence

Treatment of painful CIPN

Agent	Evidence
Duloxetine 30 → 60 mg	Only agent with moderate recommendation (ASCO 2020) — CALGB 170601 (Smith 2013); more effective in oxaliplatin than taxane neuropathy
Gabapentin, pregabalin	Widely used; RCT evidence for CIPN negative/weak (gabapentin RCT negative)
TCAs (nortriptyline, amitriptyline)	Weak; side effects
Topical baclofen–amitriptyline–ketamine gel, capsaicin 8 % patch	Small studies
Physiotherapy, balance training, falls prevention	For sensory ataxia

Five facts that get asked. Cisplatin = **ganglionopathy with coasting**. Oxaliplatin = **cold-induced acute dysaesthesia**. Vincristine = **sensory first, then motor + autonomic; disaster in CMT; never intrathecal**. Bortezomib = **give SC**. Duloxetine = **only recommended treatment**; no drug prevents CIPN.

Exam angles

- Numb hands and sensory ataxia 3 months after finishing cisplatin, still worsening → **coasting**.
- Throat tightness and hand paraesthesia triggered by cold drinks during infusion → **oxaliplatin acute neurotoxicity**.
- Child with ALL develops severe weakness after first vincristine doses; father has pes cavus → **undiagnosed CMT1A**.
- Painful CIPN, best evidence → **duloxetine**.

Psychiatric Features of Chronic Traumatic Encephalopathy

2022

Frameworks: NINDS–NIBIB consensus neuropathological criteria (McKee 2016; second consensus 2021); **NINDS consensus diagnostic criteria for traumatic encephalopathy syndrome (TES)** (Katz et al., *Neurology* 2021).

Concepts

CTE	A neuropathological diagnosis — a tauopathy linked to repetitive head impacts (RHI)
TES	The clinical syndrome (2021) that may reflect underlying CTE — diagnosed in life
Exposure	American football, boxing, rugby, ice hockey, soccer heading, military blast, intimate partner violence. Number of years of exposure predicts risk more than concussions
Dementia pugilistica	Historical term for boxers — now included within CTE

Neuropathology (pathognomonic lesion)

- **p-tau aggregates in neurons (and astrocytes) around small vessels at the depths of cortical sulci**, in an irregular pattern.
- Distinct from Alzheimer's (diffuse amyloid plaques and tangles) and ageing-related tau astrogliopathy (ARTAG).
- Supportive: dilated third ventricle, **cavum septum pellucidum**, mammillary body and thalamic atrophy, TDP-43 co-pathology.
- Staging I–IV (McKee) — now simplified to **low and high CTE** (2021).

Clinical features (TES 2021)

Domain	Features
Core — cognitive impairment	Episodic memory and/or executive dysfunction, objectively documented and progressive
Core — neurobehavioural dysregulation	Explosiveness, impulsivity, rage, emotional lability, disinhibition
Supportive	Delayed onset (years after exposure), parkinsonism, other motor signs (dysarthria, ataxia), depression, anxiety, apathy, paranoia , progressive course
Excluded	Better explained by another disorder; symptoms must not be fully accounted for by persistent post-concussive symptoms

TES requires: substantial RHI exposure + core cognitive impairment (neurobehavioural dysregulation alone is insufficient for the cognitive domain) + progressive course + not fully explained by another disorder. Levels of certainty for underlying CTE: **suggestive, possible, probable, definite (pathology only)**.

Psychiatric features — what the review emphasises

Feature	Comment
Depression	Commonest psychiatric symptom in autopsy series; hopelessness, suicidality
Suicidality	Elevated in former contact-sport athletes; causal link to CTE not established — confounders (substance use, chronic pain, retirement, psychiatric history)

Feature	Comment
Impulsivity, aggression, explosivity	Typical of younger presenters ("behavioural/mood variant")
Cognitive variant	Older presenters; dementia, often with mixed pathology
Substance misuse	Common, may confound
Psychosis, paranoia	Less common

Critical exam point – diagnosis. Definite CTE is post-mortem only. No validated in-vivo biomarker: tau-PET tracers (flortaucipir) bind poorly to CTE tau; plasma/CSF p-tau, NfL and GFAP are research tools. Autopsy series are biased by **selection** (families who donate brains are those worried about symptoms) – prevalence in exposed populations is **unknown**.

Management

- No disease-modifying therapy.
- Treat symptoms as in other disorders: **SSRIs/SNRIs** for depression and anxiety, mood stabilisers for explosivity, psychological therapy, suicide risk assessment, substance-use treatment, cognitive rehabilitation, parkinsonism treatment if present.
- Prevention: rule changes (no heading for children, limiting full-contact practice), concussion protocols (remove from play, graded return).
- Differential: Alzheimer's, bvFTD, depression, PTSD, chronic subdural haematoma, normal-pressure hydrocephalus, substance-related cognitive impairment.

Exam angles

- 45-year-old former rugby forward, explosive anger, depression, progressive memory decline → **suspected TES (possible CTE)** – not definite.
- The pathognomonic lesion → **perivascular p-tau at sulcal depths**.
- Best predictor of CTE pathology → **duration/intensity of repetitive head impacts**, not number of diagnosed concussions.
- Tau-PET confirms CTE → **false; no validated in-vivo test**.

Advances in Stroke Neurorehabilitation

2023

Read with: Cochrane stroke-unit review (2020); AVERT (2015); EXCITE (2006) and VECTORS (2009); RATULS (2019); FOCUS, AFFINITY, EFFECTS (fluoxetine, 2019–2020); FCET2EC (2017); VNS-REHAB (2021); ESO guidelines on post-stroke motor rehabilitation.

Principles

Principle	Evidence
Stroke unit care	The single most effective organisational intervention: less death, dependency and institutionalisation, for all stroke types and ages. Roughly one extra independent survivor for every ~20 patients treated
Early mobilisation — but gently	AVERT (2015): very early (< 24 h), high-dose, frequent mobilisation reduced the odds of a favourable outcome at 3 months. Short, frequent, low-intensity sessions are safer
Early supported discharge	Shorter hospital stay, similar or better outcomes for mild–moderate stroke
Task-specific, repetitive practice	Core of motor learning
Dose	More therapy time generally helps, but intensity very early can harm (AVERT, VECTORS)
Critical window	Spontaneous recovery is greatest in the first 3 months (proportional recovery ~70 % of initial upper-limb impairment in many), but meaningful gains are possible in chronic stroke (Queen Square programme, 2019)
Goal-setting	Patient-centred, multidisciplinary

Upper limb

Intervention	Evidence
Constraint-induced movement therapy (CIMT)	EXCITE (2006) positive in subacute stroke with some wrist/finger extension. VECTORS (2009): high-intensity CIMT in the acute phase was worse than standard dose — dose and timing matter
Robot-assisted training	RATULS (2019): not better than enhanced conventional therapy of equal dose; useful to increase practice
Vagus nerve stimulation paired with rehabilitation	VNS-REHAB (2021): clinically meaningful upper-limb improvement in chronic stroke; device approved (US 2021)
Mirror therapy, mental practice, virtual reality	Modest; VR equivalent to conventional therapy (adjunct)
Functional electrical stimulation	Modest for wrist extension
Non-invasive brain stimulation (rTMS, tDCS)	Inhibit contralesional or facilitate ipsilesional cortex — not standard care (inconsistent RCTs)

Gait and balance

- Task-oriented gait training, treadmill (with or without body-weight support); **LEAPS (2011):** early locomotor training not better than home physiotherapy of the same dose.
- Electromechanical gait trainers help non-ambulatory patients walk independently (Cochrane).
- Ankle–foot orthoses, FES for foot drop.

- Cardiorespiratory fitness training improves walking.

Pharmacological augmentation

Drug	Evidence
Fluoxetine	FLAME (2011) suggested motor benefit, but FOCUS, AFFINITY and EFFECTS (2019–2020; ~6000 patients) showed no functional benefit and more fractures (and hyponatraemia/seizures). Not recommended for recovery — use only for depression
Amphetamines, citicoline, cerebrolysin	Not recommended

Aphasia, dysphagia, cognition, mood

Domain	Points
Aphasia	Intensive speech and language therapy: FCET2EC (2017) — ≥ 10 h/week for 3 weeks improved verbal communication in chronic aphasia. Constraint-induced aphasia therapy; group therapy; communication partner training
Dysphagia	Screen before oral intake; texture modification; pharyngeal electrical stimulation (PHAST-TRAC) to aid decannulation; NG feeding early, PEG if prolonged (FOOD trial)
Neglect	Prism adaptation, visual scanning — limited evidence
Post-stroke depression	~30 %; SSRIs, psychotherapy
Post-stroke fatigue	Common, under-recognised; no proven drug
Spasticity	Botulinum toxin for focal spasticity — reduces tone and pain, improves passive function (hygiene, dressing) and goal attainment; not proven to improve active function ; combine with stretching/casting
Shoulder pain	Positioning, avoid traction, suprascapular nerve block, botulinum toxin
Central post-stroke pain	Amitriptyline, lamotrigine, pregabalin

The three trial traps. AVERT: very early **high-dose** mobilisation harms. VECTORS: **high-intensity CIMT early** harms. FOCUS/AFFINITY/EFFECTS: **fluoxetine does not improve recovery**. Stroke unit care helps everyone.

Exam angles

- Strongest evidence-based intervention to reduce death and dependency after stroke → **stroke unit care**.
- Mobilise within 24 h with intensive sessions → **AVERT: worse**.
- Fluoxetine to improve motor recovery → **no (FOCUS/AFFINITY/EFFECTS)**.
- Chronic hand weakness, already maximised therapy → **VNS paired with rehabilitation** is the newest evidence-based option.

EAN/ESRS/ERS — Sleep and Stroke

2020

Source: Bassetti et al., EAN/ERS/ESO/ESRS statement on the impact of sleep disorders on risk and outcome of stroke, *Eur J Neurol / Eur Respir J* 2020. **Read with:** SAVE (2016), SERVE-HF (2015).

Why it matters

Sleep disorders are both **risk factors** for stroke and **modifiers of recovery**. Sleep-disordered breathing (SDB) is the commonest and best studied.

Topic	Key points
Prevalence of SDB after stroke	AHI ≥ 5 in 50–70 % ; AHI ≥ 30 in ~30 %; obstructive more than central
SDB as a risk factor	Moderate–severe OSA roughly doubles stroke risk, independent of other factors; also associated with AF, hypertension, wake-up stroke
SDB and outcome	Associated with early neurological worsening, poorer functional outcome, recurrence and mortality
Diagnosis	Screen all stroke/TIA patients (questionnaires are poor in stroke — STOP-BANG/Berlin underperform); use respiratory polygraphy in the stroke unit; PSG when needed

Treatment of SDB after stroke

Intervention	Evidence and statement
CPAP for OSA	Feasible in the acute/subacute phase; small RCTs suggest better neurological recovery; adherence ~50 % is the problem. EAN/ESRS: CPAP may be considered to improve outcome (weak)
CPAP for secondary prevention	SAVE (2016): CPAP in patients with OSA and established cardiovascular or cerebrovascular disease did not reduce recurrent cardiovascular events (mean use 3.3 h/night); improved sleepiness, mood and quality of life. Benefit may require ≥ 4 h/night use
Central sleep apnoea/Cheyne–Stokes	Common acutely (brainstem/bilateral lesions, heart failure), often resolves. ASV is contraindicated in HFrEF (EF ≤ 45 %) with predominantly central apnoea — SERVE-HF (2015) showed increased cardiovascular mortality
Positional therapy	Supine-dependent OSA is common after stroke

Correction to the old digest. CPAP has **not** been shown to reduce recurrent stroke or cardiovascular events (SAVE); and ASV is **not** a routine treatment for post-stroke Cheyne–Stokes respiration — it is harmful in HFrEF with central apnoea (SERVE-HF).

Other sleep–wake disorders after stroke

Disorder	Points
Hypersomnia / increased sleep need	Up to 70 % acutely; paramedian thalamic (artery of Percheron), mesencephalic and pontine strokes cause severe hypersomnia; modafinil, methylphenidate in small studies
Insomnia	~40–60 %; associated with depression, anxiety, pain; CBT-I; avoid long-term hypnotics (falls, confusion)
Post-stroke fatigue	Distinct from sleepiness; common and persistent
RLS	New-onset RLS after strokes of the basal ganglia, thalamus, corona radiata and pons
RBD	After pontine tegmental lesions (symptomatic RBD)

Disorder	Points
Circadian rhythm disturbance	Light exposure, structured day in the stroke unit; melatonin
Sleep duration	Both very short (< 5 h) and very long (> 9 h) sleep associated with higher stroke risk
Wake-up stroke	~20–25 % of strokes; IVT based on DWI-FLAIR mismatch (WAKE-UP) or perfusion mismatch (EXTEND)

Exam angles

- Stroke unit patient: best tool to detect SDB → **respiratory polygraphy** (questionnaires underperform).
- CPAP reduces recurrent vascular events in OSA + stroke → **not proven (SAVE)**.
- Central apnoea + HFrEF EF 30 % → **avoid ASV (SERVE-HF)**.
- Severe hypersomnia after bilateral paramedian thalamic infarction → **artery of Percheron**.

European Guideline — Management of Narcolepsy

2021

Source: Bassetti et al., European guideline and expert statements on the management of narcolepsy in adults and children (EAN/ERS/ESRS), *Eur J Neurol / J Sleep Res* 2021. **Diagnosis:** ICSD-3 (2014; ICSD-3-TR 2023).

ICSD-3 diagnosis

Type	Criteria
Narcolepsy type 1	Daily irrepressible sleepiness or daytime lapses into sleep ≥ 3 months, plus one or both of: (1) cataplexy + MSLT mean sleep latency ≤ 8 min and ≥ 2 SOREMPs (a SOREMP within 15 min on the preceding night's PSG may replace one MSLT SOREMP); (2) CSF hypocretin-1 ≤ 110 pg/mL (or $< \frac{1}{3}$ of normative mean)
Narcolepsy type 2	Sleepiness ≥ 3 months + MSLT ≤ 8 min and ≥ 2 SOREMPs; no cataplexy ; CSF hypocretin > 110 pg/mL or not measured ; not better explained by insufficient sleep, OSA, delayed sleep phase or drugs

Correction to the old digest. NT1 does **not** require cataplexy — **low CSF hypocretin alone (with sleepiness) is sufficient**. Thresholds are ≤ 8 min and ≤ 110 pg/mL, not " < 8 " and " < 110 ".

Clinical features

Feature	Notes
Excessive daytime sleepiness	Universal; short naps are refreshing
Cataplexy	Sudden bilateral loss of tone triggered by positive emotions (laughter, joking, surprise); seconds to < 2 min; consciousness preserved ; reflexes transiently absent; partial attacks (face, neck, knees) commonest. In children: facial hypotonia, tongue protrusion ("cataplectic facies") and complex movements near onset
Sleep paralysis, hypnagogic/hypnopompic hallucinations	Also occur in normal people
Disturbed nocturnal sleep	Fragmented
Others	Weight gain (especially children), precocious puberty in children, RBD, depression, automatic behaviour

MSLT protocol: 4–5 nap opportunities of 20 min at 2-h intervals after an overnight PSG (≥ 6 h sleep), with sleep diary or actigraphy for 1–2 weeks before, and **stimulants/REM-suppressing drugs withdrawn for ≥ 2 weeks**.

HLA-DQB1*06:02 in $\sim 98\%$ of NT1 (but $\sim 25\%$ of the general population) — a negative result makes NT1 very unlikely.

Pathophysiology of NT1: selective loss of hypothalamic hypocretin (orexin) neurons, probably autoimmune (HLA association, T-cell autoimmunity, H1N1 and Pandemrix vaccine-associated cases in 2009–10, winter onset in children).

Treatment — what the guideline recommends

Symptom	Strong recommendations	Other / weak
Excessive daytime sleepiness	Modafinil, pitolisant, sodium oxybate, solriamfetol	Methylphenidate, amphetamines (weak); armodafinil; scheduled naps
Cataplexy	Sodium oxybate, pitolisant, venlafaxine	Clomipramine, SSRIs, other antidepressants (weak)
Disturbed nocturnal sleep	Sodium oxybate	
Hallucinations, sleep paralysis	Sodium oxybate, antidepressants	
Children	Sodium oxybate and pitolisant have paediatric data/licences; modafinil off-label	

Drug	Mechanism	Key points
Modafinil	Dopamine reuptake inhibition	Headache; reduces efficacy of hormonal contraception ; not for cataplexy
Pitolisant	H3 inverse agonist — increases histamine	Effective for sleepiness and cataplexy ; not a controlled drug; reduces hormonal contraceptive efficacy
Solriamfetol	Dopamine–noradrenaline reuptake inhibitor	Sleepiness only; raises BP and heart rate
Sodium oxybate (GHB; also low-sodium and once-nightly forms)	GABA-B agonist	Treats all symptoms; taken at night (twice nightly); respiratory depression with alcohol/sedatives; avoid in untreated OSA; abuse potential
Venlafaxine, clomipramine	REM suppression	Cataplexy; abrupt withdrawal → status cataplecticus
Orexin-2 receptor agonists (oveporexton/TAK-861)	Replace missing signal	Large effects in NT1 trials (phase 2 published 2025); not yet licensed

Exam angles

- EDS + low CSF hypocretin, no cataplexy → **NT1**.
- EDS, MSLT 6 min with 3 SOREMPs, no cataplexy, hypocretin normal → **NT2**.
- One drug for sleepiness **and** cataplexy that is not a controlled substance → **pitolisant**.
- Patient stops venlafaxine abruptly and has repeated cataplexy → **status cataplecticus**.

Neurogenic Supine Hypertension

2018–2022

Source: Fanciulli et al., **Consensus statement on the definition of neurogenic supine hypertension in cardiovascular autonomic failure** by the American Autonomic Society, European Federation of Autonomic Societies (EFAS) and European Society of Hypertension, *Clin Auton Res* 2018; with EFAS/EAN educational updates. **Read with:** Gibbons et al., consensus on management of neurogenic OH (2017).

Definitions

Term	Definition
Neurogenic supine hypertension (nSH)	SBP $\geq$ 140 and/or DBP $\geq$ 90 mmHg after $\geq$ 5 min of rest in the supine position, in a patient with neurogenic OH
Severity	Mild 140–159 / 90–99; moderate 160–179 / 100–109; severe $\geq$ 180 / $\geq$ 110 mmHg
Neurogenic OH	Sustained fall $\geq$ 20/10 mmHg within 3 min of standing with an inadequate heart-rate rise (ΔHR/ ΔSBP $<$ 0.5 bpm/mmHg)
Prevalence	~50 % of patients with nOH — highest in MSA (preserved postganglionic sympathetic fibres, residual tone) and pure autonomic failure
Diagnosis	24-h ambulatory BP monitoring with a position/activity diary; look for nocturnal hypertension and loss of dipping ("reverse dipping")

The paradox

The same patient has dangerous **hypotension when upright** and **hypertension when lying**. Treatments for one worsen the other. Supine hypertension also causes **pressure natriuresis** at night $\rightarrow$ nocturia $\rightarrow$ volume depletion $\rightarrow$ **worse OH in the morning**. Long-term risks: LV hypertrophy, renal impairment, possibly stroke — but **falls and syncope from OH are usually the more immediate danger**, so **orthostatic symptoms take priority**.

Management strategy

Step	Measure	Notes
1	Avoid the supine position during the day — rest sitting in a reclining chair	
2	Sleep with head-up tilt $\sim$10–20° (raise the head end of the bed $\sim$ 15–20 cm / bed blocks or wedge)	Reduces nocturnal hypertension and natriuresis; improves morning OH. (The old digest's "30–45°" is too steep to sleep in)
3	Time pressor drugs: last dose of midodrine/droxidopa $\geq$ 4 h before bed ; avoid fludrocortisone where supine hypertension is severe	
4	Small carbohydrate snack or a glass of wine/alcohol at bedtime (post-prandial fall)	Some centres; individualise
5	Avoid drinking large volumes at night; warm baths before bed lower BP	
6	Bedtime short-acting antihypertensive if severe nSH persists: transdermal glyceryl trinitrate 0.1–0.2 mg/h (remove on rising), losartan 25–50 mg, captopril 25 mg, nifedipine 10–30 mg, clonidine 0.1 mg, hydralazine, sildenafil 25 mg	Patient must get up carefully at night (nocturia $\rightarrow$ falls)
7	Avoid long-acting antihypertensives and diuretics in the daytime	Worsen OH

Drugs for nOH and their supine-BP cost

Drug	Effect on supine BP
Pyridostigmine	Little — enhances ganglionic transmission mainly when standing
Midodrine	Raises supine BP (short-acting: time doses)
Droxidopa	Raises supine BP
Fludrocortisone	Raises supine BP; also hypokalaemia, oedema, LVH
Atomoxetine	Raises supine BP (especially MSA)

Exam angles

- MSA patient, morning syncope and supine BP 190/100 at night → **head-up tilt sleeping, pressors timed ≥ 4 h before bed, bedtime GTN patch or losartan.**
- Drug for nOH least likely to worsen supine hypertension → **pyridostigmine.**
- Definition of nSH → **$\geq 140/90$ supine after 5 min rest in a patient with nOH.**
- Why is morning OH worst? → **nocturnal pressure natriuresis.**

ABN — Myasthenia Gravis Guidelines

2025

Source: Association of British Neurologists management guidelines for myasthenia gravis (2015, updated 2025). **Read with:** International consensus guidance (Sanders 2016, Narayanaswami 2021 update); MGTX (2016) and extension (2019).

Why it matters for the FEBN. New drug classes (complement and **FcRn** inhibitors), thymectomy evidence (MGTX), the seronegative pathway and how to start steroids without a crisis.

Antibodies

Antibody	Frequency	Clinical features
AChR	~85 % of generalised, ~50 % of ocular MG	Early-onset (< 50, women, thymic hyperplasia), late-onset (men, atrophic thymus), thymoma-associated (~10–15 %)
MuSK	~5–8 % (higher in seronegative)	Women; bulbar, neck and respiratory weakness, facial/tongue atrophy; poor response/intolerance to pyridostigmine; excellent response to rituximab ; no thymectomy
LRP4	1–3 %	Mild, often ocular or limb
Seronegative	~5–10 %	Repeat with cell-based assays (clustered AChR)
Titin, RyR	—	Markers of thymoma and late-onset disease

Diagnosis

- **Antibodies first**; if negative, cell-based AChR and MuSK assays, LRP4.
- **Repetitive nerve stimulation** at 3 Hz: decrement > 10 % — sensitivity ~75 % in generalised, < 50 % in ocular MG.
- **Single-fibre EMG**: increased jitter — **most sensitive (> 90 %) but not specific** (abnormal in ALS, neuropathy, myopathy).
- **Ice-pack test** for ptosis (≥ 2 mm improvement). Edrophonium test obsolete.
- **CT or MRI of the mediastinum in all** — thymoma.
- Thyroid function (associated autoimmunity); baseline for immunosuppression (TPMT before azathioprine, hepatitis B, TB screening).

Treatment algorithm

Stage	Treatment	Practical points
Symptomatic	Pyridostigmine 30–60 mg 4–6 times daily (typical max ~360 mg/day)	Cholinergic GI effects — propantheline/glycopyrronium; less useful in MuSK
Corticosteroids	Prednisolone — start low and increase slowly (e.g. 5–10 mg alternate days, +5–10 mg per dose to ~1–1.5 mg/kg alternate days or remission)	High starting doses cause transient worsening in ~1/3, often days 5–10 — if high-dose induction is needed, admit. Ocular MG: lower doses (~0.75 mg/kg alternate days)
Steroid-sparing	Azathioprine first choice (onset 6–18 months; check TPMT); mycophenolate, methotrexate, tacrolimus, ciclosporin	Start early in generalised MG

Stage	Treatment	Practical points
Thymectomy	Thymoma: always. Non-thymomatous AChR+ generalised MG, age 18–65 → strongly recommended (MGTX) — better QMG scores and lower prednisolone at 3 and 5 years	Elective, when stable; minimally invasive (VATS/robotic) acceptable. Not for MuSK; ocular and > 65: limited evidence, individualise
Complement C5 inhibitors	Eculizumab, ravulizumab, zilucoplan (SC peptide)	AChR+ refractory/generalised MG; meningococcal vaccination ± prophylaxis
FcRn antagonists	Efgartigimod (IV/SC) — AChR+; rozanolixizumab (SC) — AChR+ and MuSK+; nipocalimab (2025) — antibody-positive gMG	Lower all IgG; onset ~1–2 weeks; cyclical dosing; infections, headache
B-cell depletion	Rituximab	MuSK+ first-line refractory option; in AChR+ evidence weaker (BeatMG negative; RINOMAX positive in new-onset)
Acute exacerbation / crisis	IVIG 2 g/kg or plasma exchange (PLEX slightly faster; preferred in MuSK)	Monitor FVC, MIP, MEP — 20/30/40 rule ; bulbar failure; intubate early; pyridostigmine usually paused while ventilated

Correction to the old digest. Efgartigimod is licensed for **AChR+** MG (not MuSK+). Rozanolixizumab and nipocalimab cover MuSK+. Intubation decisions use **FVC < 20 mL/kg / MIP > -30 / MEP < 40 cmH₂O** and bulbar status, not "FVC < 15". Steroid-induced worsening is prevented by **starting low and titrating**, not by "pyridostigmine cover".

Special situations

Situation	Points
Pregnancy	Pyridostigmine, prednisolone, azathioprine acceptable; avoid mycophenolate, methotrexate; transient neonatal MG in ~10–20 %; magnesium sulfate contraindicated for pre-eclampsia (use levetiracetam); arthrogryposis with fetal AChR antibodies
Immune checkpoint inhibitors	MG with myositis and myocarditis (triple M), high mortality — stop ICI, high-dose steroids, IVIG/PLEX, check troponin and CK
Ocular MG	Pyridostigmine, then low-dose prednisolone (reduces generalisation — EPITOME)
Surgery/anaesthesia	Avoid or reduce neuromuscular blockers; sugammadex reverses rocuronium

Drugs that worsen MG

Aminoglycosides, fluoroquinolones, macrolides (azithromycin, erythromycin), telithromycin, IV magnesium, β-blockers, quinine/hydroxychloroquine, procainamide, neuromuscular blockers, botulinum toxin, statins (occasionally), D-penicillamine (can induce MG), immune checkpoint inhibitors.

Exam angles

- AChR+ generalised MG, age 34, no thymoma → **thymectomy (MGTX)**.
- MuSK+ MG refractory to steroids → **rituximab** (PLEX for crisis).
- Started prednisolone 60 mg daily as outpatient, worse after 1 week → **steroid-induced exacerbation; should have titrated up**.
- Refractory AChR+ MG, needs fast-acting maintenance → **FcRn inhibitor or complement inhibitor (vaccinate against meningococcus)**.

EAN/MDS-ES — Invasive Therapies for Parkinson's Disease

2022

Source: Deuschl et al., European Academy of Neurology/Movement Disorder Society–European Section guideline on the treatment of Parkinson's disease: **I. Invasive therapies**, *Eur J Neurol* 2022. **Since then:** subcutaneous foslevodopa/foscarbidopa (2022–23), adaptive DBS (2025).

When to consider a device-aided therapy

Indication	Detail
Motor fluctuations	Wearing-off, unpredictable on-off, > 2 h off per day despite optimised oral therapy ("5-2-1" rule: ≥ 5 oral levodopa doses/day, ≥ 2 h off/day, ≥ 1 h troublesome dyskinesia/day suggests advanced PD)
Disabling dyskinesia	Peak-dose or diphasic
Medication-refractory tremor	DBS (STN, GPi or VIM) or focused ultrasound
Early fluctuations	EARLYSTIM (2013): STN-DBS in patients with early motor complications (≤ 3 years of fluctuations, age ≤ 60) improved quality of life more than best medical therapy — EAN recommends offering DBS in this group

Prerequisites for DBS: idiopathic PD (not atypical parkinsonism); **clear levodopa response (≥ 30 – 33 % UPDRS-III improvement in a levodopa challenge)** — the best predictor of outcome, except for tremor, which improves even if levodopa-resistant; no dementia; no uncontrolled psychiatric disease; MRI without major atrophy or vascular disease; realistic expectations; usually age < 70 – 75 (biological age matters).

The options

Therapy	Target / route	Best candidate	Key points
STN-DBS	Subthalamic nucleus	Younger, fluctuations $\pm$ dyskinesia, good cognition	Allows ~50 % medication reduction; improves off-time, dyskinesia (indirectly), tremor. Risks: haemorrhage 1–2 %, infection, dysarthria, apathy (after drug reduction), hypomania, impulsivity , possible verbal fluency decline, weight gain
GPi-DBS	Globus pallidus internus	Dyskinesia-predominant, older, mild cognitive or mood vulnerability	Direct anti-dyskinetic effect; little medication reduction; fewer cognitive/mood effects. EAN: STN and GPi similar for motor outcomes — choose by profile
VIM-DBS	Thalamus	Tremor only (rare in PD; ET)	Does not help bradykinesia/rigidity
Levodopa-carbidopa intestinal gel (LCIG)	Jejunal infusion via PEG-J	Severe fluctuations, unsuitable for DBS (age, cognition)	Reduces off-time, smooths dyskinesia; tube complications (dislocation, buried bumper, infection), polyneuropathy (B12/B6 deficiency) , weight loss. LCIG adds entacapone

Therapy	Target / route	Best candidate	Key points
Continuous SC apomorphine infusion	Subcutaneous pump	Fluctuations, unsuitable for/declining DBS; preserved cognition	TOLEDO (2018) : off-time reduced ~2 h vs placebo. Skin nodules , nausea (domperidone, ECG for QT), haemolytic anaemia (Coombs test) , hallucinations, ICDs, sleepiness
Foslevodopa/foscarbidopa SC infusion	Subcutaneous, 24 h	Fluctuations; alternative to LCIG without surgery	Pivotal trial: ~1.8 h more on-time without troublesome dyskinesia vs oral levodopa; infusion-site reactions/cellulitis ; polyneuropathy monitoring
MR-guided focused ultrasound	Unilateral VIM thalamotomy (tremor); unilateral subthalamotomy or pallidotomy (investigational/emerging)	Tremor-dominant, asymmetric, not a DBS candidate	Incisionless, immediate; irreversible and non-adjustable ; bilateral treatment limited (dysarthria, gait); paraesthesia, ataxia
Radiofrequency/gamma knife lesioning	VIM, GPi	Where DBS unavailable	

EAN 2022 — headline recommendations

1. **STN-DBS** for patients with **motor fluctuations and dyskinesia** that cannot be controlled with oral treatment — **including those with early fluctuations** (EARLYSTIM).
2. **GPi-DBS** as an alternative — similar motor benefit; consider when dyskinesia dominates or when medication reduction is not a goal.
3. **LCIG** and **SC apomorphine** for fluctuations when DBS is not suitable.
4. **Focused ultrasound / unilateral thalamotomy** for medication-refractory **tremor**.
5. **No recommendation** for routine use of experimental targets (PPN for freezing) or cell/gene therapies.

STN vs GPi in one line. STN = **reduce the drugs** (younger, full motor syndrome). GPi = **switch off the dyskinesia** without lowering drugs (older, cognitively or emotionally vulnerable). Neither improves levodopa-resistant axial symptoms (freezing in on, postural instability, dysphagia) or dementia.

What does not respond to device-aided therapy

Levodopa-resistant gait freezing and falls, dysarthria (may worsen), dysphagia, cognitive decline, autonomic failure, psychosis.

Exam angles

- 55-year-old, 8 years of PD, 4 h off/day, peak-dose dyskinesia, normal cognition → **STN-DBS**.
- 72-year-old with mild cognitive impairment and fluctuations, not a DBS candidate → **LCIG, SC apomorphine or foslevodopa infusion**.
- Apomorphine pump patient with new anaemia → **Coombs-positive haemolytic anaemia**.
- Tremor-dominant PD, frail, refuses implant → **unilateral MRgFUS thalamotomy**.

CIDP — The "Update", Autoimmune Nodopathies and Paraproteinaemic Neuropathies

2021–2024

Important: there is **no separate 2022 EAN/PNS CIDP guideline**. The current document is the **2021 second revision** (Paper 12), published simultaneously in *Eur J Neurol* and *J Peripher Nerv Syst*. Everything the old digest listed as "new in 2022" (autoimmune nodopathy, SCIg, treatment response as a supportive criterion, anti-MAG excluded) was **already in the 2021 guideline**. Check which reference the official FEBN list cites. This section keeps its number and covers the high-yield neighbours of CIDP.

What changed from 2010 to 2021 (the real update)

2010 EFNS/PNS	2021 EAN/PNS
Definite / probable / possible CIDP	CIDP / possible CIDP
"Atypical CIDP"	CIDP variants: distal, multifocal, focal, motor, sensory
DADS (with or without anti-MAG)	Distal CIDP; anti-MAG neuropathy excluded
Nodal/paranodal antibodies not addressed	Autoimmune nodopathies — a separate disease
Ultrasound not included	Nerve ultrasound a supportive criterion
—	Objective treatment response a supportive criterion
—	Subcutaneous immunoglobulin recommended for maintenance

Autoimmune nodopathies

Antibody	Target	Clinical picture
NF155 (IgG4)	Paranodal glial neurofascin-155	Young men; subacute severe distal weakness, disabling tremor , sensory ataxia, very high CSF protein , CNS demyelination in some; poor IVIG response
CNTN1 (IgG4)	Paranodal contactin-1	Older; acute/subacute GBS-like onset, sensory ataxia, nephrotic syndrome (membranous)
Caspr1 (IgG4)	Paranodal contactin-associated protein-1	GBS-like onset, neuropathic pain , respiratory failure, cranial nerves
Pan-neurofascin (NF140/186, often IgG3)	Nodal	Very severe, tetraplegic, ventilated , cranial nerves; nephrotic syndrome; responds to treatment

Pathophysiology: IgG4 antibodies block protein–protein interactions at the node rather than activating complement → **no inflammation, no macrophage demyelination** → **IVIG and steroids work poorly; rituximab works** (depletes plasmablast precursors). Test in: GBS-like onset (acute-onset CIDP), tremor and ataxia, very high CSF protein, nephrotic syndrome, IVIG non-response.

Paraproteinaemic neuropathies

Condition	Paraprotein	Features	Treatment
Anti-MAG neuropathy	IgM-κ (> 90 %)	Men > 60, distal symmetric sensory ataxia, tremor , mild distal weakness; very prolonged distal motor latencies (low terminal latency index); widened myelin lamellae on biopsy	Rituximab (modest); IVIG transient; ibrutinib (if Waldenström)
IgM-MGUS without MAG	IgM	Distal CIPD-like	IVIG may work
IgG/IgA MGUS	IgG/IgA	Treated as CIPD if criteria met	As CIPD
POEMS	λ light chain (almost always)	Polyneuropathy (painful, demyelinating with axonal loss, uniform slowing, no conduction block), Organomegaly , Endocrinopathy , M-protein , Skin changes ; sclerotic bone lesions, papilloedema, oedema, thrombocytosis, VEGF very high	Haematological : radiotherapy for solitary lesion, lenalidomide–dexamethasone, autologous stem-cell transplant. IVIG/steroids ineffective
CANOMAD	IgM against disialosyl gangliosides (GD1b, GQ1b)	Chronic Ataxic Neuropathy , Ophthalmoplegia , M-protein , cold Agglutinins , Disialosyl antibodies	IVIG, rituximab
AL amyloidosis	λ > κ	Painful small-fibre and autonomic neuropathy, carpal tunnel, cardiac/renal involvement, macroglossia	Chemotherapy (daratumumab-based)
Cryoglobulinaemia	Mixed (HCV)	Painful mononeuritis multiplex, purpura	Antivirals, rituximab

The CIPD non-responder checklist

1. Is it **CIPD** at all? (Re-read NCS — misdiagnosis in up to half of referred "CIPD" cases.)
2. **Anti-MAG**? (IgM paraprotein.)
3. **POEMS**? (λ, VEGF, bone survey, thrombocytosis.)
4. **Nodopathy**? (NF155, CNTN1, Caspr1, NF186.)
5. **Hereditary**? (CMT1, hATTR.)
6. **Amyloid, lymphoma, sarcoid** (MRI plexus, PET, biopsy)?
7. Dose and interval adequate? Objective outcome measures used?

Exam angles

- CIPD-like neuropathy, **λ paraprotein, thrombocytosis, VEGF high** → **POEMS** — **not IVIG**.
- Young man with severe sensory ataxia, tremor, CSF protein 3 g/L, IVIG failure → **NF155 nodopathy** → **rituximab**.
- Membranous nephropathy + subacute neuropathy → **CNTN1**.
- Elderly man, IgM-κ, distal ataxia and tremor → **anti-MAG**.

EAN/PNS — Guillain–Barré Syndrome

2023

Source: van Doorn et al., European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of Guillain–Barré syndrome, *Eur J Neurol / J Peripher Nerv Syst* 2023. Diagnosis follows the **NINDS criteria** (Asbury & Cornblath 1990); Brighton criteria are for epidemiology.

Diagnosis

Required	Supportive	Raises doubt
Progressive bilateral weakness of arms and legs (may start in legs)	Progression over days to ≤ 4 weeks (nadir usually within 2 weeks)	CSF white cells > 50/μL (> 10 raises doubt)
Absent or reduced reflexes in weak limbs (~10 % — especially AMAN — have normal or brisk reflexes)	Relative symmetry; mild sensory signs; cranial nerve involvement (bilateral facial palsy); autonomic dysfunction; pain (back, radicular, muscle)	Marked persistent asymmetry
	CSF albuminocytological dissociation (protein may be normal in the first week in up to 50 %)	Severe respiratory dysfunction with little limb weakness
	NCS consistent with a subtype; sural-sparing pattern (abnormal median/ulnar SNAP with normal sural)	Sensory level; bladder/bowel dysfunction at onset
	Preceding infection within 6 weeks (~2/3) — <i>C. jejuni</i> , CMV, EBV, <i>Mycoplasma</i> , influenza, Zika, hepatitis E	Fever at onset; nadir < 24 h; progression > 4 weeks

Differential to exclude: spinal cord compression or myelitis (sensory level, sphincters), brainstem stroke, botulism (descending, pupils), myasthenia, tick paralysis, hypokalaemia, critical illness neuropathy, porphyria, lymphoma/leptomeningeal disease, nodopathy.

Subtypes

Subtype	Features	Antibodies
AIDP	Commonest in Europe/North America (~70–90 %)	Usually none
AMAN	Pure motor, <i>C. jejuni</i> , Asia/Latin America; reflexes may be preserved; reversible conduction failure	GM1, GD1a
AMSAN	Severe motor-sensory axonal	GM1, GD1a
Miller Fisher	Ophthalmoplegia, ataxia, areflexia	GQ1b (~85–90 %)
Bickerstaff brainstem encephalitis	MFS + reduced consciousness, pyramidal signs	GQ1b
Pharyngeal–cervical–brachial	Bulbar, neck and arm weakness	GT1a
Paraparetic, bifacial weakness with paraesthesia		

Treatment — the recommendations

Question	Recommendation
IVIG	0.4 g/kg/day for 5 days (2 g/kg total) for patients unable to walk unaided (GBS disability score ≥ 3) within 2 weeks of onset (strong). Consider for those who can walk but are progressing quickly or have severe autonomic/bulbar weakness

Question	Recommendation
Plasma exchange	12–15 L in 4–5 exchanges over 1–2 weeks , for GBS-DS ≥ 3 within 4 weeks of onset (strong); for those able to walk within 2 weeks: 2 exchanges
IVIG vs PE	Equally effective ; IVIG easier and more available, fewer discontinuations
PE followed by IVIG	Not recommended (no added benefit)
Second IVIG course	Not recommended for poor prognosis — SID-GBS (2021) : no benefit, more serious adverse events (thromboembolism)
Corticosteroids	Oral: strongly against. IV methylprednisolone: against (alone or with IVIG)
Treatment-related fluctuation (TRF)	Repeat IVIG or PE is reasonable (weak, low evidence)
Mild GBS (can walk)	Monitor; treat if progressing
Miller Fisher syndrome	Usually no treatment — good spontaneous recovery; IVIG did not change outcome in observational data; monitor for overlap with GBS or BBE (then treat)
Pain	Gabapentinoids, TCAs or carbamazepine (weak); opioids short-term
Supportive	VTE prophylaxis , autonomic monitoring (ECG — bradyarrhythmias, BP lability), bladder/bowel, pressure care, early rehabilitation, communication and psychological support

Respiratory monitoring

Tool	Use
20/30/40 rule	FVC < 20 mL/kg, MIP weaker than -30 cmH₂O, MEP < 40 cmH₂O → high risk; ICU and consider elective intubation
FVC fall > 30 % from baseline	ICU
Single-breath count < 20	Correlates with FVC < ~1.5 L
EGRIS (Erasmus GBS Respiratory Insufficiency Score) at admission	Days from onset to admission (< 7), facial and/or bulbar weakness, MRC sum score → risk of ventilation within 1 week (1–90 %)
Clinical predictors	Rapid progression, bulbar dysfunction, neck flexion weakness , bilateral facial weakness, inability to cough, lift head or stand, autonomic instability
Oxygen saturation	Late sign — do not rely on it

Prognosis

- ~80 % walk independently at 6 months; mortality 3–7 % (higher in ventilated, elderly).
- **mEGOS** (modified Erasmus GBS Outcome Score) at admission or day 7: age, preceding diarrhoea, MRC sum score → probability of being unable to walk at 4 weeks, 3 and 6 months.
- ~20 % unable to walk at 6 months; fatigue and pain common long-term.
- Recurrence ~2–5 %.

Acute-onset CIDP (A-CIDP)

~5 % of patients initially diagnosed with GBS. Suspect when there is **deterioration > 8 weeks after onset** or ≥ 3 **treatment-related fluctuations**; also prominent sensory signs with little weakness, no cranial nerve or respiratory involvement, no preceding infection. Treat as CIDP (maintenance therapy); test nodal/paranodal antibodies.

GBS in numbers. IVIG 0.4 g/kg $\times$ 5 days within 2 weeks. PE 5 exchanges within 4 weeks. No steroids. No second IVIG (SID-GBS). 20/30/40. A-CIDP: > 8 weeks or ≥ 3 TRFs. MFS: GQ1b, usually no treatment.

Exam angles

- GBS patient at day 10, cannot walk → **IVIG 2 g/kg over 5 days** (or PE).
- Poor-prognosis patient after first IVIG course (high mEGOS) → **no second course (SID-GBS)**.
- Worsening at week 10 after improvement → **A-CIDP**.
- Ophthalmoplegia, ataxia, areflexia, anti-GQ1b → **MFS; supportive care**.
- CSF 120 cells/ μ L in suspected GBS → **reconsider: HIV, Lyme, lymphoma, CMV polyradiculitis, poliomyelitis**.

EAN — Management of Amyotrophic Lateral Sclerosis

2024

Source: Van Damme et al., European Academy of Neurology (EAN) guideline on the management of amyotrophic lateral sclerosis in collaboration with the European Reference Network for Neuromuscular Diseases (ERN EURO-NMD), *Eur J Neurol* 2024. **Diagnosis:** Gold Coast criteria (Shefner et al., *Clin Neurophysiol* 2020).

Diagnosis

Gold Coast criteria (consensus meeting 2019, published 2020) — preferred because simpler and more sensitive than El Escorial/Awaji:

1. **Progressive motor impairment**, documented by history or repeated examination, preceded by normal motor function; **and**
2. **UMN and LMN dysfunction in at least one body region** (same region for both if only one), **or LMN dysfunction in at least two body regions; and**
3. Investigations exclude other disease processes.

Body regions: bulbar, cervical, thoracic, lumbosacral. LMN dysfunction can be clinical or EMG (fibrillation/positive sharp waves or fasciculation potentials with chronic neurogenic change — Awaji).

Correction to the old digest. Gold Coast is **not** "UMN or LMN signs in ≥ 1 region". It requires **UMN + LMN in one region, or LMN in two regions** — pure UMN syndromes (PLS) are excluded.

Investigation	Purpose
EMG/NCS	LMN involvement in clinically unaffected regions; exclude conduction block (MMN), demyelination
MRI brain and cervical spine	Exclude compressive myelopathy, structural lesions
Bloods	CK, thyroid, calcium/PTH, B12, protein electrophoresis, anti-GM1 (MMN), HIV, hexosaminidase A (young)
Neurofilament light chain (serum/CSF)	Raised — supports diagnosis against mimics and predicts progression rate ; not diagnostic alone
Genetic testing	EAN 2024: offer to all patients (with counselling) — <i>C9orf72</i> , <i>SOD1</i> , <i>TARDBP</i> , <i>FUS</i> at least. Needed to identify SOD1-ALS for tofersen
Cognitive/behavioural screening	ECAS — FTD in ~10–15 %, cognitive/behavioural impairment in up to 50 %

Disease-modifying treatment — EAN 2024 positions

Drug	Mechanism	Evidence	EAN 2024
Riluzole 50 mg twice daily	Glutamate modulation	Survival +~2–3 months (1994–96 RCTs)	Recommended — offer as early as possible. Monitor LFTs monthly for 3 months then every 3 months; neutropenia rare
Edaravone (IV; oral suspension)	Free-radical scavenger	MCI186-19 (2017) — slower ALSFRS-R decline in a narrow subgroup (< 2 years, FVC ≥ 80 %, all items ≥ 2); ADORATION/oral confirmatory trial negative (2024); EMA refused licence	Not recommended (weak against / no recommendation)

Drug	Mechanism	Evidence	EAN 2024
Tofersen (intrathecal)	Antisense oligonucleotide lowering SOD1	VALOR (2022): primary endpoint at 28 weeks not met , but large falls in CSF SOD1 and plasma NfL ; open-label extension suggested slower decline with early start. FDA accelerated approval 2023; EMA approval 2024	Offer to SOD1-ALS (weak). Myelitis, aseptic meningitis, papilloedema reported
Sodium phenylbutyrate–taurursodiol (AMX0035)	—	CENTAUR positive; PHOENIX (2024) negative → withdrawn	Not recommended
High-caloric diet, high-dose methylcobalamin	—	Subgroup signals only	Not routinely

Multidisciplinary and symptomatic care

Intervention	Indication	Evidence
Multidisciplinary clinic	All patients, every ~3 months	Associated with longer survival and better quality of life
NIV	Symptoms of respiratory insufficiency (orthopnoea, morning headache, poor sleep) or FVC < 50 % , SNIP < 40 cmH ₂ O, nocturnal hypoventilation/hypercapnia	Bourke 2006 RCT: median survival ~7 months longer in patients without severe bulbar dysfunction; improves quality of life in all
Invasive ventilation (tracheostomy)	Informed choice	Prolongs life; locked-in risk; needs detailed advance planning
Gastrostomy (PEG/RIG/PIG)	Dysphagia, weight loss > 5–10 % , prolonged meals	Place before FVC < 50 % (procedural risk); RIG if respiratory function poor
Cough assistance	Weak cough (peak cough flow < 270 L/min)	Mechanical insufflation–exsufflation
Sialorrhoea	Anticholinergics (glycopyrronium, amitriptyline, hyoscine patch); botulinum toxin to salivary glands ; radiotherapy	
Pseudobulbar affect	Dextromethorphan–quinidine (US), SSRIs, TCAs	
Cramps	Mexiletine (RCT), quinine (EU caution), levetiracetam	
Spasticity	Baclofen, tizanidine, physiotherapy	
Communication	Eye-gaze devices, voice banking	
End of life	Advance care planning early; palliative care; opioids and benzodiazepines for dyspnoea and anxiety	

ALS in one breath. Gold Coast: UMN+LMN in one region or LMN in two. Riluzole for everyone. Genetic testing for everyone — **tofersen for SOD1**. Edaravone and AMX0035: not recommended in Europe. NIV when symptomatic or FVC < 50 % (~7 months survival). PEG before FVC < 50 %. MDT clinic.

Exam angles

- LMN signs in cervical and lumbar regions with progression, no UMN signs → **meets Gold Coast**.
- Which ALS patients should have genetic testing (EAN 2024)? → **all, with counselling**.
- SOD1 mutation → **tofersen**; biomarker that falls on treatment → **plasma/CSF NfL**.
- Orthopnoea and morning headache, FVC 62 % → **start NIV (symptoms are enough)**.

Rapid-Fire, Numbers and Final Checklist

Rapid-fire — three lines per paper

#	Topic	Pearls
1	CVST	LMWH even with haemorrhage · warfarin (or dabigatran) 3–12 months · no steroids; craniectomy for herniation
2	Thrombectomy	0–6 h: LVO + CTA · 6–24 h: salvageable tissue (DAWN/DEFUSE-3/collaterals) · large core and basilar now included; bridging IVT
3	DLB	4 core features · indicative: DaT, MIBG, REM without atonia · no haloperidol; ChEI first
4	Neuromodulation	Surgery evaluation after 2 failed drugs · RNS = closed-loop, bilateral MTLE · ANT-DBS: depression/memory (SANTE)
5	Cluster	O ₂ 12–15 L/min + SC sumatriptan · verapamil with ECGs · galcanezumab episodic only
6	MS palliative	Early, concurrent, home-based · ACP before crises · nabiximols, intrathecal baclofen; exercise for fatigue
7	Neurosyphilis	Benzylpenicillin 18–24 MU/day × 10–14 d · CSF-VDRL specific, CSF FTA-ABS sensitive · ocular/otic = treat as neurosyphilis
8	PD neuropsychiatry	Psychosis: stop anticholinergics → amantadine → agonists, then clozapine/quetiapine · ICD ~14 %: stop agonist · rivastigmine for PDD
9	Coma / post-arrest	CRS-R ≥ 5 times · ≥ 72 h, M ≤ 3, ≥ 2 predictors · absent N20, NSE > 60, malignant EEG, diffuse anoxic imaging
10	TBI	SBP ≥ 100/110 · ICP > 22, CPP 60–70 · TXA within 3 h; no steroids; DC saves life, more disability
11	Vasculitis	GCA: steroids before biopsy, tocilizumab · EGPA/PAN = mononeuritis multiplex · RCVS ≠ PACNS (no steroids)
12	CIDP 2021	CIDP / possible CIDP only · motor CIDP: IVIG not steroids · SCIg maintenance (PATH)
13	CIPN	Cisplatin ganglionopathy + coasting · oxaliplatin cold dysaesthesia · duloxetine only recommended drug
14	CTE	Perivascular p-tau at sulcal depths · post-mortem only · TES 2021 clinical criteria
15	Stroke rehab	Stroke unit care · AVERT and VECTORS: early high intensity harms · fluoxetine no benefit
16	Sleep and stroke	SDB in 50–70 % · polygraphy, not questionnaires · SAVE neutral; ASV harmful in HFrEF
17	Narcolepsy	NT1 = cataplexy + MSLT or hypocretin ≤ 110 · MSLT ≤ 8 min + ≥ 2 SOREMPs · pitolisant/oxybate treat sleepiness + cataplexy
18	Supine hypertension	≥ 140/90 supine · head-up ~10–20°, pressors ≥ 4 h before bed · bedtime GTN patch or losartan
19	MG	Thymectomy AChR+ 18–65 (MGTX) · MuSK → rituximab · FcRn and C5 inhibitors; start steroids low
20	PD invasive	STN reduces drugs; GPi treats dyskinesia · EARLYSTIM · LCIG/apomorphine/foslevodopa when DBS unsuitable
21	Nodopathies & paraproteins	NF155 tremor, CNTN1 nephrotic — rituximab · anti-MAG IgM-κ · POEMS λ + VEGF
22	GBS	IVIG 0.4 g/kg × 5 (≤ 2 wk) or PE (≤ 4 wk) · no steroids, no 2nd IVIG · A-CIDP > 8 wk or ≥ 3 TRFs
23	ALS	Gold Coast · riluzole for all, tofersen for SOD1 · NIV symptoms or FVC < 50 %; PEG before FVC < 50 %

Numbers to know

Number	Meaning	Paper
3–12 months	Oral anticoagulation after CVT	1

Number	Meaning	Paper
49 % vs 13 %	DAWN functional independence	2
2.6	HERMES NNT for less disability	2
1 + 1	1 core feature + 1 indicative biomarker = probable DLB	3
2 drugs	Definition of drug resistance	4
~75 %	RNS median reduction at 9 years	4
12–15 L/min	Oxygen for cluster	5
15–180 min, ≤ 8/day	Cluster attack duration and frequency	5
18–24 MU/day, 10–14 days	Penicillin for neurosyphilis	7
~14 %	ICDs on dopamine agonists (DOMINION)	8
≥ 72 h, ≥ 2 predictors	Post-arrest prognostication	9
NSE > 60 µg/L	Poor outcome marker at 48/72 h	9
22 / 60–70 mmHg	ICP threshold / CPP target	10
1 g within 3 h	Tranexamic acid in TBI	10
≥ 8 weeks	CIDP time course	12
0.2–0.4 g/kg weekly	SCIg maintenance (PATH)	12
≤ 8 min, ≥ 2 SOREMPs, ≤ 110 pg/mL	Narcolepsy	17
140/90	Neurogenic supine hypertension	18
20/30/40	FVC mL/kg / MIP / MEP	19, 22
18–65	MGTX thymectomy age range	19
≥ 30 %	Levodopa challenge response for DBS	20
0.4 g/kg × 5 days	IVIg in GBS	22
12–15 L, 4–5 exchanges	Plasma exchange in GBS	22
> 50 cells/µL	CSF count against GBS	22
FVC < 50 %	NIV and PEG timing in ALS	23
~7 months	NIV survival gain (Bourke)	23

Final checklist

Closed book — know by heart. CVT anticoagulation with ICH · thrombectomy windows and large core · DLB criteria (probable vs possible) · RNS vs VNS vs DBS · cluster acute and preventive · neurosyphilis CSF tests · PD psychosis hierarchy · post-arrest predictors and timing · TBI targets, TXA, DECRA/RESCUEicp · GCA steroids before biopsy · CIDP 2021 categories · CIPN patterns · CTE post-mortem · AVERT/VECTORS/fluoxetine · SAVE and SERVE-HF · NT1 vs NT2 · nSH definition · MG antibodies and new biologics · STN vs GPi · nodopathies and POEMS · GBS treatment and A-CIDP · Gold Coast, tofersen, NIV.

Open book — bring printed. This digest (tabbed 1–23) + *The Neurology Tract* + your main textbook. Use the "Numbers to know" table for doses and thresholds; the exam-angle tables mirror how stems are written.

In scientia salus

Success is not luck — it is the result of methodical work and accumulated knowledge. The exam only confirms what you already know.